ORIGINAL ARTICLE

Stroke risk factors, subtypes, and 30-day case fatality in Abuja, Nigeria

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ABSTRACT

Background: Stroke is the second leading cause of death and the leading cause of adult disability worldwide. A better understanding of stroke risk factors and outcome may help guide efforts at reducing the community burden of stroke. This study aimed to understand stroke risk factors, imaging subtypes, and 30-day outcomes among adult Nigerians. **Materials and Methods:** We prospectively recruited all patients presenting with acute stroke at the National Hospital Abuja between January 2010 and June 2012. We assessed clinical and laboratory variables, as well as brain computerized tomography, magnetic resonance imaging, and carotid Doppler ultrasound scans. We also assessed case fatality and functional outcome at 30 days after stroke. **Results:** Of 272 patients studied, 168 (61.8%) were males. Age at presentation (mean ± standard deviation) was 56.4 ± 12.7 years in males and 52.9 ± 14.8 years in females (P = 0.039). Neuroimaging was obtained in 96.7% patients, revealing cerebral infarction (61.8%), intracerebral hemorrhage (ICH) (34.8%), and subarachnoid hemorrhage (SAH) (3.4%). Carotid plaques or stenosis ≥50% were detected in 53.2% patients with cerebral infarction. Stroke risk factors included hypertension (82.7%), obesity (32.6%), diabetes (23.5%), hyperlipidemia (18.4%), atrial fibrillation (9.2%), and cigarette smoking (7.7%). At 30 days after stroke, case-fatality rate was 18.8%, whereas modified Rankin Scale (mRS) scores for cerebral infarction, ICH, and SAH were 3.71, 4.21, and 4.56, respectively. Atrial fibrillation, a previous stroke, and age older than 50 years were all associated with worse mRS scores at 30 days. **Conclusion:** Although hypertension, obesity, diabetes mellitus, and atrial fibrillation were important stroke risk factors, in many patients, these were detected only after a stroke. While the commonest stroke subtype was cerebral infarction, observed in almost two-third of patients, SAH was associated with the highest case-fatality rate at 30 days of 44.4%. Larger population-based studies may provide additional data on stroke incidence and outcome among Nigerians.

Key words: Case fatality, cerebral infarction, hypertension, Nigeria, stroke

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INTRODUCTION

Stroke is the second leading cause of death and the leading cause of adult disability worldwide.[1] Stroke prevention strategies depend on risk factor modification, which is possible with knowledge derived from clinical studies. Such studies employ brain imaging to exclude stroke mimics and classify stroke subtypes.[2] Neuroimaging also has important implications for clinical practice. It aids decisions regarding acute stroke care, the extent of laboratory investigations, and the prediction of likely outcomes.

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Unfortunately, most studies on stroke in Nigeria involve little or no imaging protocols,[3-8] largely because most health centers lack facilities for computerized tomography (CT) scanning, magnetic resonance imaging (MRI), and carotid Doppler ultrasound scanning. Often, where those facilities are available, they are unaffordable.[4,7]

In two studies from Southwest Nigeria,[4,6] only 2 of 101 and none of 708 patients with suspected stroke had brain CT scans. In other studies from Northwest[7] and central[8] Nigeria, brain scans were obtained in only 6 of 81 and none of 76 patients. One study[9] did not describe imaging findings altogether, and it is unclear whether patients had had brain scans. Owing to these limitations, most studies rely on World Health Organization (WHO) criteria and the Siriraj Stroke Score to distinguish between cerebral infarction and hemorrhage.[6,7,9] However, the sensitivity and specificity of both scores are as low as 35-63%, according to validation studies using brain CT scans as the gold standard.[10,11] Furthermore, stroke scores do not exclude cerebral abscesses or tumors mimicking stroke; they also do not distinguish subarachnoid hemorrhage (SAH) from intracerebral hemorrhage (ICH).

Thus, current knowledge on stroke in Nigeria may be incomplete, and may not represent the profile of patients observed in routine clinical practice. To address this issue, we performed a prospective study at the National Hospital Abuja, Nigeria. We aimed to ascertain stroke risk factors, clinical and imaging subtypes, 30-day fatality, and functional outcome in a large adult cohort.

