

## Frequency of Stress Hyperglycemia in Acute Ischemic Stroke with Immediate Mortality

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## Abstract

## Original Research Article

**Introduction:** Stroke is a leading cause of morbidity, death, and a significant socioeconomic burden. This is especially true in poor nations like Bangladesh, where the health-care system, including rehabilitation, is out of reach for the average citizen. This life-threatening ailment impacts not only the patients but also their families. The goal of this hospital-based study was to determine stroke-related in-hospital mortality. For various reasons, the findings of our study are important to stroke care in our setting. Attention to modifiable variables that have a negative influence on stroke outcome (e.g. hyperglycemia and comorbidities) may help to reduce stroke mortality, which is particularly high in poor countries. The aim of the study was to evaluate the frequency of stress hyperglycemia in acute ischemic stroke cases, and observe the difference in mortality and morbidity among patients with hyperglycemia and normoglycemia. **Methods:** This observational cross-sectional study was conducted at the Department of Medicine, Sir Salimullah Medical College & Mitford Hospital, Dhaka, Bangladesh. The study duration was 6 months, from April 2017 to October 2017. The purposive sampling technique was used to select a total of 100 consecutively attending first-ever acute ischemic stroke patients attending the study hospital within 72 hours of stroke onset. **Result:** Among the participants, the majority (54%) were between the age range of 41-55 years, with a mean age of 58.37 ( $\pm 6.23$ ) years. The male: female ratio was 1.7:1. Over half the participants were from urban areas, and 29% were housewives while 25% were businessmen. Unilateral weakness, speech disturbance, and headache were the most common clinical presentations. During admission, the majority were conscious, while 7% were unconscious. Stress hyperglycemia was observed in 29% of the cases. Recovery rates were higher among normoglycemic patients. **Conclusion:** Present study showed that stress hyperglycemia is frequent during acute ischemic stroke and it influences the patient's outcome. Identifying hyperglycemia as a marker for poor functional recovery and in-hospital mortality has provided a rationale for the pursuit of tight glucose control. Benefits of tight glucose control include reduced mortality and decreased infection rates. Stroke patients who have stress have been associated with a higher risk of poor functional recovery and death. Mortality risk was greater in patients who had hyperglycemia than in those with normoglycemia.

**Keywords:** Hyperglycemia, Normoglycemia, Stress, Ischemic, Stroke.

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## INTRODUCTION

In both industrialized and developing nations, cerebrovascular accident (CVA) remains the most prevalent neurological condition. Cardiovascular disease and cancer, it is the third leading cause of mortality. The burden of stroke on patients, their families, and treating physicians continues to rise. Various controllable and non-modifiable risk variables influence the neurological

outcome. Admission (stress) hyperglycemia is one of the modifiable risk factors that harm the neurological outcome. Various studies have shown that diabetes people had a worse prognosis and neurological damage following an acute stroke than non-diabetic patients. Stress hyperglycemia is now emerging as a second important predictor for stroke patients' neurological outcomes [1]. Hyperglycemic people had an elevated risk of death one year after an ischemic stroke (IS),

according to studies that include data from both diabetic and non-diabetic subjects [2, 3]. Stroke is a condition. In general, there are two forms of stroke: ischemic (which occurs in almost 85% of cases) and hemorrhagic (which occurs in around 15% of cases). Ischemic stroke can be moderate or transitory (referred to as a small stroke or transient ischemic attack) or very severe (referred to as a large ischemic stroke), but the fundamental reasons are the same [4]. Hypertension, atherosclerosis, diabetes, smoking, dyslipidemia, and coronary artery disease are all risk factors for ischemic stroke [5]. During an acute ischemic stroke, hyperglycemia is prevalent [6]. According to several studies, entry blood glucose is increased in more than 40% of individuals with acute ischemic stroke, with diabetes mellitus being the most prevalent cause [7, 8]. Blood glucose rises after acute stroke are linked to a combination of factors, including a lack of food and stress response with impaired glucose metabolism. The most common cause of ischemic stroke is a loss of blood flow to all or part of the brain, depriving neurons of crucial glucose and oxygen. If the deprivation is severe and protracted, normal cellular processes are disrupted, and the neuronal cell membrane eventually breaks down, resulting in cell death. Ischemia can also develop as a result of oxygen deprivation alone (hypoxic-ischemic damage, as seen in patients who have a cardiac arrest, respiratory collapse, or both) or glucose deprivation alone (as seen in patients who have a cardiac arrest, respiratory collapse, or both) (as may occur with insulin overdoses in diabetic patients). Because of obstruction of a big or tiny artery, ischemic stroke usually exclusively affects a part of the brain. In the event of several emboli or a single embolus that breaks up as it travels, it may grow rapidly in various arterial areas. When an artery is blocked and blood supply to the brain is cut off, the normal function of the neurons fed by that artery is very immediately inhibited. Several variables impact the outcome of a stroke, including the kind of stroke, the severity of the stroke, the predisposing factor(s), related factors, the occurrence of sequelae, access to specialized treatment, and the availability of stroke care facilities [9, 10]. Hyperglycemia at the time of a stroke is one of the theoretically controllable variables linked to a poor outcome in acute stroke. Although the exact association between hyperglycemia and stroke outcome (whether causative or suggestive of a more severe stroke) is unknown, possible pathways by which hyperglycemia causes harm has been proposed [11-13]. Regardless of the etiology (or diabetes status), hyperglycemia has been identified in multiple experimental and clinical investigations as a predictor of poor prognosis in acute stroke. Short-term death, as defined by the 30-day case fatality rate, was shown to be considerably greater in hyperglycemic patients (41%) than in normoglycemic patients in research (21%) [9]. The goal of this study was

