ORIGINAL ARTICLE

Frequency of Hyperglycemia in Non-Diabetics Presenting with Acute Stroke

MUHAMMAD FAYYAZ, ABDUL RASHEED, SIDRA SABA, *MUHAMMAD SALEH HASSAN, ZUNAIRA HUSSAIN*

ABSTRACT

Aim: To determine the frequency of hyperglycemia in non-diabetics presenting with acute stroke
Methods: A total of 171 patientspresented with acute stroke i.e. <24 hours duration of age 30-70 years and both genders were included. Patients with known diabetes mellitus, head injury, recurrent attacks and h/o anticoagulant drugs or steroid use were excluded. After taking relevant history, blood sample of each patient was drawn and sent to the pathology laboratory for measurement of blood glucose levels and. Blood glucose levels > 11.1mmol/l (200mg/dl) was considered as hyperglycemia and noted as present or absent.
Results: Mean age was 53.82±10.31years. Out of the 171 patients, 89(52.05%) were male patients and 82 (47.95%) were female patients. Mean duration of disease was 10.29±6.53 hours. Mean BMI was 28.41±5.33kg/m^2. Hyperglycemia was found in 44(25.73%) patients, whereas there was no hyperglycemia in 127(73.27%) patients
Conclusion: This study concluded that frequency of neo-onset hyperglycemia in non-diabetic patients presenting with acute stroke is high, so great care could be taken in these particular patients and early recognition and management of this condition should be done in order to reduce the morbidity and mortality of the community.
Keywords: Stroke, ischemic, glucose, IHD, CVA, CVI

INTRODUCTION

A stroke, occasionally referred to as a cerebrovascular accident (CVA), cerebrovascular insult (CVI), or colloquially brain attack is the loss of function ofbrain due to a disturbance in the supply of blood supply to brain. This disturbance is due to eitherhemorrhage or ischemia (lack of blood flow)[1]. Ischemia is caused by either blockage of a blood vessel via thrombosis or arterial embolism, or by cerebral hypoperfusion[2]. Hemorrhagic stroke is caused by bleeding of blood vessels of the brain, either directly into the brain parenchyma or into the subarachnoid space surrounding brain tissue[3]. About 800,000 people suffer strokes each year in USA; about 82-92% of these strokes are ischemic.[4] Stroke is the second leading cause of adult disability and death after IHD(ischemic heart disease)[5].

Hyperglycemia is most frequently seen in patients admitted to hospital for acute ischemic stroke, and can last for many days beyond the acute phase[6]. Pre-existing hyperglycemia is found more commonly in patients presenting with acute stroke, and is reported to be present in 20 to 50% of patients. In many studies of thrombolytic agents, hyperglycemia occurred in about 20-30% of the patients. Although confounded by other factors, like severity of the infarct, hyperglycemia in the face of acute stroke worsens clinical outcome. Non-diabetic hyperglycemic ischemic stroke patients have a 3-fold higher 30-day mortality and diabetic patients have a 2-fold 30-day mortality[7]. In many studies involving thrombolytic and anticoagulation therapy in patients of stroke, hyperglycemia appears to be an independent risk factor for worsened outcome. In addition, hyperglycemia has been suggested as an independent risk factor in hemorrhagic conversion of the stroke after administration of thrombolytic therapy[8,9].

As there was no local study done on this subject in recent past, this study would determine the frequency of neo-onset hyperglycemia in non-diabetic patients presenting with acute stroke. With the help of this study we could determine the magnitude of problem i.e. new-onset hyperglycemia in acute stroke, and could design our routine practice guidelines for early recognition and management of this condition in order to reduce the morbidity and mortality of the community.

MATERIAL AND METHODS

This cross sectional study which was conducted at Department of Medicine, Bahawal Victoria Hospital

Department of Medicine, Quaid-Azam Medical College/B.V. Hospital, Bahawalpur
Correspondence to Dr. Muhammad Fayyaz, Associate Professor House 7, BVH Colony Bahawalpur. Cell No. 03326368870 Email. drmuhammadfayyaz@gmail.com

Bahawalpur from October 2014 to April 2015. An approval was taken from institutional review committee and written informed consent was taken from every patient's attendant. Total 171 non-diabetics presenting with acute stroke were included in this study. All non-diabetics who were presented with acute stroke i.e., <24 hours duration and having age between 30 to 70 years of both genders were included in this study. All patients history diabetes mellitus, patients with head injury, patients with h/o anticoagulant drugs or steroid use, patients with recurrent attack and patients with acromegaly or hypergonadisim were excluded from the study.

