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STRESS INDUCED HYPERGLYCEMIA IN STROKE PATIENTS

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ABSTRACT

Background: Stroke is the third most common cause of death in developed countries and second most common cause of death worldwide. High proportion of patients may develop hyperglycemia after an acute stress such as stroke or myocardial infarction even in the absence of preexisting diagnosis of diabetes mellitus. Prolonged stress hyperglycemia in ischemic stroke increases the risk of in-hospital 28- day mortality, especially in non-diabetic patients.

Aims and objectives: to determine the frequency of stress-induced hyperglycemia in non-diabetic patients with ischemic or hemorrhagic stroke. **Subjects and methods:** A total of 255 patients admitted with acute stroke, fulfilling the inclusion criteria were included in the study. After informed consent capillary blood glucose was monitored at the time of admission and after every 8-hour for three days. Glycosylated hemoglobin (hba1c) was measured simultaneously. **Results:** Hyperglycemia was noted in 67 (26.32%) patients. Out of which 50 (74.6%) presented with ischemic stroke while only 17 (25.4%) were associated with hemorrhagic stroke. Undiagnosed diabetes was found in 10% cases. **Conclusion:** Stress related hyperglycemia after acute stroke was found in 26% of patients especially those with high BMI, visceral obesity and positive family history for diabetes.

Key words: Ischemic stroke, stress hyperglycemia, acute stroke, acute hyperglycemia.

BACKGROUND

Stroke is the third common cause of death in the world after coronary heart disease and cancer especially in the elderly.^(1, 2) In 2010, world-wide prevalence of stroke was 33 million.⁽³⁾ Contrary to decline in the incidence of the disease in the western population, the burden of the disease in South Asian countries (India, Pakistan, Bangladesh, and Sri Lanka) has inclined and is expected to rise.⁽³⁾ Hyperglycemia during acute illness can be due to some drugs such as systemic corticosteroids, thiazides, phenytoin, phenothiazines, protease-inhibitors, and beta-agonists or as a result of "stress hyperglycemia" where counter-regulatory hormones such as glucagon, cortisol, catecholamines, and growth hormone promote hepatic gluconeogenesis. Hyperglycemia detected during acute illness may also be the first clinical evidence of underlying undiagnosed type 2 diabetes mellitus.⁽⁴⁾ High proportion of patients may develop hyperglycemia after an acute stress such as stroke or myocardial infarction even in the absence of preexisting diagnosis of diabetes mellitus.⁵ Hyperglycemia during hospital admission, in patients who are not known to have diabetes associated with adverse outcomes.^(5, 6)

Hyperglycemia after stroke increases during the first 12 hours and then decreases or establishes within one to few weeks. Prolonged stress hyperglycemia in ischemic stroke patients increases the risk of in-hospital 28- day mortality, especially in non-diabetic patients.^(7, 8, and 9) Few regional studies have been done on this subject especially in Asian region,^(10, 11) where incidence of stroke and diabetes mellitus both are increasing. Therefore there was need to collect data representing our population to gain better understanding and to determine the magnitude of hyperglycemia in previously non-diabetic patients after acute stroke. The objective of the study was to determine the frequency of stress induced hyperglycemia in non-diabetics patients with ischemic or hemorrhagic stroke.

METHOD

The study was conducted at medical ward of jinnah medical college hospital located in sub-urban area of city Karachi, Pakistan. Study was conducted for six months, from July to December 2013. Sample size was 255 patients (as calculated on the basis of prevalence of hyperglycemia in non-diabetics acute stroke patients

which is 21%.¹⁰ non- probability purposive sampling technique was used. Patients > 15 years of age, non-diabetic, presenting with acute stroke (ischemic or hemorrhagic) were included.

Table 1: Baseline characters of stroke patients;

	Ischemic stroke n=167	Hemorrhagic stroke n=88
Mean age	54.2+ 6.8	59.1+ 8.2
Male	103(61.7%)	48(54.5%)
Female	64(38.3%)	40(45.5%)
Smokers	58(34.7%)	28(31.8%)
Mean BMI	32.5	27.5
Family history of diabetes mellitus	26 (57.8%)	19 (42.2%)

Table 2: Frequency of hyperglycemia in stroke sub-types;

	Ischemic n=167	Hemorrhagic n=88
Euglycemia	105(62.9%)	68 (77.3%)
Stress hyperglycemia	50 (30%)	17 (19.3%)
Undiagnosed diabetes	12(7.1%)	3(3.4%)

Patients diagnosed as transient ischemic attack, brain imaging showing features, like tumor, CNS infections or trauma, having metabolic disorders like, diabetes mellitus, chronic liver disease, sepsis and renal failure, all were excluded. Patients receiving intravenous dextrose, systemic corticosteroids, thiazides, phenytoin , phenothiazines, protease-inhibitors, and beta-agonists, which promote hyperglycemia by inducing hepatic gluconeogenesis were also excluded. Informed consent was taken before enrolling for the study, from the conscious patients otherwise from the next of kins. Demographic data, age, gender, body mass index (BMI), smoking status, family history of diabetes was recorded for each patient. Blood pressure was recorded using aneroid sphygmomanometer, waist circumference was also recorded. Capillary random blood glucose levels (at least two hours after last feed) were monitored, at the time of admission and after every 8-hour for first 72 hours (using accu-check active glucometer).

