NATURE AND OUTCOME OF STROKES IN ADULT ZAMBIAN PATIENTS ADMITTED AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA

BY

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DISSERTATION

NATURE AND OUTCOME OF STROKES IN ADULT ZAMBIAN PATIENTS ADMITTED AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA

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DECLARATION

I hereby declare that this dissertation represents my own work and has not been presented either wholly or in part for a degree at the University of Zambia or at any other University.

Signed _____

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ABSTRACT

INTRODUCTION:

Stroke is an important cause of morbidity and mortality at UTH.
It is important to know the nature of stroke and the clinical outcome of different types of strokes in our setting.

This study was designed to determine the frequency and types of strokes in patients admitted at UTH and to describe the demographic characteristics of ischemic and hemorrhagic strokes. We also wanted to compare the clinical outcomes of ischemic versus hemorrhagic strokes.

METHODOLOGY

This research was a hospital based cohort study of adult Zambian strokes patients who were admitted at the University Teaching Hospital in Lusaka, Zambia from July to December 2010. Participants were assessed for cardiovascular and other risk factors, and general and neurologic examinations were performed. National institute of health stroke scale (NIHSS), modified Rankin scale (mRS), Glasgow outcome scale (GOS), Glasgow coma scale (GCS) were recorded. All information was entered to a Microsoft Office Access 2007 form. Analysis was performed on all selected variables using Epi Info 2005 version 3.3.2 software. We assessed characteristics, risk factors and investigations by stroke type using a Chi square test or Fisher exact test for categorical variables and student t test and ANOVAs for continuous variables. Stepwise logistic regression analysis was performed for risk factors. We considered a level of $p < 0.05$ as statistically significant.

RESULTS

250 patients with brain imaging confirmed strokes were assessed. Ischemic strokes represented 65% of all strokes as compared to hemorrhagic strokes found in 35%. Strokes occurred in relatively young patients with mean age of 55 ± 18years at onset of stroke with no sex difference. Hypertension was the main risk factor for ischemic and hemorrhagic strokes, it was found in 71% of participants. Other risk factors were current alcohol intake (32.6%), previous strokes (23.6%), family history of strokes (23.2%), HIV infection (25.7%), hypercholesterolemia (14%), tobacco smoking/sniffing (13.4%), atrial fibrillation (10.8%) and dilated Cardiomyopathy (9.6%). In regression analysis hypertension was independently associated with hemorrhagic strokes while atrial fibrillation and HIV infection were more common in patients with ischemic strokes. In-hospital Stroke mortality was 40%. 33% of ischemic strokes patients died compared to 53% for hemorrhagic strokes (p=0.0008). Factors associated with increased mortality were female sex, GCS≤8, pneumonia, NIHSS≥14 and hemorrhagic type of stroke. HIV infection was not associated with increased stroke mortality.

CONCLUSION

Stroke is an important cause of admission and death at UTH. 65% of strokes are ischemic and 35% are hemorrhagic. Strokes occur in relatively young patients compared to western cohorts. It is associated with high in-hospital mortality (40%). Factors associated with stroke in-hospital mortality at UTH were female sex, GCS≤8, NIHSS≥14 and pneumonia.

DEDICATION

I dedicate this work to my family, for the time taken away from you to collect data and write up, my wife Dr Kon A Kanund and my children Alex, Ben, Patrick, Bright and Gift Mukomena. You have been of great support especially Bright Mukomena, you could wait for so many hours before sleeping while I was working, for sure God will reward you one day.

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To the government and the people of this peaceful nation, for ensuring conducive environment during my study period, sincerely thanks.

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ABBREVIATIONS

AF - Atrial fibrillation
CAD - Coronary Artery Disease
CADASIL - Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy
CT scan - Computerised Tomography Scan
DCM - Dilated Cardiomyopathy
ECG - Electrocardiography
GCS - Glasgow coma scale
GOS - Glasgow outcome scale
HHD - Hypertensive Heart Disease
HIV - Human Immune Deficiency Virus
HS - Hemorrhagic stroke
ICH - Intracerebral haemorrhage
IQR - Inter Quartile Ratio
IS - Ischemic Stroke
MRI - Magnetic Resonance Imaging
mRS - Modified Rankin Scale
NIHSS - National Institute of health Stroke Scale
OR - Odd ratio
RHD - Rheumatic Heart Disease
RPR - Reagen Plasma Reagent
SAH - Subarachnoid haemorrhage
SOL - Space occupying lesions
TIA - Transient ischemic Attack
UTH - University Teaching Hospital

CHAPTER 1

INTRODUCTION

Stroke, a focal neurological deficit of sudden onset, is an important public health problem. It has been recognized in high income countries as an important cause of death and disability for many years.[1] Stroke is responsible for nearly 10% of deaths each year in industrialized countries; in the United States of America it is the third leading cause of death after coronary heart disease and cancer.[2-4]

The clinical syndrome of stroke is characterized by an acute loss of focal brain function lasting more than 24 hours or leading to (earlier) death, which is thought to be due to either inadequate blood supply to a part of the brain as a result of low blood flow, thrombosis or embolism associated with diseases of the blood vessels, heart or blood (ischemic stroke or cerebral infarction) or spontaneous haemorrhage into or over the brain substance (primary intracerebral haemorrhage, intraventricular haemorrhage and subarachnoid haemorrhage respectively)**.**[4,5] This, by convention does not include cerebral haemorrhage caused by trauma.[5] The acute loss of focal brain function lasting less than 24 hours is called transient ischemic attack (TIA).[4,5]

The common underlying causes of occlusion of a cerebral artery are: embolism via or from the heart (20%), large artery atherothrombosis or thromboembolism (45-50%), small artery microatheroma/lipohyalinosis (25%), other arteriopathies such as dissection and arteritis (5%), haematological disorders causing a prothrombotic state (<5%).[5,6]

The burden of non communicable diseases such as stroke and other vascular diseases is increasing in Sub-Saharan Africa, adding to the infectious and poverty related disease burden, straining further the limited health care resources.[1]As a population undergoes health transition, the pattern of vascular disease is thought to change from one dominated by stroke, with a high proportion caused by cerebral haemorrhage, to a pattern dominated by coronary heart disease, peripheral vascular disease, and atherosclerotic stroke.[1]

In 2008, the overall stroke incidence rates in low to middle income countries had, for the first time, exceeded the level of stroke incidence seen in high-income countries, by 20%.[7] Stroke admissions to hospital are clearly rising in Sub-Saharan Africa, although this could be due to easier access to medical care, increasing stroke incidence, and ageing of the population.[1]

Despite a high burden, there are few available data on stroke types and outcome in Sub-Saharan Africa. Prospective descriptive data are rare in most Sub-Saharan African countries. The prevalence, incidence of stroke types and outcome in most Sub-Saharan African countries remain unclear.[1,7,8] Little is known about the nature and outcome of stroke in patients admitted at the University Teaching Hospital in Lusaka. The purpose of this study was to determine the nature, the common risk factors of stroke and the clinical outcome of ischemic strokes compared to haemorrhagic strokes in patients admitted at the University Teaching Hospital.

CHAPTER 2

LITERATURE REVIEW

Stroke is a heterogeneous condition made up of three pathological types: cerebral infarction, cerebral haemorrhage and subarachnoid haemorrhage. Cerebral infarction or ischemic stroke is then further divided into various subtypes, such as intracranial small vessel disease, large-vessel atherosclerotic disease, and embolism from the heart.[9] These types and subtypes differ in terms of cause, outcome and treatment.[9,10]

Fifteen million people worldwide suffer a stroke each year with devastating effects; one third of these individuals die and another one third remain permanently disabled.[11] The burden of stroke is globally increasing and in countries such as the United States of America, more than 780,000 new or recurrent strokes and 240,000 TIAs occur each year.[12]

The incidence of stroke in black population is a public health issue. Studies in the USA and UK found stroke incidence in blacks with an approximate two fold increased risk compared to white groups regardless of the country of origin or ethnicity.[13,14] In white people, about 80 to 85% of strokes are ischemic; while in blacks and Asians the proportion is reported to be lower at about 60 to 70%.[15]

In the Republic of South Africa, the crude prevalence was 300/100 000 with prevalence higher in females than males.[16] Nigeria estimates its prevalence of stroke to be 1.14 per 1000 with the 30-day case fatality rate as high as 40%.[17] A retrospective study at Port Harcourt University Teaching Hospital in Nigeria reported cerebral infarction in 67.3% of patients with strokes.[18] However, studies in Tanzania and the Democratic republic of Congo found more cerebral hemorrhages, respectively 60% and 52% of admitted strokes patients had cerebral hemorrhages.[19,20]

The 2004 WHO health report, which used updated techniques based on those developed for the global burden of disease studies to estimate cause of death in WHO member countries in 2002, found that there were about 359000 stroke deaths (3% of all deaths) in Africa compared with almost 1.5 million (16% of all deaths) in

Europe.[21] Stroke caused an estimated 52% of vascular death (deaths caused by either stroke or ischemic heart disease) in Africa compared with 38% of vascular deaths in high income Europe, showing higher ratio of stroke death to coronary death in Africa.[21]

Stroke risk factors are divided into those that are modifiable and those that are not.[7,19] The major risk factors[22] are summarized in table 1.