Patients with no history of diabetes in past and normal HbA1c level (≤5.6%) on presentation was labeled as non-diabetic. As per WHO definition acute stroke is defined as "rapidly developing symptoms/ signs (<24 hours duration) of focal (weakness of one side of body, speech disturbances and cranial nerve palsy) and at a time global loss (loss of consciousness i.e., GCS<8/15) of cerebral function without apparent cause other than that of vascular origin" and non-contrast CT brain showed loss of gray-white interface, hypodensity of basal ganglia and insular cortex, high attenuating (bright) clot and the low attenuating (dark) cerebrospinal fluid (CSF) and normal brain tissue. After taking relevant history, blood pressure and BMI of each patient was calculated and looked for hypertension (yes/no) and obese/non-obese. Then blood sample of each patient was drawn and sent to the pathology laboratory of the institution for measurement of blood glucose levels and lipid profile for assessing dyslipidemia. Blood glucose levels > 11.1 mmol/l (200 mg/dl) was considered as hyperglycemia and noted as present or absent. All this data was recorded on a predesigned proforma.

All the collected data was entered in SPSS version 17 and analyzed. Mean and SD was calculated for numerical variables. Frequencies was calculated for categorical variables. Chi-square test was used as test of association. P value ≤ 0.05 was considered as significant.

RESULTS

Age range in this study was from 30 to 70 years with mean age of 53.82 ± 10.31years. Hyperglycemia was found in 44 (25.73%) patients. (Fig. 1) Stratification of hyperglycemia was done for age groups. Majority of the patients 53 (30.99%) were between 51 to 60 years of age. When Stratification of hyperglycemia was done for age groups, it was found that there was no significant (P:0.686) difference between different age groups (Table 1).

Out of the 171 patients, 89(52.05%) were male and 82 (47.95%) were females with male to female ratio of 1.1:1. Hyperglycemia was found in 19 (21.35%) male patients and 25(30.49%) female patients. There was no significant (0.172) difference between male and female (Table 2).

Mean duration of disease was 10.29±6.53 hours. Stratification of hyperglycemia was done for duration of disease. Two groups were made ≤12 hours and >12 hours duration of disease. Total 110 (64.33%) patients found with ≤12 hours of duration of disease and hyperglycemia was found in 25(22.73%) patients, 61(35.67%) patients with >12 hours duration of disease and 19(31.15%) patients were found with hyperglycemia. No association (P:0.228) of hyperglycemia with duration of disease was found (Table 3)

Among the 171 patients, 93 (54.39%) found with Hemorrhagic stroke and 78 (45.61%) found with Ischemic stroke and hyperglycemia was found in 24 (25.81%) and 20 (25.64%) patients with hemorrhagic stroke and ischemic stroke respectively. Insignificant (0.980) association of hyperglycemia with type of stroke was found. (Table 4)

Fig 1: Percentage of patients with Hyperglycemia (n=171).

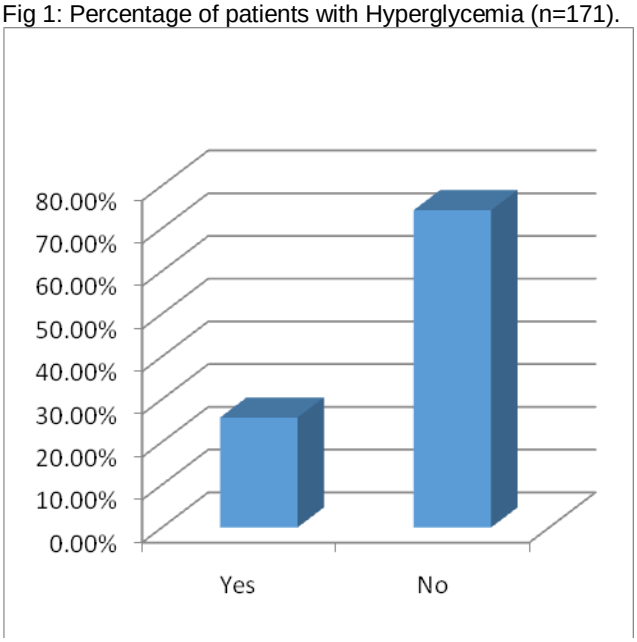

Table 1: Stratification of Hyperglycemia with respect to age groups.

Age (years)	Hyperglycemia		
	Yes	No	Total
30-40	04(17.39%)	19(82.61%)	23(13.45%)
41-50	13(29.55%)	31(70.45%)	44(25.73%)
51-60	15(28.30%)	38(71.70%)	53(30.99%)
61-70	12(23.53%)	39(76.47%)	51(29.82%)
Total	44(25.73%)	127(74.27%)	171

P value: 0.686

Table 2: Stratification of Hyperglycemia with respect to gender.

