International Journal of Advanced Biotechnology and Research (IJBR)
ISSN 0976-2612, Online ISSN 2278–599X,
Vol-9, Issue-2, 2018, pp87-94
http://www.bipublication.com

Research Article

Frequency of Hyperglycemia in Non-Diabetics Presenting With Acute Stroke.

[1]Zunurain, [2]Muhammad Shehzad Rae

and [3]Taimoor Nawaz khan

[1]Senior Medical Officer, RHC Abdul Hakim.
[2]Medical Officer, THQ Thal (MNS) Hospital, Layyah
[3]Incharge Medical officer, BHU Dhuddian, Tehsil chunnian, District Kasur

ABSTRACT

Objective: To determine the frequency of hyperglycemia in non-diabetics presenting with acute stroke.
Materials & 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 andh/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 > 11.1 mmol/l (200 mg/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 and 82 (47.95%) were females with male to female ratio of 1.1:1. Mean duration of disease was 10.29 ± 6.53 hours. Mean BMI was 28.41 ± 5.33 kg/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, high.

INTRODUCTION

A stroke, sometimes referred to as a cerebrovascular accident (CVA), cerebrovascular insult (CVI), or colloquially brain attack is the loss of brain function due to a disturbance in the blood supply to the brain. This disturbance is due to either ischemia (lack of blood flow) or hemorrhage.[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] Nearly 800,000 people suffer strokes each year in the United States; 82-92% of these strokes are ischemic.[4] Stroke is the second leading cause of adult death and disability after ischemic heart disease.[5]

Furthermore, 20-40% of patients with ischemic infarction may develop hemorrhagic transformation within one week after ictus.[6,7]Differentiating between these different types of stroke is an essential part of the initial workup of these patients because the subsequent management of each patient is vastly different. Neuroimaging plays a vital role in the workup of acute stroke by providing information essential to accurately triage patients, expedite clinical decision making with regards to treatment, and improve outcomes in patients presenting with acute stroke.[8] Rapid and accurate diagnosis is

crucial since the only drug currently approved by the FDA for treatment of acute ischemic stroke is intravenous tissue plasminogen activator (tPA) administered within 3 hours of stroke onset.[9]

Hyperglycemia (elevated levels of blood glucose) is frequently observed in patients admitted to hospital for acute ischemic stroke, and can last for several days beyond the acute phase.[10] Preexisting hyperglycemia is found commonly in patients presenting with acute stroke, and is reported to be present in 20 to 50% of patients.

In many trials of thrombolytic agents, hyperglycemia occurred in about 20-30% of subjects. Although confounded by other factors, such as severity of the infarct, hyperglycemia in the face of acute stroke worsens clinical outcome. Nondiabetic hyperglycemic ischemic stroke patients have a 3-fold higher 30-day mortality and diabetic patients have a 2-fold 30-day mortality.[11]

In several trials involving thrombolytic and anticoagulation therapy in patients with 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.

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.[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.[13] Zahra F et al[14] in his study has found 20% stroke patients with hyperglycemia who were previously non-diabetics.

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.

OPERATIONAL DEFINITIONS:

1. **Non-Diabetics:** no history of diabetes in past and normal HbA1c level (≤5.6%) on presentation was labeled as non-diabetic.
2. **Acute Stroke:** 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 atime 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.

STUDY DESIGN: Descriptive, Cross-sectional study.

SETTING: RHC Abdul Hakim.

DURATION OF STUDY: February 2017 to August 2017

Inclusion Criteria:

- All non-diabetics who will be presented with acute stroke i.e. <24 hours duration (as per operational definitions).
- Age between 30 to 70 years of both genders.

Exclusion Criteria:

- All patients with no history of diabetes in past and HbA1c level >5.6%.
- Patients with known diabetes mellitus.
- Patients with head injury.
- Patients with h/o anticoagulant drugs or steroid use.
- Patients with recurrent attack.
- Patients with acromegaly or

hypergonadisim.

Data collection procedure:

After approval from local ethical committee, 171 patients admitted to the RHC Abdul Hakim, fulfilling the Inclusion/Exclusion criteria were selected. Informed, written consent was taken from each patient's attendant.

After taking relevant history, blood pressure and BMI of each patient was calculated and looked for hypertension (yes/no) and obese/non-obese as per-operational definition. 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 (as per-operatioanl definition). 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 which contained two parts i.e. part 1st contained the patients bio-data while part 2nd contained the study variables (Annexure-I).