Table 1. Major risk factors of strokes

Modifiable Risk factors	Non Modifiable Risk factors
Hypertension	Age
Diabetes mellitus	Sex
Hypercholesterolemia	Family history of strokes
Smoking/passive smoking	History of previous strokes
Heavy alcohol consumption	Race/Ethnicity
Obesity	
Physical inactivity	
Diet(Low fruit and vegetable consumption)	

Increasing age is a major unmodifiable risk factor for strokes in all studies, whether in developed or developing countries.[22,23] Other well established risk factors for stroke include heart diseases (atrial fibrillation, heart failure, and rheumatic heart diseases), hypercoagulation states, increased plasma fibrinogen levels, hypercholesterolemia, homocystinuria and homocysteinemia.[5,10,21] African, Hispanic or Asian origins are risks factors for cerebral hemorrhages.[24,25] Congophilic amyloid angiopathy, sympathomimetic drugs, coagulopathies, and small arteriovenous malformations also cause brain hemorrhages.[26]

In South Africa, Hospital-based studies have found the following prevalence of modifiable stroke risk factors in people admitted with stroke:[27,28,29]hypertension in patients with cerebral infarction 32-76%, hypertension in patients with cerebral Haemorrhage 76-93%, diabetes mellitus 3-10%, hypercholesterolemia <2-10%,[29] atrial fibrillation 1-7%, cigarette smoking 15-28%, and previous stroke or transient ischemic attack 2-7%.

In the Southern Africa Stroke Prevention Initiative (SASPI) study of stroke prevalence in rural South Africans, hypertension was again the most common risk factor: hypertension 71%, diabetes mellitus 12%, cigarette smoking 9%, and current alcohol use 20%.[30]

Hypertension is a major risk factor for strokes.[21,22,27] Most haemorrhages in the brain parenchyma arising in the region of the small arteries that serve the basal ganglia, thalamus, and brain stem and are caused by an arteriopathy of chronic hypertension. This disorder causes either occlusions with lacunae infarction or leakages that are brain haemorrhages. Chronic hypertension stimulates the brain's blood vessels to make gradual, adaptive changes in an attempt to preserve the blood-brain barrier. One gradual change that may develop is lipohyalinosis. Subintimal fibroblast proliferation occurs, with an accumulation of lipid-laden macrophages and cholesterol deposits; this results in hyalinization and lipidosis of the blood vessels. This process segmentally affects the smaller penetrating arteries and may account for many lacunar infarcts of the basal ganglia and thalamus. Lipohyalinosis may be an intermediate stage between fibrinoid necrosis from severe hypertension and microatheromas from long-standing hypertension. Plasma leakage from persistently elevated blood pressures also can result in hyaline degeneration of the cerebral blood vessels. Serum protein accumulates in the basement membranes of the arterioles and results in collagen formation. Arterial sclerosis and fibrinoid necrosis may occur, as well as focal aneurysmal dilatation (Charcot-Bouchard intracerebral microaneurysm).[31]

Two theories about the mechanism of intracranial bleeding related to hypertensive small-vessel disease have been developed as follows:[31,32,33]

- The first theory states that the hemorrhage may arise from rupture of the damaged blood vessel. The rupture is believed to occur at Charcot-Bouchard aneurysms.[11] This theory remains controversial. Studies have reported incidences of hypertensive intracranial hemorrhage that occurred in the absence of these microaneurysms. What are believed to be aneurysms actually may be the twists and coils of tortuous small vessels, which on cross

section with some histologic stains may mimic the appearance of Charcot-Bouchard aneurysms.

- The second theory states that brain infarction eventually results in vascular compromise. The first theory, intraparenchymal hemorrhage secondary to rupture of the vessel, is accepted more widely.

The interstroke study, a case control study of risk factors conducted in 22 countries (both low and high income), found ischemic stroke in 78% and Intracerebral haemorrhagic in 22%. Significant risk factors for all strokes were: history of hypertension; current smoking; waist-to-hip ratio; diet risk score; physical inactivity; diabetes mellitus; alcohol intake for more than 30 drinks per month or binge drinking; psychosocial stress and depression; cardiac causes and ratio of apolipoproteins B to A1. These risk factors were all significant for ischemic stroke, whereas hypertension, smoking**,** waist-to-hip ratio, diet, and alcohol intake were significant risk factors for intracerebral haemorrhagic stroke.[34]

There are many reasons why someone who is immunosuppressed with HIV may present with a stroke (e.g., as a result of tuberculous meningitis, toxoplasmosis affecting cerebral blood vessels or even cardiac disease).[35] HIV has been associated with coagulation abnormalities, such as Protein S deficiency, but this was not found to be an important cause of stroke in a case series from Chris Hani Baragwanath Hospital in Johannesburg.[36] HIV infection causes an intracranial small vessel vasculopathy,[37,38] and an extra-cranial large artery vasculitis,[39,40] but only one study in South Africa has fairly convincingly found HIV to be an independent risk for stroke.[41]The Durban Stroke Register found 20% of young black stroke patients to be HIV positive and have HIV associated stroke, but in the older rural SASPI stroke prevalence study only 2% of stroke patients were thought to be HIV positive.[29,30] In both studies, these figures probably reflect the HIV prevalence in the general population. In Zambia, at the University Teaching Hospital (UTH), Lambwe found high incidence of HIV infection with CD4 count below 200 cells/ µl among young stroke patients.[42]

Several studies suggest a familial aggregation of stroke, although a few studies have not detected any familial risk of stroke. Family history and twin's studies support the

existence of genetic susceptibility to stroke. Familial aggregation can be caused by genetic factors, a shared environment or the complex interplay between genetic and environmental factors.[43]

Several Mendelian disorders are known to be associated with an increased risk of stroke such as hemoglobinopathies, dyslipoproteinemias and cardioembolic disorders. Mutation in the NOTCH3 gene causing cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy has been analyzed in large pedigrees (CADASIL).[44] Other hemoglobinopathies such as Sickle cell anaemia are also associated with stroke.

The incidence of stroke in black population is a public health issue. Studies in the USA and UK found stroke incidence in blacks with an approximate two fold increased risk compared to white groups regardless of the country of origin or ethnicity.[14,24]

In the Republic of South Africa (SA), Connor ran a stroke register at the Johannesburg hospital and found more cerebral infarctions in stroke patients but black patients had double the proportion of cerebral hemorrhages found in white patients. Hypertension and diabetes mellitus were found to be equally common in both white and black stroke patients. Black stroke patients were younger, had low cholesterol levels, smoked less, and were more likely to have dilated cardiomyopathy and rheumatic heart diseases than white patients, but less likely to have atrial fibrillation.[45]

A study in rural South Africa, found that stroke caused 5.5% of all deaths in a rural population of Limpopo Province between 1992 and 1995. The overall crude stroke mortality rate was 127/100 000 (95% CI, 93 to 160). (A direct comparison to other study must be made with caution, as the South African figures are not age-adjusted to Segi's world population).[46,47] However, as the South African rural population demographic structure is typical of a developing country population, we might expect the mortality figures to increase on adjustment.[46,47] However; a high mortality may reflect either a high incidence of stroke or a high case fatality rate or both.[5]

Special tools are needed for stroke studies. Neurological impairment is measured using the National Institute of Health Stroke Scale (NIHSS).[48] Disability after stroke is measured using the modified Rankin scale and the Barthel index. The Stroke outcome is measured using the Glasgow outcome scale.[49]

CHAPTER 3

STATEMENT OF THE PROBLEM

Stroke is an important cause of morbidity and mortality at UTH. In developed countries stroke has been extensively studied; types of strokes, risk factors and causes have been established; while in Sub-Saharan Africa including in Zambia, despite a high burden, there are few available data on stroke types and prospective descriptive data are rare.[1,8]

At UTH, little is known about the nature of stroke and the outcome for different types of stroke in patients admitted at UTH. The Johannesburg hospital stroke register ran by Connor found that black patients with stroke in South Africa compared to white patients were younger, had more cerebral haemorrhages, smoked less and had less evidence of large artery atherosclerosis; whether these findings are similar in Zambians stroke patients, had to be clarified.

