

Research Article

A study of stress hyperglycemia and its relationship with the neurological outcome in patients presenting with acute ischemic stroke

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ABSTRACT

Background: Cerebrovascular accident (CVA) continues to be the most common neurological disease in the developed and developing countries. It also stands as the 3rd more common cause of death after cardiovascular disease and cancer. Stroke related burden keeps rising among the patients, their relatives and treating consultants. The neurological outcome depends on various modifiable and non-modifiable risk factors. Among the modifiable risk factors, admission (stress) hyperglycemia has a deleterious effect on the neurological outcome. It is well known by various studies that diabetic patients have more severe outcome and neurological disability after acute stroke than the non-diabetic patients. Now stress hyperglycemia is also becoming a second serious marker to affect the neurological outcome of these stroke patients. The aim was to study the blood sugar level and its correlation with the neurological outcome among the acute ischemic stroke patients on admission and at third month of follow-up.

Methods: It is a prospective and comparative study done in a tertiary care hospital. Adult patients (> 40 years) presenting with acute ischemic stroke were neurologically stratified based on National Institutes of Health Stroke Scale (NIHSS) and admission blood sugars were noted. They were subdivided into 3 groups. Group 1 consisting of 31 normoglycemic patients, group 2 consisting of 32 stress hyperglycemic patients and group 3 consisting of 40 Type 2 diabetes mellitus (T2DM) patients. They were again reassessed after 3 months with FBS, PPBS and neurological recovery by NIHSS. Chi-square test / Fischer exact test was used to compare between 3 groups. A p-value of <0.005 was considered statistically significant.

Results: The normoglycemic individuals had much better functional recovery when compared with stress hyperglycemia and diabetes mellitus groups (p <0.001) at 3 months.

Conclusions: Abnormally high blood sugar at the time of presentation in acute stroke patient, significantly alter functional recovery at 3rd month of follow-up. Hence admission blood sugar level may be used as a surrogate marker to predict functional recovery.

Keywords: Cerebro vascular accident, Stress hyperglycaemia, Normoglycemia, Diabetes mellitus, National Institute of Health Stroke Score

INTRODUCTION

Stroke is a common cause of emergency admission which is associated with increased mortality, morbidity and poor

quality of life. After coronary artery disease and cancer, stroke is the 3rd most common cause of death in elderly.¹ The outcome of stroke is influenced by various factors including severity, type of stroke, predisposing factors,

and related complications and care facilities.² Admission hyperglycemia is among the potentially modifiable factors which affect the outcome of stroke. Various clinical and experimental studies have shown that admission hyperglycemia has an adverse effect on the neurological and short term outcomes in ischemic stroke.³⁻⁶ This acute hyperglycemia in stroke is not always due to type 2 diabetes mellitus, but instead may be due to stress response mediated partly by release of cortisol and norepinephrine.⁷

Stress hyperglycemia generally refers to a transient hyperglycemia during illnesses and restricted to individuals without prior evidence of DM. This stress hyperglycemia usually resolves spontaneously after the acute phase of illness. Stress hyperglycemia has been studied in acute myocardial infarction and cerebrovascular event and its outcomes.⁹

In spite of vastly available data and recent updates on stroke, there are no clear guidelines to support whether this hyperglycemia needs to be treated or not. Still controversies exist on whether this stress hyperglycemia is harmful and affect the outcome in acute ischemic stroke. Hence the present study was done to assess the presence of stress hyperglycemia and its effect on neurological recovery at 3rd month by comparing with normoglycaemic and T2DM patients presenting with acute ischaemic stroke.

METHODS

This prospective comparative study was done at Mahatma Gandhi Medical College and Research Institute, Pillaiyarkuppam, Puducherry, India. All those patients fulfilling the inclusion criteria presenting with acute ischaemic stroke to emergency department or to the out-patient department of general medicine were enrolled in the study. It included 103 adult patients with acute ischaemic stroke of both the sexes. All the participants were evaluated by detailed history, clinical examination and severity assessment by NIHSS score. Ischemic stroke was defined by CT brain (normal CT brain scan or recent infarct in the clinically relevant area on scan done within 72 hours of stroke). The admission blood sugar was

estimated in all patients and was later categorized in to 3 groups. Hyperglycemia was defined as a blood sugar level of more than 140 mg/dl. The patients were subdivided into 3 groups based on FBS, PPBS and HbA1c level.

Group 1: Normal admission blood glucose level with normal FBS, PPBS and HbA1c.

