Stroke Characteristics and Outcomes of Adult Patients Admitted to the University Teaching Hospital, Lusaka, Zambia

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Abstract: *Objectives:* Despite the high burden of strokes globally and among people of African origin in particular, there are few available data on stroke in most countries of sub-Saharan Africa (SSA), including Zambia. The aim of this study was to describe the characteristics and outcomes of stroke in adult Zambian patients admitted to the University Teaching Hospital (UTH) in Lusaka. *Methods:* The study was conducted at the UTH, which is the only tertiary hospital in the country, from July to December 2010. Stroke was confirmed by neurological examination and CT scan of the brain. Participants were assessed for risk factors and severity of stroke. Outcome measures included in-hospital stroke mortality and disability (modified Rankin score and Glasgow outcome scale on discharge). *Results:* A total of 250 consecutive stroke patients were included in the study. Of these 162 (65%) patients had ischemic and 88 (35%) hemorrhagic strokes. The mean age was 55 ±18years. Hypertension was most common risk factor for both strokes. Other risk factors included: alcohol intake (32.6%), previous stroke (23.6%), family history of stroke (23.2%), HIV infection (25.4%), hypercholesterolemia (14%) andtobacco smoking/sniffing (13.4%). In-hospital stroke mortality was 40%. Factors independently associated with mortality were female sex, pneumonia, Glasgow Coma Scale (GCS) ≤ 8 and stroke severity at admission. *Conclusions:* Stroke in Zambian patients occurs at a relatively young age and frequency of intracerebral hemorrhage is higher than that reported in developed countries. Hypertension is common risk factor for both types of strokes. Family history of stroke is one of important risk factor. In-hospital stroke mortality is high at UTH. HIV infection is independently associated with ischemic stroke.

Keywords: Stroke characteristics, Outcome, Sub-Saharan Africa, Zambia.

INTRODUCTION

Stroke is the second leading cause of death worldwide, and the leading cause of acquired disability in adults in most regions [1, 2]. Countries of low and middle income have the largest burden of stroke, accounting for more than 85% of stroke mortality worldwide [3, 4]. The overall stroke incidence rates in low to middle income countries exceeds the level of stroke incidence seen in high-income countries, by 20% [4-6]. The burden of non communicable diseases such as stroke and other cardiovascular diseases is increasing in Sub-Saharan Africa, adding to the tropical diseases burden, further straining the limited health care resources [4]. Despitethe documented high burden of strokes globally and among people of African origin in particular, the prevalence, risk factors, stroke types, environment and genetic causes of stroke remain unclear in most countries of sub-Saharan Africa, including Zambia [4, 7]. Zambia is a country of about 12 million people located in Southern Africa bordered by eight other African countries. It has one large tertiary hospital located in Lusaka, the University Teaching Hospital (UTH). The aim of this study was to describe the clinical stroke characteristics and outcomes of adult patients admitted to the UTH in Lusaka, Zambia.

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METHODS

Study Population

Consecutive patients aged 18 years or older admitted between June and December 2010 with the diagnosis of stroke, were enrolled. We included only patient who had stroke confirmed by neurological examination and brain CT scan. Patients who had no brain imaging done and those with head injury were excluded. Stroke was defined according to the WHO definition [8]. Daily physical checks/reviews were made of emergency room, admission ward and in-patient wards for stroke patients. After finding the stroke patients, the participants or their relatives were informed about the stroke study and consent was sought. We also provided them with an information sheet or read/explained it to them (for those who could not read). Informed consent was obtained from all patients or proxy.

