Section: Miscellaneous

Original Research Article

CLINICAL OUTCOME IN ISCHAEMIC STROKE PATIENTS WITH RELATION TO BLOOD GLUCOSE AT PRESENTATION

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Abstract

Background: Stroke or cerebrovascular accident is one of the leading causes of mortality around the world. Raised blood glucose is common in the initial phase of stroke. Extensive experimental evidence in stroke models supports that hyperglycaemia has adverse effects on tissue outcomes. In this study, we aim to determine the prevalence of stress hyperglycaemia among the patients of acute ischaemic stroke and to find a correlation between random blood glucose in the early phase of stroke patients and the severity of stroke and prognosis with respect to in-hospital outcomes. **Materials and Methods:** A total of 106 patients above 12 years of age getting admitted within 24 hrs of the onset of symptoms of ischaemic stroke were studied. Blood sugar was recorded within 24 hrs of the onset of stroke. We calculated the prevalence of stress hyperglycaemia among patients of acute ischaemic stroke. We also evaluated the severity of stroke in relation to the National Institute of Health Stroke Scale (NIHSS) and compared it with the glycaemic status of the patients at presentation. **Result:** In our study, the prevalence of stress hyperglycaemia among patients of acute ischaemic stroke was 17.9%. The mean NIHSS score among the patients with hyperglycaemia at presentation having RBS between 140-199 was 10.52 and those with RBS >200 were 17.86 as compared to 7.16 in normoglycaemic group. The relation between RBS on presentation and NIHSS score resulted in a p value of <0.001, suggesting that patients with hyperglycaemia at presentation had a higher NIHSS score hence having a poorer outcome as compared to the euglycaemic patients. Admission day hyperglycaemia is associated with a higher NIHSS score compared to normoglycaemia thus associated with poor prognosis. **Conclusion:** Stress hyperglycaemia was seen in a significant number of acute ischaemic stroke patients. Admission day elevated glucose was associated with higher NIHSS score and thus was significant predictor of mortality and poor outcome after an acute stroke.

INTRODUCTION

A stroke, or cerebrovascular accident, is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause.[1] There are mainly two types of strokes: haemorrhagic and ischaemic. Ischaemia occurs within seconds after cessation of blood supply and haemorrhagic progressing to infarction in minutes. Signs and symptoms of stroke are highly variable and can include an inability to move or feel on one side or part of the body, problems with understanding or expression, a sense of world rotation to the side.[2] If the symptoms resolve within 24 hours, this is known as a transient ischaemic attack (TIA), with no radiological evidence of brain injury. Hypertension being one of the major risk factors for stroke, other risk factors includes smoking, diabetes mellitus, and obesity, dyslipidaemia, past history of stroke, TIA, or atrial fibrillation.[3] Diagnosis is usually made using investigations like Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) of the brain. Elevated blood glucose is common in the early phase of stroke.[4] The prevalence of hyperglycaemia has been observed in two thirds of all ischaemic stroke subtypes on admission.[5] Extensive experimental evidence in stroke models supports that hyperglycaemia has adverse effects on

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tissue outcomes, and an association between blood glucose and functional outcomes has been found in an increasing number of clinical studies. Hyperglycaemia per se is associated with increased morbidity and mortality in stroke patients.[6] Additionally, 30% to 40% of patients admitted with ischaemic stroke had been found hyperglycaemic, usually without a previous history of diabetes mellitus.[7]

Although there are many studies suggesting an association between hyperglycaemia and clinical outcome in ischaemic stroke patients, the SHINE randomized clinical trial for Intensive vs Standard treatment of hyperglycaemia and functional outcome in patients with acute ischaemic stroke showed that intensive glucose control did not improve 90-day functional outcomes when compared to compared with standard glucose control.[8]

Hyperglycaemia is a manifestation of multiple pathways conversing together. There may be influence of ethnicity on these pathways. Thus, it is necessary to evaluate whether hyperglycaemia is associated with adverse outcomes in our native population. No such studies have been carried out here.

MATERIALS AND METHODS

The present study was undertaken with the primary objective to find the prevalence of stress hyperglycaemia among patients with Acute Ischaemic Stroke (AIS). Our secondary objectives were to determine the relationship between blood glucose level at presentation with respect to clinical outcome of ischaemic stroke patients in terms of mortality and morbidity to determine the relationship between diabetic, stress hyperglycaemic and non-diabetic ischaemic stroke patients with respect to their severity in terms of National Institute of Health Stroke Scale (NIHSS) score.