Group 2: Stress hyperglycemia (>140 mg/dl) with normal FBS, PPBS and HbA1c.

Group 3: Diabetes mellitus (newly/previously diagnosed).

All the patients were followed up with neurological assessment by NIHSS score, FBS, PPBS and HbA1C after 3 months of acute ischaemic stroke.

Patients with recurrent ischemic stroke, haemorrhagic stroke, stroke with related complication (aspiration pneumonia, septicemia) were excluded from the study.

This study was done with the declaration of Helsinki and institutional human committee of Mahatma Gandhi Medical College and Research Institute, Puducherry, India approved it.

Statistical methods

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented as mean \pm SD (min-max) and results on categorical measurements are presented in numbers (%). A p-value of < 0.05 was considered to be statistically significant.

RESULTS

In the present study we had 103 stroke patients with acute ischemic stroke. The predominant distribution was among the male gender in all the 3 groups. The mean age of presentation with CVA was 68.68 \pm 4.41 years in group 1 as compared to 65.47 \pm 6.90 years in group 2 and 61.98 \pm 4.23 years in group 3, which was found to be statistically significant (p <0.001) (Table 1).

Table 1: Demographical profile among the 3 groups.

	Normoglycemic (N= 31)	Stress hyperglycemic (N=32)	Diabetes mellitus (N=40)	p value
Age	68.68 \pm 4.41	65.47 \pm 6.90	61.98 \pm 4.23	<0.001
Sex (M:F)	20:11	21:11	27:13	
BMI	23.26 \pm 3.88	22.95 \pm 2.72	26.21 \pm 2.78	<0.001

The body mass index in group 1 was 23.26 \pm 3.88 as compared to 22.95 \pm 2.72 in group 2 and 26.21 \pm 2.78 in

group 3, which was found to be statistically significant (p<0.001) (Table 1).

Hypertension was present in 9 (29%) patients in group 1, as compared to 13 (40.6%) patients in group 2 and 20(50%) patients in group 3 (Table 2).

About 5 (15.6%) patients in group 2 and 10 (25%) patients in group 3 had underlying coronary artery disease (CAD). While none of the patients in group 1 had

CAD as co-morbidity (Table 2). About 10 (32.3%) patients in group 1, 11 (34.4%) patients in group 2 and 17 (42.5%) patients in group 3 were smokers. Similarly alcoholism was present in 6 (19.4%) patients in group 1, as compared to 8 (25%) patients in group 2 and 16 (40%) patients in group 3 (Table 2).

Table 2: Risk factor among the stroke 3 groups.

	Normoglycemic (N=31)	Stress hyperglycemic (N=32)	Diabetes mellitus (N=40)
Hypertension	9 (29%)	13 (40.6%)	20 (50%)
CAD	0	5 (15.6%)	10 (25%)
Smoking	10 (32.3%)	11 (34.4%)	17 (42.5%)
Alcoholism	6 (19.4)	8 (25%)	16 (40%)

Table 3: RBS, FBS and PPBS of the 3 groups at admission and on follow up.

	Normoglycemic (N=31)	Stress hyperglycemic (N=32)	Diabetes mellitus (N=40)	p value
RBS				
Admission	124.68±11.39	181.38±18.03	206.88±31.92	<0.001
FBS				
Admission	101.23±6.75	93.00±11.25	150.68±17.37	<0.001
After 3month	81.42±5.40	85.47±5.14	120.95±7.51	<0.001
p value	<0.001	<0.002	0.286	
PPBS				
Admission	128.97±5.94	126.53±5.99	171.48±16.53	<0.001
After 3 month	122.94±4.02	123.19±3.16	159.55±12.35	<0.001
p-value	<0.001	<0.009	<0.001	
HbA1c	5.76±0.11	5.86±0.26	7.19±0.51	<0.001

The mean admission random blood glucose (RBS) level was 124.68±11.39 mg/dl, 181.38±18.03 mg/dl and 206.88±31.92 mg/dl among the normoglycemic, stress hyperglycemic and diabetic groups respectively which was found to be statistically significant with a p-value of <0.001 (Table 3).

The mean FBS in group 1, group 2 and group 3 was 101.23±6.75 mg/dl, 93.00±11.25 mg/dl and 150.68±17.37 mg/dl respectively at admission, which was found to be statistically significant (p <0.001) (Table 3). At 3 months of follow up, the mean FBS was 81.42±5.40 mg/dl, 85.47±5.14 mg/dl and 120.95±7.51 mg/dl respectively in group 1, group 2 and group 3 respectively, which was statistically significant (p <0.001).

