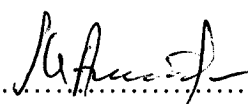
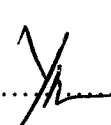


APPROVAL PAGE

This dissertation of NASON LAMBWE has been approved as fulfilling the requirements or partial fulfillment of the requirements for the award of Master of Medicine in INTERNAL MEDICINE by the University of Zambia.

Examiners

1. Signature.......... Date.....1/06/05.....
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**THE UNIVERSITY OF ZAMBIA
SCHOOL OF MEDINE
DEPARTMENT OF INTERNAL MEDICINE**

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**TITLE: STROKE IN THE YOUNG ADULTS AT THE UNIVERSITY
TEACHING HOSPITAL, LUSAKA**

**A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT
OF THE REQUIREMENTS FOR THE MASTERS OF MEDICINE
DEGREE IN INTERNAL MEDICINE**



DISSERTATION

**TITLE: STROKE IN YOUNG ADULTS (15-45 YEARS
AT UNIVERSITY TEACHING HOSPITAL (UTH)**

RESEARCH : DR. N. LAMBWE, BScHB, MBChB

SUPERVISOR: PROF. M. ATADZHANOV, MD DSc

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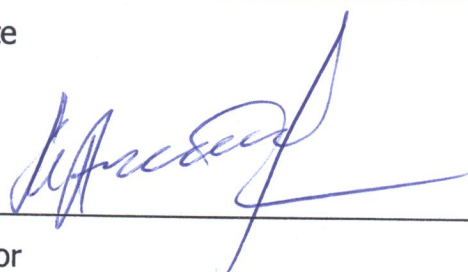
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DECLARATION


I hereby declare that this dissertation nor part thereof has not been presented for any other degree.

It is not currently submitted for any degree.

Signed:  _____
Candidate

Signed:  _____
Supervisor

Signed:  _____
Co-supervisor

Signed:  _____
Head of Department

DEDICATION

I dedicate this piece of work to you my wife Aggie, children Nathan, Grace and Elijah and sister Kayula. You have been of great support and encouragement when dad was pre-occupied with the dissertation to the exclusion of family life that is normal.

I did this to show that by this kind of hard work we must live.

"One who is slack in his work is brother to one who destroys"

Proverbs 18:9

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Nason

ABBREVIATIONS

ICH	-	Intracranial haemorrhage
SAH	-	Subarachnoid
TIA	-	Transient Ischaemic Attack
APC	-	Activated Protein C
PNH	-	Paroxysmal Nocturnal Haemoglobinuria
LP(a)	-	Lipoprotein a
AVMs	-	Arterio Venous Malformations
AIDS	-	Acquired Immune Deficiency Syndrome
CMV	-	Cytomegalovirus
CADASIL	-	Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy
HIV	-	Human Immune Deficiency Virus
AHA	-	American Heart Association
SCD	-	Sickle Cell Disease
DM	-	Diabetes Mellitus
MS	-	Mitral Stenosis
DVT	-	Deep Vein Thrombosis
CVS	-	Cardiovascular System
UTH	-	University Teaching Hospital
RPR	-	Reagen Plasma Reagent
RBS	-	random Blood Sugar
Hb	-	Haemoglobin
ESR	-	Erythrocyte Sedimentation Rate
ECG	-	Electrocardiogram
CT Scan	-	Computerised Tomography Scan
CVD	-	Cerebrovascular Disease

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ABSTRACT

Study Setting

This six month prospective case controlled study involving sixty patients was conducted at the University Teaching Hospital, Lusaka, Zambia.

Objectives

To study the relationship between strokes in the young adults (15-45 years) and HIV infection.

Design and Methods

Thirty young adults conveniently chosen who presented with stroke were counselled and had an HIV test done. After a full history and examination, investigation done included RPR, CT, RBS, ECG, ECHO, LP, FBC, U/E, CD4 and LFT. A matched control group of thirty patients was also recruited.