It was a hospital based prospective observational study. Ethical clearance was obtained from the ethical committee of the institution and was conducted from 1st June 2022 to 31st May 2023 for a period of one year.

The prevalence of hyperglycaemia in acute stroke is 38%.[9] Therefore, to determine the prevalence of stress hyperglycaemia with a confidence of 95% and margin of error of 10%, 91 patients were required. To account for an attrition of 15%, we intended to include 106 patients.

Our study included any patient aged 12 years and above with first episode of ischaemic stroke getting admitted within 24 hrs of onset of symptoms and whose blood sugar was recorded within 24 hrs of onset of stroke.

Patients with haemorrhagic stroke, tumour, subarachnoid haemorrhage, brain abscess or who received intravenous glucose before or during the study period and the ones prepared for thrombolysis were excluded from our study.

Written and informed consent was obtained from each participant/attendant of participant who presented within 24 hrs of onset of symptoms of stroke. A detailed history was taken and a complete physical examination was done as per proforma. Once clinical diagnosis of acute stroke was made, venous blood sample was taken within 24 hours of onset of symptoms and sent for glucose estimation. Random blood sugar was estimated using the VITROS 5600 integrated system.

Then, a CT scan of brain was done using SIEMEN'S SOMATOMS SPIRIT SPIRAL CT SCANNER to confirm the diagnosis, detect the type of stroke, detect the size of lesion (Small <5mm, Medium 5-10mm, Large >10mm or involving more than one vascular territory), detect site of lesion, detect any midline shift or cerebral oedema. Those with haemorrhage, tumour, subarachnoid haemorrhage or brain abscess were excluded from the study.

A detailed neurological examination was carried out again between 48 hours to 72 hours and were labelled as minor, moderate, moderate to severe or severe stroke based on NIHSS score, 0 - No stroke symptoms, 1-4 - Minor stroke, 5-15 - Moderate Stroke, 16-20 - Moderate to severe stroke and 21-42 - Severe Stroke. Patients were observed for 7 days for their in-hospital outcome in the form of death, poor, moderate and good improvement. Patients who were unable to return to any form of work,[10] persistent disability,[11] need for residential placement,[12] dependent in activities of daily living,[13] and stable deficit with no recovery,[10] were classified as poor outcome. Patients whose symptoms improved, who were independent in performing day to day activities, improvement in motor function and aphasia and no persistent disability were classified as good outcome. Patients whose symptoms were in between these two groups like they could perform most of their day to day activities with some help, improving disabilities but were unable to return to work as still required some assistance were classified as moderate outcome.

An RBS value of >140 mg/dl was considered as elevated blood glucose level. In patients with blood sugar more than 140 mg/dl and without a history of diabetes, HbA1c was performed. The normal HbA1c ranges from 3.8% to 6.4%. Hence the patients can be divided into four groups:

a. Blood sugar less than 140mg/dl – Non-diabetic (Euglycaemics)
b. History of Diabetes – Known Diabetics
c. Blood sugar >140mg/dl with HbA1c >6.4%, without history of diabetes – Newly detected Diabetic
d. Blood sugar >140mg/dl with HbA1c <6.4, without history of diabetes – Stress Hyperglycaemic.[14]

Other routine investigations like Complete blood count (CBC), Kidney function test (KFT), Serum

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electrolytes, ESR, Lipid profile, Urine analysis, ECG, chest X-ray, 2D echo, carotid artery and vertebral artery doppler and MRI brain(if required) were done. The levels of RBS at the time of admission were compared with the scores obtained via NIHSS and was looked for association and prognosis.

Statistical analysis was done using the Statistical Package for the Social Sciences (SPSS) software version 19.0 (IBM SPSS, US) software with regression modules installed. Microsoft excels and word has been used to generate graphs, tables, etc. Results on continuous measurements are on mean and SD (min-max) and results on categorical measurements are presented in number (%). The level of significance was taken at 5% to assess significance.

RESULTS

1. Demographic Data of the study population(Table 1)

The study population belonged to the Northeastern states of India mostly from Meghalaya and Assam (both Rural and Urban).

2. PREVALENCE OF STRESS HYPERGLYCAEMIA IN ACUTE ISCHAEMIC STROKE PATIENTS

Prevalence was calculated using the formula:

Prevalence = (Total number with disease) / (Population at risk for the disease)[15]

During a period of 1 year from 1st June 2022 to 31st May 2023.