to determine the prevalence of stress hyperglycemia in acute ischemic stroke and its link to short-term mortality. The goal of the trial was to start treating non-diabetic stroke patients with hyperglycemia to reduce mortality and morbidity.

## OBJECTIVE

### General Objective

- To observe the frequency of stress hyperglycemia in acute ischemic stroke patients.
- To find out short-term mortality in normoglycemic acute ischemic stroke patients.

## METHODS

This observational cross-sectional study was conducted at the Department of Medicine, Sir Salimullah Medical College & Mitford Hospital, Dhaka, Bangladesh. The study duration was 6 months, from April 2017 to October 2017. The purposive sampling technique was used to select a total of 100 consecutively attending first-ever acute ischemic stroke patients attending the study hospital within 72 hours of stroke onset. Informed written consent was obtained from each of the participants prior to their admission to the study, and ethical approval was also obtained from the ethical review committee of the study hospital. Patient confidentiality was maintained by providing a unique ID to each participant while collecting data. The modifiable Rankin Scale (MRS) was used for measuring the degree of disability or dependence in the daily activities of stroke patients. In stroke patients, stress hyperglycemia was defined (in the absence of known diabetes) as a plasma glucose level of above  $>7.8$  mmol/L. Patients were observed for 2 weeks from the time of admission. All the collected data questionnaire was checked very carefully to identify errors in collecting data. Data processing work consisted of registration of schedules, editing, coding and computerization, preparation of dummy tables, analysis, and matching data.

### Inclusion Criteria

- First-ever acute ischemic stroke
- Admission to study within  $\leq 72$  hours of stroke onset
- Patients who had given consent to participate in the study.

### Exclusion Criteria

- Mentally ill.
- Unable to answer the criteria question.
- Known cases of steroid therapy
- Patients with atrial fibrillation, infective endocarditis, heart failure

## RESULTS

**Table 1: Social-demographic characteristics of participants**

Characteristics	Frequency	Percentage
<b>Age</b>		
≤40	8	8
41-55	54	54
56-70	24	24
>70	14	14
Mean ± SD	58.37 (±6.23)	
<b>Gender</b>		
Male	64	64
Female	36	36
Male: Female Ratio	1.7:1	
<b>Residence</b>		
Rural	31	31
Urban	58	58
Sub-urban/slum	11	11
<b>Occupation</b>		
Service holder	11	11
Retired	16	16
Daily worker	19	19
House wife	29	29
Business	25	25

In this series, the maximum numbers of patients (54%) were between 41-55 years of age group, next (24%) were between the age group of 56-70 years, with a mean age of 58.37 (±6.23) years. 64% were male and 36% were female. The male and female ratio was 1.7:1.

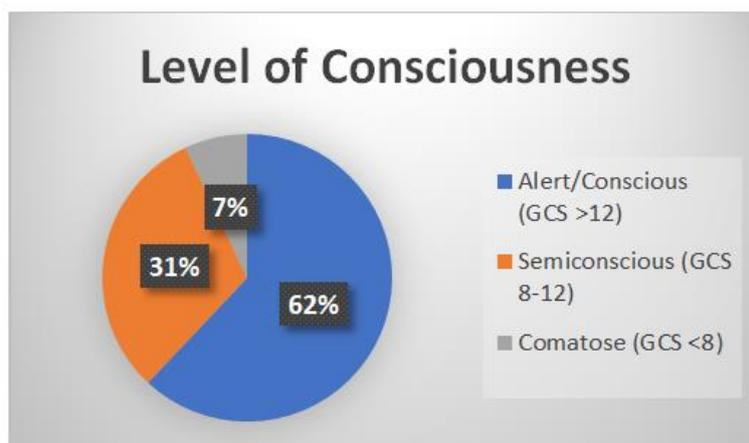
Large numbers of respondents came from urban areas (58), followed by rural areas (31) and 11% from sub-urban/slum areas. The majority of the patients comprised housewives (29.0%) followed by a businessman at 25.0%.