MATERIALS AND METHODS

This was a prospective study conducted at the National Hospital, a tertiary referral hospital in Abuja, Nigeria's Federal Capital Territory (FCT). We enrolled all patients with acute stroke presenting to the emergency department, intensive care unit, and in-patient wards of the hospital between January 2010 and June 30, 2012. Ethical clearance was obtained from the hospital research ethics committee, while patients or their proxies signed informed consent.

Demographic, clinical, and laboratory data were obtained from patients or their proxies and entered in a structured datasheet. Patients were interviewed and examined by two neurologists, who noted education status and pre-morbid history of prior stroke or transient ischemic attack, hypertension, diabetes, hyperlipidemia, atrial fibrillation, sickle cell disease, congestive heart failure, cigarette smoking, alcohol use, and use of prescription drugs. Examination findings noted included body mass index (BMI), blood pressure, and cardiovascular and neurologic signs at admission and during in-patient care.

Laboratory investigations included fasting plasma glucose and lipid profile, serum chemistry, full blood count, erythrocyte sedimentation rate (ESR), and screening for human immunodeficiency virus (HIV) types 1 and 2 infections. Young stroke patients (age ≤50 years) had further tests, including hemoglobin genotype, plasma homocysteine, serum anticardiolipin antibodies, and proteins C and S and antithrombin-III assays.

Stroke was defined according to WHO criteria.[12] Obesity was defined as a BMI of 30 kg/m^2 or greater. Hypertension was defined as a previous physician diagnosis of hypertension or blood pressure readings consistently ≥140/90 mmHg. Diabetes was defined as a previous physician diagnosis or fasting plasma glucose ≥7 mmol/L. Hyperlipidemia was deemed to be present if a patient had been taking lipid-lowering agents or had total cholesterol >240 mg/dl, triglycerides >200 mg/dl, or low-density lipoprotein cholesterol >160 mg/dl, according to Adult Treatment Panel-III (ATP-III) guidelines of the National Cholesterol Education Program (NCEP).[13]

Brain imaging was performed with CT or MRI. To classify cerebral infarction (CI), we adopted the Oxfordshire Community Stroke Project (OCSP) classification by Bamford *et al*.,[2] which uses imaging and clinical criteria to categorize strokes into total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), posterior circulation infarcts (POCI), and lacunar infarcts (LACI). ICH and SAH were classified according to the anatomical site of bleed on brain scans.

Carotid Doppler ultrasound scanning was performed using a power Doppler scanner. Abnormalities noted in the common and internal carotid arteries included intimal thickening, presence of atheromatous plaques, and carotid lumen stenosis. These were graded according to the Society of Radiologists in Ultrasound Consensus Conference recommendations.[14]

Treatment outcomes were assessed with the modified Rankin Scale (mRS), which was administered at 1 month after stroke, either during in-patient care or at the clinic. Discharged patients were booked for follow-up at the neurology clinic, and caregivers were contacted on telephone to ascertain the reason for missed appointments. Record was made of all deaths (and their causes) within 30 days of stroke during in-hospital care and after discharge. In ascertaining causes of death, we examined medical records and nursing charts, and interviewed doctors, nursing staff, and family members of the deceased who were present at the time of death.

To identify stroke patients who may have died before a neurologic consultation, a daily review was made of all deaths recorded at the emergency department, neurosurgical beds, and the intensive care unit (ICU) throughout the study period.

Statistical analysis was performed with statistical package for the social sciences (SPSS) version 14.0 software. Means of continuous variables were compared using Student's unpaired *t* test, whereas categorical variables were analyzed by the Chi-square test. *P* values less than 0.05 were considered significant.

RESULTS

A total of 272 patients presented with acute stroke, of whom 168 (61.8%) were males, thereby giving a male-to-female ratio of 1.6:1. Age at presentation was 56.4 ± 12.7 years (mean ± SD) in males and 52.9 ± 14.8

years in females, a difference that was statistically significant (P = 0.039). Other clinical and laboratory variables are shown in Tables 1 and 2.