This study of the nature, the risks factors and the outcome of different types of stroke at UTH will help both the clinicians and the managers to plan for stroke treatment and prevention (both primary and secondary) and reduce stroke related morbidity and mortality at UTH.

HYPOTHESIS

- Ischemic strokes are more common than hemorrhagic strokes in adults stroke patients admitted at the University Teaching Hospital (UTH)
- And that, patients admitted to UTH with ischemic strokes have lower in-hospital mortality than patients admitted to UTH with hemorrhagic strokes.

Study justification

Stroke is a global public health problem with incidence in black populations approximately two fold higher compared to white populations and the proportion of cerebral haemorrhage in black stroke patients is almost double that of white stroke patients.[3,4,5] There is an increase in both stroke morbidity and mortality at UTH over the last decade. Stroke mortality has doubled over the last two years increasing from

1.7% to 4 % of all UTH medical death (audits). Health workers at UTH face more cases of stroke admissions than before. Hence in order to put in place prevention and treatment guidelines and improve management and reduce stroke morbidity and mortality, this study on the nature, the risk factors and outcome associated with different types of stroke was conducted at UTH.

Most resources in Sub Saharan Africa are allocated towards control and treatment of infectious diseases such as HIV infection and AIDS, tuberculosis, and malaria, neglecting the increasing burden of non communicable diseases such as stroke.
A study such as this one will help draw attention to non communicable diseases as well. Furthermore the results of this study will be availed to UTH managers and researchers for further planning and further stroke research.

GENERAL OBJECTIVE

To determine the nature and clinical outcome of different types of stroke in patients admitted at UTH in order to put in place prevention and treatment guidelines.

SPECIFIC OBJECTIVES

1. To determine the demographic characteristics of ischemic and hemorrhagic strokes in patients admitted at UTH.
2. To determine the types of stroke in patients admitted at UTH.
3. To determine the frequency of stroke risk factors in patients with ischemic and hemorrhagic stroke admitted at UTH.
4. To determine the clinical outcome of ischemic stroke compared to hemorrhagic stroke in patients admitted at UTH.

CHAPTER 4

RESEARCH METHODOLOGY

We conducted this descriptive in-patient cohort study at the University Teaching Hospital in Lusaka which is the only tertiary hospital in Zambia. It provides health care (secondary and tertiary) to much of the Lusaka population and the patients referred from all the provinces of Zambia.

Our target population were all consecutive patients admitted to UTH with diagnosis of stroke (and those developing stroke while on the wards) who met the inclusion criteria. We recruited patients from July to December 2010.

Inclusion criteria

a) 18 years and above
b) Admitting diagnosis of stroke (or patients developing stroke while on the ward) confirmed by brain imaging.

Exclusion criteria

a) Failure to obtain consent
b) Cerebral haemorrhages secondary to trauma.

Study process

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 nature and outcome of stroke study and consent was sought. We also provided them with an information sheet or read/explained it to them (in case of illiteracy). On obtaining the consent, the patient's demographic details and risk factors for stroke were documented on a datasheet/ questionnaire by study physician. We defined stroke according to the WHO criteria as rapidly developing signs of focal disturbance of cerebral function leading to death or lasting longer than 24hours, with no apparent causes other than vascular.

The case definitions of the risk factors included the following:

Hypertension → 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 140mmhg systolic or 90 mmhg diastolic before the stroke or persisting after the acute event (World Health Organization) or evidence of left ventricular hypertrophy on ECG or Echo.[50]

Diabetes mellitus → patients 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.[51]

Hypercholesterolemia → serum cholesterol > 5.2 mmol/L or prestroke treatment with a cholesterol lowering agent.[52]

Cigarettes smoking → was defined as self (or relatives recall) declared as current, former for more than one year or never smoked.[45]

Alcohol consumption→ was defined as self (or relatives recall) declared never, ex-drinker for more than one year, current alcohol use.[45]

History of transient ischemic attack (TIA)/ previous stroke and a family history of stroke were also documented. The referral status of the patient (referral from Lusaka urban vs from outside of Lusaka or rural setting) and HIV status were also recorded. Other risk factors included: cardiovascular diseases such as dilated cardiomyopathy (DCM), rheumatic heart diseases (RHD), atrial fibrillation (AF), hypertensive heart disease (HHD) and coronary artery disease (CAD).

The patient examination included a detailed general and neurological assessment, measurement of the patient's blood pressure and examination for any potential sources of emboli. We assessed the patient for signs of focal neurological deficit. The study physician was trained to carry out a full neurological assessment. The patient's admission National Institutes of Health Stroke Scale (NIHSS) and Glasgow Coma scale (GCS), the discharge modified Rankin stroke scale (mRS) and the Glasgow Outcome Scale (GOS) were recorded.[48,49] We reviewed the patients and all questionnaires and scans and other investigations done personally and assigned a

final diagnosis and type of stroke.[22,45] We decided not to use the Siriraji and Guy hospital stroke scores as there were found not to be reliable in Africans populations.[53] We also included patients who had a stroke within 3 months irrespective of their reason for admission if clear documentation excluding trauma as a cause of neurological deficit was available or within 6 months if the stroke was the main reason for seeking assistance.

Access to brain imaging was according to attending unit (physician) request and hospital policy of using the siemens somatom sensation open CT scan available at the cancer disease hospital (CDH) (within UTH premises) during the period of the study.

Ethical considerations

The proposal was approved by the University of Zambia (UNZA) Biomedical Research Ethic Committee (UNZA/REC) and UTH Management and the department of Medicine taking into account the Helsinki declaration.[54]

Data collection

The data was collected using a questionnaire. The questionnaire extracted information regarding patient's social demographic factors, risk factors, general and neurological examinations, NIHSS score, modified Rankin scale score and Glasgow outcome scale score. Collected information was checked for completeness then entered onto a Microsoft Office Access form.

Variables

The dependant variables were types of stroke and in-hospital outcome (modified Rankin scale score and Glasgow outcome scale score).

The independent variables of interest in the study were: patient demographics, risk factors and strokes characteristics (i.e. NIHSS score, GCS,).

Data analysis

The sample size was calculated at 5% significance level with 95% confidence interval using the formula: $N= z^2 \times PQ/d^2$, where $Z=1.96^2$ fixed constant at $\alpha = 0.05$ and Q=100-p. Estimates from UTH preliminary data were that strokes admissions accounted for 10 to 20% of patients in emergency wards and that among admitted strokes patients an estimated 80% have ischemic and 20% hemorrhagic (Audits from Emergency ward and CT scan). Thus, the calculated sample size after taking into account above parameters was 250 patients. We utilised convenient sampling.

Analysis was performed using Epi info 2005 version 3.3.2. Information was imported from Microsoft Office Access 2007. Student t test and ANOVAs were used for normally distributed data, for non Gaussian data we used Mann-Whitney/Wilcoxon (Kruskal- Wallis) test to compare medians. Chi-square was used for categorical variables (Yates correction and Fisher's exact test were used where the numbers in the cells were limited). For continuous variables means and percentages were used while proportions and percentages were used for categorical variables. Stepwise logistic regression analysis was used to determine the association of risk factors to strokes types.

CHAPTER 5

RESULTS

284 consecutive stroke patients who presented to UTH from July to Dec 2010 were assessed. 250 (88% of stroke patients admitted to UTH during study period) had stroke confirmed by brain imaging. 34(12%) stroke patients who did not have access to brain imaging were excluded from analysis.

Married patients were more likely to have access to brain imaging then patients who were not married (never married, separated and widowed) (p=0.013).There was no statistically significant difference of age (p=0.376), sex (p=0.441), residence (Urban/outside Lusaka urban) (p=0.134), time from onset to admission (p=0.396) and stroke severity (NIHSS) (p=0.225) between patients who had brain imaging to those who did not. For the rest of analysis, we excluded patients without brain imaging and considered for analysis only 250 patients who had brain imaging done.

Baseline characteristics of strokes are described in table 2. Of 250 patients with brain imaging confirmed strokes, 103 were male and 147 were female with male to female ratio of 0.7. Cerebral infarction was the cause of stroke in 65% (162/250) and hemorrhagic stroke was found in 35% (88/250) of patients. For both strokes, mean age at presentation was 55 ± 18 years (median age 55, range 18 to 91). Mean age for ischemic strokes was 55 ± 18 years (median56, range 18 to 91) compared to 56 ± 16 years (median55, range 18to85) for hemorrhagic strokes (p=0.1591).Only 44 patients (32%) with ischemic strokes patients had access to secondary or tertiary education compared to 37(49%) for hemorrhagic stroke (p=0.16). 126 (55.7%) of both strokes were still in active employment prior to stroke. Hemorrhagic strokes patients were more likely to be referred within 12 hours to UTH compared to ischemic strokes patients; however chance could not be excluded (p=0.05).

