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ACUTE STROKE;
STUDY OF HYPERGLYCEMIA IN NON-DIABETIC PATIENTS

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ABSTRACT... Objectives: To find out the frequency of hyperglycemia in non-diabetic patients presenting with acute stroke. **Study Design:** Cross sectional study. **Setting:** Department of Medicine, Dera Ghazi Khan Hospital, D.G Khan. **Period:** September 2014 to March 2015. **Materials & Methods:** Total 150 non-diabetics presented with acute stroke i.e. <24 hours duration of age 30-70 years either male or female 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 blood glucose levels and blood glucose levels > 11.1 mmol/l (200 mg/dl) was considered as hyperglycemia and noted on pre-designed proforma. **Results:** Mean age was 54.82 ± 11.44 years. Total 32 (21.33%) patients found with hyperglycemia. Male patients were 80 (53.33%) and female patients were 70 (46.67%) and hyperglycemia was found in 14 (17.5%) male patients and 18 (25.71%) female patients. Insignificant of hyperglycemia with age, gender, duration of disease and type of stroke was detected. **Conclusion:** Results of this study reveals 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.

Key words: Ischemic, non-diabetic, stroke, glucose, IHD, CVA, CVI

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INTRODUCTION

A stroke is the loss of function of brain due to a disturbance in supply of blood to brain and stroke can be divided into hemorrhagic stroke and ischemic stroke.[1] Ischemic stroke is caused by 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 commonly seen in patients admitted to hospital with acute ischemic stroke, and can last for many days beyond the acute phase.[6] Pre-existing hyperglycemia is found more frequently 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]

No local data available on this topic. Purpose of this study is to 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 was a cross sectional study and conducted at the Department of Medicine, Dera Ghazi Khan Hospital, D.G Khan from September 2014 to March 2015. An approval was taken from institutional review committee and written informed consent was taken from every patients' attendant. Total 150 non-diabetic male or female patients who were presented with acute stroke (<24 hours) and having age between 30 years to 70 years were included in this study. All patients with history of 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 mellitus in past and normal HbA1c level (≤5.6%) on presentation was labeled as non-diabetic. As per WHO criteria, 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, hypo density 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 sample of each patient was drawn and sent to the pathology laboratory of the institution for blood glucose levels. Blood glucose levels > 11.1 mmol/l (200 mg/dl) was considered as hyperglycemia and noted in pre-designed proforma along with demographic profile of the patients.

All the collected data was entered in SPSS version 20 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

In this study total 150 non-diabetics presenting with acute stroke were included. Minimum age was 30 years and maximum age was 70 years with mean age of 54.82 ± 11.44 years. Out of 150 patients, 32 (21.33%) patients found with hyperglycemia. (Figure-1) Patients were divided into 4 age groups i.e. age group 30-40 years, age group 41-50 years, age group 51-60 years and age group 61-70 years. Twenty one (13.45%) belonged to age group 30-40 years followed by 36 (25.73%) to age group 41-50 years, 44 (30.99%) to age group 51-60 years and 49 (29.82%) to age group 61-70 years and hyperglycemia was found in 03 (14.29%), 11 (30.56%), 7 (15.91%) and 11 (22.45%) patients respectively. Statistically insignificant (P = 0.355) association of hyperglycemia with age was found. (Table-I)