Data analysis procedure:

Statistical analysis was performed using SPSS version 20.0. Mean and standard deviation was calculated for age, duration of disease and BMI. Frequency and percentage was calculated for gender, type of stroke (hemorrhagic/ischemic), hypertension (yes/no), dyslipidemia (yes/no), smoking (yes/no) and hyperglycemia (present / absent). Effect modifiers like age, gender, duration of disease, type of stroke (hemorrhagic/ischemic), hypertension (yes/no), smoking (yes/no), dyslipidemia (yes/no) and BMI (obese/non-obese) were controlled through stratifications. Post-stratification Chi square was applied to see their effects on the hyperglycemia and 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. Majority of the patients 53 (30.99%) were between 51 to 60 years of age as shown in Table I. 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 (Figure I). %age of patients according to type of stroke and co-morbid conditions are shown in Figure II and Table II respectively. Mean duration of disease was 10.29 ± 6.53 hours. Mean BMI was 28.41 ± 5.33 kg/m^2.

Hyperglycemia was found in 44 (25.73%) patients, whereas there was no hyperglycemia in 127 (73.27%) patients as shown in Figure III. When Stratification of hyperglycemia was done on age groups, it was found that there was no significant difference between different age groups as shown in Table III while the stratification of hyperglycemia with respect to gender has shown in Table IV which also showed no significant difference between male and female.

Table V & VI have shown the stratification of hyperglycemia with respect to duration of disease and type of stroke respectively. Stratification of co-morbid conditions i.e. smoking, hypertension, dyslipidemia and BMI, are shown in Table VII, VIII, IX and X respectively.

Table-I: Age distribution of patients (n=171).

Age (in years)	No. of Patients	%age
30-40	23	13.45
41-50	44	25.73
51-60	53	30.99
61-70	51	29.82

Mean ± SD = 53.82 ± 10.31 years

Figure-I: %age of patients according to gender (n=171).

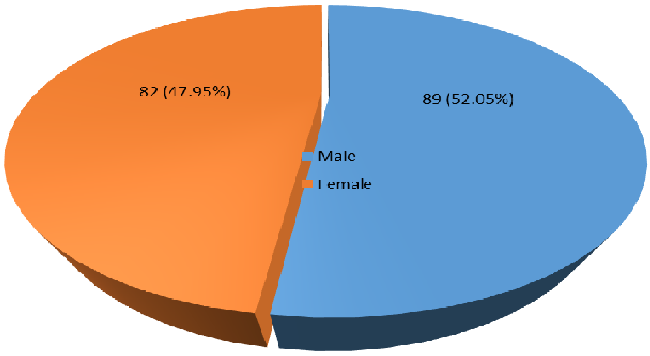

Figure II: %age of patients according to type of stroke (n=171)

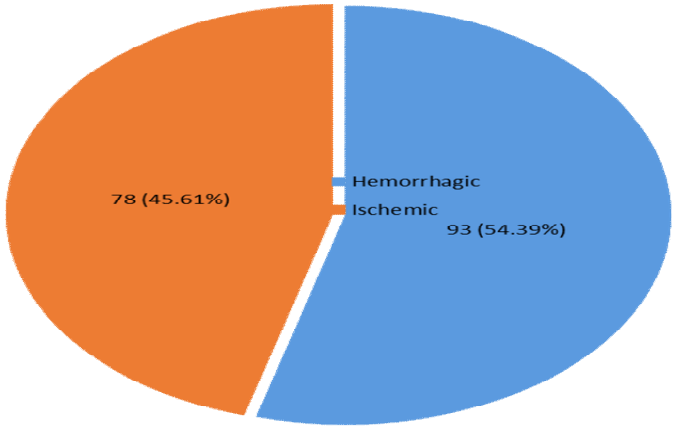

Table II: %age of patients with status of co-morbid conditions (n=171)

Confounding variables		Frequency	%age
Smoking	Yes	73	42.69
	No	98	57.31
Hypertension	Yes	119	69.59
	No	52	30.41
Dyslipidemia	Yes	102	59.65
	No	69	40.35
BMI	Obese	88	51.46
	Non-obese	83	48.54

Figure III: %age of patients with Hyperglycemia (n=171).