**Table 2: Clinical presentations of the participants**

Presentation	Frequency	Percentage
Unilateral weakness/ hemiplegia	86	86
Speech disturbance	52	52
Visual deficit	27	27
Visuo-spatial dysfunction	24	24
Ataxia	19	19
Headache	35	35
Seizure	18	18
Sphincter problem	23	23
Vomiting	15	15
Hiccup	12	12
Coma	7	7

Unilateral weakness, speech disturbance and headache were the commonest presentation in ischemic stroke (86.0%, 52.0% & 35.0% of patients respectively).

Other clinical manifestations were visual deficit (27.0%), Sphincter problem (23.0%), vomiting (15.0%), ataxia (19.0%) and Seizure (18.0%).



**Figure 1: Level of consciousness among the participants according to GCS score**

Among the 100 cases, (62.0%) were alert or conscious, (31.0%) were semiconscious and seven cases were unconscious following the GCS scoring system

**Table 3: Risk factor assessment of the study participants**

Risk factors	Frequency	Percentage
Hypertension	63	63
Smoking	37	37
Coronary Heart Diseases	12	12
Obesity	23	23
Family history of CVD,CAD	47	47
Dyslipidaemia	13	13

Among all the risk factors hypertension was the most common risk factor, present in 63.0% of cases; the

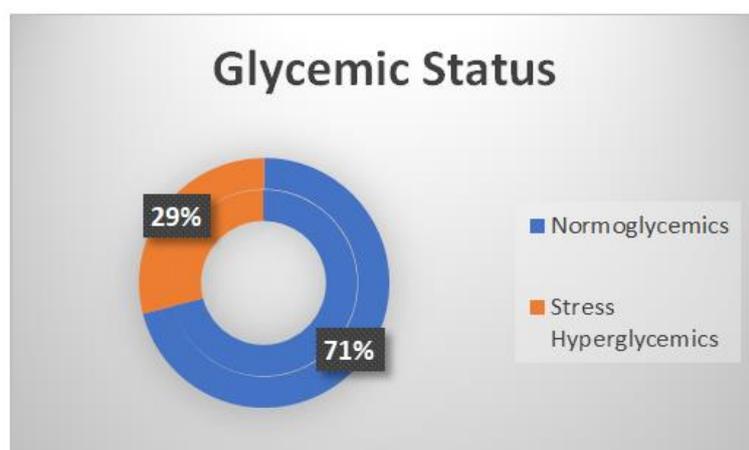
next common risk factors are smoking 37%, and coronary heart disease 12% of patients.

**Table 4: Assessment of blood sugar levels in the study population (n=100)**

Blood sugar level (mmol/L)	Frequency	Percentage
<6.1	56	56.0
6.1-7.7	15	15.0
≥7.8	29	29.0

According to the operational definition of acute stress, hyperglycemia is referred to as an elevation of blood glucose level (>7.8 mmol/L). In this study

amongst ischemic stroke patients, 71.0% of patients were found to have blood sugar levels  $\leq 7.7$  whereas 29.0% of patients were blood sugar levels  $\geq 7.8$  mmol/L.



**Figure 2: The frequency of different glycemic statuses among the participant's**

Prevalence of acute stress hyperglycemia in stroke patients was detected at 29.0%. Normo-glycemic status was in the remaining 71.0% of patients.

**Table 5: Comparison of hospital outcomes of the participants by glycemic status**

Outcome	Frequency		Total
	Normoglycemic	Stress hyperglycemic	
Recovered	64(90.1%)	15(51.7%)	79
No improvement	5(7.0%)	9(31.0%)	14
Expired	2(2.8%)	5(17.2%)	7
<b>Total</b>	<b>71</b>	<b>29</b>	<b>100</b>

Patients' symptoms, degree of disability or dependence on the daily activities, and clinical outcomes were evaluated and measured by the modified Rankin Scale (MRS). The study shows that 81.0% of the patients recovered (MRS score 0 to 2), among them maximum were Normoglycemic patients (90.1% vs 51.7%). Fourteen patients were having poor outcomes, disabled

and they were discharged on request or risk bond (MRS score 3 to 5). In this study, 7.0% expired during hospital stay (MRS score 6). In expired cases, the maximum was Stress hyperglycemic patients (2.8% vs 17.2%). So in-hospital outcome is very poor in Stress hyperglycemic patients.

