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ISCHEMIC STROKE;

FREQUENCY OF RAISED HEMOGLOBIN A1c IN PATIENTS PRESENTING WITH ISCHEMIC STROKE

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ABSTRACT… Background: Patients with acute ischemic stroke frequently test positive for hyperglycemia, which is associated with a poor clinical outcome. This association between poor glycemic control and an unfavorable prognosis is particularly evident in patients with persistent hyperglycemia, patients without a known history of diabetes mellitus (DM), and patients with cortical infarction. **Objective:** To determine the frequency of raised hemoglobin A1c in patients presenting with ischemic stroke. **Material & Methods: Study design:** Retrospective study. **Setting:** Department of Medicine, Independent University Hospital, Faisalabad. **Duration:** 6 months. **Data collection procedure:** Reports of 150 patients fulfilling selection criteria were selected from medical record section of Independent University Hospital, Faisalabad. Demographic details were obtained. Then medical record of patients was assessed for presence of HbA1c. If HbA1c of patients was reported ≥ 6.5%, then raised HbA1c was labeled. **Results:** In this study raised HbA1C level in patients presenting with ischemic stroke was 25%. Among these patients the most affected age group of patients was 41-60 years. Female patients were more effected than male patients. Among these patients only 27% were diabetic while 73% were non-diabetic, 54% were smokers, 32% patients were hypertensive and in 14% patients hyperlipidemia was seen. All these factors were not significantly associated with raised HbA1c level in patients presenting with ischemic stroke. **Conclusion:** Results of this study demonstrate a high frequency of raised HbA1c level in patients presenting with ischemic stroke. i.e. 25%. So keeping in mind these findings it is recommended that stroke patients should also be screened for hyperglycemia or increased HbA1c so that patients can be prevented from development of permanent hyperglycemia or other complications associated with it.

Key words: Hemoglobin, A1c, ischemic stroke

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INTRODUCTION

Patients with acute ischemic stroke frequently test positive for hyperglycemia, which is associated with a poor clinical outcome. This association between poor glycemic control and an unfavorable prognosis is particularly evident in patients with persistent hyperglycemia, patients without a known history of diabetes mellitus (DM), and patients with cortical infarction.[1]

Hyperglycemia in relation to acute ischemic stroke is common both in patients with and in patients without a diagnosis of DM, and it has been suggested to worsen survival. However, recent results from several clinical studies indicate that particularly patients with stroke and stress hyperglycemia, but not diabetes, have increased mortality.[2-4]

Glucose level appears to influence infarct volume growth and neurological deterioration, particularly in non-diabetic patients with ischemic stroke.[4] But it is considered that hyperglycemia at the onset of acute ischemic stroke may negatively impact not only acute morbidity but also brain recovery. Establishing hyperglycemia treatment protocols is challenging, given the variation among patients and acute stroke care settings.[5]

Kamouchi et al. in 2011, showing that patients with acute ischemic stroke and DM had more unfavorable outcome, the higher HbA1c they

had. A recent study by Li et al., is one of the few studies systematically investigating the role of HbA1c on stroke outcome, regardless of a pre-stroke diagnosis of DM; their results show that elevated HbA1c level relates to stroke severity and poor prognosis in the whole study population; however, only patients with brainstem infarction were included in this study.[6, 7]

In a study conducted in Faisalabad in 2006, the frequency of raised HbA1c was 56.4% in patients presenting with ischemic stroke.[8] But another study conducted , the frequency of raised HbA1c was 13.2% in patients presenting with ischemic stroke.[9]

Rationale of this study is to assess the frequency of raised hemoglobin A1c in patients presenting with ischemic stroke. Literature has showed controversial results as one study showed that hyperglycemia can be present in >50% cases and can be a high risk for poor prognosis in patients with ischemic stroke, but another study showed that the extent of hyperglycemia was very low. So, it creates a dispute whether to be aware for hyperglycemia or not. So we want to conduct this study to confirm the extent of problem in local population. This will improve our knowledge and practice and we will be able to recommend that stroke patients should also be screened for hyperglycemia or increased HbA1c so that patients can be prevented from development of permanent hyperglycemia or other complications associated with it.

