Relationship between diabetes mellitus and acute stroke: Predictive role of stress hyperglycemic ratio in mortality of acute stroke

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Abstract

Background: Stress induced hyperglycemia is one of the commonest metabolic disorder in Acute stroke. The general objective of the study is to determine the prevalence of stress induced hyperglycemia and the predictive value of Stress Hyperglycemic Ratio (SHR) on mortality in acute stroke.
Methodology: This study population included all the patients admitted into the acute stroke ward within the six- month study period at Lagos State University Teaching Hospital (LASUTH) Nigeria. Clinical and sociodemographic data such as age, diabetes mellitus status prior to stroke, brain imaging of confirmed stroke, random blood glucose at admission and glycated hemoglobin. The Stress Induced Hyperglycemic Ratio (SHR) was calculated.
Results: Most patients with DM had acute ischemic stroke (p value 0.005, OR (CI), 3.25 (1.40-7.64). The incidence of SIH was 35%. Over 60% of those who were discharged had no incidence of SIH, hence absence of SIH appears to be a good prognostic factor. Majority of those who died from acute stroke had higher glycated hemoglobin and random blood glucose . The SHR was not predictive of the type of stroke or the mortality in acute stroke.
Conclusion: Stress Hyperglycemic ratio (SHR) appears not to play a significant role on determining the type of stroke and mortality in acute stroke.

Relation entre le diabète sucré et l'AVC aigu : rôle prédictif du rapport hyperglycémique de stress dans la mortalité liée à l'AVC aigu

Résumé
Contexte de l'étude: L'hyperglycémie induite par le stress est l'un des troubles métaboliques les plus courants dans les accidents vasculaires cérébraux aigus. Déterminer la prévalence de l'hyperglycémie induite par le stress et la valeur prédictive du rapport hyperglycémique de stress (RSH) sur la mortalité lors d'accidents vasculaires cérébraux aigus.
Méthode de l'étude*:* Cette population étudiée comprenait tous les patients admis dans le service d'AVC aigu au cours de la période d'étude de six mois à l'hôpital universitaire de l'État de Lagos (LASUTH) au Nigéria. Données cliniques et sociodémographiques telles que l'âge, le statut du diabète sucré avant l'accident vasculaire cérébral, l'imagerie cérébrale d'un accident vasculaire cérébral confirmé, la glycémie aléatoire à l'admission et l'hémoglobine glyquée. Le rapport hyperglycémique induit par le stress (RHS) a été calculé.
Résultat de l'étude*:* La plupart des patients atteints de diabète ont eu un accident vasculaire cérébral ischémique aigu (valeur p 0,005, OR(IC), 3,25 (1,40-7,64). L'incidence de le RHS était de 35 %. Plus de 60 % de ceux qui ont obtenu leur congé n'avaient aucune incidence de Le RHS, donc L'absence de RHS semble être un bon facteur pronostique. La majorité des personnes décédées d'un AVC aigu avaient une hémoglobine glyquée et une glycémie aléatoire. Le RHS n'était pas prédictif du type d'AVC ni de la mortalité en cas d'AVC aigu.
Conclusion*:* Le rapport hyperglycémique de stress (RHS) ne semble pas jouer un rôle significatif dans la détermination du type d'accident vasculaire cérébral et de la mortalité en cas d'accident vasculaire cérébral aigu

INTRODUCTION

Dysglycemia is a common metabolic disorder in Acute Stroke. Stress Induced Hyperglycemia (SIH) is a complication of acute illness and it is one of the commonest dysglycemia reported in acute stroke even in the absence of diabetes mellitus (1). Stress induced hyperglycemia is associated with high risk of mortality in stroke (1). As a result, early diagnosis and use of glucose lowering medications including insulin reduces the degree of brain damage and mortality in acute stroke (2).

Diabetes is one of the established risk factors for stroke with associated poorer outcomes such as high mortality, repeat stroke, poor functional outcomes with longer hospital stay (3). Other risk factors of acute stroke are hypertension, dyslipidemia, hyperuricemia among others (3). Factors responsible for mortality in acute stroke are interwoven with an interplay of multiple risk factors contributing to increased incidence.

Various studies in Nigeria have shown the prevalence of diabetes mellitus to range between 0.8% to 4.4% in rural areas(4,5,6) while the urban areas reported higher prevalence of 4.6% to 7% (7,8,9). Uloko et al recently reported an overall prevalence of 5.77% in Nigeria (9). The International Diabetes Federation (IDF) projected a geometric rise in DM from 643 million in 2030 to 783 million in 2045 (10).