Clinical Procedure

Within 24 hours of admission, we obtained medical history, conducted general and neurological examination and brain C T scan done. The patient's demographic details and

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Table 1. Baseline Characteristics of Zambian Patients with Ischemic and Hemorrhagic Strokes

Characteristics	TotalN=250	Ischemic Strokes N=162	Intracerebral Hemorrhagen=88	P Value
Age, mean (SD)	55(18)	55(18)	56(16)	0.62
Male sex, n (%)	103(41.2)	67(41.4)	36(40.9)	0.52
Marital status n=215 (%)				
Married	138(64.2)	90(62.1)	48(60)	0.96
Never married	19(8.8)	12(8.3)	7(8.8)	
Separated/divorced	58(26.9)	33(29.8)	25(31.3)	
Residence n=229 (%)				
Lusaka Urban	176(76.8)	107(74)	69(82)	0.08
Other referral	53(23.1)	38(26.2)	15(17.9)	
Employment, n=226 (%)				
Current employment	126(55.7)	78(52.7)	48(61.5)	0.07
EX/None	100(44.2)	70(47.2)	30(38.4)	
Time from onset to admission, n=242 (%)				
< 3 hours	32(13.2)	17(10.7)	15(18.1)	0.05
6 to 12 hours	35(14.4)	19(12)	16(19.2)	
>24 hours	175(72.3)	123(77.4)	52(62.7)	

risk factors for stroke were documented on a data collection sheet by study physician. Risk factors for stroke included: hypertension, diabetes mellitus, elevated cholesterol, atrial fibrillation, past history of myocardial infarction accompanied by any signs of ischemic heart disease on ECG, tobacco smoking/sniffing (current smoker, former smoker for more than one year, never smoked), alcohol consumption (never, ex drinker for more than one year, current alcohol use), history of transient ischemic attack, and a family history of stroke. Case definition for hypertension was current use of antihypertensive medication, history of being diagnosed as hypertensive by a doctor prior to stroke, documented blood pressure of greater than or equal to 140 mmhg systolic or 90 mmhg diastolic before the stroke or persisting after the acute event or evidence of left ventricular hypertrophy on ECG or echocardiogram [9]. Diabetes mellitus was diagnosed when patient was taking antidiabetics drugs prior to stroke, if a doctor had diagnosed type I or type II diabetes before stroke or if the patient had a documented non fasting blood glucose of greater than 11.1 mmol/L or fasting blood glucose of greater than 7.0 mmol/L after the acute phase of stroke to exclude acute transient elevation of glucose as a stress response after stroke [10]. Elevated cholesterol was considered ifserum fasting cholesterol was > 5.2 mmol/L or prestroke treatment with a cholesterol lowering agent [11]. Other risk factors included:HIV infection,cardiovascular diseases such as dilated cardiomyopathy (DCM), rheumatic heart diseases (RHD), atrial fibrillation (AF), hypertensive heart disease (HHD), coronary artery disease (CAD). The referral status of the patient (referral from Lusaka urban vs. outside of Lusaka or rural setting) was also has been recorded.

The severity of stroke was evaluated on admission using the National Institutes of Health Stroke Scale (NIHSS) [12]. NIHSS is a validated and widely used neurological stroke scale that evaluates level of consciousness, eye movement, visual field, facial palsy, power in limbs, ataxia, sensation, aphasia and neglect. Stroke outcome was measured using the modified Rankin stroke scale (mRS) and the Glasgow Outcome Scale (GOS) at discharge [12-14].

Analysis

The study was approved by UNZA Biomedical Research Ethic Committee (UNZA/REC).Data was entered onto a *Microsoft Office Access 2007* form. Analysis was performed using *Epi info 2005 version 3.3.2*. Means and medians were calculated to summarize continuous variables and compared ischemic and hemorrhagic strokes using Student t test for normally distributed data while for non Gaussian data we used Mann-Whitney/Wilcoxon (Kruskal- Wallis) test to compare medians. Chi-square was used for categorical variables. Stepwise logistic regression analysis was used to determine the association of risk factors to strokes types and the associations of factors to outcome. A probability value less than 0.05 was considered statistically significant.

RESULTS

A total of 250 consecutive patients were included in the study. Of these, 65% (162/250) of patients had ischemic stroke and 35% (88/250) had hemorrhagic stroke. Table **1** outlines distribution of baseline characteristics of ischemic and hemorrhagic strokes. The mean age at presentation was 55 years (SD±18) and 58.8% (147/250) patients were female. Most (72.3%) patients were admitted more than 24 hours after stroke onset.

