SHORT TERM MORTALITY PREDICTORS AND CLINICAL PROFILE IN SUBJECTS OF ACUTE STROKE WITH SPECIAL EMPHASIS ON THRIVE SCORE AND STRESS HYPERGLYCEMIA

Dr. Dhermendra Pratap Singh,[1] Dr. Yatish[2*]

[1]MD Medicine, Associate Professor, Department of General Medicine, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh

[2*]MD Medicine, Assistant Professor, Department of General Medicine, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh

Corresponding author:
Dr. Yatish Chaudhary
Email id: ***yatish.chaudhary09@gmail.com***

Type of study: Original Research Paper

==========

ABSTRCT

Background: In various critical illnesses including myocardial infarction and stroke, acute and transient hyperglycemia and stress hyperglycemia have been studied extensively. One reliable and predictable factor to study mortality in these diseases is THRIVE score seen in previous studies. However, data concerning this is scarce in literature for Indian subjects.

Objectives: The present study was conducted to assess the short-term mortality predictors and clinical profile in subjects of acute stroke with special emphasis on THRIVE score and stress hyperglycemia.

Methods: The study included 120 subjects with acute stroke reported within 24 hours of stroke with either confirmed WHO diagnosis criteria or CT evidence of stroke. In all the included subjects, THRIVE score values and blood glucose levels were assessed after admission of the subjects. The severity of stroke was assessed using NIHSS scores and disability was assessed using mRS scores.

Results: Group III with subjects having hyperglycemia without diabetes at admission, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%. (n=56), 76.78% (n=43) subjects died and 23.21% (n=13) subjects survived. Group IV had subjects that were non-diabetic and did not have hyperglycemia, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%. (n=20), 30% (n=6) subjects died and 70% (n=14) subjects survived (Table 2). THRIVE score ≥6 (n=64), 70.31% (n=45) subjects died, whereas, for subjects with THRIVE scores of <6, 51.78% (n=29) subjects died. Group I had 15 subjects where mRS >4 showing poor functional outcomes was seen in 46.6% (n=7) of study subjects. In Group II having 5 subjects, 20% (n=1) subjects had mRS >4 showing poor functional outcomes. In Group III subjects had hyperglycemia without diabetes at admission, no history of diabetes

and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%, of 13 subjects, 30.76% (n=4) subjects showed poor functional outcomes at discharge with mRS >4.

Conclusion: The present study concludes that a significantly poor prognostic factor in acute stroke subjects was stress hyperglycemia, whereas, THRIVE score was also found to be a reliable prognostic factor. Further assessment of these factors as a definitive predictive tool for assessing mortality needs to be assessed further.

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

INTRODUCTION

One of the leading causes of significant mortality and morbidity in recent times is stroke which means being stuck with a deadly blow. Also, as of 2016, stroke contributes the second largest cause of death globally following ischemic heart diseases. Mortality rates were higher in subjects with hemorrhagic shock in comparison to subjects with ischemic stroke. The outcome following stroke is governed by many factors including complications, predisposing factors, stroke type, and/or severity. The risk factors associated with strokes are various where few are modifiable including sedentary lifestyle, alcohol consumption, smoking, dyslipidemia, and hypertension, whereas, other risk factors are non-modifiable including ethnicity, gender, and age. One of the modifiable risk factors for stroke is admission hyperglycemia or stress hyperglycemia.[1]

Previous literature data has established that acute stroke is associated with admission hyperglycemia as its short-term outcome. The occurrence of this acute hyperglycemia is attributed to the release of norepinephrine and cortisol owing to the stress and not linked to the type 2 diabetes mellitus exclusively. Poor clinical outcomes are seen in subjects with acute hyperglycemia in subjects with stroke where various mechanisms are associated with this stress including cerebral vasculopathy induced by hyperglycemia, increased free fatty acid pool interfering with vasodilation, and/or direct tissue damage mediated by lactate and intracellular acidosis in the ischemic brain.[2]

One study conducted in 2004 had suggested that mortality is seen in subjects with ischemic stroke when they have suggested that increased risk of mortality is seen in subjects with fever>38^0c, higher age, and NIHSS score. Another study conducted in 2006 presented Essen ICH scores which was a new prognostic model which assessed variables like consciousness levels, NIHSS score, and age. In various critical illnesses including myocardial infarction and stroke, acute and transient hyperglycemia and stress hyperglycemia have been studied extensively.[3]

The role of stress hyperglycemia as an independent factor in depicting the prognosis of acute stroke is not yet clear. Previous literature data has also established the role of THRIVE (totaled health risks in vascular events) scores in predicting outcomes of acute stroke. THRIVE scores are calculated with atrial fibrillation, diabetes mellitus, presence of hypertension, presence of hypertension, and age. However, data concerning this is scarce in the literature.[4] Hence, the

ISSN: 0975-3583, 0976-2833 VOL13, ISSUE 08, 2022

present study was conducted to assess the short-term mortality predictors and clinical profile in subjects of acute stroke with special emphasis on THRIVE score and stress hyperglycemia.