Prevalence of stress hyperglycaemia = Number of stress hyperglycaemia/total population

P = 19/106 * 100 = 17.9 %

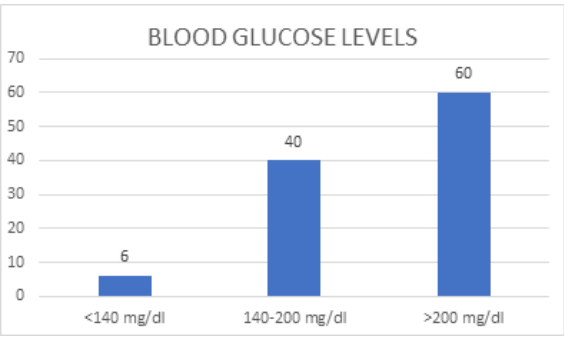

Figure 1: Column diagram of Ischaemic stroke patients showing blood glucose levels at presentation

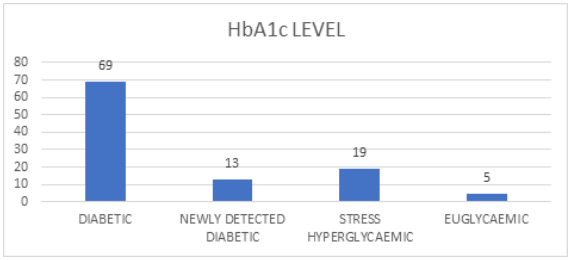

Fig 2: Column diagram of Ischaemic stroke patients showing HbA1c levels

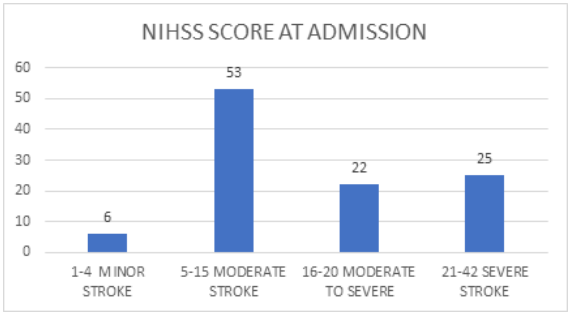

Fig 3: Column diagram showing NIHSS score at admission in Ischaemic stroke patients

3. IN-HOSPITAL OUTCOME

The patients were observed for a period of 7 days for their In-hospital outcome.

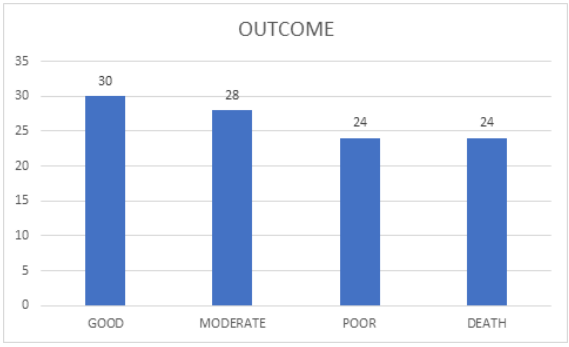

Fig 4: Column diagram showing In-Hospital Outcome of the patients with Ischaemic stroke

4. ASSOCIATION BETWEEN RBS AND NIHSS SCORE- There was a positive and significant correlation between RBS and NIHSS score with a p value <0.001.

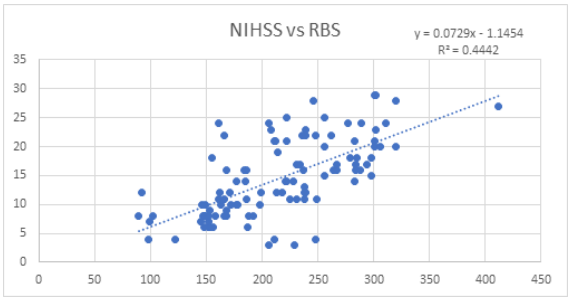

Fig 5: Scatter diagram showing Correlation between NIHSS and RBS in Ischaemic stroke patients.

