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A STUDY OF HYPERGLYCAEMIA AND ITS PROGNOSTIC EFFECT ON NEUROLOGICAL OUTCOME IN PATIENTS PRESENTING WITH ACUTE ISCHEMIC STROKE.

General Medicine

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ABSTRACT

Background: Cerebrovascular stroke is the third most common leading cause death worldwide after coronary heart disease (CAD) and cancer. The prevalence of stroke and its complications are increasing in last decades which make a large burden to patients, society and also treating physician. The neurological outcome of stroke is depending on various risk factor like age, sex, diabetes, hypertension, smoking, temperature, blood sugar level etc. Among these risk factor admission (stress) hyperglycaemia may adversely affect the outcome of stroke which can be modified by better blood sugar management both in diabetics and nondiabetics (stress hyperglycaemia). Now stress hyperglycaemia is also become a important marker which adversely affect the outcome stroke. In this study we evaluate correlation between blood sugar level and neurological outcome of is chaemic stroke on admission and after three months follow up.

Methods: It is a prospective and comparative study at A.N.M.M.C Gaya. 103 patients with ischemic stroke with age more than 40 years included. These patients National Institute of Health Stroke Score (NIHSS) and blood sugar level noted at time of admission. These patients divided in three group first group with normoglycemia second group with stress hyperglycaemia and third group with T2DM patients. These groups were again reassessed after 3 months with FBS, PPBS and neurological recovery by NHISS. 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 patients of first group(normoglycemic) had good functional recovery compared to second (stress hyperglycaemia) and third group (diabetes mellitus) groups ($p<0.001$) at 3 months.

Conclusions: High blood sugar level at the time of admission in patients of stroke may adversely affect the neurological outcome. So, blood sugar level at the time of admission may be used as important prognostic indicator for functional recovery.

KEYWORDS

Cerebrovascular accident, Stress hyperglycaemia, Normoglycemia, Diabetes mellitus, National Institute Of Health Stroke Score

INTRODUCTION

Cerebrovascular accident (CVA) is third most common leading cause of death worldwide. The world health organisation (WHO) defines stroke as" rapidly developing clinical sign of focal/global disturbance of cerebral functions with symptoms lasting for 24 hours or longer or leading to death with no apparent cause other than vascular origin". Among 80% of stroke are ischemic, rest being due to haemorrhage. Acute hyperglycaemic response to stress has been recognised since Claude Bernard's observations more than a century ago. This stress hyperglycaemia exemplifies the obligatory metabolic rearrangement to cope with critical stress. The concept evolved as glucose become identified as metabolic mirror of the severity and outcome of critical illness. 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 hyperglycaemia is among the potentially modifiable factor`s which affect the outcome of stroke. Various clinical and experimental studies have shown that admission hyperglycaemia has an adverse effect on the neurological and short term outcomes in ischemic stroke.[3-6] This acute hyperglycaemia in stroke is not always due to type 2 diabetes mellitus, but it may be due to stress response mediated partly by release of cortisol and norepinephrine.[7] Stress hyperglycaemia generally refers to a transient hyperglycaemia during illnesses and restricted to individuals without prior evidence of DM. This stress hyperglycaemia usually resolves spontaneously after the acute phase of illness. Stress hyperglycaemia 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 hyperglycaemia needs to be treated or not. Still controversies exist on whether this stress hyperglycaemia is harmful and affect the outcome in acute ischemic stroke. Hence the present study was done to assess the presence of stress hyperglycaemia and its effect on neurological recovery at 3rd month by comparing with normoglycemic and T2DM patients presenting with acute ischaemic stroke.

METHODS

This prospective comparative study was done at Anugrah Narayan Magadh Medical College Gaya. 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. Stress hyperglycaemia was defined as a blood sugar level of more than 140 mg/dl. The patients were subdivided into 3 groups based on fasting blood sugar (FBS), post prandial (PPBS) and HbA1c level.

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

Group 2: Stress hyperglycaemia (>140 mg/dl) with normal HbA1c and no history of diabetes mellitus.

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, septicaemia) were excluded from the study.

Statistical methods

Descriptive and inferential statistical analysis has been carried out in

the present study. Results on continuous measurements are presented as mean ±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±4.41years in group 1 as compared to 65.47±6.90 years in group 2 and 61.98±4.23 years 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).

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 group 1, group 2 and group 3(diabetic) 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 m g / d l , 85.47±5.14 mg/dl and 120.95±7.51 mg/d 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 the NIHSS score re-assessment after 3 months 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

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 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 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).

DISCUSSION

All the 40 (100%) patients in group 3 had a higher month, 3 (9.7%) patients in group 1, 15 (46.9%) patients NIHSS score of >13, whereas 23 (74.2%) patients in in group 2 and 38 (95%) patients in group 3 had group 1 and 30 (93.8%) patients in group 2 had a score of persistent high NIHSS score of >13, which was >13 which was statistically significant (p=0.001) statistically significant (p <0.001). (Table 5). When all the patients were reassessed at 3rd 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 hyperglycaemic 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 hyperglycaemic 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, 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 haemorrhagic 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 nondiabetic 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 glycaemic status of the patients.

The admission RBS was the one used to categories the 3 groups. The cut off range for stress hyperglycaemia 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 nondiabetic 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 hyperglycaemia, 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 hyperglycaemic and the diabetic group respectively, with a statistical significance.[10] Admission hyperglycaemia is shown to have a higher mortality and lower functional outcome in the non-thrombolysed stroke patients and also a greater level of intracerebral haemorrhage 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 hyperglycaemic 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]

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 hyperglycaemic group when compared to 8.00 in the normoglycemic group and also concluded that admission hyperglycaemia 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 hyperglycaemic 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 hyperglycaemic groups had a lesser functional recovery compared to the normoglycemic group. Hence the admission hyperglycaemic levels do have significance on the functional neurological recovery. Sarah E et al, in her systemic overview also concluded that hyperglycaemia does elevate the risk of lower functional recovery in nondiabetic stroke patients.[3] Kolawole W et al did not find any significance in functional outcome with respect to admission blood sugars.[13]

CONCLUSION

Admission hyperglycaemia is better prognostic indicator for functional and neurological recovery in patients with ischaemic stroke. Better management of hyperglycaemia may improve neurological recovery and outcome instroke.

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 1: Demo graphical profile among the 3 groups.

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

The body mass index in group 1 was 23.26±3.88 as group 3, which was found to be statistically significant compared to 22.95±2.72 in group 2 and 26.21±2.78 in (p<0.001) (Table 1).

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

Table 4: 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%)	

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