Table **2** displays risks factors for ischemic and hemorrhagic strokes. A total of 23.6% (59/250)patients had previous strokes. Hypertension was the most common risk factor for ischemic and hemorrhagic strokes, occurring in 71% of all strokes, with a significantlyhigher rate of hypertension in

Table 2. Risk Factors by Strokes Types

Characteristics	Total N=250	Ischemic Strokes N=162	Intracerebral Hemorrhage N=88	Odds Ratio 95% CI	P Value
Previous stroke, n (%)	59 (23.6)	39 (25)	20 (23.3)	1.1 (0.58-1.9)	0.409
Hypertension n (%)	178(71)	104(64)	74(84)	0.34 (0.18-0.65)	0.003
Alcohol Use, n=245 (%)					
Current	80 (32.6)	47(29.4)	33(38.8)	0.75 (0.44-1.28)	0.069
Ex	24 (9.7)	17(10.6)	7(8.2)		
Never	141 (57.5)	96(60)	45(52.7)		
HIV infection present n=185 (%)	47 (25.4)	40(31.7)	7(11.8)	3.79 (1.62-8.88)	0.003
Family history of stroke	58 (23.2)	35(21.6)	23(26.1)	0.78 (0.42-1.42)	0.210
Cholesterol ≥ 6mmol/L	35 (14)	22(13.5)	13(14.7)	0.91 (0.43-1.95)	0.394
Tobacco Use (Smoking/Sniffing) n=245					
Current	33(13.4)	24(15%)	9(10.6)	1.10 (0.56-2.23)	0.087
Never	199(81.2)	129(80.6)	70(82.4)		
Ex	13(5.3)	7(4.4)	6(7.1)		
Diabetes mellitus, n (%)	30(12.2)	20(12.3)	10(11.3)	1.10 (0.49-2.56)	0.417
Atrial fibrillation	27(10.8)	23(14)	4(4.5)	3.48 (1.16-10.39)	0.008
Dilated Cardiomyopathy	24(9.6)	19(11.7)	5(5.6)	2.21 (0.79-6.13)	0.061

Table 3. Severity and Outcome by Strokes Types

Characteristics	Total N=250	Ischemic Strokes N=162	Intracerebral hemorrhage N=88	P value
Neurologic impairment (NIHSS)				
Mean total(SD)	12.4(±8)			
Mild impairment(≤5)	53(21.2)	40(24.7)	13(14.8)	0.03
Moderate impairment(6 to 13)	103(41.2)	71(43.8)	32(36.3)	
Severe impairment(≥14)	94(37.6)	51(31.4)	43(48.8)	
Modified Rankin Scale				
Mean total(SD)	2.8(0.9)	2.7(0.91)	2.9(0.95)	0.013
Good outcome (<3), n (%)	103(41.2)	75(46.3)	28(31.8)	
Moderate to severe Disability (≥3), n (%)	147(58.8)	87(53.7)	60(68.2)	
GOS at discharge, n (%)				0.02
Good recovery=1	23(9.2)	18(11.1)	5(5.7)	
Moderate disability=2	80(32)	60(37)	20(22.7)	
Severe disability=3	40(16)	26(16)	14(15.9)	
Vegetative state=4	5(2)	3(1.9)	2(2.3)	
Death=5	101(40.4)	54(33.3)	47(53.4)	0.001

patients with hemorrhagic stroke (p=0.003). A total of 25.4% of all stroke patients were positive for HIV infection,with significantly higher rates of infection among patients with ischemic stroke compared to ICH(p=0.003). On multivariate analysis, factors independently associated with ischemic strokes were atrial fibrillation and HIV infection. Hypertension favored hemorrhagic stroke.

Table **3** outlines strokes severity and outcome. The mean NIHSS for all strokes was 12.4 ± 8.5. Patients with hemorrhagic stroke had significantly more severe strokes compared to patients with ischemic strokes, respectively mean NIHSS 14.5 ± 9.1 and mean NIHSS 11.1 ± 8 (p=0.006). Mean mRS at discharge was 2.8 ± 0.91 for all strokes, respectively 2.7 ± 0.95 for ischemic stroke and 2.9 ± 0.95 for hemorrhagic stroke. GOS mean for all strokes was 3.3 ± 1.5 (median 3, IQR 2 to 5). Mean GOS for ischemic strokes was 3 ± 1.4 and 3.75 ± 1.4 for hemorrhagic strokes. The in-hospital stroke mortality was worse for hemorrhagic compared to ischemic as expected (P=0.001). Forty percent of all strokes patients died (33.3% of ischemic strokes patients died compared to 53.4% of hemorrhagic strokes).