Results

The results showed 25 (83.3%) of stroke patients were positive for HIV while the seroprevalence in the control group was (53.3%). The median age for strokes was 29 and the other major risk factor apart from HIV infection was cardiovascular abnormalities, which were present in 3 patients (10%). Most of the patients had stigmata of retroviral disease although most of the investigations were negative for HIV related pathogens. The major CT scan finding was normal except for one patient who had suspected toxoplasmosis. Many patients had anemia of chronic ill health and generally reported late to the hospital.

Conclusion

HIV is strongly associated with strokes in the young adults.

CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

Stroke, a focal neurological deficit (1), is the third leading cause of death in the United States. It is the most common neurological problem in the world (2-3). There's little data on the incidence and prevalence of strokes in the African setting. Stroke is nonetheless an increasing problem (4). Though stroke incidence increases with age, it does occur across all age groups. Its occurrence in the younger age groups is not rare (5). Stroke is catastrophic event in any individual's life and is especially tragic in children with potential long-term disability and burden for the victims, families and community (6).

The causes of stroke in the young are varied. With Human Immunodeficiency Virus (HIV), it is expected that the number of cases of strokes will be higher. Not much work has been done on the relationship between HIV and stroke in the young. There's an association between HIV and cerebrovascular disease (CVD). CVD may take the form of transient ischaemic attacks (TIAs), or thrombo-embolic or haemorrhagic strokes.

Stroke increases both morbidity and mortality in patients with HIV/AIDS. HIV-positive patients are at risk for strokes at much younger ages than typically are associated with stroke (7).

Less than 5% of all strokes occur in subjects less than 45 years of age in Western countries (8). Occurrence of between 19% and 30% was reported in the developing countries (9). Morbidity and mortality is high in blacks (10).

smoking, alcohol consumption any illicit drug use) can significantly increase the rate of stroke among young adults in a community. Smoking is a risk factor for ischaemic strokes. This is due to increased fibrogen levels and platelet adhesiveness and reduced cerebral blood flow mainly due to atheroma formation (14). Marijuana smoking increases the risk of arterial thrombosis in individuals heterozygous for factor V Leiden (15). Cocaine and heroine use predispose to cerebral vascular disease. Cocaine can cause hypertension which lead to haemorrhagic strokes and Ischaemia through vasospasms. Heroin causes vasculitis. Its non-soluble contaminants occlude blood vessels. Heavy alcohol drinking and particularly binge drinkers are exposed to a higher risk for cardioembolic strokes (16). Hypertension is strongly associated with subsequent stroke risk whereas hypercholestromia is related to death from non-haemorrhagic stroke (13).

Atherosclerosis is a common cause of stroke. Fatty deposits and platelets collect on the wall of the arteries forming plaques. If it involves the internal carotid artery it is an important cause of stroke (17). Diabetes mellitus and increased cholesterol levels among many others predispose to atherosclerosis. Diabetes Mellitus doubles the risk of stroke.

The risk of stroke is increased in current oral contraceptive users (18). There's an association of 3 fold increase of strokes.

Age is an important non-modifiable risk for stroke. Risk doubles every decade (4). The risk is strongest from cerebral infarction, primary intracranial haemorrhage and subarachnoid haemorrhage. Male sex is most prominent in the middle age as a risk factor for stroke. History of transient ischaemic attack (TIA) or stroke itself increases the chance of further strokes. Diseases causing increased blood viscosity predispose to cerebral infarction. Patients with blood

dyscrasias are prone to recurrent strokes. Victims are usually younger than stroke patients in the general population (19).

There is thrombosis in the cerebral vasculature leading to ischaemic cerebrovascular events. Thrombosis is due to platelet function abnormality, inherited haemostatic abnormality or vascular injury. Mutations of factor V Leiden (i.e. activated protein C resistance (APC) of prothrombin gene mutation (FII G20210A) is associated with tendency towards ischaemic strokes (20).

Resistance to activated protein C (APC) is the most frequent cause of thrombophilia and a well-known risk factor for deep and cerebral vein thrombosis (21). APC is associated more with venous sinus thrombosis than arterial mechanism hence paradoxical embolism. Protein C, Protein S and ant thrombin III deficiencies are all frequently associated with cerebral thrombosis.