The mean PPBS in group 1, group 2 and group 3 was 128.97±5.94 mg/dl, 126.53±5.99 mg/dl and 171.48±16.53 mg/dl respectively, which was statistically significant (p <0.001). At 3 months of follow up, the

mean PPBS was 122.94±4.02 mg/dl, 123.19±3.16 mg/dl and 159.55±12.35 mg/dl respectively, which was statistically significant (p <0.001) (Table 3).

The mean levels of total cholesterol (p=0.003), LDL-cholesterol (p <0.001), HDL-cholesterol (p=0.001), TG (p <0.001) and VLDL-cholesterol (p<0.001) was significantly different between the three groups (Table 4).

The NIHSS score on admission was 14.06±2.58, 15.50±2.49 and 18.13±2.67 among the group 1, group 2 and group 3 respectively, which was found to be statistically significant with a p value of 0.001. Similarly the NIHSS score re-assessment after 3 month was 9.90±2.43, 12.41±1.78 and 15.93±2.14 between the group 1, group 2 and group 3 respectively, which was statistically significant (p <0.001). The score improvement difference was 4.161, 3.094 and 2.20 among group 1, group 2, and group 3 respectively (Table 3).

All the 40 (100%) patients in group 3 had a higher NIHSS score of >13, whereas 23 (74.2%) patients in group 1 and 30 (93.8%) patients in group 2 had a score of >13 which was statistically significant ($p=0.001$) (Table 5). When all the patients were reassessed at 3rd

month, 3 (9.7%) patients in group 1, 15 (46.9%) patients in group 2 and 38 (95%) patients in group 3 had persistent high NIHSS score of >13, which was statistically significant ($p < 0.001$).

Table 4: Lipid profile among the 3 stroke groups.

	Normoglycemic (N=31)	Stress hyperglycemic (N=32)	Diabetes mellitus (N=40)	p-value
TC	189.55±7.70	191.78±9.28	204.58±29.71	0.003
LDL	109.50±8.10	112.52±8.13	129.94±29.75	<0.001
HDL	48.00±4.23	46.06±4.32	37.78±4.02	0.001
TGL	159.97±10.78	167.88±8.72	184.98±18.84	<0.001
VLDL	23.32±2.76	25.31±1.84	25.83±2.17	<0.001

Table 5: The mean NIHSS score and score grading at and after 3 months of admission.

NIHSS score	Normoglycemic (N=31)	Stress hyperglycemic (N=32)	Diabetes mellitus (N=40)	p-value
Admission	14.06±2.58	15.50±2.49	18.13±2.67	<0.001
After 3 months	9.90±2.43	12.41±1.78	15.93±2.14	<0.001
Difference	4.161	3.094	2.20	
NIHSS score severity				
Admission				
<13	8(25.8%)	2(6.3%)	0	0.001
>13	23(74.2%)	30(93.8%)	40(100%)	
After 3 months				
<13	28(90.3%)	17(53.1%)	2(5%)	0.001
>13	3(9.7%)	15(46.9%)	38(95%)	

DISCUSSION

In the present study, the stroke onset was at an earlier age with group 3, followed by group 2 and group 1. Akbar DH et al in his study observed a lower average age among the new hyperglycemic groups as compared to the non-diabetic and diabetic groups which was proven to be statistically significant with p value of < 0.001.⁶ They also observed a lower average age of 56.9±8.5, 51.5±4.3 and 45.3±2.1 among the diabetes, new hyperglycemic and non-diabetic stroke patients respectively. Athanasia et al in his study had a higher average age ranges in which the diabetic group had 77.4±6.4 years as compared to 77.3±5.2 years in the non-diabetic stroke group.⁹

In the present study, predominantly male patients were affected in all the 3 groups. Akbar DH et al showed predominance in male among the diabetic and non-diabetic stroke patients and female predominance among the new hyperglycemic stroke patients.⁶ Umpierrez et al on the other hand showed a female predominance among all his groups.¹⁰

In the present study we noticed that the diabetic group (group 3) had a higher level of BMI which was similar to the study done by Akbar DH et al and Umpierrez et al.^{6,10}

In the present study, hypertension was the common comorbidity associated with stroke and the numbers were significantly higher in group 3. Tanmoy WM et al in his study showed an equal number of hypertension between the diabetic and non-diabetic strokes group.¹¹ Mansoureh T et al in his study found that hypertension history was higher among the ischaemic stroke than the hemorrhagic stroke patients with a statistical significant p value of 0.006.¹²

In the present study, smoking was observed in all the 3 groups, with group 3 having a higher number when compared to the other 2 groups. Tanmoy WM et al observed a similar finding, where the number of smokers was high in diabetic group when compared to non-diabetic stroke group.¹¹ But on the contrary Akbar DH et al in his study observed a higher number of smokers in non-diabetic group when compared to diabetic stroke group.⁶ In spite of knowing the fact that smoking is a risk factor for stroke, it could not be concluded that smoking influences the glycemic status of the patients.