Stress Induced Hyperglycemia has been linked to increased severity and poorer outcome of stroke even in patients without previous history of diabetes mellitus (11,12). Also studies have shown association between SIH and the varied outcomes of stroke in patients with diabetes mellitus (11,13). There is currently no agreed definition of stress hyperglycemia and the patients are generally classified as known diabetes, newly diagnosed, and hospital-related hyperglycemia (14,15,16,17). The stress hyperglycemia ratio (SHR) is a new method for determining stress related hyperglycemia. It is calculated using the values of glycated hemoglobin (HBA1c) and random blood glucose after Stroke (18).

Few studies on patients with acute ischemic stroke and diabetes showed that the using SHR as indicators of stress hyperglycemia could be better predictors for the severity and poor outcome of stroke (19,20,21).

There are few reported studies on relationship of severity of diabetes mellitus in acute stroke (14,15,16,17). Few of the studies available showed the relationship of diabetes mellitus in acute stroke but there is paucity of data on predictive role of SHR on acute stroke in Nigeria (15,16,17,18,19). This study aims to demonstrate the relationship of severity of stress induced hyperglycemia and SHR in acute stroke with its predictive role in the mortality of stroke. This would guide the clinicians in the management of acute stroke

MATERIALS AND METHODS

This was a retrospective study conducted at the Lagos State University Teaching Hospital (LASUTH). The study population includes all the patients 18 years and above admitted into the acute stroke ward within the six- month study period between May 2023 to October 2023 with confirmed brain imaging of either ischemic or hemorrhagic stroke using CT or MRI scans.

The definition of SIH was random blood glucose greater than 140mg/dl (10). Also, new diagnosis of DM was made based on HBA1C greater or equal to 6.5% while prediabetes was HBA1c between 5.7% to 6.4%(10). The Stress Hyperglycemic Ratio (SHR) was calculated using the formula, glucose at admission (random glucose) ÷ estimated average glucose while estimated average glucose is calculated with (28.7 X HBA1c) ÷ 46.7(18).

The study was performed in line with the principles of the declaration of Helsinki. Ethical approval was obtained from the Health Research and Ethics Committee of LASUTH on the 17th May 2023 with approval number of LREC/06/10/2131. Clinical and sociodemographic data were retrieved from case note using the study questionnaire. These were age, sex, occupation, religion, marital status, diabetes mellitus status prior to stroke, complete blood count, brain imaging of confirmed stroke, random blood glucose and glycated hemoglobin.

The analysis was done using SPSS version 26 and a P value of < 0.05 was considered significant. Data were presented as descriptive statistics such as means, standard deviation, frequencies and percentages. Associations between variables were assessed using the chi-square test and Analysis of variance.

RESULTS

The total number of study population was 100. The table 1 shows majority of the patients were above 65years (44.0%). The mean age was 61.0 ± 13.4 while their age range was 35 to 90 years. There were more males than females (62% and 38%), 86% were married while 3% were single. The largest majority 54(54.0%) were

employed.

The table 2 shows 22% mortality in acute stroke while 78% was alive. Eight (17.8%) of the subjects who initially reported not being diabetic were found to be diabetic. Twenty-two of the subjects who were previously diabetic were not within the target glycated hemoglobin of 6.5% and less.

The prevalence of SIH as 35% in the study as shown in figure 1. The overall prevalence of prediabetes in acute stroke was 15% in this study as shown in table 3. There was higher prevalence of stroke in elderly patients which accounted for 43% of the study population. Patients with DM had more ischemic stroke {23(51.1%)}compared to hemorrhagic stroke {22 (48.9%)}. Stress induced hyperglycemia and SHR were not predictive of the type of stroke or mortality in acute stroke.

There was 0% mortality recorded in patients who were less than 45 years compared with 22% mortality in those greater than 45 years (p value 0.026). Highest percentage of mortality (81.8%) as seen in those with less than 14 days of admission (p value 0.013). Majority of those with less than 14 days of admission had diabetes with higher glycated hemoglobin of 7.60 ±1.76 compared with those with greater than 14 days of admission 8.97±2.89 which was statistically significant (p value 0.013). Also, they had higher random blood glucose (p value 0.036) as shown in table 4

Those who had SIH were mainly not previously diagnosed with diabetes mellitus (54.5%) compared with those with diabetes (8.9%) which was statistically significant (p value 0.001) as depicted in table 5.

DISCUSSION

Stress Induced Hyperglycemia is common in acute stroke and occurs in about 30-50% of patients without diabetes mellitus (23,24,25). This is similar to the findings in our study with over 50% of SIH occurring in non-diabetes patient.