Sickle cell anaemia predisposes to strokes. It causes vasculopathies and stasis in small arteries and this is the principle mechanism by which it causes strokes.

In dysfibrinogenemia, which is genetically caused there is hypofibrinolysis. Fibrinogen molecules form clots that bind with increased avidity to platelets to promote thrombosis (19) especially in young individuals.

Hyperviscosity is also caused by polycythaemia vera which causes diminished cerebral blood flow. Essential thrombocytopaenia and paroxysmal nocturnal haemoglobinuria (PNH) cause cerebrovascular thrombotic events.

Coagulation factor XIII which is involved in haemostasis, fibrinolysis, vascular remodeling and tissue repair is implicated in haemorrhagic strokes. Phe 204 and Leu 564 variants of the factor may be markers for genetic susceptibility to haemorrhagic strokes in women less than 45 years (22). Hyperhomocystinaemia

is a factor in stroke. Stroke patients have homocysteine levels one and half times those for age and sex matched controls. Mechanism is mainly vasculopathy and an arterial more than venous strokes are caused (21). Cystathione beta synthase deficient homozygous individuals develop premature arteriosclerosis and others experience stroke early in life.

Hyperhomocystinaemia is more commonly acquired. Causes of the acquired forms are

- Dietary deficiency of folic acid
- Dietary deficiency of vitamin B12
- Use of anticoagulants e.g. phenytoin
- Renal insufficiency

Antiphospholipid syndrome occurs in 10% patients with ischaemic strokes and number higher in younger patients. There is a hyper-coagulable state and cerebrovascular endotheliopathy (19). A lupus anticoagulant or antiphospholipid antibody is present.

Anticardiolipin antibodies are a heterogeneous group of antiphospholipid antibodies that are associated with arterial and venous thrombosis. They confer a strong independent risk for venous thromboembolism (23). Increased lipoprotein (a) Lp (a) is a potent risk factor for stroke especially in young individuals (19).

Cardiac causes and risk factors for stroke have generally been discussed under cardioembolic stroke. They may be asymptomatic (24). Atrial fibrillation, even in the absence of rheumatic valvular disease predisposes patients to embolic complications (25). In another study, atrial fibrillation has a small impact on morbidity and mortality in young patients with normal hearts (26). In infective endocarditis neurological complication pose a significant problem (27). In

patients of left atrial myxoma younger and male patients have more neurological symptom and female patients have more systemic symptoms (28). There is a relationship between atrial septal anomalies and latent atrial vulnerability in unexplained ischaemic stroke of young adults (29). Cardioembolic stroke is largely preventable making measures of primary prevention valuable (30).

Intracranial arteriovenous malformations (AVMS) are typically diagnosed before the patient has reached the age of 40 years. More than 50% of AVMS present with intracranial haemorrhage (31).

Infection is an important cause and predisposing factor for stroke in young individuals.

HIV infection of the central nervous system is an early event after initial exposure. Virus infected monocytes cross the blood brain barrier. Microphage factors induced by HIV have been shown to have neurotoxic effects (32).

CNS involvement in HIV is due to the neurotoxic products of HIV virus and the cytokine abnormality secondary to immune dysregulation (33). The virally induced cytokine, interleukin 1 and tumour necrosis factor alpha have both been implicated. Autopsy and imaging studies often reveal evidence of clinically silent cerebrovascular disease in HIV patients (7).

HIV causes cerebral vasculopathy, which can lead to stroke syndromes. HIV predisposes to opportunistic central nervous infection, which also cause strokes in the young adults.

Toxoplasmosis is a leading cause of focal CNS disease in Acquired Immune Deficiency Disease (AIDS). Symptoms and signs are seizures, hemiparesis, hemianopia, aphasia ataxia and cranial nerve palsies (36).