Table 4. Factors Associated with Stroke Mortality Among Patients at the University Teaching Hospital in Lusaka

Characteristics	Total N=250	Died N=101	Survived N= 149	OR(95%CI)	P value
Female sex, n (%)	147(58.8)	65(64.3)	82(55)	2.21 (1.31-3.71)	0.001
Pneumonia, n (%)	28(11.2)	26(26.2)	2(1.4)	25.48 (5.88-110.2)	<0.0001
GCS < 8, n (%)	54(21.6)	51(50.5)	3(2)	49.98 (14.94-167.2)	<0.0001
Neurologic impairment (NIHSS≥ 14), n (%)	96(38.4)	83(82.2)	13(8.7)	48.24 (22.47-103.5)	<0.0001
HIV positive status, n (%)	47(18.8)	18(17.8)	29(19.7)	0.89 (0.46-1.72)	0.376
Stroke type (Hemorrhagic), n (%)	88(35.2)	47(46.5)	41(27.5)	3.14(1.86-5.29)	<0.0001
Previous Stroke, n (%)	59(23.6)	23(23)	36(25.4)	0.92(0.51-1.68)	0.402
Time onset to admission ≥24 hours, n (%)	175(70)	72(71.2)	103(69.1)	1.11 (0.63-1.92)	0.359
Distance from UTH (outside Lusaka), n (%)	55(22)	19(19)	36(24.2)	0.72(0.39-1.36)	0.161

As shown in Table **4**, factors independently associated with increased stroke mortality were female sex, pneumonia, stroke severity, low GCS at admission and hemorrhagic type of stroke. HIV infection status was not independently associated with increased stroke mortality.

DISCUSSION

There has been no previous published data in Zambia on stroke characteristics and outcome. We carried out this study to describe the stroke characteristics and outcomes of a consecutive series of adult patients admitted at UTH in Lusaka, Zambia. Our findings showed that 65% of patients had ischemic stroke and 35% had hemorrhagic stroke. The mean age of stroke at presentation was 55 years. Hypertension was most common risk factor for both types of stroke. Other important risk factors included alcohol intake, HIV infection, previous history of stroke and family history of stroke. In-hospital mortality was 40%. Factors independently associated with mortality were female sex, pneumonia and stroke severity. The access to brain imaging at UTH was relatively low compared to developed countries but was higher than reported in other African countries such as Mauritania (58%) [15]. In our study, which was comparable to the region, the prevalence of hemorrhagic stroke was more than found in western cohorts [15-22]. Hospital based studies in other African countries found results in accordance with ours; in Senegal 70% of strokes were ischemic while others ranged from 63.3% in Zimbabwe to 84.5% of ischemic strokes in Libya [17-19]. However, intracerebral hemorrhage in some African countries was even more prevalent than ischemic stroke; making up to 60% of all strokes in 2 hospital based studies in Ghana, Tanzania and 52% in the Democratic Republic of the Congo [20-22]. We suggest this difference with western data could be as a result of differences in study design (hospital based) and environment and genetic interactions in different population groups.

Mean age for all strokes was 55 years (SD±18) with no significant difference between ischemic and hemorrhagic stroke. Our patients were younger than in western cohort [23]. Moreover 30% of our patients were below 45 years. The European Registers of Stroke (EROS) reported median age of 73 years (IQR 62 to 81) [23]. However, the mean age of our patients was similar to that of other hospital based studies from Sub-Saharan Africa. In Senegal the mean age was 60.4 years, 58 years in the Gambia and 51 years in South Africa [17, 24, 25]. Some studies found hemorrhagic strokes patients to be significantly younger compared to ischemic strokes with mean age of 51 years in Senegal, 49 years in Zimbabwe and 56 years in Mauritania [17, 26, 15]. Our findings are in agreement with literature indicating that the proportion of stroke in age 45 or younger is higher in Africa compared to high-income countries [27]. This dissimilarity could be explained by difference in population pyramid and high prevalence of hypertension, HIV infection and familial aggregation of stroke in our study population.