Hyperglycemia has been associated with poor functional outcome and increasing mortality in acute stroke especially non diabetic patients (11,12,26). Greater than 60% of those that were alive had absence of SIH, hence the absence of SIH is a good prognostic factor in the mortality of acute stroke. However, calculated Stress Hyperglycemic Ratio (SHR) was not predictive of the type of stroke or the outcome of acute stroke.

Most DM patient had ischemic stroke compared to hemorrhagic stroke. This was similar to the findings by O'Donnell who reported higher odds ratio for ischemic stroke compared to hemorrhagic stroke in patient with DM (3). The presence DM and also the occurrence of SIH had influence on mortality of patients with acute stroke.

Majority of those with acute stroke admission duration less than 14 days had the highest mortality. This accounted for 72% of the total death. It is interesting to note that those with duration of admission less than 14 days had significantly higher glycated hemoglobin, random plasma glucose and overall average plasma glucose compared to those who survived acute stroke showing the role of hyperglycemia in mortality of acute stroke.

Increasing age was also associated with increased mortality and poor prognosis. This was similar to the findings by Kelly-Hayes M et al who demonstrated doubling effect of acute stroke with each decade after 45 years (27). The highest prevalence of stroke was seen in patients greater or equal to 65 years of age accounting for 43% of the total population. Also, increasing age has been shown to increase mortality in acute stroke. There was no mortality recorded in those less than 45 years. Hemorrhagic stroke occurred only in younger patients (less than 45 years). In our study the incidence of stroke was found to rise with increasing age.

The presence or absence of diagnosis of diabetes mellitus as a single risk factor was not predictive of the outcomes of acute stroke. This implies that the factors that influence the duration (14 days) and mortality in acute stroke are most likely multifactorial.

CONCLUSION

Stress Induced Hyperglycemia plays a vital role in mortality of acute stroke. However, Stress Hyperglycemic ratio (SHR) appears not to play a significant role in determining the type of stroke and mortality in acute stroke.

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Table 1: Sociodemographic characteristics of study participants

Variable	Frequency N= 100	Percentage (%)
Age Group (Yrs)		
? 45	15	15.0
45 – 64	41	41.0
= 65	44	44.0
Age range	**35 – 90**	
Mean ± SD	**61.0 ± 13.4**	
Sex		
Male	62	62.0
Female	38	38.0
Marital Status		
Married	86	86.0
Single	3	3.0
Widowed	11	11.0
Religion		
Christianity	79	79.0
Islam	20	20.0
Hindu	1	1.0
Occupation		
Clergy	2	2.0
Employed	54	54.0
Retired	40	40.0
Unemployed	4	4.0

Table 2: Clinical characteristics of subject with acute stroke

Variable	Frequency (N= 100)	Percentage (%)
Previous history of diabetes mellitus		
No	63	63.0
Yes	37	37..0
Previous history of hypertension		
No	25	25
Yes	75	75
Types of Strokes		
Hemorrhagic	62	62.0
Ischemic	38	38.0
Outcome of Strokes		
Dead	22	22.0
Alive	78	78.0
Diabetic glycemic Status(n=45)		
Previously Diagnosed	37	82.2
Newly Diagnosed	8	17.8
Glycemic Control(n=37)		
Controlled	15	40.5
Uncontrolled	22	59.5
Mean ± SD	**7.0 ± 2.7**	

Table 3: Relationship between clinical and biochemical factors and the type of acute stroke.

Parameters	Ischemic stroke Number (%)	Hemorrhagic stroke Number (%)	Total Number (%)	P value	OR (CI)
Age					
<45 years	0 (0.0)	15 (100)	15 (100)	**0.004**	
45-64 years	18(42.9)	24(57.1)	42 (100)		
=65 years	20 (46.5)	23(53.5)	43 (100)		
Sex					
Male	21 (33.9)	41(66.1)	62 (100)	0.277	0.633 (0.27-1.45)
Female	17 (44.7)	21(55.3)	38 (100)		
DM					
Yes	23 (51.1)	22(48.9)	45 (100)	**0.015**	**2.788 (1.212-6.412)**
No	15(27.3)	40(72.7)	55(100)		
Prediabetes					
Yes	4(26.7)	11(73.3)	15(100)	0.327	0.545 (0.160-1.855)
No	34 (40.0)	51 (60.0)	85(100)		
SIH					
Yes	12 (35.3)	22(64.7)	34 (100)	0.689	0.839 (0.365-1.982)
No	26 (39.4)	40(60.6)	66(100)		
SHR					
= 75%	4(33.3)	34(38.6)	38 (100)	0.723	0.794 (0.22-2.841)
=75%	8 (66.7)	54 (61.4)	62(100)		
Outcome					
Alive	30(38.5)	48(61.5)	78 (100)	0.858	1.094 (0.410-2.918)
Dead	8(36.4)	14 (63.6)	22(100)		
Duration of admission					
<14 days	5(41.7)	7(58.3)	12 (100)	0.780	1.190 (0.349-4.057)
= 14 days	33(37.5)	55(62.5)	88 (100)		