**Table 6: Comparison of mortality and morbidity among groups**

Glycemic type	Frequency	Percentage
<b>Mortality n=7</b>		
Normoglycemic	2	28.50%
Stress hyperglycemic	5	71.50%
<b>Relative Risk</b>	2.5	
<b>Morbidity n=14</b>		
Normoglycemic	5	35.80%
Stress hyperglycemic	9	64.20%
<b>Relative Risk</b>	1.7	

The risk of death in hyperglycemia was 71.5%, while the risk of death in Normoglycemic was 28.5%. Relative risk was 2.5, as patients with acute ischemic stroke with stress hyperglycemia were 2.5 times more likely to die than Normoglycemic. The risk of morbidity in hyperglycemia was 64.2%, while the risk of morbidity in Normoglycemic was 35.8%. Relative risk was 1.7, as patients with acute ischemic stroke with stress hyperglycemia were 1.7 times less likely to improve as compared to Normoglycemic.

## DISCUSSION

Stroke, after coronary heart disease and cancer, is the third biggest cause of mortality globally. Ischemic infarcts, in particular, are one of the most prevalent and deadly illnesses [14, 15]. A study found that even a minor increase in blood glucose levels was related to a more than two-fold increased risk of short-term death in nondiabetic individuals who had ischemic strokes when compared to the normoglycemic group [16]. Even in the absence of a prior diagnosis of diabetes, a substantial proportion of individuals who experience acute stress such as a stroke or myocardial infarction may acquire hyperglycemia [17-19]. Among the present study participants, the maximum numbers of patients (54%) were between 41-55 years of age group, and the next (24%) were between the age group of 56-70 years, with a mean value 58.37 ( $\pm 6.23$ ) years. Out of 100 cases, 64% were male and 36% were female. The male and female

ratio was 1.7:1. The maximum number of respondents (58) came from urban areas. These findings were in accordance with the findings of home and abroad [20-22]. Unilateral weakness, speech disturbance, and headache were the commonest presentation in ischemic stroke cases in the present study. Other clinical manifestations were visual deficit (27.0%), Sphincter problem (23.0%), vomiting (15.0%), ataxia (19.0%) and Seizure (18.0%). At the time of admission, a thorough physical examination and neurological evaluation were performed. Among the 100 cases, 62.0% were alert or conscious, 31.0% were semiconscious and seven cases were unconscious. Among all risk factors, hypertension was the most common risk factor, present in 63.0% of cases; the next common risk factors are smoking 37%, and coronary heart disease 12% of patients. According to the operational definition of acute stress, hyperglycemia is referred to as an elevation of blood glucose level ( $>7.8$  mmol/L). The present study demonstrated that the prevalence of acute stress hyperglycemia in stroke patients was 29.0%, while Normoglycemic status was in the remaining 71.0% of patients. This was similar to the findings of several other studies with similar stress hyperglycemia rates [9, 23-26]. In a study conducted in a similar tertiary setting like ours, Ogunrin *et al* documented a lower prevalence rate of 28% but acknowledged that the retrospective design of that study may have affected their results as only 100 of their 163 cases had blood glucose estimated on admission [27].

Patients' symptoms, degree of disability or dependence on the daily activities, and clinical outcomes were evaluated and measured by the modified Rankin Scale (MRS). The present study showed that 81.0% of the patients had successfully recovered, among whom the frequency of normoglycemic patients was higher compared to stress hyperglycemic patients (90.1% vs 51.7%). Among the 29 stress hyperglycemia patients, 31% had a poor outcome, and 7% had died, compared to 70% with poor outcome and a 2.8% mortality rate among the 71 normoglycemic patients. This higher adverse outcome rate among stress hyperglycemia patients was supported by many other studies [28-30]. On the evaluation of mortality, the risk of death in hyperglycemia was 71.5% and in Normoglycemic was 28.5% with a relative risk of 2.5. So patients with acute ischemic stroke with stress hyperglycemia were 2.5 times more likely to die than Normoglycemic. Even in survivors, functional outcome was worse in the hyperglycemic group.

### Limitations of the Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

### CONCLUSION

The present study showed that stress hyperglycemia is frequent during acute ischemic stroke and it influences the patient's outcome. Identifying hyperglycemia as a marker for poor functional recovery and in-hospital mortality has provided a rationale for the pursuit of tight glucose control. Benefits of tight glucose control include reduced mortality and decreased infection rates. Stroke patients who have stress have been associated with a higher risk of poor functional recovery and death. Mortality risk was greater in patients who had hyperglycemia than in those with normoglycemia.

### RECOMMENDATION

The study recommended multi-centre study with large sample size, which can give more reliable findings for the issue.

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**Conflict of interest:** None declared.

**Ethical approval:** The study was approved by the Institutional Ethics Committee.

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