TABLE 2. Baseline characteristics of Zambian patients with ischemic and hemorrhagic strokes.

Characteristics	Total N=250	Ischemic Strokes N=162	Intracerebral hemorrhage N=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 (%)				0.96
Married	138(64.2)	90(62.1)	48(60)	
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 (%)				0.08
Lusaka Urban	176(76.8)	107(74)	69(82)	
Other referral	53(23.1)	38(26.2)	15(17.9)	
Secondary and tertiary Education, n (%)	81(38)	44(32)	37(49)	0.16
Employment, n=226 (%)				0.07
Current	126(55.7)	78(52.7)	48(61.5)	
EX/None	100(44.2)	70(47.2)	30(38.4)	
Time from onset to admission, n=242 (%)				0.05
< 3 hours	32(13.2)	17(10.7)	15(18.1)	
6 to 12 hours	35(14.4)	19(12)	16(19.2)	
>24 hours	175(72.3)	123(77.4)	52(62.7)	

Table 3 outlined the major risk factors. Hypertension was the main risk factor for strokes (71% of both strokes), occurring respectively in 64% of ischemic and 84% of hemorrhagic strokes, which is significantly different (p=0.0003). Poor compliance to medication was reported in 58% of patients including 4 patients who were using copper bracelets around wrist presumably to control blood pressure. Mean cholesterol for both strokes was 4.8 ± 1.49 mmol/ L. Mean cholesterol difference between ischemic (4.8 ± 1.6 mmol/ L) and hemorrhagic (4.9 mmol/ L) strokes was not statistically significant (p=0.62). HIV test was done in 78% of participants and not done in 22% (consent not obtained to carry on the test). HIV infection was found in 47 (25.7%) of both strokes patients who were tested for HIV infection. Of which 40 (85.1%) had significantly ischemic strokes compared to 7 (14.8%) who had hemorrhagic strokes (p=0.003).

Atrial fibrillation was more frequently found in ischemic (14%) compared to hemorrhagic (4.5%) strokes (p=0.008). Tobacco use (smoking/sniffing) was found in 33 (13.4%) of both strokes. 5.3% of all strokes patients were ex smokers. There was no significant difference for current tobacco use status (smoking/sniffing) between ischemic (15%) and hemorrhagic (10.6%) strokes (p= 0.087). Current alcohol intake was found in 32.6% of all strokes. However, the difference in current alcohol intake frequency between ischemic (29.4%) and hemorrhagic (38.8%) strokes was not statistically significant (p=0.14). Other risk factors for all strokes were previous strokes (23.6%), family history of strokes (23.2%), hypercholesterolemia (14%), diabetes mellitus, and dilated cardiomyopathy (9.6%).

Table 3. Risk factors by strokes types. Univariate analysis.

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)	0.0003
Alcohol use, n=245					
Current n (%)	80(32.6)	47(29.4)	33(38.8)	0.75 (0.44-1.28)	0.14
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(32)	7(12)	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)	0.21
cholesterol≥6mmol/L	35(14)	22(13.5)	13(14.7)	0.91 (0.43-1.95)	0.394
Tobacco use n=245 (%) (smoking/sniffing)					
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)	0.06

Table 4. Risk factors by stroke types: Multivariate analysis.

Characteristics	Total N=250	Ischemic Strokes N=162	Hemorrhagic Strokes N=88	Odds ratio (95%CI)	P value
Male sex (M/F)	103(41.2)	67(41.4)	36(40.9)	0.83(0.46-1.49)	0.546
Hypertension Y/N	178(71.2)	104(64)	74(84)	0.34(0.17-0.70)	0.003
Atrial fibrillation Y/N	27(10.8)	23(14)	4(4.4)	5.03(1.64-15.39)	0.004
Tobacco use Y/N	33(13.4)	24(15)	9(10.6)	0.68(0.30-1.55)	0.367
Diabetes mellitus Y/N	30(12.2)	20(12.3)	10(11.3)	1.61(0.69-3.77)	0.267
HIV infection Y/N	47(18.8)	40(24.7)	7(8.1)	3.00(1.20-7.51)	0.018
HIV unknown/N	65(26)	36(22.2)	29(33.7)	0.74 (0.39-1.39)	0.348

As shown in table 4, multivariate logistic regression analysis was performed to determine the independent association of cardiovascular risk factors on stroke types. Factors independently associated with ischemic strokes as opposed to hemorrhagic strokes were atrial fibrillation and HIV infection. Hypertension was associated with more hemorrhagic strokes. Neither tobacco use nor diabetes mellitus favored either of the strokes.

Table 5. Severity and outcomes by stroke types.

Characteristics	Total N=250	Ischemic Strokes N=162	Intracerebral hemorrhage N=88	P value
GCS, mean (SD)	10.4(3.4)	11(3)	9.5(3.5)	0.003
Neurologic impairment (NIHSS)				
Mean (SD)	12.4(8)	11.4(8.3)	15.2(9.4)	0.001
Mild impairment (≤5), n (%)	53(21.2)	40(24.7)	13(14.8)	
Moderate impairment (6 to 13), n (%)	103(41.2)	71(43.8)	32(36.3)	
Severe impairment (≥14), n (%)	94(37.6)	51(31.4)	43(48.8)	
Modified Rankin Scale at discharge				
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

Stroke severity and outcomes are described in table 5. Hemorrhagic stroke patients had significantly lower Glasgow coma scale compared to ischemic stroke, respectively mean GCS 9.5 ± 3.5 (median 9,range 3 to15) and mean GCS 11 ± 3 (median 11, range 3 to 15) (p=0.003). The mean admission NIHSS for all strokes was 12.4±8. As expected, patients with hemorrhagic stroke had significantly more severe strokes (mean NIHSS 15.2±9.4) compared to patients with ischemic stroke (mean NIHSS 11.4±8.3) (p=0.001). Glasgow outcome scale (GOS) mean for both 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 outcome was worse with hemorrhagic strokes as expected (p= 0.0008).

Mean modified Rankin scale (mRS) at discharge was 2.8 ± 0.9 for all strokes. Mean mRS for ischemic strokes was 2.7 ± 0.95 (median 3, IQR 2 to 3) and 2.9 ± 0.95 (median 3, IQR 2 to 3) for hemorrhagic strokes. There was no significant difference in term of disability at discharge (p=0.116). 101(40.4%) of all strokes patients died. 54 (33.3%) of ischemic strokes patients died compared to 47(53.4%) of hemorrhagic strokes. Hemorrhagic strokes were associated with higher mortality (p=0.001).

Table 6. 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
Age>75	37(14.8)	16(15.8)	21(14.1)	1.14 (0.56-2.32)	0.351
Female sex, n (%)	147(58.8)	65(64.3)	82(55)	2.21 (1.31-3.71)	0.001
Pneumonia	28(11.2)	26(26.2)	2(1.4)	25.48 (5.88-110.2)	<0.0001
GCS < 8	54(21.6)	51(50.5)	3(2)	49.98 (14.94-167.2)	<0.0001
Neurologic impairment (NIHSS≥ 14)	96(38.4)	83(82.2)	13(8.7)	48.24 (22.47-103.5)	<0.0001
HIV positive	47(18.8)	18(17.8)	29(19.7)	0.89 (0.46-1.72)	0.376
HIV unknown	65(26)	36(36.6)	29(19.7)	2.29 (1.29-4.07)	0.002
Stroke types (Hemorrhagic)	88(35.2)	47(46.5)	41(27.5)	3.14(1.86-5.29)	<0.0001
Previous Stroke Y/N	59(23.6)	23(23)	36(25.4)	0.92(0.51-1.68)	0.402
Time onset to admission ≥24 hours	175(70)	72(71.2)	103(69.1)	1.11 (0.63-1.92)	0.359
Distance from UTH (outside Lusaka urban)	55(22)	19(19)	36(24.2)	0.72(0.39-1.36)	0.161

Factors associated with stroke mortality are described in table 6. Factors independently associated with stroke mortality were female sex (OR 2.21; 95% CI, 1.31 to 3.71), pneumonia (OR 25.48; 95% CI, 1.34 to 110.20), low Glasgow Coma Scale (GCS<8) (OR 49.98; 95% CI, 14.94 to 167.20), NIHSS ≥ 14 (OR 48.24; 95% CI, 22.47 to 103.50) and Hemorrhagic type of stroke (OR 3.14; 95%CI, 1.86 to 5.29). HIV positive status was not associated with increased stroke mortality (OR

0.90; 95% CI, 0.47 to1.72). Previous strokes, presentation to hospital after 24 hours, distance from hospital (Lusaka urban or referral outside Lusaka urban) did neither favor mortality nor good outcome.