Gender	Hyperglycemia		
	Yes	No	Total
Male	19(21.35%)	70(78.65%)	89(52.05%)
Female	25(30.49%)	57(69.51%)	82(47.95%)
Total	44(25.73%)	127(74.27%)	171

P value: 0.172

Table 3: Stratification of Hyperglycemia with respect to duration of disease.

Duration of disease	Hyperglycemia		
	Yes	No	Total
≤12 hours	25(22.73%)	85(77.27%)	110(64.33%)
>12 hours	19(31.15%)	42(68.85%)	61(35.67%)
Total	44(25.73%)	127(74.27%)	171

P value: 0.228

Table 4: Stratification of Hyperglycemia with respect to Type of Stroke.

Type of Stroke	Hyperglycemia		
	Yes	No	Total
Hemorrhagic	24(25.81%)	69(74.19%)	93(54.39%)
Ischemic	20(25.64%)	58(74.36%)	78(45.61%)
Total	44(25.73%)	127(74.27%)	171

P value: 0.980

DISCUSSION

The glycemia is one of the parameters that shall be controlled in the ictus unit. The hyperglycemia in the ischemic ictus is very usual and is present in the acute phase of the ictus in approximately 20-25% of the patients, affecting 100% of the diabetic patients during the first 8 hours and up to 50% of the non-diabetic patients. These are normally moderate values of hyperglycemia[10,11]. The relative risk of mortality in non-diabetic patients who show hyperglycemia in the acute phase of the ictus increases three times[12].

It is known that in diabetic and non-diabetic patients the presence of hyperglycemia at admission is associated to an incorrect evolution after the ictus, conferring a worse functional prognosis and higher rates of brain hemorrhages, both in diabetic and non-diabetic patients. The history of diabetes mellitus is also associated per se to an inadequate prognosis. It was recommended to treat the glycemias over 200mg/dl in the acute ictus long ago in order to avoid the harmful effects of the hyperglycemia. At present, the consensus guidelines of the American Heart Association (AHA) and the ictus recommend starting treatment with insulin as from values of 140-185 mg/dl (class II, C evidence level)[13].

In our study, hyperglycemia was found in 44(25.73%) patients, whereas there was no hyperglycemia in 127(73.27%) patients. In a study that evaluated the dynamics of the hyperglycemia in the acute ictus, taking a baseline control and another after 24hours, it could be observed that the non-diabetic patients withhyperglycemia kept both at admission and after 24 hours showed higher rates of dependence, mortality and brain hemorrhages. The different adaptation of the organism to the hyperglycemia in both groups of patients, with the starting of different mechanisms to face the hyperglycemia, with an already organized adaptationin the diabetic patients, might explain these differences[14].

The prevalence of previously recognized diabetes mellitus (DM) in acute stroke patients is estimated between 8 - 20%. About 6 - 42% of acute stroke patients have previously un-recognized DM[15]. In a study of supratentorial strokes, DM was diagnosed in 24.8% patients while transient hyperglycemia was seen in 36.3%patients[16]. Zahra F et al[10] in his study has found 20% stroke patients with hyperglycemia who were previously non-diabetics. Zafar A et al[17] in his study has found that in non-diabetics, 58% had ischaemic stroke while 42% had intracerebral haemorrhage.

Hyperglycemia is very common in patients of acute stroke, occurring in upto 60% of patients and is believed to aggravate cerebral ischaemia.[16] It leads to intracellular acidosis, accumulation of extra cellular Glutamate, cerebral oedema, blood-brain barrier disruption, and tendency for haemorrhagic transformation[18]. It is observed that between 20-40% of patients admitted with ischaemic stroke are hyperglycemic, often without a pre-existing diagnosis of diabetes[15] which can be due to stress hyperglycemia or undiagnosed diabetes exposed during an acute incident.

The multicenter study GLIAS (Glycemia in Acute Stroke), tried to determine the threshold of the glycemia on which the wrong evolution of the patients could be observed. The cut point was stated in 155mg/dl. Any increase of the glycemia over this value during the first 48 hours after the ictus conferred an inadequate prognosis as regards to higher rates of discapacity (score >2 in the modified Rankin scale [MRS] and mortality[19].

Van Kooten et al found a significant association between hyperglycemia on admission and stroke outcome, did not find a correlation between catecholamine and glucose levels, implying that increased stress was not responsible for the hyperglycemia[20].

In one study it was reported that 8 to 63% of non-diabetic and 39% to 83% of diabetic patients with ischemic stroke had hyperglycemia.[21] Blood glucose levels seem to decline within the first 24 hours after stroke onset, but they rise again after 24 to 88 hours, regardless of whether the patient has DM. This late

hyperglycemic phase is probably the result of impaired glucose metabolism that only becomes evident once the patient resumes feeding after an initial fasting period[17].

