Original Article

Association Between Admission Hyperglycemia and Outcome in Acute Stroke Patients

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Abstract

Background : Patients with acute ischemic stroke have been found to have a higher risk of hemorrhagic transformation of infarcts and post-thrombolytic hemorrhage if their blood glucose level is high.

Aims and Objectives : The aim of the study was to assess the relationship between admission blood sugar levels and the clinical outcome of patients admitted to the hospital within 24 hours of the onset of stroke.

Materials and Methods : Among 50 patients admitted to a Tertiary Care Centre in Salem, Tamil Nadu, within the first 24 hours after suffering a stroke, a cross-sectional analytical study was conducted between January, 2020 and December, 2021. The study included all patients over 35 years of age, of both genders, who presented to the hospital with a stroke and fulfilled the eligibility requirements. The National Institutes of Health Stroke Scale is used to test the extent of stroke in each individual patient.

Results : About a third of the patients were between the ages of 51 and 60. Nearly 64% of the patients were male. Most (64%) patients had co-morbidity hypertension, followed by a history of Diabetes Mellitus (42%). The severity of stroke among patients who presented with raised blood sugar was significantly higher when compared with patients who presented with euglycemia. Patients who presented with hyperglycemia had a 46.5% higher mortality rate than those who were euglycemic (4.5%). The mortality among patients who presented with hemorrhagic stroke was higher (33.3%) than that of among those with ischemic stroke (26.3%), though no statistical significance was seen.

Conclusion : In this study, it was discovered that stroke patients had high rates of hyperglycemia at the time of presentation, which was associated with increased stroke severity and mortality. As a result, hyperglycemia in people with an acute stroke should be taken into account as a sign of a poor prognosis.

Key words : Diabetes Mellitus, Ischemic Stroke, Hemorrhagic Stroke, Stroke.

The World Health Organization (WHO) defined stroke in 1970 as a quickly growing clinical symptom of the focal (or global) disruption of brain function that lasts more than 24 hours or results in death, with no obvious explanation other than a vascular origin[1].

Over the past two decades, the burden of stroke has continued to increase globally, especially in low and middle-income countries[2]. Stroke occurs at a rate that varies greatly from country to country, with the age-adjusted incidence rate ranging from 58 to 151 per 1,00,000 in studies conducted within the past two decades[3]. The incidence of stroke increases by approximately 25% in adults from 20 to 64 years of age, low and middle-income countries account for 18% of that burden[2].

Editor's Comment :

- Patients with acute ischemic stroke have a higher risk of hemorrhagic transformation of infarcts and post-thrombolytic hemorrhage if their blood glucose level is high.
- This study shows that hyperglycemia is highly prevalent among patients with stroke at the time of presentation, and that it is associated with worse stroke outcomes. Therefore, hyperglycemia should be considered as an indicator of a poor prognosis in patients with acute stroke.

Stroke outcomes depend on a large number of variables, such as the severity of the initial stroke, stroke care standards, and the unique characteristics of each patient. It is imperative that treating physicians and clinicians identify the predictors of stroke outcome and case fatality in order to provide patients at high risk of death with effective therapy and management. Some aspects of acute stroke care necessitate action

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at the administrative or public health level, whereas others are patient-specific and necessitate individualized clinical intervention. One such factor is high blood sugar, which has been associated with poor outcomes in stroke survivors[4].

It is a common sign of an impending stroke. Patients with preexisting Diabetes Mellitus or those who suffer a sudden neurological injury may experience this stress reaction[5]. Van Kooten, *et al* have mentioned in their literature that the prevalence of high blood sugar in stroke patients ranging from 5.6% to 45.2%[6]. This wide variation in prevalence may be due to the different definitions of hyperglycemia across different settings, the time blood glucose was measured, and the inclusion or exclusion of diabetic patients in the studies[7]. Hyperglycemia has been shown to negatively affect stroke outcomes in a variety of clinical and experimental settings. Patients with acute ischemic stroke have been shown to have a higher risk of hemorrhagic transformation of infarcts and post-thrombolytic hemorrhage if their blood glucose levels are high[8].

Compared to stroke patients with lower blood glucose levels, those with hyperglycemia after a stroke have a significantly higher risk of short-term death and a higher chance of poor functional recovery. Stroke severity was found to increase with admission blood glucose values above 108 mg/dl, according to a meta-analysis and systematic review of 32 studies. Stroke outcomes can be mitigated through primary and secondary level interventions aimed at preventing hyperglycemia and providing optimal treatment for lowering blood glucose levels following a stroke[9]. This study examined the association between admission blood sugar levels and the clinical outcome of patients hospitalized within 24 hours of the onset of stroke.