Objective
To assess the frequency of raised hemoglobin A1c in patients presenting with ischemic stroke.

OPERATIONAL DEFINITION

Ischemic stroke
It is defined as thrombotic stroke occurs when diseased or damaged cerebral arteries become blocked by the formation of a blood clot within the brain detected on CT scan.

Raised HbA1c
It will be labeled if HbA1c>7% at time of presentation of patient.

MATERIAL & METHODS

Study design
Retrospective study.

Setting
Department of Medicine, Independent University Hospital, Faisalabad.

Duration
6 months from the date of approval of synopsis.

Sample Size
Sample size of 150cases is calculated with 95% confidence level, 5.5% margin of error and taking expected percentage of raised HbA1c i.e. 13.2% in patients presenting with ischemic stroke.

Sampling techniques
Non-probability, consecutive sampling.

SELECTION CRITERIA

Inclusion criteria
Patients of 40-80 years age of either gender diagnosed with ischemic stroke (as per operational definition) presenting in emergency.

Exclusion criteria
- Patients with history of ischemic stroke (medical record)
- Patients with transient ischemic attack and those with intracerebral haemorrhage (on CT scan)
- Patients with recent blood transfusion or a haemoglobinopathy (on history and medical record)

DATA COLLECTION PROCEDURE
Reports of 150patients fulfilling selection criteria will be selected from medical record section of hospital, Department of Medicine, Independent University Hospital, Faisalabad. Demographic details (name, age, gender and BMI) will be obtained. Then medical record of patients will be assessed for presence of HbA1c. If HbA1c of patients would be reported >7%, then raised HbA1c will be labeled (as per operational

definition). All this information will be noted on proforma (attached).

STATISTICAL ANALYSIS

IBM SPSS version 21 will be used for entry and analysis of data. All quantitative variables like age, BMI and HbA1c level will be presented in the form of mean and standard deviation. All qualitative variables like gender, history of DM and raisedHbA1c will be presented in the form of frequency and percentage. Data will be stratified for age, gender, smoking, hypertension, hyperlipidemia and history of DM. Chi-square test will be applied to compare the raised HbA1c in stratified groups. P-value of <0.05 will be taken as significant.

RESULTS

The mean age of the patients was 55.14±15.10 years the minimum age was 30 years and maximum was 80 years. (Table-I)

There were 81(54%) males and 69 (46%) females in our study. (Graph-1)

The mean BMI was 25.99±4.20 kg/m²the minimum BMI was 20 kg/m² and maximum was 35 kg/m². (Table-II)

The mean duration of Ischemic stroke was 9.58±7.48 days the minimum duration was 1 day and maximum was 25 days. (Table-III)
There were 30(20%) patients with diabetes mellitus and 120(80%) without diabetes mellitus. (Graph-2)

There were 65(43.3%) smokers and 85(56.7%) nonsmokers in our study. (Graph-3)

There were 46 (30.7%) patients with hypertension and 104 (69.3%) without hypertension in our study. (Table-IV)

There were 25 (16.7%) patients with hyperlipidemia and 125 (83.3%) without hyperlipidemia. (Table-V)

The mean HbA1c was 5.99±1.48 mmol/mol. Minimum HbA1c was 4mmol/mol and maximum was 10 mmol/mol. (Table-VI)

There were 37(24.7%) patients with raised HbA1c and 113 (75.3%) had normal HbA1c. (Graph-4)

There was no significant association between age groups and HbA1c as the p-value is not significant (p-value=0.58). i.e. HbA1c (Raised): 20-40 years: 19%, 41-60 years:49% & 61-80 years:32% (Table-VII)

