

Metabolic Disorders and Other Common Risk Factors in Acute Stroke: A Tertiary Hospital Experience

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Abstract

Background: Despite categorical milestones improvements in the prevention and treatment over the last decades, stroke is still a devastating disease. The case fatality of stroke is as high as 40%. Established “traditional” risk factors like hypertension, diabetes mellitus and dyslipidemia are common in addition to some modifiable risk factors like alcohol and smoking. Stroke patients with advanced renal function impairments are at high risk due to cardiovascular complications. Studies have shown that increased morbidity, mortality and disability are common in stroke patients with metabolic disorders or risk factors. **Methodology:** This is a cross sectional retrospective study of 95 patients admitted with acute stroke from June 2020 to July 2021 in the Lagos State University Hospital (LASUTH) Ikeja. The institution is a tertiary referral center. The inclusion criteria were patients with acute stroke who were admitted in the acute stroke wards within 24 hours of occurrence and had adequate clinical information and neuroimaging (CT/MRI) reports. Patients with space occupying lesions or head injury were excluded. The data was analyzed using SPSS 23.0. The analysis included frequency proportion, mean with standard deviation, percentage tables and suitable graphs. The Chi square test used to determine association among categorical variables. Statistical significance was taken as $P \leq 0.05$. **Result:** The mean age of the patients was 61.0 ± 13.4 with age range from 35 to 90 years. There were more males (63.2%) than females (36.8%). Sixty-five (65%) were admitted with hemorrhagic stroke while 35 (35%) had ischemic stroke. The risks factors identified were hypertension (71%), diabetes mellitus (35%), 18 (51.4%) of the DM were controlled while 25 (26.3%) had dyslipidemia. Eight subjects (8.0%) had eGFR of 30-59 ml/min. Twenty (20%) took significant alcohol while 8 (8.4%) had significant smoking history. **Conclusion:** The study showed that hemorrhagic stroke was more prevalent than ischemic stroke. The commonest risk factors identified were diabetes mellitus, hypertension, dyslipidemia and smoking. There was a statistically significant association between hypertension ($P=0.03$), Medical history of diabetes ($P=0.02$) and stroke types. Patients who had history of diabetes mellitus are 3 times likely to develop ischemic stroke CI at 95% 1.118– 8.141.

Keywords: Stroke, Metabolic Disorders, Risk factors

INTRODUCTION

Despite categorical milestones improvements in primary prevention strategies and acute treatment over the last decades, stroke is still a devastating disease.¹ In the European Union (EU), stroke is the second most common cause of death and a leading cause of adult disability.² Studies in Asia have reported varying levels of prevalence, mortality and disease burden.

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The overall incidence of stroke in Asia varied between 116 and 483/100 000 per year.³ In Nigeria, the frequency of stroke hospitalization ranges between 0.9 to 4.0% and 0.5 to 45% of neurological admissions. It's also responsible for about 3.7% of emergency medical admissions and found to be eighth leading cause of death. Regarding all types of strokes, 88% are classified as ischemic, and remaining 12% comprise of haemorrhagic, either sub-arachnoid (9%) or intra-cerebral (3%)⁴

Hypertension (HTN), dyslipidemia, diabetes mellitus (DM), cigarette smoking and sedentary lifestyle are all modifiable risk factors that predispose individuals to stroke.⁵ Dyslipidemia is the presence of abnormal levels of lipids or lipoproteins in the blood, which includes elevated low density lipoprotein cholesterol (LDL-C), elevated triglyceride (TG) and reduced high density lipoprotein cholesterol (HDL-C).⁶ Dyslipidemia is a risk factor for cerebral infarction by promoting formation of atherosclerosis.⁷ Hypertension is the most important etiological risk factor for stroke.⁸ Diabetes is notably a paramount cause of stroke by causing metabolic derangement.⁹

Elevated values of blood urea and creatinine are biochemical markers of glomerular disease. It is a well-established fact that patients with chronic kidney disease are prone to cardiovascular events like stroke with its attendant morbidity and mortality.¹⁰ Patients with chronic kidney disease (CKD) stages 3-5 have worse survival and diminished functional outcomes following stroke.¹¹ The risk of stroke is 5-30 times higher in patients with chronic kidney disease, especially on dialysis.^{11,12} Case fatality rates are also higher reaching almost 90%¹². A recent meta-analysis incorporating data from 33 studies reported a 43% independent risk of stroke with eGFR < 60mls/min.¹² Smoking plays a significant independent risk factor for ischemic stroke, and the pathogenesis is multifactorial: modification of lipid chemical, hyperfibrinogenemia, reduced fibrinolytic activity polycythemia, and aggregation of platelets thus leading to formation of fat laden plaques and atherosclerosis.¹³

This study aims to identify metabolic disorder and other risk factors known to cause acute stroke in a bid to detect them earlier and advert cardiovascular morbidity and mortality.