Materials and Methods

Study Settings :

Salem is a city located on the banks of the Thirumanimutharu River in the Indian state of Tamil Nadu. It is the sixth-largest urban agglomeration in the state by population and the fifth-largest city in Tamil Nadu by area, covering an area of 124 km^2. The Tertiary Care Centre is located in the rural area of Salem, and the hospital has 560 beds. The Department of General Medicine normally provides 24-hour service to more than one lakh outpatients per year, mainly to the people of Salem and partly to the neighboring districts of Erode and Namakkal. A hospital-based cross-sectional analytical study was carried out among patients hospitalized in a Tertiary Care Centre twenty-four hours after stroke.

Study Period and Study Population :

This study was conducted for two years, from January, 2020 to December, 2021. All patients above 35 years of age of both genders presented to the hospital with a stroke and fulfilled the eligibility requirements.

Ethical consideration : The approval for this study was obtained from the ethical clearance from the Institutional Ethics Committee on Human Subjects (Approval No. VMKVMC&H/IEC/20/16). Following clearance from the Institutional Ethics Committee, patients were recruited after getting written informed consent.

Selection of Study Participants :

Inclusion Criteria : Patients admitted to a Tertiary Care Centre's Department of General Medicine within twenty-four hours after the beginning of a stroke, patients who had no previous history of stroke, ie, patients experiencing their first stroke episode and blood sugar levels measured within twenty-four hours of the stroke

Exclusion Criteria : Patients who had received glucose intravenously prior to admission, patients who had passed away prior to establishing a history of diabetes and patients who had symptoms of stroke related to diseases.

Sample Size Determination and Sampling Method :

The long-term follow-up study of 811 patients with acute stroke confirmed by Computed Tomography noticed that the prevalence of hemorrhagic stroke was 14%[4]. Considering this prevalence, the minimum sample size of 47 was calculated using the formula $3.84*pq/d^2$, where prevalence (p) = 14, q (1-p) = 86, and precision (d) = 10, with a 95% Confidence Interval. All consecutive stroke patients, from January, 2020 to December, 2021, who attended the General Medicine Department at a Tertiary Care Centre and who fit the inclusion criteria were enrolled in the study.

Data collection procedure : A semi-structured questionnaire was used by the principal investigator using a one-on-one interview method to collect data. Each individual was given a thorough clinical examination, history was obtained and a clinical diagnosis was determined. All patients underwent an

Electrocardiogram, Chest X-ray and assessment of Blood Pressure, Glucose, Urea, Creatinine, Electrolytes, Hemoglobin, total and differential count, Urine Sugar, Albumin, Deposits and Urinalysis. Each patient's stroke severity is determined using the NIH Stroke Scale (NIHSS). The next step was for all patients to get a CT scan of the brain to confirm the diagnosis and identify the specific type of stroke. A venous blood sample is obtained within 24 hours of the onset of symptoms once a clinical diagnosis of acute stroke has been made and then forwarded to the laboratory for glucose determination. After 30 days of observation, the patients' outcomes were recorded as either death, poor, moderate or good improvement.

Study Tool :

(1) The National Institute of Health Stroke Scale (NIHSS)

The original description of this 15-item, 42-point clinical deficit measure was published in 1989. With an increased deficit, the score also increases. A maximum score of 42 points is accorded for a person who died and a score of more than 14 is used to define severe stroke[10]. The scale is simple, reliable, valid and compares agreeably with other scales. However, left hemisphere strokes have a tendency to be rated higher than right hemisphere strokes, often by roughly 4 points for the same extent of infarction[11].

(2) Glycemic status based on HbA1c level

(i) History of Diabetes : known diabetics

(ii) Non-diabetic blood glucose levels were considered as less than 6.1% mmol/l (euglycemic)

(iii) Blood glucose levels greater than 6.1mmol/l without a history of diabetes and hemoglobin A1c values greater than 6.4% were considered to indicate newly diagnosed diabetes.

(iv) Greater than 6.1 mmol/l blood glucose without history of diabetes, and hemoglobin A1c of less than 6.4% were considered as Stress hyperglycemic.

(3) Prognosis of the patient

(i) Patients who were unable to return to any type of employment, had permanent disability, required residential placement, were reliant on activities of daily living and had a stable deficit with no improvement were categorized as having a poor outcome.

(ii) Patients whose symptoms improved, who were independent in their day-to-day activities, whose motor function and aphasia improved and who did not have a persistent handicap were categorized as having a good outcome.

(iii) Patients who performed between these two groups were classified as having a moderate outcome.

Data processing and analysis : The obtained data were entered into Microsoft Excel (Redmond, WA: Microsoft Corporation) and analyzed with SPSS version 21 software (IBM Corp, Armonk, NY). For continuous variables such as age and the NIH severity scale, the mean and Standard Deviation were employed, as were frequency and percentages for gender, clinical outcome, etc. The chi-square test or Fisher's exact test was done to see the association of the glycemic status of patients with outcome.