Approximately 45% patients presented first to our hospital, whereas 55% were referred from other hospitals. Brain CT or MRI scans were obtained in 263 patients, representing 96.7% of the study population. These showed 61.8% patients had CI, 34.7% had ICH, and 3.4% had SAH. Nine patients did not have brain scans, owing to financial constraints (three patients), unstable clinical states (four patients), and self-discharge (two patients).

We admitted 91.2% patients, whereas 8.8% were seen as outpatients. Patients spent a median of 11 days and a mean of 18.2 days before death or discharge. Hospital stay was longest for SAH patients (51.3 days), compared to CI (18.1 days) or ICH (13.9 days) patients.

Among 163 patients with ischemic stroke, stroke subtypes composed of TACI (19.9%), PACI (43.5%), POCI (17.4%) and LACI (19.3%). In those with ICH, lobar hemorrhage was most common (35.1%), followed by bleeding at the basal ganglia (28.7%), thalami (18.1%), pons (9.6%), cerebellum (5.3%) and midbrain (2.1%). Three patients bled at multiple sites.

Of the nine patients with SAH, CT, or MR angiography was performed in seven, and revealed abnormalities in three. These were an arterio-venous malformation, a posterior communicating artery aneurysm and multiple aneurysms of anterior cerebral arteries.

Carotid Doppler ultrasound scanning was performed on 47 patients with CI, and showed abnormalities amongst 30. Seventeen patients had atheromatous plaques, while 26 had lumen stenosis involving carotid arteries ipsilateral to CI. In three patients, stenosis involved the contralateral carotids only. One patient had an ipsilateral carotid body tumor, but died before histologic confirmation.

Atrial fibrillation was prevalent among 25 patients, of

Table 1: Clinical and laboratory profile of acute stroke patients

Age distribution	All patients (*n*=272)	Men (*n*=168)	Women (*n*=104)	*P* value
Age, years (mean±SD)	55.1±13.6	56.4±12.7	52.9±14.8	0.039
Age range in years, number (%)				
25-34	17 (6.2)	5 (3.0)	12 (11.5)	
35-44	44 (16.2)	25 (14.9)	19 (18.3)	
45-54	78 (28.7)	50 (29.8)	28 (26.9)	
55-64	61 (22.4)	41 (24.4)	20 (19.2)	
65-74	48 (17.6)	33 (19.6)	15 (14.4)	
75-84	21 (7.7)	13 (7.7)	8 (7.7)	
≥85	3 (1.1)	1 (0.6)	2 (1.9)	
Physical and laboratory findings (mean±SD)				
Body mass index, kg/m^2	31.9±5.3	30.9±3.9	33.2±6.5	0.20
Systolic BP, mmHg	158.2±35.8	158.6±36.3	157.6±35.2	0.81
Diastolic BP, mmHg	95.6±22.0	96.9±23.7	93.5±18.8	0.24
Fasting glucose, mmol/L	6.22±2.27	6.06±2.01	6.45±2.62	0.39
Total cholesterol, mg/dl	195.7±53.3	189.2±51.0	206.4±55.7	0.03
HDL cholesterol, mg/dl	46.5±19.1	44.6±19.7	48.6±18.3	0.37
LDL cholesterol, mg/dl	124.1±46.6	120.4±45.1	130.4±48.7	0.20
Triglycerides, mg/dl	118.7±57.6	113.6±51.1	127.4±66.7	0.13

BP – Blood pressure; SD – Standard deviation; LDL – Low-density lipoprotein; HDL – High-density lipoprotein