Table 4: Relationship between clinical and biochemical factors with the outcome of stroke

Clinical Parameters	Alive Number (%)	Dead Number (%)	Total Number (%)	P value (chi square)
Age				
<45 years	15 (100.0)	0.0 (0.0)	15 (100)	**0.026**
=45 years	63 (74.1)	22(25.9)	85 (100)	
DM				
Yes	35 (77.8)	10(22.2)	45 (100)	0.961
No	43(78.2)	12 (21.8)	55(100)	
SHR				
= 75%	10(83.3)	2(16.7)	12 (100)	0.634
=75%	68 (77.3)	20(22.7)	88(100)	
Duration of admission				
<14 days	6(50.0)	6(50.0)	78 (100)	**0.013**
= 14 days	72(81.8)	16(18.2)	22 (100)	
Biochemical Parameters	**<14 days (mean ±SD)**	**≥14 days (mean ±SD)**	**P value**	**Confidence interval**
HBA1C	8.97±2.89	7.60±1.76	**0.036**	6.62-7.84
FBS	150.40±37.38	133.68±44.84	0.431	122.10-149.16
SHR VALUES	1.33±0.36	1.26±0.35	0.667	1.16-1.37
RBS	271.40±130.66	185.45±59.10	**0.013**	172.68-218.20
Average glucose	210.68±82.81	154.27±50.64	**0.036**	143.29-178.36

Table 5: Relationship between stress induced hyperglycemia and clinical factors

Parameters	Presence Number (%)	Absence Number (%)	Total Number (%)	P value
Age				
<45 years	6 (40.0)	9 (60)	15 (100)	0.953
=45 years	28(32.9)	57(67.1)	85(100)	
Sex				
Male	17 (27.4)	45(72.6)	62 (100)	0.076
Female	17 (44.7)	21(55.3)	38 (100)	
DM				
Yes	4(8.9)	41(91.1)	45 (100)	**0.001**
No	30 (54.5)	25 (45.5)	55(100)	
Prediabetes				
Yes	5(33.3)	10(66.7)	15(100)	0.953
No	29(34.1)	56(65.9)	85(100)	
Outcomes				
Alive	30(38.5)	48(61.5)	78 (100)	0.076
Dead	4 (18.2)	18 (81.8)	22(100)	
Duration of admission				
<14 days	3(25.0)	9(75.0)	12 (100)	0.483
= 14 days	31(35.2)	57(64.8)	88 (100)	

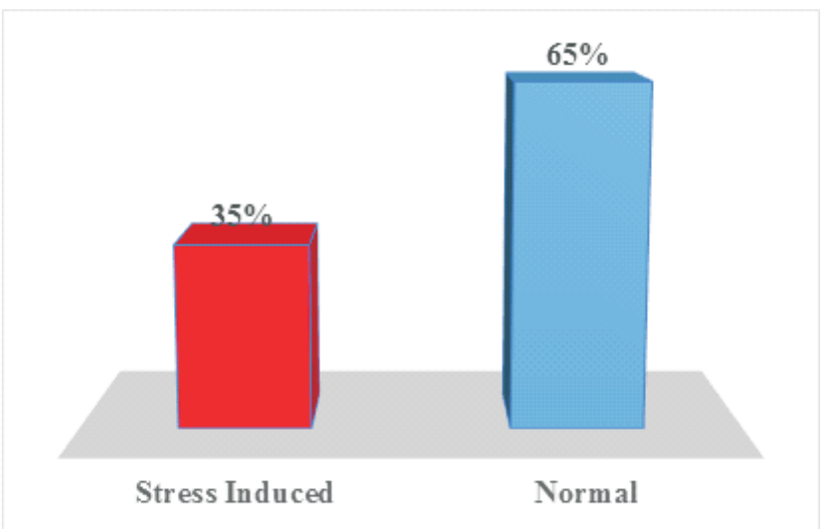

Figure 1: Prevalence of Stress Induced Hyperglycemia in Acute Stroke.

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