Results

Nearly 32% of the patients were between the ages of 51 and 60, and nearly two-thirds (64%) were men. Nearly 64% of patients had hypertension as a co-morbidity, followed by a history of diabetes mellitus (42%). Only 10% of patients had coronary artery disease, while 16% had hypercholesterolemia. Almost one-third of the patients had a history of smoking and 16% had a history of alcohol consumption. Approximately 62% of the patients had stage 2 hypertension, followed by stage 1 hypertension (20%). Table 1 describes the distribution of the patients' characteristics.

The newly diagnosed hyperglycemia cases had the highest mortality rate (80%), followed by the stress hyperglycemia cases (50 percent). In addition, the severity of stroke in patients who presented with elevated blood sugar was significantly greater than in patients with euglycemia. Table 2 describes the relationship between the patient's blood sugar level at the time of the stroke and the severity of the stroke.

Patients with elevated blood sugar had a significantly higher mortality rate (46.4%) than those who presented with euglycemia (4.5%). In addition, the mortality rate among those newly diagnosed with diabetes was significantly higher than that of those with other glycemic statuses. Table 3 describes the relationship between a patient's blood sugar level when they were admitted and the outcome of their condition, broken down by glycemic status.

Patients who presented with a hemorrhagic stroke had a higher mortality rate (33.3%) than those who

Table 1 — *The distribution of the patients' characteristics (N=50)*

Variable	Frequency (n=50)	Percentage (%)
Age Group :		
50 years	11	22%
51-60 years	16	32%
61-70 years	9	18%
>70 years	14	28%
Gender :		
Male	32	64%
Female	18	36%
Co-morbidities :		
Diabetes Mellitus	21	42%
Hypertension	32	64%
Coronary artery disease	5	10%
Hyper-cholesterolaemia	8	16%
Others*	5	10%
Personal habits :		
Smoking	16	32%
Alcohol	8	16%
Classification of Blood Pressure :		
Normal	4	8%
Pre-hypertension	5	30%
Stage 1 Hypertension	10	20%
Stage 2 Hypertension	31	62%

*Atrial fibrillation, Rheumatic heart disease, Dilated cardiomyopathy, Mitral valve prolapse

presented with an ischemic stroke (26.3%), although this difference was not statistically significant. Moreover, in patients with ischemic stroke, stress hyperglycemia and newly diagnosed hyperglycemia were likely associated with a higher mortality rate. In contrast, only one of the patients who presented with a hemorrhagic stroke was euglycemic, and the two patients newly diagnosed with hyperglycemia had died. Table 4 describes the association between glycemic status and outcome based on the type of stroke.

Discussion

Stroke outcomes depend on a wide variety of variables, such as the severity of the initial stroke, current stroke care guidelines, and individual patient characteristics. It is of the utmost importance for the treating physician or clinician to identify the predictors of stroke outcome and case fatality so that specific and appropriate treatment and management strategies can be applied to patients at high risk of death.

One characteristic that predicts a worse prognosis after a stroke is a patient's increased blood glucose

Table 3 — *Association of blood sugar level at admission and outcome of patients according to different glycemic status*

Glycemic Status	Favorable outcome (n=36)	Death, (n=14)	P value
Association of blood sugar level at admission and outcome			
Euglycemia	21 (95.5%)	1 (4.5%)	0.001*
Raised Blood Sugar	15 (53.6%)	13 (46.4%)	
The outcome of patients according to different glycemic status			
Euglycemia	20 (95.2%)	1 (4.8%)	0.003*
Stress Hyperglycemia	2 (50%)	2 (50%)	
Newly diagnosed diabetes	1 (20%)	4 (80%)	
Known Diabetes	13 (65%)	7 (35%)	

*Statistically significant value (p value <0.05)

Table 4 — *Association of glycemic status and outcome according to stroke type*

Association of glycemic status and outcome according to stroke type	Glycemic Status	Favorable outcome	Death	P value
Ischemic Stroke	Euglycemic	20(100%)	0(0%)	0.001*
	Stress Hyperglycemia	1(33.3%)	2(66.7%)	
	Newly detected Hyperglycemia	1(33.3%)	2(66.7%)	
	Known Diabetes	6(50%)	6(50%)	
Hemorrhagic Stroke	Euglycemic	0(0%)	1 (100%)	0.04*
	Stress Hyperglycemia	1(100%)	0(0%)	
	Newly detected Hyperglycemia	0(0%)	2(100%)	
	Known Diabetes	7(87.5%)	1(12.5%)	

*Statistically significant value (p value <0.05)

Table 2 — *Association of blood sugar level at the stroke severity and prognosis of the patient*