Table 2: Prevalence of classic stroke risk factors among acute stroke patients

Risk factor, *n* (%)	All patients (*n*=272)	Men (*n*=168)	Women (*n*=104)	*P* value
History of TIA	10 (3.7)	4 (2.4)	6 (5.8)	0.35
Previous stroke	51 (18.8)	34 (20.2)	17 (16.3)	0.43
Obesity	48/147 (32.6)	24/94 (25.5)	24/53 (45.3)	0.018
Current cigarette smoking	21 (7.7)	20 (11.9)	1 (1.0)	0.001
Hypertension	225 (82.7)	142 (84.5)	83 (79.8)	0.20
Diabetes mellitus	64 (23.5)	39 (23.2)	25 (24.0)	0.49
Hyperlipidemia	50 (18.4)	29 (17.3)	21 (20.2)	0.63
Atrial fibrillation	25 (9.2)	18 (10.7)	7 (6.7)	0.38
Congestive heart failure	7 (2.6)	5 (3.0)	2 (1.9)	0.43
HIV infection	10 (3.7)	4 (2.4)	6 (5.8)	0.19
Carotid plaque/stenosis≥50%	25/47 (53.2)	15/27 (55.5)	10/20 (50.0)	0.52

HIV – Human immunodeficiency virus; TIA – Transient ischemic attack whom one had been on warfarin and two had been taking aspirin at the time of stroke. None of the other 22 patients had been on anticoagulant or antiplatelet therapy.

Of 111 young stroke patients, 27 had no classic risk factors for CI or ICH, such as hypertension, diabetes, hyperlipidemia, atrial fibrillation and cigarette smoking. In this group of cryptogenic stroke, one patient had hyperhomocysteinemia but all others tested negative for thrombophilia screening and sickle cell disease.

Among 248 patients admitted for acute care, 49 died in the hospital within 30 days of a stroke, giving an in-hospital mortality rate of 19.8%. While two other patients died within 30 days of a stroke after discharge from hospital, none of the 24 cases seen as out-patients died within that period.

Thus, case fatality rate at one month was 51/272 (18.8%) for all strokes, and was higher for SAH (44.4%), compared to ICH (31.9%) or CI (8.0%) (P = 0.001). Half of all deaths (48.9%) occurred within 3 days of admission and 81% occurred in the first week. Causes of death included neurologic deterioration in 64.0% (i.e., massive cerebral edema, shift of midline structures, or herniation/compression of the brainstem), aspiration pneumonia or sepsis (10.0%), cardiac arrest (i.e., ventricular fibrillation or asystole; 4.0%), pulmonary edema (4.0%), pulmonary embolism (4.0%), multi-organ failure (4.0%) and unknown (10.0%). No patient had an autopsy.

Mean mRS scores at 30 days were 3.71, 4.21, and 4.56 for CI, ICH, and SAH, respectively. Mean mRS scores were not different between males and females (3.91 ± 1.67 vs. 3.95 ± 1.57; P = 0.877). To identify the effects of other variables on 30-day outcome, we compared patients with mRS scores of 0-2 to those with scores of 3-6, which indicate good and poor outcomes, respectively [Table 3]. Factors associated with poor outcome included a previous stroke, age older than 50 years and presence of atrial fibrillation. There was a trend for good outcome in those with tertiary education, but this effect did not reach statistical significance.

DISCUSSION

The age and gender distribution of our patients are consistent with previous findings in urban centres.[7,8,15] It would seem stroke affects younger Nigerians than Tanzanians,[16] African Americans and US Caucasians.[17] Possible explanations are a younger age of the Nigerian population and the cosmopolitan nature of Abuja, which attracts still younger people seeking jobs.

In this study, CI was the most common stroke subtype. Among patients with CI, we found PACI, TACI, LACI, and POCI to be significant in that order. In the original OCSP study,[2] Bamford *et al*. reported similar findings, except for TACI, which was least common in Oxfordshire but second in prevalence in our study. This was not surprising, since a large number of our patients had unrecognized vascular risk factors. This group would likely have extensive lipohyalinosis and atherosclerosis of cervical and cerebral arteries, resulting in a high proportion of TACI in the event of a CI.