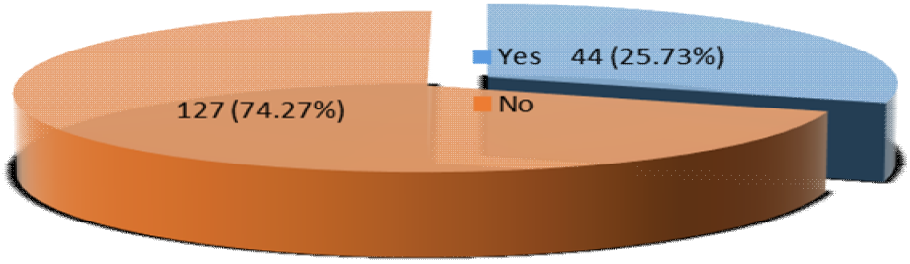

Table III: Stratification of Hyperglycemia with respect to age groups.

Age (years)	Hyperglycemia		p-value
	Yes	No	
30-40	04 (17.39%)	19 (82.61%)	
41-50	13 (29.55%)	31 (70.45%)	
51-60	15 (28.30%)	38 (71.70%)	
61-70	12 (23.53%)	39 (76.47%)	**0.686**

Table IV: Stratification of Hyperglycemia with respect to gender.

	Hyperglycemia		**p-value**
Gender	Yes	No	
Male	19 (21.35%)	70 (78.65%)	
Female	25 (30.49%)	57 (69.51%)	**0.172**

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

Duration of disease (in hours)	**Hyperglycemia**		**p-value**
	Yes	No	
≤12 hours	25 (22.73%)	85 (77.27%)	
>12 hours	19 (31.15%)	42 (68.85%)	**0.228**

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

	Hyperglycemia		**p-value**
Type of Stroke	Yes	No	
Hemorrhagic	24 (25.81%)	69 (74.19%)	
Ischemic	20 (25.64%)	58 (74.36%)	**0.980**

Table VII: Stratification of Hyperglycemia with respect to Smoking.

	Hyperglycemia		**p-value**
Smoking	Yes	No	
Yes	19 (26.03%)	54 (73.97%)	
No	25 (25.51%)	73 (74.49%)	**0.939**

Table VIII: Stratification of Hyperglycemia with respect to Hypertension.

	Hyperglycemia		**p-value**
Hypertension	Yes	No	
Yes	35 (29.41%)	84 (70.59%)	
No	09 (17.31%)	43 (82.69%)	**0.096**

Table IX: Stratification of Hyperglycemia with respect to Dyslipidemia.

	Hyperglycemia		**p-value**
Dyslipidemia	Yes	No	
Yes	30 (29.41%)	72 (70.59%)	
No	14 (20.29%)	55 (79.71%)	**0.181**

Table X: Stratification of Hyperglycemia with respect to BMI.

	Hyperglycemia		**p-value**
BMI	Yes	No	
Obese	24 (27.27%)	64 (72.73%)	
Non-obese	20 (24.10%)	63 (75.90%)	**0.635**

DISCUSSION

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 inthe 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 showedhigher rates of dependence, mortality and brain hemorrhages.The different adaptation of the organism to the hyperglycemia inboth groups of patients, with the starting of different mechanismsto face the hyperglycemia, with an already organized adaptationin the diabetic patients, might explain these differences.[15]

The prevalence of previously recognized diabetes mellitus in acute stroke patients is estimated between 8 - 20%. About 6 - 42% of acute stroke patients have previously un-recognized diabetes mellitus.[16] In a study of supratentorial strokes, diabetes mellitus was diagnosed in 24.8% patients while transient hyperglycemia was seen in 36.3% of patients.[17] Zahra F et al[14] in his study has found 20% stroke patients with hyperglycemia who were

previously non-diabetics. Zafar A et al[18] in his study has found that in non-diabetics, 29 (58.0%) had ischaemic stroke while 21 (42.0%) had intracerebralhaemorrhage.

