
Original Research Article

A Study On The Clinical Outcome In Ischemic Stroke Patient With Hyperglycemia In A Tertiary Care Hospital Of Southern Bihar

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Received: 15-07-2020 / Revised: 21-08-2020 / Accepted: 25-09-2020

Abstract

Background: Previous research has been able to establish an association between diabetes/ increased sugar levels and increased mortality, length of hospital stay, readmission rates, and poorer functional and rehabilitation outcomes after stroke. The present study was done to assess the link of the blood sugar levels with acute stroke and thereby evaluate the severity and prognosis of stroke with reference to hyperglycemia.**Materials and method**: The blood sugar and HbA1C levels at the time of admission were recorded. The severity of stroke for each patient is calculated based on NIH stroke scale, which takes the clinical findings in to account and each criteria awarded specific points. The Student's *t*-test was applied for the comparing the mean values, Chi-square test for the comparison of frequencies and Spearman's correlation test for correlation between the 2 variables.**Results:** Maximum number of the subjects in the present study belonged to the age group of 51-60 years with predominance among the males. High sugar levels as assessed by Random blood sugar and HbA1C levels was associated with increased severity of stroke as per NIH stroke class severity and poor functional outcome as well as the mortality.

Conclusion: There is a linear correlation between admission day hyperglycemia and the severity of ischemic stroke. There is a good correlation between glucose level at the time of admission and the ischemic stroke outcome.

Keywords: Diabetes mellitus, HbA1C level, Blood sugar level, Ischemic Stroke

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Introduction

Stroke is one of the major causes of disability and mortality all over the world.[1,2] Given its major socioeconomic burden, there is always a need to improve our understanding of its high risk population, complications, and prognosis.Diabetes is a major risk factor for stroke occurrence.[3] Hyperglycemia (blood glucose level >6.1mmol/L or 121 mg/dL) is common in early phase of stroke, even in patients without a previous diagnosis of diabetes mellitus. It has been found in two thirds of all stroke patients and in almost half of ischemic stroke patients.[4,5]

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High glucose levels predict a larger infarct size, poor clinical outcome and a higher risk of mortality, and are independent from other predictors of a poor prognosis such as age, diabetic status and stroke severity.[6,7-12] Several mechanisms seem to account for the high frequency of hyperglycemia observed in patients with acute ischemic stroke, and various pathophysiological mechanisms have been proposed to account for the detrimental effect of hyperglycemia on the ischemic brain.A recent meta-analysis of prospective and case-control studies confirmed the importance of early stress hyperglycemia as a predictor of stroke outcome, but debate continues as to whether the effect is independent of pre-existing diagnosis of diabetes or initial stroke severity. It is still not clear what cut-off value of the mean blood glucose level (MBGL) should be considered safe in diabetic and non-diabetic patients.[13]Pulsinelli and colleagues found that neurological outcome was worse in patients with blood glucose levels > 120 mg/dl (6.7 mmol/l).[14] In a systematic review of hyperglycaemia and poststroke outcomes, Capes and colleagues included 32 studies and found that admission blood glucose > 108–144 mg/dl (6–8 mmol/l) was associated with increased in-hospital or 30-day mortality (relative risk of 3.1, in patients without diabetes compared to 1.3, in patients with diabetes).[15]Although hyperglycaemia is often attributed solely to the physiological stress of the acute stroke event, elevated blood glucose levels may reflect underlying glucose intolerance or diabetes mellitus. Approximately one-third of all patients with diabetes have undiagnosed diabetes (i.e. not recognized by their clinician).[16] Current guidelines recommend screening patients for diabetes if they have one or more risk factors for diabetes (e.g. age more than 45 years, hypertension, lipid abnormality, vascular disease, etc.).[17]The under-diagnosis of diabetes in the general population, together with the strong association of diabetes with stroke (stroke is often due to either micro- or macrovascular disease, and stroke patients often have other risk factors for diabetes),[18,19] suggests a rationale for screening all hyperglycaemic stroke patients for diabetes. A diagnosis of diabetes in a stroke patient would probably change the clinical management of that patient, specifically with respect to lipid and blood pressure management.[20,21]The present study was done to assess the link of the blood sugar levels with acute stroke and thereby evaluate the severity and prognosis of stroke with reference to hyperglycemia.

Materials and method

The study included 100 of acute ischemic stroke patients reporting to the ICU of Narayan Medical College & Hospital, Bihar between July 2019 to December 2019.