Our findings also differed only slightly from those of the INTERSTROKE study, a multinational case-control study of stroke risk factors across 22 high and low-income countries, including Nigeria, where four centers had participated.[18] In that study, ischemic stroke subtypes were PACI, LACI, POCI and TACI, in order of prevalence. Again, this disparity with our findings was likely due to more advanced atherosclerosis among our cohort, since INTERSTROKE involved patients in high-income countries with better control of vascular risk factors.

We found hypertension to be the most prevalent risk factor for stroke, being present in four-fifths of our patients. This was consistent with previous findings in Nigeria and

Table 3: Effects of demographic and clinical variables on 30-day outcome among patients with cerebral infarction or hemorrhage

Demographic/clinical variable	Good outcome (mRS 0-2) (%)	Poor outcome (mRS 3-6) (%)	*P* value
Female gender	40.9	40.4	1.00
Age≤50 years	59.1	37.9	0.02
Tertiary education	59.5	43.1	0.08
History of TIA	8.3	9.2	1.00
Previous stroke	2.3	25.6	0.001
Current cigarette smoking	6.8	8.3	1.00
Obesity	38.7	33.8	0.66
Diabetes	15.9	21.1	0.53
Hypertension	88.6	80.1	0.27
Hyperlipidemia	20.5	17.4	0.66
Atrial fibrillation	0.0	15.4	0.008
Congestive heart failure	0.0	9.1	0.58
HIV infection	2.3	3.7	1.00

HIV – Human immunodeficiency virus; mRS – modified Rankin scale; TIA – Transient ischemic attack. Tertiary education denotes a university degree or a polytechnic higher national diploma elsewhere.[8,15] Indeed, a meta-analysis of several studies has found a continuous and graded relationship between blood pressure and stroke risk in many populations, with higher levels of blood pressure conferring greater risks of stroke in hypertensive and normotensive subjects.[19] Antihypertensive drug treatment has been shown to reduce stroke risk by as much as 32%.[20] Unfortunately, a fifth of hypertensive subjects in our cohort had been unaware of their condition before they had a stroke. This suggests the need for better efforts at detecting and treating hypertension in Nigeria.

Yet, under-diagnosis of vascular risk factors is not limited to sub-Saharan Africa. A study in Southeastern United States has detected unrecognized hypertension and dyslipidemia among 18.7% and 59.1% of stroke survivors, respectively.[21]

Diabetes mellitus was prevalent in a quarter of our patients. Similar findings were reported in INTERSTROKE, in which diabetes was prevalent among 21% patients with ischemic stroke, and was responsible for 5% and 7.9% of the total population attributable risks of stroke, and ischemic stroke, respectively.[18]

Karaye *et al*. reported a 67.9% prevalence of dyslipidemia among stroke patients in Kano, Northwest Nigeria.[7] That figure was more than thrice the prevalence of hyperlipidemia in our study. However, we have used a more restricted definition based on the ATP-III-NCEP guideline recommendations,[13] whereas investigators in Kano used a broader definition and lower thresholds of cholesterol values. Another reason may be the dietary habits of the Hausa-Fulani of Kano, who consume large quantities of animal fat in form of fried cheese in their diets. Other local studies[4,6,8] have not reported serum cholesterol values, perhaps because they were retrospective reviews lacking results of serum lipids.

Atrial fibrillation (AF) was prevalent among 25 of our patients, of whom 18 had CI. Previous studies[4,7-9] have reported 0.6-8.9% prevalence of atrial fibrillation or cardiac arrhythmia among Nigerians with stroke of varied classes. In North America, AF increases stroke risk by five-fold and contributes to 10% of the yearly incidence of ischemic strokes.[22] In the INTERSTROKE study, atrial fibrillation or flutter and other cardiac conditions were prevalent in 14% patients with ischemic stroke, contributing to 6.7% and 8.5% of the population attributable risks of stroke, and ischemic stroke, respectively.[18]

Stroke risk stratification schemes have been proposed for use in AF. A widely utilized scheme is the $CHADS_2$ score, an acronym for congestive heart failure, hypertension, age 75 years or older, diabetes and a prior stroke or TIA.[22,23] A score of two or more on this scheme implies a high risk of stroke, while a score of less than 2 implies low risk. On the basis of this and other findings, the American Heart Association and European Society of Cardiology both recommend oral anticoagulant therapy or aspirin to prevent stroke in patients with AF at high and low risk risks, respectively.[24]