Hyperglycemia is common in patients with acute stroke, occurring in upto 60% of patients and is believed to aggravate cerebral ischaemia.[17] It leads to intracellular acidosis, accumulation of extra cellular Glutamate, cerebral oedema, blood-brain barrier disruption, and tendency for haemorrhagic transformation.[19] It is observed that between 20 - 40% of patients admitted with ischaemic stroke are hyperglycemic, often without a pre-existing diagnosis of diabetes,[16] 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 155 mg/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. This happened independently from the ictus seriousness, the size of the infarction, the age of the patient and the presence or not of previous diabetes.[20] In a post hocanalysis of this same study, it could be observed that 40% of the patients with hyperglycemia kept values of >155 mg/dl in spite of the hypoglycemiant treatment.[21]

Hyperglycemic stroke patients without a previous diagnosis of diabetes are not routinely screened for diabetes.[17] Diabetes guidelines recommend aggressive screening for type 2 diabetes mellitus in Asian patients as they are considered to have a higher risk of developing diabetes and potentially worse prognosis. Current guidelines also recommend screening patients for diabetes if they have 1 or more risk factors for diabetes for e.g. age > 45 years, hypertension, lipid abnormalities, vascular disease.[22] van Kootenet 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.[23]Tuomilehtoet al[24] calculated that 16% of all stroke mortality in men and 33% in women could be directly attributed to diabetes. However, one local study could not show much difference in the outcome in the diabetics versus non diabetics.[25]

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.

REFERENCES

1. Sims NR, Muyderman H. Mitochondria, oxidative metabolism and cell death in stroke. BiochimicaetBiophysicaActa. 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. Mullins ME, Lev MH, Schellingerhout D, Gonzalez RG, Schaefer PW. Intracranial

hemorrhage complicating acute stroke: how common is hemorrhagic stroke on initial head CT scan and how often is initial clinical diagnosis of acute stroke eventually confirmed?.*AJNR Am J Neuroradiol.* Oct 2005;26(9):2207-12.
7. Nighoghossian N, Hermier M, Adeleine P, Blanc-Lasserre K, Derex L, Honnorat J. Old microbleeds are a potential risk factor for cerebral bleeding after ischemic stroke: a gradient-echo T2-weighted brain MRI study. *Stroke*. Mar 2002;33(3):735-42.
8. Dirnagl U, Iadecola C, Moskowitz MA. Pathobiology of ischaemic stroke: an integrated view. *Trends Neurosci*. Sep 1999;22(9):391-7.
9. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. *N Engl J Med*. Dec 14 1995;333(24):1581-7.
10. 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.
11. 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.
12. Samiullah S, Hafiz S, Iftikhar Q, Khalid S. Frequency of metabolic syndrome and its various components in patients with ischemic stroke. Int J Med Med Sci. 2011;3:247-51.
13. Arrojo FG, Munoz AH, Rodriguez BA. Recommendations for an adequate glycemic control during hospitalization after a stroke episode. Av Diabetol. 2010;26:408-13.
14. 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.
15. Yong M, Kaste M. Dynamic of hyperglycemia as a predictor of stroke outcome in the ECASS-II. Stroke. 2008;39:2749-55.
16. Christopher SG, Janice EOC and Hilary L. Diabetes hyperglycemia and recovery from stroke. Geriatrics and Gerontology International. 2001;1:2-7.
17. 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.
18. 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.
19. Nadya K, Shmuel L, Hilla K. The Role of Hyperglycemia in Acute Stroke. Arch Neurol. 2001;58:1209-12.
20. 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.
21. Fuentes B, Ortega-Casarrubios MA, Sanjose B, Castillo J, Leira R, Serena J, et al. Persistent hyperglycemia >155 mg/dl in acute ischemic stroke patients: how well are we correcting it? Implications for outcome. Stroke. 2010 Aug 19 [Epub ahead of print].
22. Gray CS, Hildreth AJ, Sandercock PA, O'Connell JE, Johnston DE, Cartlidge NE, et al. GIST Trialists Collaboration. Glucose-potassium-insulin infusions in the management of post-stroke hyperglycaemia: the UK Glucose Insulin in Stroke Trial (GIST-UK). Lancet Neurol. 2007;6:397-406.
23. 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.
24. Tuomilehto J, Rastenyte D, Jousilahti

P, Sarti C, Vartiainen E. Diabetes mellitus as a risk factor for death from stroke. Prospective study of the middle-aged Finnish population. Stroke. 1996;27:210–15.

25. Basir F, Ali S, Aziz H. Stroke recovery and outcome in diabetes. J Coll Physicians Surg Pak. 2001;11:736–8.