CHAPTER 6

DISCUSSION

We carried out an in-hospital cohort study to determine the stroke types, risk factors and clinical outcomes at the UTH in Lusaka, Zambia. No previous data was available locally on stroke types and clinical outcomes.

88% of strokes patients had access to brain imaging. Married patients had better access to brain imaging compared to single, separated and divorced. The access to brain imaging is relatively low compared to developed countries. But in Africa this is a very good access as part of UTH emergency care of stroke because countries such as Mauritania report only 58% of brain CT scan done among patients presenting to emergency department with presumed stroke.[55]

Stroke types

65% of patients had ischemic strokes and 35% had hemorrhagic strokes. Although hospital based strokes studies may bias the inclusion of cerebral hemorrhages which often has a more dramatic presentation.[56,57]Among our strokes patients, hemorrhagic strokes patients were brought in early and had more severe stroke. Some hospital based studies in Africa 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.[58] Conversely, hemorrhagic strokes were more frequently reported in other studies, making up to 60% of all strokes in 2 hospital based studies in Ghana[68] and Tanzania.[59] A study in the Democratic Republic of the Congo also found hemorrhagic strokes in 52% of participants.[19]

Age

Mean age for all strokes was 55 ± 18 years with 30% of all strokes patients below 45 years old. 14.8% of all strokes patients were more than 75 years old. This is typical of other studies of strokes in Sub-Saharan Africa.[60,61,62,63] In Senegal the mean age was 60.4 years, 58 years in the Gambia and 51 years in South Africa.[61,62] However we cannot ignore the possibility of hospital-admission bias influencing the age of patients in our and other hospital-based studies in Sub-Saharan Africa.

The mean age for ischemic strokes was 55 years and 56 years for hemorrhagic strokes. However a study in Senegal found hemorrhagic strokes patients to be significantly younger with mean age of 51 years compared to ischemic strokes patients who had mean of 64.2years.[62]

Time from onset to admission

72.3% of our stroke patients were admitted 24 hours or more after the onset of strokes. Late presentation of stroke patients was also reported in the Senegalese study in which the mean time to presentation was 2 days, ranging from 0 to 45days.[62]

Cardiovascular and other risk factors

Hypertension was the main risk factor as it was found in 71% of all strokes. Hypertensive patients presented significantly with more hemorrhagic strokes than ischemic. Hypertensive patients presenting with strokes were significantly non compliant to medication. Abundant observational and experimental evidence has demonstrated the strong relationship between blood pressure control and stroke, and the efficacy of blood pressure treatment to lower stroke risk.[64,65,66] Moreover, both the Heart Outcomes Prevention Evaluation (HOPE)[67] and the Perindopril Protection Against Recurrent Stroke Study (PROGRESS)[68] studies have demonstrated that reduction in the risk of stroke extends to patients with only moderately high levels of blood pressure. Despite available evidence, compliance to treatment remains poor in Africa. In Tanzania, less than 20% of hypertensive subjects were aware of their diagnosis, approximately 10% of them were treated, and less than 1% were controlled.[63,64] We are glad that an ongoing study on compliance among hypertensive patients was being conducted at UTH during the same time of our study, as the results would shed more light on the factors associated with this significant poor compliance to medication. Hypertension was reported to be important stroke risk factor in many studies across Africa encountered in 32.3% to 68% of ischemic strokes and in 44% to 93.1% of hemorrhagic strokes. Our findings are similar to these studies across Africa, such as study from South Africa and Senegal.[28,62]

Other important risk factors were diabetes mellitus and atrial fibrillation found significantly more among ischemic stroke patients.

HIV infection was encountered in 25.7% of all strokes who were tested for HIV infection. Although the prevalence in the general population in Zambia is 14%, we

found significant difference between ischemic and hemorrhagic strokes. The mean CD4 count was 155 cells/µl confirming a study done previously which found significant association of HIV and stroke in the young with CD4 count below 200 cells/µl.[42] In South Africa, The Durban stroke register found 20% of young black stroke patients to be HIV positive and have HIV-associated stroke,[30] but in the older rural SASPI stroke prevalence study only 2% of stroke patients were thought to be HIV positive.[30]

Factors independently associated with ischemic strokes as opposed to hemorrhagic strokes were atrial fibrillation and HIV infection while hypertension favored hemorrhagic strokes. Sex, Tobacco smoking/sniffing, previous strokes and diabetes mellitus favored neither ischemic stroke nor hemorrhagic strokes in our patients.
A multivariate logistic regression analysis in a Danish study showed that diabetes favored ischemic strokes but neither hypertension nor sex favored either of the strokes types.[66]

Stroke severity and clinical outcome

NIHSS mean in all strokes was 12.4 ± 8.5. Stroke severity was similar to patients in a South African study[45] which reported a mean NIHSS of 12 ± 9 but in the Gambia stroke was more severe with mean NIHSS of 16 ± 7.

Stroke Mortality

40% of all strokes patients died. 33.3% of ischemic strokes patients died compared to 53.4% of hemorrhagic strokes. Hemorrhagic strokes were associated with more death. The case fatality rate was high compared to western cohorts but in Africa the findings are similar to a Nigerian study which found high mortality with the 30 days stroke case fatality rate as high as 40%[8,17] and the Gambia study[8] which found in-hospital case fatality rate of 41%.

Factors associated with mortality in stroke patients at UTH

Factors independently associated with mortality among UTH stroke patients were female sex, pneumonia, low Glasgow Coma Scale (GCS<8) and NIHSS ≥ 14. Our findings were similar to the Gambian study.[8] In the Gambia, a study found that severity of stroke was high on admission especially in women and was strongly

correlated to the outcome[8] and consciousness level on admission were strong predictors of the mortality risk. Swallowing difficulties at admission, fever and lung infection were independently risk factors of the lethal outcome. Other predictor of mortality among our stroke patients was hemorrhagic type of stroke.

We found being female had an associated higher mortality, which was comparable to what has been reported in other studies such as the Canadian study of differences in strokes outcome based on sex.[69] It was found in this study that women had poor outcome compared to men unless treated with thrombolysis.[69]Among our patients we found that 36.9% of women were widowed compared to only 3.2% of men being widowers. We also found that widowed or single patients had poor access to brain imaging. Widowed female stroke patients might not have the necessary support during illness. HIV positive status, previous strokes, presentation to hospital after 24 hours, distance from hospital did neither favor mortality nor good outcome.

Study limitations

Hospital based study such as this one is unlikely to reflect strokes in the community, as not all stroke patients are admitted to the hospital. In addition we had utilized convenient sampling so this also reduces the generalizability of the study.

There are several reasons postulated why stroke patients may not be admitted to the hospital including:

- early death before hospital admission. (This could be the case in our study as late presentation was not associated with increased mortality in our study).
- limited resources, such as lack of transportation for stroke patients.
- mild stroke patients attending out patients clinics.
- and ignorance to seek medical help.

The other limitation was financial, as not all our patients were fully investigated.
We will not under estimate the possibility of recall bias concerning risk factors such as family history of strokes and age as some patients or their relatives could not remember their exact date of birth.

CHAPTER 7

CONCLUSION

The study found that ischemic stroke occurred in 65% of patients with stroke while hemorrhagic stroke was found in 35% with no difference in gender between the two types. Married patients had better access to brain imaging. Strokes among our participants occur in relatively younger patients compared to western cohorts as the mean age at presentation was found to be 55 ± 18 years. Mean age for ischemic strokes was 55 ± 18 years and 56 ± 16 years for hemorrhagic strokes.

Factors independently associated with ischemic stroke among participants were atrial fibrillation and HIV infection. Hypertension was found to be associated with hemorrhagic strokes. Strokes were severe and in-hospital mortality was high and was found to be 40% for all strokes. Hemorrhagic type of strokes was associated with worse outcome as expected. In-Hospital mortality was 53% for hemorrhagic strokes and 33% for ischemic strokes.

Factors independently associated with mortality were: Female sex, stroke severity (NIHSS $\geq$ 14), Low GCS ($\leq$ 8), hemorrhagic type of strokes and pneumonia. We also found that HIV positive status, distance from hospital and presentation after 24 hours were not predictors of stroke mortality.

RECOMMENDATIONS

We carried out the study of the nature and outcome of strokes at UTH and in view of our findings, we recommend the following:

1. Complete general and neurologic assessment of stroke patients including documentation of admission GCS and NIHSS should be performed at UTH, as these were found to be strong predictors of stroke mortality in our setting. Brain CT scans should be done on admission within 24hours on all strokes patients.

2. The social services of UTH should pay more attention to vulnerable groups such as the widows, single and divorced patients as they were found to have significantly low access to brain imaging.

3. Health education to be promoted to encourage the community to bring stroke patients early to the hospital and the stroke referral from the district to be done early. Health education should also address stroke prevention.