METHODOLOGY

This is a hospital based cross sectional retrospective

study of 95 patients with acute stroke admitted in the acute stroke ward of the neurology unit of the Lagos State University Teaching Hospital (LASUTH) Ikeja from June 2020 to July 2021. The institution is a tertiary referral center. Consent and approval for the study was obtained from the ethical committee of the institution. Data was collected from case records of the patients using a pre-structured questionnaire. The inclusion criteria were all patients with acute stroke admitted within 48 hours of occurrence and had adequate clinical documentation and neuroimaging reports (CT scan or MRI). Patients who have history of hypertension, diabetes mellitus, dyslipidemia, smoking and alcohol were included. Patients with history of space occupying lesions or head injury were excluded.

Dyslipidemia was defined using the Third Report of the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP-III) guideline. Diabetes was diagnosed if patient had a history, was on drug therapy for diabetes and or laboratory investigations was indicative of diabetes and not stress hyperglycemia. Patients who were normoglycemic at the time of presentation but with history of diabetes or on oral hypoglycaemic agents or insulin were also classified as diabetic.

Stress hyperglycemia was defined as blood glucose of 180mg/dl or above in patients without pre-existing diabetes and glycosylated hemoglobin results were within the normal range. Significant smoking history was taken as more than 20 pack years in both sexes. Significant alcohol history is defined as taking more than 21 units per week in males and more than 14iu per week for females.

Estimated glomerular filtration rate was (eGFR) was deduced using the Modification of Diet in Renal Disease (MDRD-eGFR) equation. Data obtained from the case records were analysed using SPSS 23.0. The analysis included frequency proportion, mean with standard deviation, percentage tables and suitable graphs. Chi square test used to determine association between variables. Statistical significance was taken as $P \leq 0.05$.

Note: (NCEP ATP III) National cholesterol education programme adult treatment panel prevalence of the metabolic syndrome in postmenopausal Latin American women. *Climacteric*. 2007 Jan 1;10(2):164-70.

MDRD (Modification of diet in renal disease) Van Biesen W, Vanholder R, Veys N, Verbeke F, Delanghe J, De Bacquer D, Lameire N. The importance of standardization of creatinine in the

implementation of guidelines and recommendations for CKD: implications for CKD management programmes. Nephrology Dialysis Transplantation. 2006 Jan 1;21(1):77-83.

RESULTS

A total of 95 patients recruited from stroke wards at Lagos state university teaching hospital was used in this study. The age range was 35 to 90 years. The highest majority of the patients 36(36.0%) were within the age group of 65 to 79 years, while the lowest number of patients 7(7.0%) were within the age of 80 to 94 years. The mean age of the patients was 61.0 ± 13.4.

Table 1: Demographic characteristics of the patients

Variable	Frequency N= 95	Percentage (%)
Age Range	35 - 90	
Age Group		
☐☐☐	62	65.3
>65	33	34.7
Mean ± SD	61.0 ± 13.4	
Sex		
Male	60	63.2
Female	35	36.8
Marital Status		
Married	81	85.3
Single	3	3.2
Widowed	11	11.5
Religion		
Christianity	74	77.9
Islam	20	21.0
Hindu	1	1.1
Occupation		
Civil servant	14	14.7
Retired	38	40.0
self employed	37	39.0
Unemployed	4	4.2
Others	2	2.1

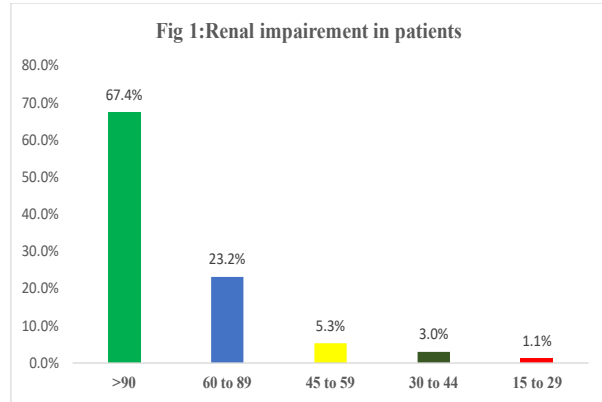


Fig 1: Renal Impairment in Patients in the 5 stages of CKD
Table 4: Glycemic control among diabetes patients

Variable	Frequency n= 35	Percentage (%)
HBA1C FOR DM PTS		
Controlled	18	51.4
Uncontrolled	17	48.6
Mean ± SD	6.1 ± 3.6	

DM=Diabetes Mellitus, PTS= Patients.