Selection of study subjects

The Patients were selected on the following basis

Inclusion criteria:

1. Patients should be above the age of forty
2. Patients should have been admitted within twenty four hours of onset of symptoms
3. This should be the first cerebro vascular accident for the patient
4. Blood sugar recorded with in twenty four hours of the onset of stroke

Exclusion criteria

1. Patients admitted after twenty four hours of stroke
2. Those patients who received intravenous glucose before or during study period
3. Patients with reliable information about diabetes could not be obtained
4. Patients who died before it could be established whether or not they had diabetes
5. Illness presented with stroke like symptoms

Study procedure

Complete history was taken, clinical examination was done and clinical diagnosis for each patient was arrived. Blood pressure measurement, blood sugar, urea, creatinine, electrolytes, hemoglobin, total count, differential count; urine sugar, albumin, deposits; electrocardiogram and chest X ray done for all patients. The severity of stroke for each patient is calculated based on NIH stroke scale, which takes the clinical findings in to account and each criteria awarded specific points. The points were added, with a maximum of forty two points.

Table 1:NHSS Score and stroke severity

NIHSS Score	Stroke severity
0	No stroke symptoms
1-4	Minor stroke
5-15	Moderate stroke
16-20	Moderate to severe stroke
21-42	Severe stroke

Once clinical diagnosis of acute stroke was made, the venous blood sample was taken, within 24 hours of onset of symptoms, and sent to laboratory for glucose estimation. In patients with blood sugar more than 6.1 mmol/l (110 mg/dl)[22] and without a history of diabetes, Hemoglobin A1c was performed. (Hemoglobin A1C is structurally similar to hemoglobin A except for the addition of glucose.

CT

computerized tomography, CT, of the brain was performed in all patients to : Confirm the diagnosis Detect the type of stroke Detect the size of lesion (small

< 5mm; Medium 5 – 10 mm; Large > 10 mm or involving more than one vascular territory) Locate the site of lesion Identify the presence of cerebral edema or midline shift.

Follow-up

The patients were followed up for thirty days and outcome in the form of death; poor, moderate and good improvement was recorded. Patients who were unable to return to any form of work, persistent disability, need for residential placement, dependent in activities of daily life, and stable deficit with no recovery were classified as those with poor outcome.Patient whose symptoms improved, who were independent in attending day to day activities, improvement in motor function and aphasia and no persistent disability were grouped as patients with good outcome. Patients who fared in between these two groups were grouped as those with moderate outcome.

Statistical analysis

The data was entered into the Microsoft excel and analyzed using the SPSS version 25.0. The Student's *t*-test was applied for the comparing the mean values, Chi-square test for the comparison of frequencies and Spearman's correlation test for correlation between the 2 variables. The p-value was considered to be at the significance level when it was below 0.05.

Results

There was a male preponderance in our study with 62.0% males. Majority of the patients belonged to 51-60 years age group (28.0%) followed by 61-70 years (26.0%), above 70 years (25.0%) and 40-50 years (21.0%).

The distribution of the risk factors among the study population showed that 38.0% were hypertensive, 74.0% had prior history of diabetes mellitus and 62.0% had abnormal lipid levels. History of smoking and alcohol was reported among 34.0% and 30.0% subjects respectively. (Table 2)At the time of the admission, normal random blood glucose levels were reported among 38.0% while the remaining 62.0% had elevated blood glucose levels. As per the HbA1C values, Diabetes was reported among 65.0% patients, with 15.0% newly detected diabetics and 32.0% had stress hyperglycemia. (Table 2)The stroke severity was assessed with NIH Stroke scaling system. The patients with hyperglycemia had statistically significantly higher score in comparison to the Euglycemic patients as assessed by the random blood glucose levels and HbA1c levels. (Table 3, 4)

Our study clearly shows a positive correlation ($r = 0.71$) between admission day sugar value and the outcome of stroke. Higher admission day elevated blood glucose level has increased mortality and high risk of poor functional recovery. (Table 5)At the end of thirty day follow-up, good functional recovery was reported among 75.0% patients with normal blood glucose levels. Whereas, 4.6%, 6.7% and 12.5% known diabetic, newly detected and stress hyperglycemics had good functional recovery. High mortality and poor functional outcome at the end of 30 day period of follow-up was reported among known diabetic, newly detected and stress hyperglycemics. (Table 6)

Discussion

Clinical outcome after stroke is highly variable and depends on many factors.[22] Accurate assessment of the expected outcome is important for clinical decision-making, to guide patient management and improve rehabilitation. It is also needed to plan discharge and to provide appropriate prognostic information to patients and his/her relatives.[23]

The stroke patients in the current study were in the age range of 41-75 years of age with majority in the age range of 51-60 and 61-70 years which was quite similar to the study by *Subhash et al*, maximum patients were in the age group of 60–69 years (40%) in diabetic stroke and 60–69 (27.5%) in the non-diabetic group.

Men were found to experience stroke more frequently in our study which was in similarity to the findings by *Subhash et al*, men were at a greater risk for stroke in both diabetic and non-diabetic group. Women often did not seek health care and believed in natural cure or native medicine. This possibly explains the significant decrease in the female gender.