Table 3: Comparison of characters between euglycemic and stress hyperglycemia groups;

	Stress hyperglycemia n=67	Euglycemia n= 173	P values
Mean systolic blood pressure	165.2 mmhg	168.4	0.67
Mean bmi	33.31	27.52	<0.001
Mean waist circumference	48.4 inches	41.2 inches	< 0.001
Family history of diabetes	35 (52%)	10(5.7%)	<0.001
Smokers	42 (62%)	44(24%)	0.423

HbA1c (glycosylated hemoglobin) was measured simultaneously. A confirmed value of hba1c at or above 6.5% was used as diagnostic for diabetes mellitus as recommended by the american diabetes association¹¹ Stress hyperglycemia was labeled if blood glucose \geq 140mg/dl any time during first 72 hours when hba1c was < 6.5. Undiagnosed diabetes was diagnosed when blood sugar was >140 mg/dl and HbA1c > 6.5. Data

was analyzed using spss version 21. Quantitative data i.e age, BMI, systolic blood pressure, waist circumference were presented as mean + SD, while qualitative data gender, smoking, family history of diabetes and frequency of stress hyperglycemia were presented as frequencies or percentages. Statistical analysis was performed using chi-square for qualitative variables and students t test for quantitative data. P value of 0.05 or less was considered as the level of significance.

RESULTS

A total of 255 patients admitted with cerebrovascular accident (stroke) were evaluated, out of which 167 (65.4%) had ischemic stroke while 88(34.5%) had hemorrhagic stroke. In ischemic group 103(61.7%) were male and 64(38.3%) were female. In hemorrhagic group 48(54.5%) were male and 40(45.5%) were female. Mean age was 54.2 + 6.82 years in ischemic group while 59.1+ 8.2 in hemorrhagic group. In ischemic group 58(34.7%) were smoker and in hemorrhagic group 28(31.8%) were smoker. Mean BMI (body mass index) was 32.5 in ischemic group while 27.5 in hemorrhagic group. Family history of diabetes was positive in 26 (57.77%) patients with ischemic stroke while 19 (42.22%) patients with hemorrhagic stroke. (table 1) In ischemic group, 105 (62.9%) were euglycemic, 50 (30%) had stress hyperglycemia and 12 (7.1%) had underlying undiagnosed diabetes. In hemorrhagic group 68(77.3%) were euglycemic, 17(19.3%) had stress hyperglycemia while 3 (3.4%) had undiagnosed diabetes. (table 2) On comparison of different features in euglycemic and stress hyperglycemic patients there was statistically significant difference in mean bmi and mean waist size. (p value <0.001) Moreover positive family history of diabetes mellitus was found to be more common in patients with stress hyperglycemia; however there was no significant difference systolic blood pressure and frequency of smoking. (table 3)

DISCUSSION

Hyperglycemia detected during acute illness is associated with adverse outcomes. Among patients without known diabetes admitted to hospital with myocardial infarction (MI), stroke, pneumonia, and exacerbation of chronic obstructive pulmonary disease (COPD), higher glucose levels are associated with in-hospital and longterm mortality, intensive care unit admission, prolonged length of stay, and discharge to long-term nursing^(12,13) Our study evaluated stress induced hyperglycemia in patients with acute stroke found that 26.3% patients had hyperglycemia in the

absence of diabetes mellitus. This result was comparable to other studies ^(7,10,14,15). We also observed that stress hyperglycemia was in patients with ischemic than hemorrhagic stroke which is different from some studies ⁽⁷⁾. We observed that over all 6% patient had undiagnosed diabetes at the time of admission. The prevalence of recognized diabetes mellitus in acute stroke patients is between 8% to 20%, but between 6% to 42% of patients may have undiagnosed diabetes mellitus before presentation ⁽¹⁶⁾ In comparison of various characters in patients with euglycemia and stress hyperglycemia, we observed that stress hyperglycemia was significantly common in patients with high BMI and central obesity(higher waist circumference), the same observation was seen in other studies.^(17,18,19,20) It was also noted that patients with stress hyperglycemia had greater incidence of diabetes mellitus in first degree relatives than patients with euglycemia. However there was no significant difference in systolic blood pressure in between two groups.

CONCLUSION

Stress related hyperglycemia after acute stroke was found in 26% of patients especially those with high BMI, visceral obesity and positive family history for diabetes. These patients can constitute a high risk group requiring close monitoring of blood sugars and thus preventing complications. Further studies should be directed towards determining mortality and complications related to stress induced hyperglycemia and the effects of management on patient outcome.

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Author's contribution:

Dr. Aziz u rehman: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review

Dr. Ajeet Kumar: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review

Dr. Salma Razzaque: Data collection, data analysis, manuscript writing, manuscript review

Dr. Ashok Kumar: Data analysis, manuscript writing, manuscript review

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