4. More neurologists and radiologists should be trained to help address this serious problem in Zambia.

5. Finally, we recommend that a much bigger community based stroke study be done in Zambia. This will enable us to have a better picture of strokes in this country and in Africa in general.

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APPENDIX

Appendix 1: Information sheet for Nature and outcome of stroke study

You are invited to take part in a study looking at the nature of stroke in patients admitted to UTH. This study is being done as part of requirement for a master of internal medicine. Information about this study is supplied in this document. One of the study team will be on hand to explain the contents and answer all your questions. Please make sure that you understand everything in this document. If you decide to participate you will be asked to give consent before you take part.

Participation in this study is completely voluntary. You are under no obligation to take part. You are free to withdraw from this study at any time. This will have no consequences for your medical care. No financial reward will be given to any persons taking part in this study.

Title of study

NATURE AND OUTCOME OF STROKE IN ADULT ZAMBIAN PATIENTS ADMITTED AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA.

- **Who is doing the study?**

Dr Patrice Mukomena Ntanda is the principal investigator under the supervision of Professor Masharip Atadhzanov. The principle investigator is responsible for the day to day running of the study. We can be contacted via Department of medicine, University Teaching Hospital, **Lusaka, Zambia**

Tel: 00260979832265, 0977775662

EMAIL: patricemuko@yahoo.fr, masharip@yahoo.com.

The study has been approved by the Medical Ethics Committees of the University of Zambia and the school of medicine post graduate forum. They can be contacted on the following number: +260 1 256067 or at this address: Biomedical Research Ethics Committee, University of Zambia, Ridgeway Campus, PO Box 50110, Lusaka, Zambia

- **What is the purpose of this study?**

Stroke is a major health problem in the world and increasingly in Zambia. Cerebrovascular accident may occur as a result of hemorrhage or infarction in the brain. It is an emergency and early diagnosis is important to save life. Patients presenting with stroke can have some

risk factors such as diabetes, hypertension, high cholesterol, smoking and others may also have members of the family affected earlier on.

The aim of this project is to see the number of people presenting to UTH with stroke, determine the nature and the outcome of stroke. In addition we want to see the contribution of other factors like hypertension, diabetes, high cholesterol, Smoking and compare the outcome of ischemic to hemorrhagic stroke.

- **What is stroke?**

Stroke is a sudden manifestation of a neurological deficit of vascular origin lasting more than 24 hours.

- **Procedure of the study**

1. If you agree to take part in this project you will be asked to sign or print a consent form. You will be given a copy of this information sheet and the consent form to keep.
2. You (patient or relatives if aphasic or unconscious) will then be interviewed. The interview will start with questions about your age, sex and place where you live. You will then be asked questions about your illness including the symptoms and length of time you have been unwell. You will be asked questions about your past medical history. You will be asked a few questions related to your general health and the health of yours parents and siblings. The interview will take about 30 minutes or less.
3. Your medical notes will be reviewed and your progress while you are an inpatient at UTH will be followed.
4. Investigations done/reviewed during this Study will include Brain Imaging(CT Scan), blood for lipid profile, coagulation profile, full blood count, DNA extraction/analysis, Lipidogram, Random and fasting blood glucose, Echocardiography, Electrocardiography and Urinalysis.

The information you give in the interview and in the notes will be analyzed with the other results from the study and will be kept strictly confidential.

- **Are there any risks for people taking part in this study?**

Some of the questions in the interview related to your health and your family history are personal and may cause you distress. If the interview is distressing you we will not continue.

Taking part in the interview will not interrupt your clinical care.

While we will be reviewing your notes and investigations we will not be directly involved in your clinical care, physician attending to you will be in charge of your treatment and care.

- **Benefits**

The main benefit from this study will be a greater understanding of the nature and outcome of stroke in patients admitted to UTH and a better understanding of the risk factors in patients with stroke presenting to UTH. We hope this will lead to adequate planning and care for patients with stroke at UTH in the future.

- **Confidentiality**

All information that you give in the interview and we obtain from your records will be kept confidential. Your identity will not be disclosed in any report or publication that results from this study. The data we collect will be kept securely and it will only be accessible to medical staff taking part in the research. The research ethics committees of the University of Zambia and the department of medicine/UTH may review the data for verification purposes.

If you have any questions about this study please ask them now. If you have any later questions or concerns please contact, Dr Patrice Mukomena Ntanda or Professor Masharip Atadzhanov at the above address. Please keep this information sheet in a safe place, thank you.

Appendix 2: informed consent form for nature and outcome of stroke study:

1. I have been invited to take part in a research project being conducted at the University Teaching Hospital by Dr Patrice Mukomena Ntanda and Professor Masharip Atadhzanov department of medicine, UTH, Lusaka, Zambia; Tel:00260979832265.
2. The study is being supervised by professor Atadzhanov, Department of medicine, School of Medicine, UNZA. Tel 00260977775662.
3. I have been told the purposes of this research and understand the processes involved. I understand the potential distress that may occur.
4. I have been given a list of names and addresses of people and institutions I may contact in relation to this research. I have read the information in the **nature and outcome of stroke information sheet** or have had it read or explained to me.
5. I have had the opportunity to ask questions and have had these answered satisfactorily.
6. I understand that I have the right to refuse to participate in this study or withdraw from the study at any time. I understand that refusing to take part or withdrawing from the study will in no way compromise my clinical care.
7. I agree to take part in the study

Participant's information:

Signature (or fingerprint): _____

Surname:

Name: _____

Date: _____

The person who conducts the informed consent discussion must also sign and date this form.

Signature: _____

Date: _____

Surname: _____

Name: _____

Signature of witness, if applicable.

Witnessed by: (print name): _____

Signature of Witness: _____

Date _____

QUESTIONAIRE FOR NATURE AND OUTCOME OF STROKE STUDY

A. Personal details

1. STUDY ID: _____
2. File Number: _____
3. RESIDENCE(City or village name): _____
4. Township of residence: _____

5. Phone number of patient or next of kin_____

6. Age_____ or date of birth _____

7. Sex: □ Male □ Female

8. Profession: _____

9. Educational level: □ Unknown □ None
   □ Primary □ College
   □ Secondary □ University

10. Marital status: □ Single □ Married
    □ Widowed □ Divorced

11. Tribe_____

12. Date of registration_____

B. Clinical evaluation

13. Date of onset of presenting Stroke symptoms _____ Time_____

□Woke with symptoms (If woke with symptoms use time that patient went to sleep well)

14. Date of Admission to UTH _____Time

15. CT Scan Brain ☐ Done ☐ Not done Date _____Time_____

16. Date of blood draw_____

17. What is the Stroke Subtype?

☐ Intracerebral hemorrhage ☐ Ischemic small vessel (Lacunar)

☐ Ischemic Large artery ☐ SAH

☐ Cardioembolic ☐ Undetermined

☐ CT not done

18. PMHx/Risks Factors:

Previous Stroke yes ☐ No ☐

HTN Yes ☐ No ☐

MI/CAD yes ☐ No ☐

CHF yes ☐ No ☐

Hyperlipidemia yes ☐ No ☐

Diabetes Mellitus yes ☐ No ☐

Atrial Fibrillation yes ☐ No ☐

Valvular Heart Disease yes ☐ No ☐

Miscarriage Yes ☐ No ☐

Family hx of stroke: Yes ☐ No ☐

Obesity Yes ☐ No ☐

Smoker Current ☐ Ex>1year ☐ Never ☐

Alcohol Current ☐ Ex>1year ☐ Never ☐

Sickle cell disease yes ☐ No ☐

HIV infection Yes ☐ No ☐

CD4 Count _____

Other _____

19**. Home medications** ☐ Aspirin ☐ Warfarin ☐ B blockers

☐ Ca++ channel blocker ☐ ACE inhibitors

Compliance
Yes ☐
No ☐

☐ Antiretroviral ☐ Oral hypoglycaemic
☐ Lipid lowering drugs ☐ others ☐ none

20. **Rev of Systems** : ☐ Fever ☐ Chest pain ☐ SOB/DOE

☐ RTI ☐ Dyspepsia ☐ Hemoptysis

☐ Headache/ Neckache

Physical exam:

21 Vital Sign: BP___ HR____ RR____ T_____ Adm RBS_____ Chol____

22 **Mental Status:** ☐Alert/responsive (0)

☐Arouses only to pain (2)

☐Unarousable /reflexive withdrawal (3)

☐Doesn't know age (1)

☐ Doesn't know name (1)

☐Doesn't follow close/open eyes (1)

☐Doesn't follow close/open hand (1)

Sub-Total1 _____

23. **GAZE/EOMs** (Horizontal): ☐ Normal (0) ☐Impaired (1) ☐Forced (2)

24. **Visual Field**: ☐ Normal (0) ☐Partial loss (quadrant) (1)