The admission RBS was the one used to categorize the 3 groups. The cut off range for stress hyperglycemia was taken as 140 mg/dl.^{5,14} We choose to use this cut off in view of the conclusion made by Sarah EC et al, that non-diabetic survivors with an admission level RBS between 121 to 144 mg/dl had a greater risk of poor functional

recovery.³ There are few other studies, which had used the same range. Akbar DH et al and Umpierrez et al both used 2 values to define hyperglycemia, fasting blood glucose level of >126mg/dl and a random blood glucose level of >200mg/dl.^{6,10} Umpierrez et al in his study showed a mean RBG (mmol/l) of 6.3±0.4, 10.6±0.6 and 14.3±1.8 among the normoglycemic, new hyperglycemic and the diabetic group respectively, with a statistical significance.¹⁰ Admission hyperglycemia is shown to have a higher mortality and lower functional outcome in the non-thrombolysed stroke patients and also a greater level of intracerebral hemorrhage in thrombolysed patients.¹⁴⁻¹⁶

In the present study, the mean FBS, PPBS was significantly higher in group 3 followed by group 2 and group 1 which was statistically significant. Tanmoy WM et al had a mean FBS and PPBS of 101.56±6.02 and 127.16±4.93 among the non-diabetic compared to 181.70±12.39 and 284.09±41.25 in the diabetic group.¹¹ In his study, the mean FBS and PPBS of the normoglycemic stroke patient were similar to our observation, but the diabetic group had a much higher mean value. There was no previous study showing the mean FBS and PPBS level in the stress hyperglycemic group. Also no data was available on comparing at 3 months of follow up. In the present study, the HbA1c was found to be significantly higher in the group 3. Similarly other studies of Tanmoy WM et al and Gill et al showed greater values of HbA1c in the diabetes related group.^{11,17}

Dyslipidemia is a major risk for cardiovascular disease and cerebrovascular disease. Stroke patient with dyslipidemia have higher risk of atherosclerosis of the carotid. In the present study, the mean TC, TG, LDL-C and VLDL-C were significantly higher in group 3 and group 2 when compared with group 1. But the level HDL-C was significantly lower in group 3 when compared to group 1 and 2. A similar observation was seen by Jeetendrakumar et al.¹⁸ Stress hyperglycemic groups had a higher level of TGL, LDL and VLDL which was found to be statistical significant. Ogbera et al in his study found that the mean triglyceride level was higher among the ischemic stroke compared to the hemorrhagic stroke.¹⁹

In the present study, the NIHSS score at the time of admission, group 3 and group 2 showed a higher severity score when compared to group 1. Kolawole W et al in his study found that the median admission NIHSS was 14.00 in the hyperglycemic group when compared to 8.00 in the normoglycemic group and also concluded that admission hyperglycemia is a significant predictor for short term outcomes.¹³ The NIHSS score assessment after 3 month was 9.90±2.43, 12.41±1.78 and 15.93±2.14 with a differences of 4.161, 3.094 and 2.20 among the normoglycemic, stress hyperglycemic and diabetes groups respectively which was found to be statistically significant with p value of <0.001. This clearly showed that the diabetes and stress hyperglycemic groups had a

lesser functional recovery compared to the normoglycemic group. Hence the admission hyperglycemic levels do have significance on the functional neurological recovery. Sarah E et al, in her systemic overview also concluded that hyperglycemia does elevate the risk of lower functional recovery in non-diabetic stroke patients.³ Kolawole W et al did not find any significance in functional outcome with respect to admission blood sugars.¹³

CONCLUSION

Admission hyperglycemia in acute ischaemic stroke is a long time known factor and many studies about its significance and related impact on the short and long term outcome of stroke is available. Establishing its relation on the functional neurological outcome brings us to the awareness that good achievement of blood glucose has a significant role in improving the neurological outcome and also the quality of life of the patient. Further studies are required with larger sample size to determine its independent role in neurological outcome, including Indian population.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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