MATERIALS AND METHODS

The present observational study was conducted to assess the short-term mortality predictors and clinical profile in subjects of acute stroke with special emphasis on THRIVE score and stress hyperglycemia. The present study was conducted at Department of General Medicine, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh after obtaining clearance from the concerned Ethical committee. The study included a total of 120 subjects from both genders with acute stroke reported within 24 hours of stroke with either confirmed WHO diagnosis criteria (rapidly developing focal neurological deficit lasting 24 hours or more) or CT evidence of stroke. After explaining the detailed study design, informed consent was taken from all the study subjects. The exclusion criteria for the study were subjects with aneurysms and coagulopathies, vascular malformations, traumatic hematomas, secondary hyperglycemia, recurrent stroke, and/or Transient Ischemic Attacks (TIA) and reported after 24 hours.

After final inclusion, detailed history was recorded for all the subjects followed by clinical examination. The history was also recorded for the Glassgow coma scale, comorbidities, hypertension, and diabetes history. CT brain and neurologic examination were considered for the diagnosis of hemorrhagic stroke and ischemic stroke within 72 hours. This was followed by recording the ECG (Electrocardiogram) for all the subjects at baseline. Venous blood was collected using the sterile and aseptic method from all subjects for assessing lipid profile, CRP (C-reactive protein levels), Glycosylated hemoglobin (HbA1c), blood glucose, and CBC (Complete blood count).

Blood investigations were done at baseline, 12, 48, and 72 hours after admission, and discharge. Drug intake history was recorded for cyclosporine, oral contraceptives, glucocorticoids, beta-blockers, and thiazides where drug intake was considered as exclusion criteria. After blood analysis, the blood glucose level of more than 140 mg/dl was considered a hyperglycemic state.

A total of 120 study subjects were divided into 4 groups depending on glucose levels at admission, HbA1c levels, history of oral hypoglycemics, and history of diabetes.

Group I: included subjects with diabetes history, glucose >140mg/dl, HbA1c >6.5%, and history of diabetes medicine.

Group II included subjects having diabetes and were without hyperglycemia when admitted, had a history of diabetes and medicine, glucose less than 140mg/dl, and HbA1c levels of >6.5%.

Group III included subjects having hyperglycemia without diabetes at admission, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%

Group IV included subjects that were non-diabetic and did not have hyperglycemia, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%

All the included subjects were assessed during their complete course of hospitalization for recovery by assessing the Glasgow coma scale, discharge/ mortality, hospital stay duration, comorbidities, and complications including sepsis. For each study participant, THRIVE scores were calculated with atrial fibrillation, hypertension, and diabetes history. Modified Rankin Scale(mRS) was used to assess the functional recovery on discharge.

The collected data were subjected to the statistical evaluation using SPSS software version 21 (Chicago, IL, USA) and one-way ANOVA and t-test for results formulation. The data were expressed in percentage and number, and mean and standard deviation. The level of significance was kept at $p<0.05$.

RESULTS

The present observational study was conducted to assess the short-term mortality predictors and clinical profile in subjects of acute stroke with special emphasis on THRIVE score and stress hyperglycemia. The study included a total of 120 subjects from both genders in the age range of 18-94 years and the mean age of 66.91±15.98 years. The demographic characteristics of the study subjects are listed in Table 1. The age of the subjects that died was significantly higher of age 69.58±14.93 compared to survivors who had the age of 62.78±16.88 years (p=0.01). There were 70.21% (n=33) females and 29.78% (n=14) males in the survivors compared to69.86% (n=51) females and 30.13% (n=22) males among non-survivors. This was non-significant with p=0.93. Hemorrhagic stroke was diagnosed in 48.93% (n=23) survivors and 50.68% (n=37) non-survivors, whereas, ischemic shock was seen in 51.06% (n=24) survivors and 49.31% (n=36) non-survivors. This difference was non-significant (p=0.08). 44.68% (n=21) subjects presented in less than 12 hours among survivors and 53.42% (n=39) among non-survivors (p=0.26). Mean HbA1c, cholesterol, and Hb scores had non-significant differences among survivors and non-survivors with respective values of 0.58, 0.37, and 0.12 respectively. Mean NIHSS scores were significantly higher among non-survivors with 27.13±6.42 compared to survivors who had a score of 24.53±6.82 with p=0.01. The mean GCS score was significantly lesser in non-survivors (7.58±2.79) compared to survivors (8.77±2.29) with p=0.006 (Table 1).