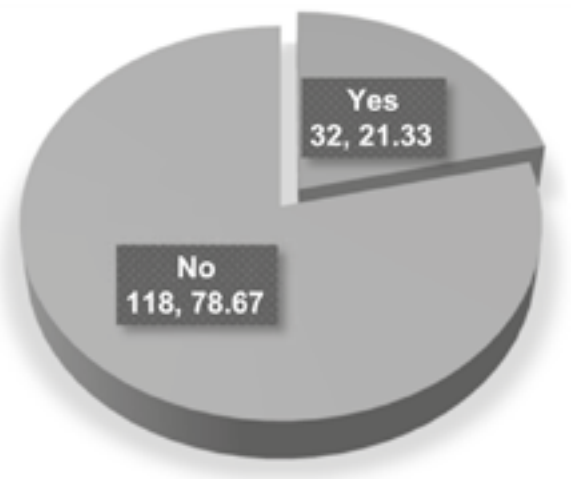

Figure-1. Frequency of hyperglycemia

Age (years)	Hyperglycemia			p-value
	Yes (%)	No (%)	Total (%)	
30-40	03 (14.29)	18 (85.71)	21 (13.45)	0.355
41-50	11 (30.56)	25 (69.44)	36 (25.73)	
51-60	7 (15.91)	37 (84.09)	44 (30.99)	
61-70	11 (22.45)	38 (77.55)	49 (29.82)	
Total	32 (21.33)	118 (78.67)	150	

Table-I. Association of hyperglycemia with age

Male patients were 80 (53.33%) and female patients were 70 (46.67%) and hyperglycemia was found in 14 (17.5%) male patients and 18 (25.71%) female patients. Association between hyperglycemia and gender was statistically insignificant (P = 0.301). (Table-II) Stratification of hyperglycemia was done for duration of disease. Two groups were made ≤12 hours and >12 hours duration of disease. Total 96 (64%) patients found with ≤12 hours of duration of disease and hyperglycemia was found in 18 (18.75%) patients, 54 (36%) patients found with >12 hours duration of disease and 14 (25.93%) patients were found with hyperglycemia. No association (P = 0.409) of hyperglycemia with duration of disease was found. (Table-III).

Gender	Hyperglycemia			p-value
	Yes (%)	No (%)	Total (%)	
Male	14 (17.5)	66 (82.5)	80 (53.33)	0.301
Female	18 (25.71)	52 (74.29)	70 (46.67)	
Total	32 (21.33)	118 (78.67)	150	

Table-II. Association of hyperglycemia with gender

Duration of disease (in hours)	Hyperglycemia			p-value
	Yes (%)	No (%)	Total (%)	
≤12 hours	18 (18.75)	78 (81.25)	96 (64)	0.409
>12 hours	14 (25.93)	40 (74.07)	54 (36)	
Total	32 (21.33)	118 (78.67)	150	

Table-III. Association of hyperglycemia with duration of disease

Out of 150 patients, 81 (54%) found with Hemorrhagic stroke and 69 (46%) found with Ischemic stroke and hyperglycemia was found in 17 (20.99%) and 15 (21.74%) patients with hemorrhagic stroke and ischemic stroke respectively. Insignificant (P = 0.920) association of hyperglycemia with type of stroke was found. (Table-IV)

Type of Stroke	Hyperglycemia			p-value
	Yes (%)	No (%)	Total (%)	
Hemorrhagic	17 (20.99)	64 (79.01)	81 (54)	0.920
Ischemic	15 (21.74)	54 (78.26)	69 (46)	
Total	32 (21.33)	118 (78.67)	150	

Table-IV. Association of hyperglycemia with type of Stroke.

DISCUSSION

Hyperglycemia in the ischemic ictus is very usual and is present in the acute phase of the ictus in approximately 20% to 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.[10-12]

In both 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. It was recommended to treat the glycemias over 200 mg/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 present study, 21.33% patients found with hyperglycemia. In a study that evaluated the dynamics of the hyperglycemia in the acute ictus, taking a baseline control and another after 24 hours, it could be observed that the non-diabetic patients with hyperglycemia 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 adaptation in the diabetic patients, might explain these differences.[14]

The prevalence of previously recognized diabetes mellitus (DM) in acute stroke patients is estimated between 8% to 20%. About 6% to 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 et al[10] in his study has found 20% stroke patients with hyperglycemia who were previously non-diabetics. Zafar et al[17] in his study has found that in non-diabetics, 58.0% had ischemic stroke while 42.0% had intracerebral hemorrhage.

Hyperglycemia is frequently found in patients of acute stroke, occurring in up to 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 hemorrhagic transformation.[18] It is observed that between 20% to 40% of patients admitted with ischemic 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 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.[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

Results of this study reveals 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.

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"Only those who dare to fail greatly can ever achieve greatly."

Robert F. Kennedy

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