Male to female ratio was 0.7 while in South Africa it was previously reported to be 1.0 [25]. As expected, most admissions with strokes (76.8%) were from Lusaka. Most stroke patients (72.3%) were admitted more than 24 hours after the onset of strokes. Hypertension (71%) was the most common risk factor of all stroke patients. The INTERHEART and the INTERSTROKE studies also reported hypertension as an important risk factor [27, 28]. Both the HOPE and PROGRESS studies have demonstrated that reduction in the risk of stroke extends to patients with only moderately high levels of blood pressure [29, 30]. Our findings are similar to studies in South Africa and Senegal [17, 25]. Previous stroke was found in 23.6 % of patients. Since this data was not available in the country, we included these patients in our analysis as well. Alcohol use among our stroke patients was more frequently (32.6%) reported than in other African studies [25].

Relationship between HIV infection and stroke is widely discussed in literature [31-35]. Although the prevalence of HIV infection in the general population in Zambia is 14%, 25.4 % of our stroke patients were HIV positive. In comparison, the Durban Stroke Register in South Africa found 20% of young black stroke patients to be HIV positive and had HIV-associated stroke, but in the older rural SASPI stroke prevalence study only 2% of stroke patients were HIV positive [31, 32]. We also found that HIV infection was significantly more prevalent among our ischemic (31.7%) compared to hemorrhagic stroke patients (11.8%). In our study the mean CD4 count was 155cell/uL.

A family history of vascular disease has been reported as independent risk factor for both ischemic and hemorrhagic stroke [36, 37]. In our study, positive family history of stroke

was high (23.6%). This could be partly explained by the relatively young age of our patients as family history was found to be a risk factor especially in stroke patients presenting before 65 years [36]. Other potential explanations include familial aggregation of stroke risk factors such as hypertension and diabetes, and other environmental factors. Factors favoring ischemic strokes as opposed to hemorrhagic strokes were atrial fibrillation, HIV infection while hypertension favored hemorrhagic strokes. Most of our patients had moderate to severe strokes (NIHSS mean of 12.4 ± 8.5),as expected hemorrhagic strokes were more severe. Stroke severity was similar to patients in SAbut in the Gambia stroke was reported to be more severe [24, 25]. In-hospital mortality was40% of all strokes which is much higher than that of developed countries [7, 23]. Thirty three percent of ischemic strokes patients died compared to 53.4% of hemorrhagic strokes. In-hospital stroke mortality was higher compared to western cohorts but was comparable to other studies in the region. A Nigerian study found high mortality with the 30 days stroke mortality as high as 40% and in the Gambia a study found in-hospital mortality of 41% [38, 24]. Factors independently associated with mortality among UTH stroke patients were female sex, pneumonia, stroke types and severity. These findings were similar to the Gambian study [24].

This could be explained by late presentation, as most of our patients were admitted more than 24 hours after onset, the severity of stroke and the high frequency of ICH in our stroke patients. Another possible contribution to the high in-hospital stroke mortality could be the absence of a stroke care unit which has been shown to benefit patients with both ischemic and hemorrhagic strokes [39].

One of our study limitations was the hospital design, which is not representative of all strokes occurring in the community. Nonetheless, our inclusion criteria was restricted to patients who had brain imaging confirmed strokes making it to the best of our knowledge the first of this kind in our setting.

In conclusion, stroke in Zambian patients occurs at a relatively young age and frequency of ICH is higher than that reported in developed countries. Hypertension is the most common risk factor for both types of strokes. In-hospital stroke mortality is high at UTH Lusaka, Zambia. Parental and sibling history of stroke is one of important risk factor. HIV infection is independently associated with ischemic strokes.

DISCLOSURE

M. Atadzhanov, P.N. Mukomena, S. Lakhi, O. A. Ross, J. F. Meschia, have nothing to disclose.

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CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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