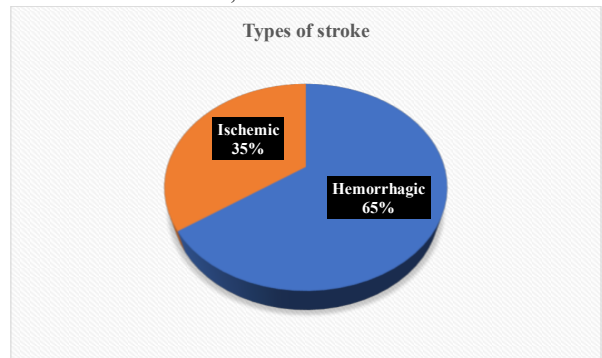


Fig 2: Most common Types of Strokes.

Table 2: Clinical characteristics of patients with stroke

Variable	Freq N= 95	Percentage (%)
Significant alcohol intake		
No	76	80.0
Yes	19	20.0
Significant smoking		
No	87	91.6
Yes	8	8.4
Previous history of diabetes mellitus		
No	60	63.2
Yes	35	36.8
Previous history of hypertension		
No	24	25.3
Yes	71	74.7
Previous history of Stroke		
No	85	89.5
Yes	10	10.5
First degree family history of diabetic mellitus		
No	84	88.4
Yes	11	11.6
First degree family history of hypertension		
No	83	87.4
Yes	12	12.6
First degree family history of Stroke		
No	94	98.9
Yes	1	1.1
Patients with more than one risk factors		
HTN and DM	30	31.6
HTN, DM, DYSL	12	12.6
HTN, DM, DYSL, STR	4	4.2
HTN, DM, DYSL, STR, ALCH	2	2.1
HTN, DM, DYSL, STR, ALCH, SMOK	1	1.1
NO Established risk factors	46	48.4

HTN=Hypertension, DM= Diabetes Mellitus, DYSL=Dyslipidemia, ALCH= Significant Alcohol, STR=Stroke, SMOK= Significant Smoking.

Table 3: Metabolic Disorder Associated with Patients

Variable	Frequency N= 95	Percentage (%)
FBS (mg/dl)		
Hyperglycemia	26	27.4
Normal	69	72.6
Stress induced Hyperglycemia	0	00.0
Mean ± SD	94.0 ± 57.9	
Serum lipid(mg/dl)		
Dyslipidemia	25	26.3
Normal	70	73.7

The mean fasting blood sugar of the patients was 94.0 ± 57.9mg/dl. More than half of the patients 25(26.3%) presented with dyslipidemia.

Table 5: Association between risk factors and stroke.

Variable	Stroke (Freq (%) (N=95)		X ²	Df	P=Value
	Hemorrhagic (n=62)	Ischemic (n=33)			
Age Group					
≤65	43(69.4)	19(30.6)	1.138	1	0.178
>65	19(57.6)	14(42.4)			
Sex					
Female	21(60.0)	14(40.0)	0.677	1	0.273
Male	41(68.3)	19(31.7)			
Hypertension					
Not hypertensive	20(83.3)	4(16.7)	4.625	1	0.025*
Hypertensive	42(59.2)	29(40.8)			
Significant alcohol intake					
Non-User	51(67.1)	25(32.9)	0.569	1	0.310
User	11(57.9)	8(42.1)			
Significant smoking					
Non-Smokers	58(66.7)	29(33.3)	0.898	1	0.281
Smokers	4(50.0)	4(50.0)			
Medical History of DM					
None Diabetic	46(76.7)	14(23.3)	9.342	1	0.02*
Known diabetic	16(45.7)	19(54.3)			

X²= Chi Square, DF= Degree of freedom, * = Statistically significant, DM= Diabetes Mellitus.

Table 6: Binary logistic regression between diabetes and stroke.

Predictor	Coefficient	df	Sig.	Odd ratio	95% C.I for Odd ratio	
					Lower	Upper
Diabetics	1.104	1	.029	3.017	1.118	8.141

Patients who had medical history of diabetes mellitus are 3times likely to develop ischemic stroke CI at 95% 1.118 – 8.141.