On the whole, it is concluded that frequency of neo-onset hyperglycemia in non-diabetic patients presenting with acute stroke is high, so great care could be taken in these particular patients and early recognition and management of this condition should be done in order to reduce the morbidity and mortality of the community.

CONCLUSION

This study concluded that frequency of neo-onset hyperglycemia in non-diabetic patients presenting with acute stroke is high. So, we recommend that in every patient of acute stroke, hyperglycemia should be taken into consideration and its early recognition and management should be done in order to reduce the morbidity and mortality of the community.

REFERENCE

1. Sims NR, Muyderman H. Mitochondria, oxidative metabolism and cell death in stroke. Biochimica et Biophysica Acta. 2009;1802(1):80–91.
2. Fonarow GC, Saver JL, Smith EE, Broderick JP, Kleindorfer DO, Sacco RL, et al. Relationship of national institutes of health stroke scale to 30-day mortality in medicare beneficiaries with acute ischemic stroke. *J Am Heart Assoc*. 2012;1(1):42-50.
3. Vinay K. Robbins and Cotran pathologic basis of disease. (8th ed). Philadelphia, PA: Saunders/Elsevier. 2010; pp. 1290–98.
4. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. *Circulation.* 2012;125(1):e2-e220.
5. Arshi S, Naheed F, Badshah M, Naz F, Nisa F. Hemorrhagic and ischemic stroke; frequency in hypertensive patients presenting with stroke at Pakistan Institute of Medical Sciences, Islamabad. Professional Med J. 2012;19(3):1-5.
6. Marjukka H, Jaakko T, Markku M, Coen DA S, Kalevi P, Bjorn Z, et al. Hyperglycemia and incidence of ischemic and hemorrhagic stroke-comparison between fasting and 2-hour glucose criteria. Stroke. 2009;40:1633-7.
7. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. *Stroke.* Oct 2001;32(10):2426-32.
8. Adams HP, Adams RJ, Brott T, del Zoppo GJ, Furlan A, Goldstein LB, et al. Guidelines for the Early Management of Patients With Ischemic Stroke A Scientific Statement From the Stroke Council of the American Stroke Association. Stroke. 2003 Apr 1;34(4):1056–83.
9. Miller DJ, Simpson JR, Silver B. Safety of Thrombolysis in Acute Ischemic Stroke: A Review of Complications, Risk Factors, and Newer Technologies. Neurohospitalist. 2011 Jul;1(3):138–47.
10. Zahra F, Kidwai SS, Siddiqi SA, Khan RM. Frequency of newly diagnosed diabetes mellitus in acute ischaemic stroke patients. J Coll Physicians Surg Pak. 2012;22(4):226-9.
11. Lloyd-Jones D, Adams R, Carnethon M. Heart disease and stroke statistics--2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. Jan 27 2009;119(3):480-6.
12. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. Stroke. 2001;32:2426-32.
13. Adams HP, Del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. Circulation. 2007;115:e478-534.
14. Yong M, Kaste M. Dynamic of hyperglycemia as a predictor of stroke outcome in the ECASS-II. Stroke. 2008;39:2749-55.
15. Christopher SG, Janice EOC and Hilary L. Diabetes hyperglycemia and recovery from stroke. Geriatrics and Gerontology International. 2001;1:2-7.
16. Szczudlik A, Slowik A, Turaj W, Wyrwicz-Petkow U, Pera J, Dziedzic T, et al. Transient hyperglycemia in ischemic stroke patients. J Neurol Sci. 2001;189:105-11.
17. Zafar A, Shahid SK, Siddiqui M, Khan FS. Pattern of stroke in type 2 diabetic subjects versus non diabetic subjects. J Ayub Med Coll Abbottabad. 2007;19(4):64-7.
18. Nadya K, Shmuel L, Hilla K. The Role of Hyperglycemia in Acute Stroke. Arch Neurol. 2001;58:1209-12.
19. Fuentes B, Castillo J, San Jose B, Leira R, Serena J, Vivancos J, et al. The prognostic value of capillary glucose levels in acute stroke: the GLycemia in Acute Stroke (GLIAS) study. Stroke. 2009;40:562-8.
20. Van KF, Hoogerbrugge N, Naarding P, Koudstaal PJ. Hyperglycemia in the acute phase of stroke is not caused by stress. Stroke 1993;24:1129-32.
21. Lindsberg PJ, Roine RO. Hyperglycemia in acute stroke. Stroke. 2004;35:363-4.