There was no significant association between gender and HbA1c as the p-value is not significant. (p-value=0.13) i.e. HbA1c (Raised): Male: 43% vs. Female: 57%. (Table-VIII)

There was no significant association between Duration of Ischemic stroke and HbA1c as the p-value is not significant (p-value=0.13). i.e. HbA1c (Raised): 1-10 Days: 57%, 11-20 day:35% & 21-30 Days:8%. (Table-IX)

There was no significant association between diabetes mellitus and HbA1c as the p-value is not significant (p-value=0.22). i.e. HbA1c (Raised): Diabetic: 27% vs. Non-Diabetic: 73%. (Table-X)

There was no significant association between smoking and HbA1c as the p-value is not significant (p-value=0.13). i.e. HbA1c (Raised): Smokers: 54% vs. Non-Smokers:46%. (Table-XI)

There was no significant association between hypertension and HbA1c as the p-value is not significant (p-value=0.79). i.e. HbA1c (Raised): Hypertensive: 32% vs. Non-Hypertensive: 68%. (Table-XII)

There was no significant association between hyperlipidemia and HbA1c as the p-value is not significant (p-value=0.55) i.e. HbA1c (Raised): Hyperlipidemia: 14% vs. Non-Hyperlipidemia: 86%. (Table-XII)

N	150
Mean	55.14
SD	15.10
Min	30
Max	80

Table-I. Descriptive statistics for age

N	150
Mean	25.99
SD	4.20
Min	20.00
Max	35.00

Table-II. Descriptive statistics for body mass index

N	150
Mean	9.58
SD	7.486
Min	1
Max	25

Table-III. Descriptive statistics for duration of ischemic stroke (days)

Hypertension	Frequency (%)
Yes	46(30.7%)
No	104(69.3%)
Total	150(100%)

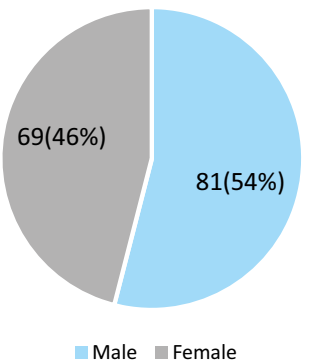
Table-IV. Hypertension status of patients

Hyperlipidemia	Frequency (%)
Yes	25(16.7%)
No	125(83.3%)
Total	150(100%)

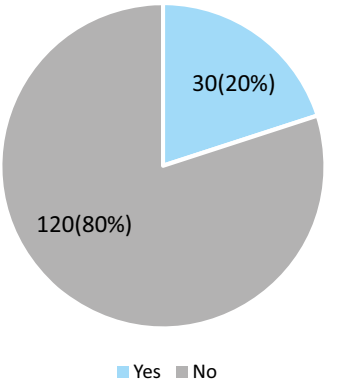
Table-V. Hyperlipidemia status of patients

N	150
Mean	5.99
SD	1.48
Min	4.0
Max	10.0

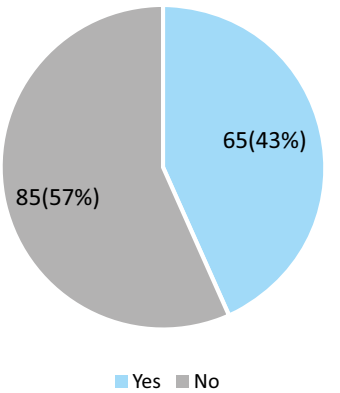
Table-VI. Descriptive statistics for HbA1c



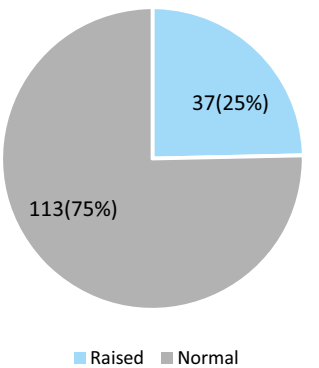
Graph-1. Gender distribution of patients