In our cohort, however, only one female with a prosthetic mitral valve and AF was taking warfarin at the time of stroke. She had a massive ICH and died soon after presentation. Of the other 24 AF patients, two had been on aspirin and none had been on anticoagulants, including 12 high-risk patients. Obviously, our AF patients were not properly managed at primary and secondary care levels. This could be due to several factors, including difficulties associated with regular monitoring of international normalized ratio.

Unlike in East[25] and Southern Africa,[26] HIV infection was not an important stroke risk factor among our patients. We noted a 3.7% HIV prevalence, which was even lower than the Nigerian national adult HIV seroprevalence rate of 4.1% in 2010.[27] However, our findings may have resulted from sampling bias, since we did not study stroke incidence in HIV positive and HIV negative individuals on a case-control basis.

To our knowledge, only one local study has previously assessed carotid anatomy in patients with vascular risk factors. Using B-mode ultrasonography, Okeahialam *et al*.[28] found a non-significant increase in carotid intima media thickness (IMT) among hypertensive and diabetic patients in Jos, central Nigeria. In the present study, however, we detected atheromatous plaques and moderate to severe stenosis in over half of patients scanned. Two factors may have accounted for this difference. First, we assessed four surrogates of carotid artery stenosis (carotid IMT, lumen diameter, flow velocities and atheromatous plaques) while Okeahialam *et al*. assessed only carotid IMT. Secondly, our sample was derived exclusively from a cohort of patients with ischemic stroke, while the Jos study enrolled diabetic and hypertensive subjects who did not necessarily have advanced atherosclerosis.

The one-month case-fatality rate of 18.8% in this study was within the range of 8.9-23.8% reported locally.[8,4] Our findings were also similar to rates of 17.8% and 17.2% found in Oxfordshire, England.[2,29] Yet, we may have under-estimated stroke-related deaths, as some patients may have died before reaching our hospital. Mortality rates provide better estimates of deaths due to stroke, but these are best assessed in community-based multi-center studies.

We have found atrial fibrillation, age over 50 years and a history of previous stroke as the only prognostic variables associated with worse outcomes at 30-days after a stroke, while other variables did not show an association [Table 3].

Chamorro *et al*. have reported age, degree of neurological impairment, infarct size on neuroimaging, ESR and serum uric acid concentrations all predicted 30-day outcome after ischemic stroke, whereas AF, hypertension and diabetes did not predict outcome.[30] However, other studies have implicated AF as a predictor of early stroke mortality and worse functional outcome.[31,32] Thus, our findings are consistent with those reported previously.

A major limitation of our study was its hospital-based design. Population-based studies allow for complete case-ascertainment of stroke in the community, but such studies require huge financial resources and manpower.

A second limitation was our failure to obtain carotid Doppler scans in a majority of patients with CI. Reasons included logistic constraints on our own part, and financial constraints on the part of some patients. However, we used the OCSP classification of ischemic strokes, which places little emphasis on carotid imaging, the reason it is preferred over other systems in resource-poor settings.

In conclusion, we have provided relevant data on the socio-demographic and clinical profile of stroke among Nigerians, as well as case-fatality and functional outcomes at 30 days after stroke. We have noted a high prevalence of under-diagnosis of vascular risk factors at levels of primary and secondary care. For instance, evidence-based guidelines recommend oral anticoagulant therapy for high-risk patients with atrial fibrillation, but only one in 13 patients had received this treatment at primary and secondary care.

We recommend for improved public awareness of vascular risk factors and better diagnostic and treatment facilities aimed at addressing those factors at levels of primary and secondary healthcare. Smoking-cessation campaigns, aggressive control of hypertension and appropriate use of anticoagulant therapy could significantly reduce the current stroke burden in Nigeria. Larger population-based studies may provide additional data on stroke incidence and outcome among Nigerians.

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