☐Complete homonymous (2) ☐Blind/bilateral (3)

25. **Facial Appearance** ☐Normal (0) ☐Minor/asymmetric/flat nasolabial fold (1)

☐Lower only (2) ☐Upper & lower palsy (3)

Sub-Total2 _____

26. MOTOR

M O T O R	Left arm (10sec)	Right arm (10sec)	Left leg (5 sec)	Right leg (5sec)
Raised extremities	**L**	**R**	**L**	**R**
Normal/no drift (0)				
Drift only (1)				
Some antigravity (2)				
No effort against gravity (3)				
No movement (4)				
Amputation/Joint fusion (9)				

Sub-Total arm3 + leg _____

27. Cerebellar ataxia: ☐ None ☐ R ☐ L
☐ One limb (1)
☐ Two limbs (2)
☐ Untestable

28. GAIT: ☐ Normal ☐ Wide base ☐ falls to ☐ R ☐ L

29. Sensory: ☐ Normal (0) ☐ R ☐ L
☐ Impaired/unilateral (1)
☐ Complete loss/bilateral (2)

30. **Language:** ☐ Normal (0)
☐ Mild/moderate aphasia, but Comprehensible (1)
☐ Severe aphasia, almost no Communication (2)
☐ Global aphasia/mute (3)

31. **Dysarthria:** ☐ Normal (0)
☐ Mild/moderate slurring (1)
☐ Severe/unintelligible (2)

32. NEGLECT: ☐ Normal (0) ! R ! L
☐ One modality (1)
☐ Two modalities (2)

Sub-Total4_____

33. STROKE CLASSIFICATION

Oxfordshire ☐ TACs ☐ LACS

❐PACS ❐POCS

Admit NIHSS = Sub-Totals 1-4_____

Admit mRankin scale _____

Admit Barthel Index score _____

Admit GCS_____

34. Stroke Outcome: Glasgow outcome Scale_____

☐ In-hospital mortality ☐ Discharge without Disability

☐ Discharge with Disability

35. Date of Discharge_____ or date of in-hospital death_____

Date

Time

Name of Physician

NIH Stroke Scale

The NINDS tPA Stroke Trial No. ___ ___ - ___ ___ ___ - ___ ___ ___

Pt. Date of Birth ___ ___ / ___ ___ / ___ ___

Hospital _____ (___ ___ - ___ ___)

Date of Exam ___ ___ / ___ ___ / ___ ___

Interval: 1 ☐ Baseline 2 ☐ 2 hours post treatment 3 ☐ 24 hours post onset of symptoms 6 minutes
4 ☐ 7–10 days 5 ☐ 3 months 6 ☐ Other _____ (___ _____)

Time: ___ ___:___ ___ 1 ☐ am 2 ☐ pm

Administer stroke scale items in the order listed. Record performance in each category after each subscale exam. Do not go back and change scores. Follow directions provided for each exam technique. Scores should reflect what the patient does, not what the clinician thinks the patient can do. The clinician should record answers while administering the exam and work quickly. Except where indicated, the patient should not be coached (i.e., repeated requests to patient to make a special effort).

IF ANY ITEM IS LEFT UNTESTED, A DETAILED EXPLANATION MUST BE CLEARLY WRITTEN ON THE FORM. ALL UNTESTED ITEMS WILL BE REVIEWED BY THE MEDICAL MONITOR, AND DISCUSSED WITH THE EXAMINER BY TELEPHONE.

Instructions	Scale Definition	Score
1a. Level of Consciousness: The investigator must choose a response, even if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.	0 = Alert; keenly responsive. 1 = Not alert, but arousable by minor stimulation to obey, answer, or respond. 2 = Not alert, requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped). 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, areflexic.	_____
1b. LOC Questions: The patient is asked the month and his/her age. The answer must be correct — there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or non-verbal cues.	0 = Answers both questions correctly. 1 = Answers one question correctly. 2 = Answers neither question correctly.	_____
1c. LOC Commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one-step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to them (pantomime) and score the result (i.e., follows none, one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored.	0 = Performs both tasks correctly 1 = Performs one task correctly 2 = Performs neither task correctly	_____

NIH Stroke Scale

The NINDS tPA Stroke Trial No. __ __ - __ __ __ - __ __ __

Pt. Date of Birth __ __ / __ __ / __ __

Hospital _____ (__ __ - __ __)

Date of Exam __ __ / __ __ / __ __

Interval: 1 ☐ Baseline 2 ☐ 2 hours post treatment 3 ☐ 24 hours post onset of symptoms 6 minutes
4 ☐ 7–10 days 5 ☐ 3 months 6 ☐ Other _____ (__ _____)

Instructions	Scale Definition	Score
2. Best Gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV or VI) score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness or other disorder of visual acuity or fields should be tested with reflexive movements and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.	0 = Normal 1 = Partial gaze palsy. This score is given when gaze is abnormal in one or both eyes, but where forced deviation or total gaze paresis are not present. 2 = Forced deviation, or total gaze paresis not overcome by the oculocephalic maneuver.	_____
3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat as appropriate. Patient must be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia is found. If patient is blind from any cause, score 3. Double simultaneous stimulation is performed at this point. If there is extinction, patient receives a 1, and the results are used to answer question 11.	0 = No visual loss 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia (blind including cortical blindness)	_____
4. Facial Palsy: Ask, or use pantomime to encourage the patient to show teeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape or other physical barrier obscures the face, these should be removed to the extent possible.	0 = Normal symmetrical movement 1 = Minor paralysis (flattened nasolabial fold, asymmetry on smiling) 2 = Partial paralysis (total or near total paralysis of lower face) 3 = Complete paralysis of one or both sides (absence of facial movement in the upper and lower face)	_____

NIH Stroke Scale

The NINDS tPA Stroke Trial No. __ __ - __ __ __ - __ __ __

Pt. Date of Birth __ __ / __ __ / __ __

Hospital _____ (__ __ - __ __)

Date of Exam __ __ / __ __ / __ __

Interval: 1 ☐ Baseline 2 ☐ 2 hours post treatment 3 ☐ 24 hours post onset of symptoms 6 minutes
4 ☐ 7–10 days 5 ☐ 3 months 6 ☐ Other _____ (__ _____)

Instructions	Scale Definition	Score
5 & 6. Motor Arm and Leg: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine) and the leg 30 degrees (always tested supine). Drift is scored if the arm falls before 10 seconds or the leg before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder or hip may the score be "9" and the examiner must clearly write the explanation for scoring as a "9."	0 = No drift, limb holds 90 (or 45) degrees for full 10 seconds. 1 = Drift, Limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. 2 = Some effort against gravity, limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. 3 = No effort against gravity, limb falls. 4 = No movement 9 = Amputation, joint fusion explain: _____ **5a. Left Arm**	_____
	5b. Right Arm	_____
	0 = No drift, leg holds 30 degrees position for full 5 seconds. 1 = Drift, leg falls by the end of the 5-second period but does not hit bed. 2 = Some effort against gravity; leg falls to bed by 5 seconds, but has some effort against gravity. 3 = No effort against gravity, leg falls to bed immediately. 4 = No movement 9 = Amputation, joint fusion explain: _____ **6a. Left Leg**	_____
	6b. Right Leg	_____

NIH Stroke Scale

The NINDS tPA Stroke Trial No. ___ ___ - ___ ___ ___ - ___ ___ ___

Pt. Date of Birth ___ ___ / ___ ___ / ___ ___

Hospital _____ (___ ___ - ___ ___)

Date of Exam ___ ___ / ___ ___ / ___ ___

Interval: 1 ☐ Baseline 2 ☐ 2 hours post treatment 3 ☐ 24 hours post onset of symptoms 6 minutes
4 ☐ 7–10 days 5 ☐ 3 months 6 ☐ Other _____ (___ _____)

Instructions	Scale Definition	Score
7. Limb Ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion may the item be scored "9," and the examiner must clearly write the explanation for not scoring. In case of blindness, test by touching nose from extended arm position.	0 = Absent 1 = Present in one limb 2 = Present in two limbs If present, is ataxia in Right arm 1 = Yes 2 = No 9 = amputation or joint fusion, explain _____ Left arm 1 = Yes 2 = No 9 = amputation or joint fusion, explain _____ Right leg 1 = Yes 2 = No 9 = amputation or joint fusion, explain _____ Left leg 1 = Yes 2 = No 9 = amputation or joint fusion, explain _____	_____ _____ _____ _____
8. Sensory: Sensation or grimace to pinprick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas [arms (not hands), legs, trunk, face] as needed to accurately check for hemisensory loss. A score of 2, "severe or total," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will therefore probably score 1 or 0. The patient with brain stem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in coma (item 1a=3) are arbitrarily given a 2 on this item.	0 = Normal; no sensory loss. 1 = Mild to moderate sensory loss; patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick but patient is aware he/she is being touched. 2 = Severe to total sensory loss; patient is not aware of being touched in the face, arm, and leg.	_____
9. Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. The patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet, and to read from the attached list of sentences. Comprehension is judged from responses here as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in coma (question 1a=3) will arbitrarily score 3 on this item. The examiner must choose a score in the patient with stupor or limited cooperation but a score of 3 should be used only if the patient is mute and follows no one-step commands.	0 = No aphasia, normal 1 = Mild to moderate aphasia; some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided material difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card from patient's response. 2 = Severe aphasia; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = Mute, global aphasia; no usable speech or auditory comprehension.	_____