DISCUSSION

Stroke incidence is related to both modifiable and non-modifiable risk factors. Aging is a known non-modifiable risk factor for incident stroke.¹⁴ According to a previous report by Palomeras Soler E and Casado Ruiz V it's been noted that the level of blood total cholesterol in both men and women increases until the age of 60 to 65 years and high cholesterol is a known risk factor for the incidence of stroke.¹⁴ In the current study, the majority of the patients were younger than 65years old, this finding differs from the result obtained by Yousufuddin M et al which noted approximately three-quarters of all strokes patients were aged ≥65 years, but somewhat similar to the result submitted by Sanuade OA et al in Ghana and Morikawa Y et al in Japan where a high incidence of stroke was reported in patients within 35–44-years old age group.^{15,16,17} The incidence rate and outcome of

stroke has been reported to vary across gender.^{18,19} In the present study, there were more male patients than females which corresponds with a research done by Danesi M et al in southwest Nigeria but not in line with the study conducted in Ghana and by Onwuchekwa AC et al in Niger Delta, South-South Nigeria.^{16,20,21} This may be because women are more sensitive to health information and health-seeking behaviors whereas the male are more likely to engage in more risk factors for stroke like cigarette smoking which is also an established risk factor for stroke.^{22,23}

Modifiable risk factors like smoking, harmful alcohol use, unhealthy diet, physical inactivity, hypertension, diabetes mellitus and dyslipidemia has been established to be associated with stroke.²⁴ Cigarette smoking is noted to increase risk of stroke, specifically Pan B et al in a meta-analysis found a 12% increase risk of stroke for each increment of 5 cigarette per day.²⁵ The prevalence of smokers recorded in the current study is lower than the prevalence submitted in another study by Parikh NS et al in the United State.²⁶ Correspondingly, heavy alcohol consumption increases the relative risk of any stroke while light or moderate alcohol consumption has been shown to be protective against ischemic stroke.²⁷ The prevalence of alcohol consumption reported in the present study differs from result obtained a retrospective analysis of 143 records by Abdul-Afeez SO et al. as well in a similar Mediterranean cohort study.^{28,29}

Hypertension has been reported to increase the risk of stroke by causing blocking or bursting of blood vessels that supply blood and oxygen to the brain leading to ischemic or hemorrhagic stroke respectively.³⁰ In the current study, hypertension accounted for the highest risk factor of stroke. This is in concordance with the findings by Habibi-Koolae M et al.³¹ Previous history of stroke is a known risk factor for the recurrence of stroke, the prevalence of patients with previous history of stroke in the present study is 10.5% however higher prevalence were reported at University College Hospital, Ibadan South-West Nigeria and in Pakistan^{28,32}

Stroke is known to be more prevalent in patients with chronic kidney disease (CKD) than in the general population, chronic kidney disease and cerebrovascular disease (CVD) share similar traditional cardiovascular risk factors.³³ In our study, 5.3% patient with stroke were found to present with stage 3a chronic kidney disease.

Dyslipidemia is a notable risk factor for cardiovascular diseases and its association with the incidence of acute stroke is well established. Excess

blood cholesterol may accumulate in the wall of the artery and thus narrowing the arteries resulting to atherosclerosis which can block the flow of blood or cause the blood to clot consequently leading to ischemic stroke³⁴ The present study finds a prevalence of dyslipidemia lower than that submitted by Olamoyegun MA et al in Ogbomoso, southwest Nigeria and Mahdi Habibi-koolae et al. in Iran.^{31,35} Previous report has noted that hyperglycemia in acute stroke patients promotes increase in cerebral infarct size and exacerbate neurologic outcome both in presence and without preexisting diabetes mellitus (stress hyperglycemia). Stress hyperglycemia could occur as a transient cause of elevated blood sugar in acute stroke due to release of hormones like cortisol and catecholamines³⁶ Incidentally, our study did not record any patients with stress hyperglycemia nor newly diagnosed diabetes mellitus patients with stroke.

The World Health Organization (WHO) and American Diabetes Association have recognized HbA1c as an additional method for diagnosing DM apart from being used to monitor its control during management. Glycosylated hemoglobin (HbA1c) \geq 6.5% is categorized as uncontrolled glycemic.³⁷ In the current study, more than half of the patients who are diabetic presented with uncontrolled glycemic level, this result is however not consistent with the result obtained in a similar study in Lagos by Ogbera AO et al.³⁸

Generally, strokes have different subtypes, it could either be classified as Hemorrhagic, and ischemic or sub-arachnoid haemorrhage stroke, the result from the current study reveals that the majority of the patient had hemorrhagic stroke which is not in agreement with the result obtained in previous study carried out in Zaria north west Nigeria³⁹ but was in accord with another study carried out in Sokoto north west Nigeria where hemorrhagic stroke was the commonest type of stroke.⁴⁰

CONCLUSION

Our study highlights hypertension and diabetes mellitus being prominent modifiable risk factors for the development of stroke however smoking, alcohol and dyslipidemia were not found to be significantly associated with acute stroke in our study. It is pertinent to identify and manage this group of patients at risk of acute strokes promptly and adequately.

Limitations

Our research is a retrospective. Population study is comparatively small, and this may not reflect true outcome obtainable in other studies also most of the patients could not afford brain imaging due to financial constraints.

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