On assessing the outcomes in the different groups of the study subjects based on the stress hyperglycemia, it was seen that in Group I had subjects with diabetes history, glucose >140mg/dl, HbA1c >6.5%, and history of diabetes medicine having 37 subjects, 59.45% (n=22) subjects died and 40.54% (n=15) survived. In Group II having subjects with diabetes and were without hyperglycemia when admitted, had a history of diabetes and medicine, glucose less than 140mg/dl, and HbA1c levels of >6.5%. (n=7), 28.57% (n=2) subjects died and 71.42% (n=5) subjects survived. In Group III; subjects having hyperglycemia without diabetes at admission having glucose level >140mg/dl, and HbA1c of <6.5% (n=56), 76.78% (n=43) subjects were died and 23.21% (n=13) subjects survived. Group IV had subjects that were non-diabetic and did not have hyperglycemia, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%. (n=20), 30% (n=6) subjects died and 70% (n=14) subjects survived (Table 2).

Concerning the mortality in the study subjects based on THRIVE scores and other parameters, it was seen that for THRIVE score ≥6 (n=64), 70.31% (n=45) subjects died, whereas, for subjects with THRIVE scores of <6, 51.78% (n=29) subjects died. In subjects with THRIVE score >6 with stress hyperglycemia (n=20), 90% (n=18) subjects died and 10% (n=2) subjects survived. In other subjects who did not have THRIVE score >6 with stress hyperglycemia, there were 100 subjects among whom 55% (n=55) subjects died and 45% (n=45) subjects survived as shown in Table 3.

Group I had 15 subjects where mRS >4 showing poor functional outcomes was seen in 46.6% (n=7) of study subjects. In Group II having 5 subjects, 20% (n=1) subjects had mRS >4 showing poor functional outcomes. In Group III subjects had hyperglycemia without diabetes at admission, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%, of 13 subjects, 30.76% (n=4) subjects showed poor functional outcomes at discharge with mRS >4. In Group IV subjects that were non-diabetic and did not have hyperglycemia, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%, among 14 subjects 14.28% (n=2) subjects showed poor functional outcomes at discharge with mRS >4 as depicted in Table 4.

DISCUSSION

In the present study, on assessing the outcomes in the different groups of the study subjects based on the stress hyperglycemia, it was seen that in Group I having subjects with diabetes history, glucose >140mg/dl, HbA1c >6.5%, and history of diabetes medicine having 37 subjects, 59.45% (n=22) subjects died and 40.54% (n=15) survived. In Group II having subjects with diabetes and were without hyperglycemia when admitted, had a history of diabetes and medicine, glucose less than 140mg/dl, and HbA1c levels of >6.5%. (n=7), 28.57% (n=2) subjects died and 71.42% (n=5) subjects survived. In Group III with subjects having hyperglycemia without diabetes at admission, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%. (n=56), 76.78% (n=43) subjects died and 23.21% (n=13) subjects survived. Group IV had subjects that were non-diabetic and did not have hyperglycemia, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%. (n=20), 30% (n=6) subjects died and 70% (n=14) subjects survived. These results were consistent with the studies of Lei C et al[5] in 2014 and Zhao Y et al[6] in 2017 where authors reported comparable outcomes in subjects with stress hyperglycemia and acute stroke in their studies.

On assessing the mortality in the study subjects based on THRIVE scores and other parameters, it was seen that for THRIVE score ≥6 (n=64), 70.31% (n=45) subjects died, whereas, for subjects with THRIVE scores of <6, 51.78% (n=29) subjects died. In subjects with THRIVE score >6 with stress hyperglycemia (n=20), 90% (n=18) subjects died and 10% (n=2) subjects survived. In other subjects who did not have THRIVE score >6 with stress hyperglycemia, there were 100 subjects among whom 55% (n=55) subjects died and 45% (n=45) subjects survived. These results were in agreement with the studies of Kongwad LI et al[7] in 2018 and Raghavendra

PBN et al[8] in 2016 where THRIVE scores of 6 or more had higher mortality compared to subjects with THRIVE scores of less than 6.