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Table 1: Demographic data and comorbidities of patients presenting with ischaemic stroke

Parameters	Values (mean +/- SD)
Age#	59.41 +/- 11.27 years
Sex (Male/Female)*	64/42
BMI#	22.90 +/- 1.58 kg/m2
Comorbidities*	
Diabetes	69
Hypertension	68
Dyslipidaemia	61
CAD	14
Modifiable Risk Factors*	
Smoking	34
Alcohol	30
Systolic Blood Pressure#	149.05 +/- 17.39 mmHg

#Mean, *Absolute Value

ASSOCIATION BETWEEN HbA1c Levels AND NIHSS SCORE

Table 2: Correlation between HbA1c and NIHSS score

HbA1c Levels	NIHSS group				total	p value
	Minor	Moderate	Moderate to severe	Severe		
Stress hyperglycaemic	2(1.9%)	17(16.0%)	0(0%)	0(0%)	19(17.9%)	
Euglycaemic	1(0.9%)	4(3.8%)	0(0%)	0(0%)	5(4.7%)	
New diabetic	0(0%)	9(8.5%)	1(0.9%)	3(2.8%)	13(12.3%)	<0.001
Diabetic	3(2.8%)	23(21.7%)	21(19.8%)	22(20.8%)	69(65.1%)	
Total	6(5.7%)	53(50%)	22(20.8%)	25(23.6%)	106(100%)	

There was a significant correlation between HbA1c Levels and NIHSS score with a p value of <0.001.

Association Between RBS And Outcome

Table 3: Correlation between RBS and outcome

Outcome	RBS Group			Total	p value
	<140	140-199	>200		
Good	2(1.9%)	18(17.0%)	10(9.4%)	30(28.3%)	
Moderate	4(3.8%)	16(15.1%)	8(7.5%)	28(26.4%)	
Poor	0(0%)	4(3.8%)	20(18.9%)	24(22.6%)	
Death	0(0%)	2(1.9%)	22(20.8%)	24(22.6%)	
Total	6(5.7%)	40(37.7%)	60(56.6%)	106(100%)	

There is a significant correlation between RBS and outcome with a p value of <0.001

DISCUSSION

A hospital-based observational study was done on 106 patients presenting to a tertiary care hospital from 1st June 2022 to 31st May 2023. Subjects who got admitted with a diagnosis of ischaemic stroke to the medical ward/ICU were included in the study.

In our study, the mean age of study population is 59.41 ± 11.27 years. Similar values were observed in the studies conducted by Youn CS, et al 2012,[16] where the mean age of the population was 66.9 ± 12.9 years. In studies done by Subhash, et al 2018,[17] the mean age in diabetics were 57.5 ± 12.7 years and non-diabetics were 61.3 ± 12.9 years.

In our study the distribution of gender showed that males were the majority (60.4%) and Females were 39.6% of the study population.

In the study conducted by Subhash, et al 2018,[17] males were 70% and females were 30% also similarly the studies of kumar, et al 2020,[18] showed that there were 62% male and 38% were female. Hence the findings were almost similar to the studies conducted by other researchers.

The mean BMI of the study population was 22.90 +/- 1.58 kg/m^2. 16.03% study population were overweight. In a similar study conducted by Yao T, et al. 2020,[19] mean BMI of the study population was 24.10 +/- 2.96 kg/m^2. This result was similar to that of our study population, hence results can be compared. Skolarus L E, et al 2014,[20] studied the association of Body Mass Index and Mortality after Acute Ischaemic Stroke. He found that severe obesity was associated with increased post stroke mortality in middle-aged and older adults.

In a study by Huang J.; et al 202,[21] during an average follow-up period of 5.5 years, when BMI was treated as a continuous variable, there were 206 onset cases (6.21%) of Ischaemic stroke and it was positively associated with the incidence of new onset Ischaemic stroke after adjusting for potential confounders.

In the study conducted by Subramanian, et al, 2019,[22] diabetes was the most common comorbidity with 68% of study population having diabetes followed by 64% of population having hypertension and 58% of population having dyslipidaemia.

The study conducted by Kumar, et al 2020,[18] showed diabetes as the most common comorbidity with 74% of population having diabetes followed by

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68% having hypertension and 62% having dyslipidaemia.

In study by Renjen, et al 2015,[23] hypertension was the most common comorbidity with 56.9% of population having hypertension followed by 34.8% having diabetes and 18% had Coronary Artery Disease. In our present study, Diabetes was the most common comorbidity with 65.1% study population having diabetes followed by hypertension, with 64.2% of population having hypertension. Dyslipidaemia was present in 57.5% and CAD was present in 13.2% of the study population.