Graph-2. Diabetes mellitus status of patients



Graph-3. Smoking status of patients



Graph-4. HBA1C status in patients

		HbA1c		Total
		Raised	Normal	
Age Group	20-40	7(19%)	26(23%)	33
	41-60	18(49%)	44(39%)	62
	61-80	12(32%)	43(38%)	55
Total		37	113	150

Table-VII. Association between age groups and HbA1c
Chi-Square Test= 1.09 **p-value**= 0.58

		HbA1c		Total
		Raised	Normal	
Gender	Male	16(43%)	65(58%)	81
	Female	21(57%)	48(42%)	69
Total		37	113	150

Table-VIII. Association between gender and HbA1c
Chi-Square Test= 2.28 **p-value**= 0.130

		HbA1c		Total
		Raised	Normal	
Duration of Ischemic stroke	**1-10**	21(57%)	66(58%)	**87**
	11-20	13(35%)	35(31%)	**48**
	21-30	3(8%)	12(11%)	**15**
Total		**37**	**113**	**150**

Table-IX. Association between duration of ischemic stroke and HbA1c
Chi-Square Test= 0.34 **p-value**= 0.844

		HbA1c		Total
		Raised	Normal	
DM	Yes	10(27%)	20(18%)	30
	No	27(73%)	93(82%)	120
Total		37	113	150

Table-X. Association between diabetes mellitus and HbA1c
Chi-Square Test= 1.51 **p-value**= 0.22

		HbA1c		Total
		Raised	Normal	
Smoking	Yes	20(54%)	45(40%)	65
	No	17(46%)	68(60%)	85
Total		37	113	150

Table-XI. Association between smoking and HbA1c
Chi-Square Test= 2.29 **p-value**= 0.13

		HbA1c		Total
		Raised	Normal	
Hypertension	Yes	12(32%)	34(30%)	46
	No	25(68%)	79(70%)	104
Total		37	113	150

Table-XII. Association between hypertension and HbA1c
Chi-Square Test= 0.072 **p-value**= 0.79

		HbA1c		Total
		Raised	Normal	
Hyperlipidemia	**Yes**	5(14%)	20(18%)	**25**
	No	32(86%)	93(82%)	**125**
Total		**37**	**113**	**150**

Table-XIII. Association between hypertension and HbA1c
Chi-Square Test= 0.35 **p-value**= 0.55

DISCUSSION

Hyperglycemiain relation to acute is common both in patients with and in patients without a diagnosis of DM, and it has been suggested to worsen survival. However, recent results from several clinical studies indicate that particularly patients with stroke and stress Hyperglycemia, but not diabetes, have increased mortality.[10,11]

In this study raised HbA1c level in patients presenting with ischemic stroke was 25%. Among these patients the most effected age group of patients was 41-60 years. Female patients were more effected than male patients. Among these patients only 27% were diabetic while 73% were non-diabetic, 54% were smokers, 32% patients were hypertensive and in 14% patients hyperlipidemia was seen. All these factors were not significantly associated with raised HbA1c level in patients presenting with ischemic stroke.

Frequency of raised HbA1c level greater than the frequency reported in the study from Faisalabad however it was greater than the frequency reported in the study from Lahore This difference in frequency of raised HbA1c level was based on mythological aspects of the studies as well as cut points and operational definitions for the study outcome and most importantly difference in the sample size.