For the functional outcomes in the study subjects, Group I had 15 subjects where mRS >4 showing poor functional outcomes was seen in 46.6% (n=7) of study subjects. In Group II having 5 subjects, 20% (n=1) subjects had mRS >4 showing poor functional outcomes. In Group III subjects had hyperglycemia without diabetes at admission, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%, of 13 subjects, 30.76% (n=4) subjects showed poor functional outcomes at discharge with mRS >4. In Group IV subjects that were non-diabetic and did not have hyperglycemia, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%, among 14 subjects 14.28% (n=2) subjects showed poor functional outcomes at discharge with mRS >4. These results were similar to the studies of Gofir A et al[9] in 2017 and Snarska KK et al[10] in 2017 where poor functional outcomes and mRS scores of >4 were seen in comparable proportion in their studies as in the present study.

CONCLUSION

Within its limitations, the present study concludes that a significantly poor prognostic factor in acute stroke subjects was stress hyperglycemia, whereas, THRIVE score was also found to be a reliable prognostic factor. Further assessment of these factors as a definitive predictive tool for assessing mortality needs to be assessed further. However, the present study had a few limitations including small sample size and geographical area biases. Hence, more longitudinal studies with a larger sample size will help reach a definitive conclusion.

REFERENCES

1. 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;10:11.
2. 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;74:133-7.
3. 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.
4. 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.
5. 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;45:1689-94.
6. 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;39:152-7.

7. 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.
8. Raghavendra Prasad B. N. Dr. Sandeep Reddy A., Dr. Prabhakar et al. Stress hyperglycemia as a prognostic marker in acute ischaemic stroke. EJPMR, 2016;3:247-56.
9. 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;127:923-9.
10. 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;13:100.

TABLES

Characteristics	**Survivors (n=47)**	**Mortality (n=73)**	**p-value**
Mean age (years)	62.78±16.88	69.58±14.93	0.01
Gender n (%)			
Females	33 (70.21)	51 (69.86)	0.93
Males	14 (29.78)	22 (30.13)	
Diagnosis n (%)			
Hemorrhagic stroke	23 (48.93)	37 (50.68)	0.08
Ischemic stroke	24 (51.06)	36 (49.31)	
Admission			
<12 hours	21 (44.68)	39 (53.42)	0.26
>12 hours	26 (55.31)	34 (46.57)	
Mean HbA1c	6.15±1.22	6.28±1.49	0.58
Mean Cholesterol	145.88±53.13	138.76±39.97	0.37
Mean Hb	11.92±1.35	12.32±1.56	0.12
Mean RBS	152.13±38.56	195.68±80.66	<0.001
Mean NIHSS	24.53±6.82	27.13±6.42	0.01
Mean GCS	8.77±2.29	7.58±2.79	0.006

Table 1: Demographic characteristics of the survivors and non-survivors in the study

Groups	**Non- survivors (n=73)**	**Survivors (n=47)**
Group I: subjects with diabetes history, glucose >140mg/dl, HbA1c >6.5%, and history of diabetes medicine. (n=37)	22 (59.45)	15 (40.54)
Group II: subjects having diabetes and were without hyperglycemia when admitted, had a history of diabetes and medicine, glucose less than 140mg/dl, and HbA1c levels of >6.5%. (n=7)	2 (28.57)	5 (71.42)
Group III subjects having hyperglycemia without diabetes at admission, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%. (n=56)	43 (76.78)	13 (23.21)
Group IV subjects that were non-diabetic and did not have hyperglycemia, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%. (n=20)	6 (30)	14 (70)

Table 2: Outcomes in the different groups of the study subjects based on stress hyperglycemia

Parameter	Mortality	Survivors
THRIVE score ≥6 (n=64)	45 (70.31)	21 (32.81)
THRIVE score <6 (n=56)	29 (51.78)	27 (48.21)
THRIVE score >6 with stress hyperglycemia (n=20)	18 (90)	2 (10)
Others (n=100)	55 (55)	45 (45)

Table 3: Mortality in the study subjects based on THRIVE scores and other criteria

Group	N	Poor functional outcomes mRS >4 (n)	Poor functional outcomes mRS >4 (%)
Group I: subjects with diabetes history, glucose >140mg/dl, HbA1c >6.5%, and history of diabetes medicine.	15	7	46.6
Group II: subjects having diabetes and were without hyperglycemia when admitted, had a history of diabetes and medicine, glucose less than 140mg/dl, and HbA1c levels of >6.5%.	5	1	20
Group III subjects having hyperglycemia without diabetes at admission, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%.	13	4	30.76
Group IV subjects that were non-diabetic and did not have hyperglycemia, no history of diabetes and anti-diabetic drugs, glucose >140mg/dl, and HbA1c of <6.5%.	14	2	14.28

Table 4: Diabetes and stress hyperglycemia correlation with mRS at discharge in the study subjects