The results of our study showed similar results with those of previous studies with respect to diabetes and hypertension, however our study had a less number of CAD patients i.e. 13.2% as compared to the study done by Rejen, et al 2015,[23] which had 18% of CAD patients.

In the study conducted by Idicula T. T., et al 2009,[24] 24% of the study population had a history of smoking. In studies done by Kumar, et al 2020,[18] 34% of the study population was observed to have a history of smoking.

In our study 32.1% of patients had a history of smoking. In the study conducted by Nagaraja, et al 2009,[25] 25.1% had a history of consumption of alcohol. In studies by Subhash et 2018,[17] an average of 33.75% (27.5% in Diabetic and 40% in non-diabetic) had a history of alcohol consumption.

In our study Alcohol consumption was seen in 28.3% of study population. These results of both smoking and alcohol consumption were similar to the results seen in the previous studies. In our study the prevalence of stress hyperglycaemia among patients of AIS was 17.9%. This was slightly lesser compared to the study conducted by Jitendra, et al 2017,[26] where the prevalence of stress hyperglycaemia in stroke patients was 24.13% while it was similar when compared to study conducted by Matz, et al 2006,[27] where prevalence of stress hyperglycaemia in stroke patients was 19.7%.

In a study by D Mi, P Wang et al 2018,[28] 59.4% were having RBS >140 mg/dl, while 40.6% were having RBS <140mg/dl. In a similar study by Kumar, et al 2020,[17] 62% patients had RBS >200 mg/dl, while 38% had RBS between 126-199 mg/dl. In our study 56.6% of the patients had blood glucose levels >200 mg/dl, and 37.7% had RBS levels between 140-200 while 5.7% of the patients had RBS <140 mg/dl. In study by Al-Weshahy A., et al 2017,[29] the mean NIHSS Score among patients with hyperglycaemia on admission was 14.9 ± 5.9 as compared to 7.8 ± 3.5 in the control group i.e those having normoglycaemia. In our study the mean NIHSS score among the patients with hyperglycaemia at presentation having RBS between 140-199 was 10.52 ± 4.2 and those with RBS >200 was 17.86 ± 6.2 as compared to 7.16 ± 2.94 in the normoglycaemic group.

The relation between RBS on presentation and NIHSS score resulted in a p value of <0.001 thus suggesting that patients with hyperglycaemia at presentation had a higher NIHSS score hence having a poorer outcome as compared to the euglycaemic patients. In another similar study conducted by Kumar, et al 2020,[17] there was a positive correlation(r=0.71, p = <0.001) between admission day sugar and outcome of stroke. Good functional recovery was reported in 75% of patients with normal blood glucose, whereas only 4.6%, 6.7%, 12.5% of known diabetic, newly detected diabetic and stress hyperglycaemic i.e. those having hyperglycaemia had good functional recovery.

In our study there was a positive correlation seen between Glycaemic status and outcome of stoked with a p value of 0.0001. Good functional recovery was seen in 20% of Euglycaemic and moderate functional recovery was seen in 80% of Euglycaemic patients whereas no death and poor outcome were seen in euglycaemic patients. These findings were suggestive of correlation between hyperglycaemia and poor outcome in a stroke patient and the findings of our studies were in par with similar studies done previously.

There are several studies determining the association between outcome in stroke and blood glucose at presentation in different parts of the country, however no such study was done in the northeastern part of the country. Hence, this study was essential in this part of the country due to difference in demography, lifestyle and dietary habits as well as knowledge and awareness regarding stroke and access to healthcare of the population here.

The limitations of this study are its small sample size, short duration of the study period and institutionalised study. Also, the management of hyperglycemia and stroke per se was not standardized. Hence, it is difficult to draw a definite inference. Therefore, a large number of prospective, epidemiological, and analytical studies are required to come to a strong and definite conclusion.

CONCLUSION

Based on the results and methodology employed, we can conclude that a significant number of patients with AIS have stress hyperglycaemia irrespective of their previous diabetic status and admission day hyperglycaemia is associated with a higher NIHSS score as compared to normoglycaemia. Admission day elevated glucose is a significant predictor of mortality and poor outcome after an acute stroke. Also, the findings of the present study demonstrate significant deleterious effects of stress hyperglycaemia on outcome of patient with acute ischaemic stroke.

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