Stroke Status		Euglycemia (n=21)	Stress Hyperglycemia (n=4)	Newly detected Hyperglycemia (n=5)	Known Diabetes, (n=20)	P value
Severity of Stroke	Mild and moderate severity (NIHSS ≤14)	18 (85.7%)	2 (50.0%)	0 (0%)	6 (30%)	0.001*
	Severe and very severe (NIHSS >14)	3 (14.3%)	2 (50.0%)	5 (100%)	14 (70%)	
Prognosis of the patient	Good	13 (61.9%)	0 (0%)	0 (0%)	1 (5%)	0.0001*
	Moderate	4 (19%)	2 (50%)	0 (0%)	6 (30%)	
	Poor	3 (14.3%)	0 (0%)	1 (20%)	6 (30%)	
	Death	1 (4.8%)	2 (50%)	4 (80%)	7 (35%)	

NIHSS - National Institutes of Health Stroke Scale. *Statistically significant value (p value <0.05)

level[10]. It is a common symptom in the early phase of acute stroke and may be due to the patient's pre-existing diabetes or a stress response to the acute neurological injury[5].

Fifty individuals with either ischemic or hemorrhagic stroke who were seen at the study location within the first 24 hours after symptoms appeared participated in the study. In this study, the majority of patients (32%) were between the ages of 51 and 60, with a mean age of 62.66±10.95 years. The average age of the participants in the study by Haobam J, *et al*[12] was 58±7.9 years and Umpierrez GE, *et al*[13] also observed similar findings where the mean age was 59±4 years. A study indicated that as developed countries experience an increase in their elderly population, the mean age of patients increases in comparison to developing countries like India, where the mean age is lower[14]. Almost two-thirds (64%) of the patients in this study were men, indicating a male preponderance. Several other studies concur with this report that male gender is a stroke risk factor[4,12,15]. This may be due to the high prevalence of undiagnosed or inadequately treated hypertension, smoking history and an abundance of other cardiovascular risk factors in men. The protective role that estrogen hormones perform in women before menopause may also have contributed to these results.

In our study, 42% of patients who presented with a stroke had diabetes, which is higher than studies conducted in western countries[16,17]. This may be attributable to a lack of awareness and a changing lifestyle in developing nations such as India, including the dietary practices of the study area.

Stroke severity was considerably higher in patients who came with hyperglycemia compared to those who presented with euglycemia (P=0.05). Patients with hyperglycemia had a median NIHSS score of 14 (IQR 10-19), while those with normoglycemia had a median NIHSS score of 11 (IQR 8-15), as shown in the study by Zewde, *et al*. However, a significant association was not observed[18]. In line with the findings of our study, Stead LG, *et al* found a significant correlation between the severity of strokes and patients' blood sugar levels[19]. Stroke severity is increased by hyperglycemia due to its multiple pathophysiological mechanisms, including increased brain damage, increased infarct size due to stimulation of vasoconstrictive factors, decreased penumbral tissue salvage due to high lactate levels and increased neurotoxicity as a direct result of inflammation and oxidative stress[7,20,21].

Patients presenting with hyperglycemia had a much higher mortality rate than those with euglycemia (p=0.05). Researchers Li J, *et al* found that non-diabetic persons' relative stress hyperglycemia is a significant risk factor for mortality within a year after an ischemic stroke[22]. Two studies have shown that patients with acute stress hyperglycemia have a greater risk of passing away while hospitalized[9,23]. Two other trials found that people whose hyperglycemia was caused by stress had a poorer functional result after a stroke[24,25]. However, Tziomalos, *et al* found no relationship between stress hyperglycemia and the risk of hospital mortality and poor functional result following stroke[26].

Patients with hyperglycemia had a higher mortality rate after an ischemic stroke, according to research by Williams, *et al*[27]. Another study found that the probability of survival after a stroke decreases as the admission blood glucose level rises[28]. The entry blood glucose level is associated with a greater death rate, as observed by Watila, *et al*[29]. These discrepancies could be because studies use various criteria to define stress hyperglycemia.

Limitation :

This study had some limitations, including the fact that just one blood sugar reading was taken upon admission. Estimates of blood sugar levels taken at later times may have helped clinicians get a clearer picture of how blood sugar levels play a role in acute stroke patients, as well as how treatment outcomes change for these patients over time. Second, since lesion size was not measured, the relationship between lesion size and stroke outcome could not be evaluated in this study.

Conclusion

This study shows that Hyperglycemia is highly prevalent among patients with stroke at the time of presentation and that it is associated with worse stroke outcomes. Therefore, hyperglycemia should be considered an indicator of a poor prognosis in patients with acute stroke. If hyperglycemia is suspected in a patient with a stroke, quick action should be considered to bring blood glucose levels down to near normal in order to lessen the negative effects of the condition.

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Competing Interests : The authors declare no competing interest.

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