In line to our findings, *Subhash et al* reported that Diabetic stroke patients with a history of hypertension were 75% and that of non-diabetic group were 42.5%. Similar results were also found in the Copenhagen stroke study.[24] Hypertension is the single most important factor for all vascular diseases, in general, cardiac and cerebral, in particular, closely followed by DM. When both are present, risk is greater. DM hastens atherosclerosis, and atherosclerosis promotes hypertension. Therefore, the prevalence of stroke is higher in diabetics, hypertensives and metabolic syndrome. Diabetic stroke patients with a history of CAD were 32.5% and that of non-diabetic group were 27.5%. The observation in the present study that previous history of CAD was more common in the DM than in the non-diabetics was similar to another study.[24 Coronary arteries as well as cerebral arteries are medium sized, and therefore, atherosclerotic changes contributory to the development of stroke also contribute to the higher incidence of stroke, more so, in diabetes.In our study, there was an increased severity of stroke as per the NIHSS classification with elevated blood sugar levels and HbA1C levels at the time of the admission which was similar to the study by *Subramiam et al*. Previous clinical trials have shown that hyperglycemia at admission is correlated with a worsened clinical outcome. In non-diabetic patients, stress hyperglycemia was associated with a 3-fold risk for fatal stroke at 30 days and a 1.4-fold risk for poor functional outcome as compared with normoglycemic patients.[15,25-27]In several thrombolysis trials, hyperglycemia has been found to be associated with decreased odds for neurological improvement and also with increased secondary haemorrhagic events, which leads to speculation that hyperglycemia might be partially responsible for the diminishing beneficial effect of rtPA and early reperfusion.[28,29] *Subramanian et al* demonstrated that ischemic patients, who had elevated admission day glucose level experienced a three and a half fold increased early mortality than euglycemics with similar results among non-diabetic patients. In the diabetic group since the sugar value before the onset of stroke was not known, the effect of stress in diabetic group could not be studied.Diabetes is typically associated with poorer functional outcome, especially in poorly controlled diabetes (HbA1c >7%). Diabetes has also been associated with worse neurological deterioration (decrease of National Institute of Health Stroke Scale points 1 at 3 months) and increased risk of hemorrhagic development in people treated with thrombolysis for ischemic stroke. An explanation for this might be incomplete recanalization after thrombolysis, as suggested in one study. Diabetes has been associated with a reduced amount of recovery after rehabilitation, higher risk of mortality in some but not all studies and a risk factor for recurrent ischemic stroke.[30]Similar to our study, *Kes et al* have shown that there is an unadjusted relative risk of in-hospital mortality within 30 days of 0.68 among non-diabetic patients and of 0.39 in diabetic patients. Non-diabetic patients with hyperglycemia had a 1.7 higher relative risk of in-hospital 28-day mortality than diabetic patients, which correlates with previous studies showing a relative risk about 2.0 times higher in non-diabetic patients than diabetic patients.[15,25-27]Studies that compared three glycemic measures – FBG vs random admission glucose vs HbA1c – consistently found that elevated FBG (≥7 mmol/L),[31] random admission glucose or blood glucose 2-hour post OGTT (≥11.1 mmol/L)[32-34] were independent predictors of poor neurological outcome,[32,34] higher rates of mortality[33,34] and stroke recurrence[34] post-stroke compared with a single HbA1c ≥6.5%. Receiver operating characteristic analysis[32] showed a different threshold of FBG in individuals with diabetes (FBG >7.8 mmol/L) compared with individuals without diabetes (FBG >6.05 mmol/L). In one study96, an elevated random glucose ≥11.1 mmol/L was a poor prognostic marker in non-diabetics or individuals with diabetes with good control (HbA1c 6.5% has also been found to be a predictor of symptomatic intracerebral hemorrhage after thrombolysis for ischemic stroke.[30]Several studies have confirmed that stress hyperglycemia is associated with a poor outcome [26,13,35]. Jorgensen and colleagues [26], in their large prospective Danish study found that plasma glucose level >11 mmol/L (>198 mg/dL) was associated with hospital mortality of 17% for non-diabetic patients, 24% for those with known diabetes and 32% for patients with hyperglycemia with no history of previous diabetes. Capes and colleagues,[15] in their systematic review found that stress hyperglycemia upon hospital admission was associated with three folds higher risk of short-term mortality compared with patients with lower glucose levels. Possible theories which are considered to cause hyperglycaemia related brain damage include; acidosis, oxidative stress, reperfusion injury, interference with glucose/sodium transport and glucose related cortisol increase.[36]On a physiological and radiological level, stress hyperglycemia has been associated with a larger infarct volume on presentation,[37,38] and might contribute to poorer stroke recovery through impairment of the fibrinolytic process[39,40] and delayed reperfusion of the ischemic penumbra.[41] Relative insulin deficiency associated with increased lipolysis associated with hyperglycemia diminishes cerebrovascular reactivity. Even in nondiabetic patients stress hyperglycemia may be a marker of deficient glucose regulation in individuals with insulin resistance and developing diabetes mellitus.[42] By provoking anaerobic metabolism, lactic acidosis, calcium overload, decreased mitochondrial function and free radical production, hyperglycemia may be a cause of the direct membrane lipid peroxidation and cell lysis in the zone of the numbra and penumbra, leading to the direct death of neurons and dysfunction of the blood-brain barrier and promoting hemorrhagic infarct conversion. Also, insulin resistance is a very well-known indirect risk factor for stroke onset due to increased thrombophilia, endothelial dysfunction and inflammation.[43]