According to a review published by Capes et al.[12], acute Hyperglycemia predicted increased risk of in-hospital mortality after ischemic stroke in non-diabetic patients and increased risk of poor functional recovery in non-diabetic stroke survivors. The recent results of Nardi et al. are also inline with this conclusion.[13]

Study by Li et al. is one of the few studies systematically investigating the role of HbA1c on stroke outcome, regardless of a prestroke diagnosis of DM; their results show that elevated HbA1c level relates to stroke severity and poor prognosis in the whole study population; however, only patients with brainstem infarction were included in this study.[14]

Several previous studies have found worse

survival in patients with Hyperglycemia.[15,16,17,]

Some research groups have reported that Hyperglycemia is a determinant of worse clinical outcome in patients with ischemic stroke without DM, but not in those with DM, while others have found a deleterious effect of Hyperglycemia on survival regardless whether or not the patients had DM. Also, Hyperglycemia was not correlated with stroke severity in an independent manner, even though it has preliminarily been linked to induction of pro coagulant state and to neurotoxicity, due to pro-oxidative and pro-inflammatory effects.[18,19]

Results from two newly published studies also show that high HbA1c is independently associated with poor outcome 1 year after stroke, supporting our findings. Nevertheless, one of the studies, based on data from the Fukuoka Stroke Registry, only included patients with known DM; moreover, none of the studies investigated the effect of HbA1c on acute stroke severity.[20,21]

Evidence is compelling that increased stroke risk is associated with high levels of total cholesterol and low-density lipoprotein, and decreased high-density lipoprotein levels. In the Helsinki young stroke registry,[22] dyslipidemia was clearly the most prominent well documented risk factor. Sunanda in his study also shown that high mean levels of total cholesterol (<0.005) and very low-density lipoprotein (<0.0001), and Triglycerides (<0.0001) levels in patients of ischemic stroke with poor glycemic control when compared with good glycemic control and Non-diabetics ischemic stroke patients.[23,24]

It is has been suggested that diabetes mellitus represents just 'the measured tip of a much larger 'dysglycemic iceberg''.[25] Raised glucose levels in the circulation may speed up the process of atherosclerosis through putative mechanisms such as oxidative stress and protein glycation of vessel walls.[26] In patients with diabetes, reducing plasma HbA1c levels by tight glycaemia control lowers the risk of subsequent microvascular disease. However, the relation of reduced HbA1c levels with macro-vascular outcomes (e.g. stroke, ischemic heart disease, peripheral vascular disease) is less clear.[27]

Studies have concluded that a progressive relation between glucose concentrations and cardiovascular disease extends below the current threshold used to define diabetes mellitus.[28] Therefore, patients without diabetes with suboptimal HbA1c levels may have a level of dysglycaemia that may not meet the criteria for a diagnosis of diabetes mellitus, but may still contribute to an adverse postoperative outcome. Plasma HbA1c would be a more useful test for trying to identify these patients preoperatively than other tests, such as fasting plasma glucose level or an oral glucose tolerance test).[29] An increased HbA1c level reflects poor long term glycemic control and has specific implications for the structure and function of the vascular bed, including small and large cerebral vessels. Increased HbA1c level might also be a marker of poor compliance, indicating an unhealthy lifestyle.

CONCLUSION

Results of this study demonstrate a high frequency of raised HbA1c level in patients presenting with ischemic stroke i.e. 25%. So keeping in mind these findings it is recommended that stroke patients should also be screened for hyperglycemia or increased HbA1c so that patients can be prevented from development of permanent hyperglycemia or other complications associated with it.

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CORRECTION

The amendment of the Professional Vol: 24, No.09 (Prof-4000) titled: "Hemorrhoidectomy; stapled versus conventional hemorrhoidectomy in terms of postoperative pain and hospital stay" on page 1316 is as under;

INCORRECT	CORRECT
Shibber Ahmed[1] MBBS, FCPS Assistant Professor of Surgery Bakhtawar Amin Medical and Dental College Multan	**Shabbir Ahmad**[1] MBBS, FCPS Assistant Professor of Surgery Bakhtawar Amin Medical and Dental College Multan

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Naveed ur Rehman	Manuscript Writing	
2	Dr. Absar Alam	Data collection	
3	Dr. Kashif Rehman	Data collection, Proof read	