NIH Stroke Scale

The NINDS tPA Stroke Trial No. ___ ___ - ___ ___ ___ - ___ ___ ___

Pt. Date of Birth ___ ___ / ___ ___ / ___ ___

Hospital _____ (___ ___ - ___ ___)

Date of Exam ___ ___ / ___ ___ / ___ ___

Interval: 1 ☐ Baseline 2 ☐ 2 hours post treatment 3 ☐ 24 hours post onset of symptoms 6 minutes
4 ☐ 7–10 days 5 ☐ 3 months 6 ☐ Other _____ (___ _____)

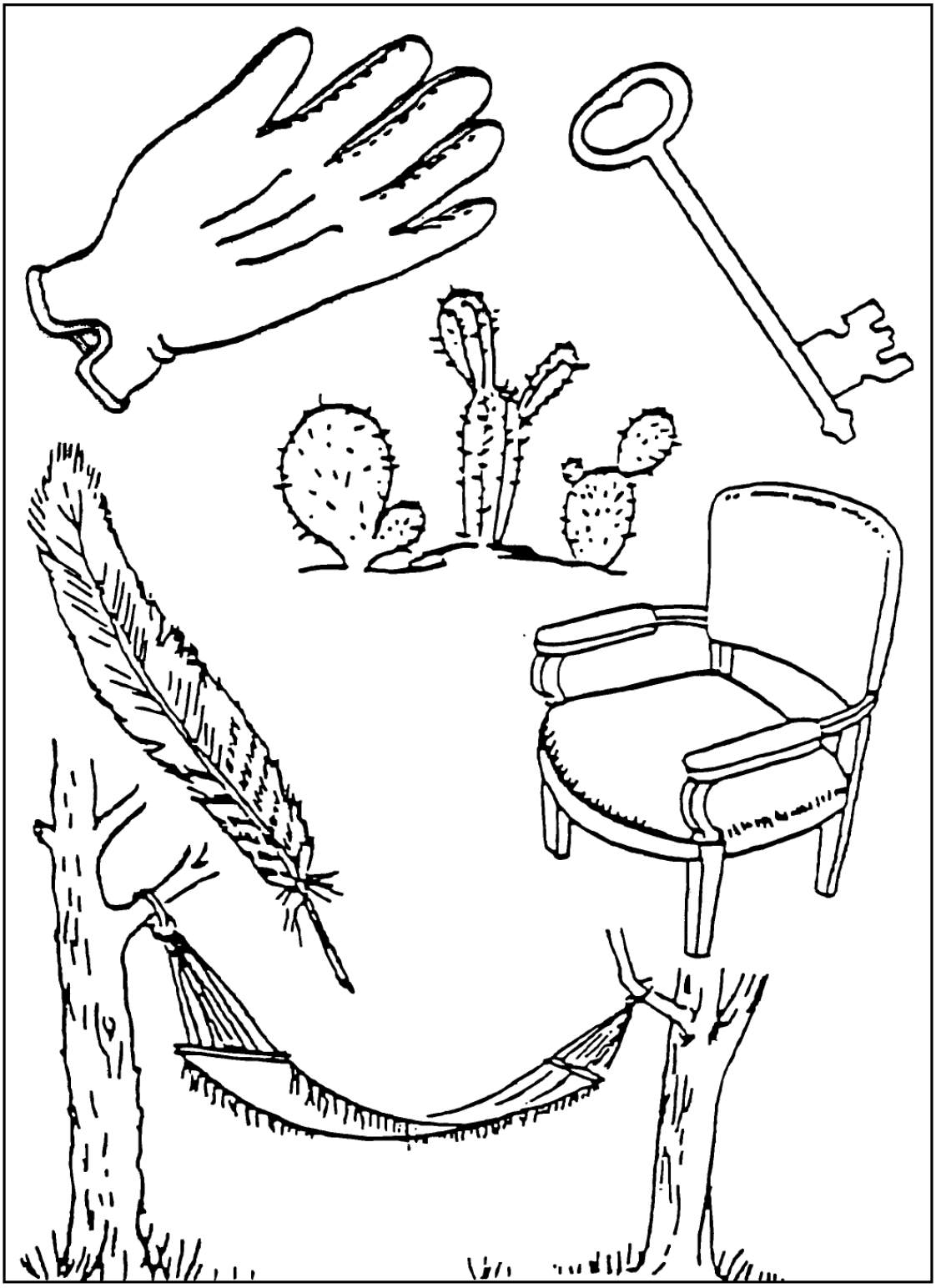
Instructions	Scale Definition	Score
10. Dysarthria: If patient is thought to be normal, an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barrier to producing speech may the item be scored "9," and the examiner must clearly write an explanation for not scoring. Do not tell the patient why he/she is being tested.	0 = Normal 1 = Mild to moderate; patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = Severe; patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric. 9 = Intubated or other physical barrier, explain _____	_____
11. Extinction and Inattention (formerly Neglect): Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.	0 = No abnormality. 1 = Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 = Profound hemi-inattention or hemi-inattention to more than one modality. Does not recognize own hand or orients to only one side of space.	_____

Additional item, not a part of the NIH Stroke Scale score.

A. Distal Motor Function: The patient's hand is held up at the forearm by the examiner and patient is asked to extend his/her fingers as much as possible. If the patient can't or doesn't extend the fingers, the examiner places the fingers in full extension and observes for any flexion movement for 5 seconds. Only the patient's first attempts are graded. Repetition of the instructions or of the testing is prohibited.	0 = Normal (No flexion after 5 seconds) 1 = At least some extension after 5 seconds, but not fully extended. Any movement of the fingers which is not upon command is not scored. 2 = No voluntary extension after 5 seconds. Movements of the fingers at another time are not scored. **a. Left Arm** **b. Right Arm**	_____ _____

12. _____ (___ ___ ___)
Person Administering Scale Code

NIH stroke scale



Modified Rankin Scale

0 □ No symptoms at all.

1 □ No significant disability despite symptoms; able to carry out all usual duties and activities.

2 □ Slight disability; unable to carry out all previous activities but able to look after own affairs without assistance.

3 □ Moderate disability requiring some help, but able to walk without assistance.

4 □ Moderate severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance.

5 □ Severe disability; bedridden and requiring constant nursing care and attention.

Glasgow Outcome Scale (GOS)

1. □ Good recovery- patient can lead a full and independent life with or without minimal neurological deficit.

2. Moderately disabled; patient has neurological and intellectual impairment but is independent.

3. Severely disabled; patient conscious but totally dependent on others to get through daily activities.

4. Vegetative survival.

5. Dead

THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

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Lusaka, Zambia

Assurance No. FWA00000338
IRB00001131 of IORG0000774

7 July, 2010
Ref.: 011-06-10

Dr Patrice Mukomena Ntanda, BScHB, MBChB
Department of Medicine
University of Zambia/UTH
LUSAKA

Dear Dr Ntanda,

RE: SUBMITTED RESEARCH PROPOSAL: **"NATURE AND OUTCOME OF STROKE IN ADULT PATIENTS ADMITTED TO THE UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA"**

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee on 27 April, 2010 where changes/clarifications were recommended. We would like to acknowledge receipt of the corrected version with clarifications. The proposal is now approved.

CONDITIONS:

- This approval is based strictly on your submitted proposal. Should there be need for you to modify or change the study design or methodology, you will need to seek clearance from the Research Ethics Committee.
- If you have need for further clarification please consult this office. Please note that it is mandatory that you submit a detailed progress report of your study to this Committee every six months and a final copy of your report at the end of the study.
- Any serious adverse events must be reported at once to this Committee.
- Please note that when your approval expires you may need to request for renewal. The request should be accompanied by a Progress Report (Progress Report Forms can be obtained from the Secretariat).
- **Ensure that a final copy of the results is submitted to this Committee.**

Yours sincerely,

Dr James Munthali
A/CHAIRPERSON

Date of approval: 7 July, 2010 **Date of expiry**: 6 July, 2011