Table 2:showing the baseline characteristics of the study population

		Number	%
Gender	**Male**	62	62.0%
	Female	38	38.0%
Age groups	**40-50 years**	21	21.0%
	51-60 years	28	28.0%
	61-70 years	26	26.0%
	Above 70 years	25	25.0%
Risk factors	**Hypertension**	68	68.0%
	Diabetes Mellitus	74	74.0%
	Dyslipidemia	62	62.0%
	Smoker	34	34.0%
	Alcoholic	30	30.0%
Glycemic status (Based on HbA1c)	**Euglycemic**	4	4.0%
	Known Diabetic	65	65.0%
	Newly Detected	15	15.0%
	Stress Hyperglycemics	16	16.0%
Based on random blood glucose	**126-199**	38	38.0%
	≥ 200	62	62.0%
Fasting blood sugar level	**< 100 mg/dL (5.6 mmol/L)**	35	35.0%
	≥ 126 mg/dL (7 mmol/L)	38	38.0%
	≥ 126 mg/dL (7 mmol/L)	27	27.0%

Table 3: showing the association of HbA1c level with severity of Stroke (NIHSS class)

	HbA1c level			
Stroke severity (NIHSS class)	**Euglycemic**	**Known Diabetic**	**Newly Detected**	**Stress Hyperglycemics**
Minor	2	0	0	3
	50.0%	0.0%	0.0%	18.8%
Moderate	2	25	9	13
	50.0%	38.5%	60.0%	81.3%
Moderate to severe	0	20	1	0
	0.0%	30.8%	6.7%	0.0%
Severe	0	20	5	0
	0.0%	30.8%	33.3%	0.0%
Chi-square value = 8.908, p-value < 0.001*				

Table 4: showing the association of Random blood sugar levels with severity of Stroke (NIHSS class)

Stroke severity (NIHSS class)	Random blood sugar level		Fasting blood sugar level		
	126-199	**> 199**	**< 100 mg/dL (5.6 mmol/L)**	**≥ 126 mg/dL (7 mmol/L)**	**≥ 126 mg/dL (7 mmol/L)**
Minor	3	2	3	1	1
	7.9%	3.2%	8.6%	2.6%	3.7%
Moderate	33	16	31	13	5
	86.8%	25.8%	88.6%	34.2%	18.5%
Moderate to severe	0	21	0	11	10
	0.0%	33.9%	0.0%	28.9%	37.0%
Severe	2	23	1	13	11
	5.3%	37.1%	2.9%	34.2%	40.7%
Chi-square value = 9.790, p-value < 0.001*			**Chi-square value = 8.148, p-value = 0.008***		

Table 5: Correlation of NIHSS score with HbA1c level and Random blood sugar level

NIHSS score	Pearson correlation coefficient (r)	p-value
HbA1C	0.801	< 0.001*
Random blood sugar level	0.512	0.021*

Table 6: showing the outcome among subjects with stroke

	HbA1c level			
Recovery	**Euglycemic**	**Known Diabetic**	**Newly Detected**	**Stress Hyperglycemics**
Death (within 30 days)	0	32	7	5
	0.0%	49.2%	46.7%	31.3%
Poor functional outcome	1	30	7	9
	25.0%	46.2%	46.7%	56.3%
Good functional recovery	3	3	1	2
	75.0%	4.6%	6.7%	12.5%
Chi-square value = 9.790, p-value < 0.001*				

Conclusion

Diabetes is a highly prevalent comorbidity in acute stroke patients, and is associated with poorer stroke outcomes compared with people without diabetes. Acute hyperglycemia is strongly associated with poorer stroke outcomes in people with or without diabetes. The elevated glucose level at the time of admission was found to be a significant predictor of mortality and poor functional outcome after acute stroke.

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Source of Support:Nil
Conflict of Interest: Nil