Cytomegalovirus (CMV) may present with focal neurological symptoms and infects brain, spinal cord, meninges and nerve routes. CMV infection of the CNS is recognized at autopsy in 5-40% of patients with AIDS in whom diagnosis was not made during life (35).

Varicella zoster can cause acute strokes. A single report described virologically confirmed large vessel vasculopathy due to varicella zoster virus without previous zoster. It develops weeks or months after zoster of contralateral trigeminal distribution (36).

HIV and syphilis may be found in the same patient. Neurosyphilis can cause a gumma, a localized chronic expanding intracranial mass causing epilepsy, raised intracranial pressure and focal signs like hemiparesis (Kumar and Clark). There is obliterative small vessel endarteritis involving the vasovasorum of the central nervous system. Neurosyphilis presents as stroke in 23% cases (37). It is relatively young adults who are affected and mostly the middle - cerebral artery. This leads to ischaemia and infarction of brain (38). Tuberculoma, cryptococcus and central nervous system lymphomas may present as stroke.

Focal signs and seizures are uncommon with chronic meningitis due to cryptococcus (1). Infection with the pork tapeworm, taenia solium causes development of cysts in the brain (neurocysticercosis). This produces cerebral infarction, TIAs and brain haemorrhage. There is cerebral arteritis and primarily it is small brain vessels that are compromised by the parasite. The subarachnoid space is the most frequent site for neurocysticercosis. It is a well-recognized cause of cerebral infarction. It may cause intracranial hypertension as well (39, 40).

Migraine is frequent in young patients with ischaemic strokes and infrequent in older patients. Patients with ischaemic strokes and migraine are mainly women with stroke features that are age dependent (41).

Other causes of stroke are uncommon. Takayasu arteritis and autoimmune disorders can lead to carotid artery dissection (42).

Air embolism can occur due to endoscopic procedure, neurosurgical procedure and as a complication of cardiac catheterization. It can cause cerebral air embolism and present as a stroke (43).

Some mitochondrial disorders are responsible for ischaemic cerebral infarction in young patients (44). Exertional heart stroke, actively common in young men predisposes to coagulopathies (45).

Stroke occurs following viper bite. There is subarachnoid or cerebral bleeding as a result of depletion of clotting factors (46). The cadasil (cerebral autosomal dominant arteriopathy with sub cortical infarcts and leucoencephalopathy) is an adult onset neurological disorder (average age of onset 45 years) characterized by recurrent strokes and dementia. It is due to mutations in the notch 3 gene (47).

Eales disease is an idiopathic obliterative vasculopathy that usually involves the peripheral retina of young adults. It mostly has associated neurological findings like myelopathy, ischaemic strokes, hemiplegia and multifocal white matter dysfunction (49).

Ischaemia is associated with pathological changes caused by the accumulation of reactive metabolites in CVA (49).

Some of the reactive metabolites are free radicals, arachdonic acid and nitric oxide. They are produced due to massive calcium ion influx leading to the destruction of the cell membranes and other essential neuronal structures (11).

In patients with intracerebral bleed usual mechanism is leakage from the small intracerebral arteries (3).

In cardioembolic strokes, stasis is an important mechanism. Others are due to attachment of materials and platelets and bacterial to the free bodies of the valves (32).

CLINICAL FEATURES

Clinically the presentation will depend on the type of the stroke and the brain site that is involved (11). Hemiparesis is the most common clinical feature of stroke (50). Cognitive impairment is present in the majority of all types of stroke and may be the sole presentation (51). Oropharyngeal dysphagia occurs in up to a third of patients presenting with a unilateral hemiplegic stroke (52). Cranial nerve palsies are common.

EFFECTS

Individuals who have survived a stroke present with varying degrees and types of neurological impairment and functional deficits (2). There is a huge impact on public health with early mortality and residual disability of stroke survivors (53). In the young adults stroke is devastating (54).

TESTS/TREATMENT

Identification and treatment of (55) risk factors reduce the causes of strokes. Poor prognostic indicators are:

- Pyrexia (hyperthermia). Induced hypothermia had a protective effect. Hypothermia reduced cerebral oxygen requirements (56).

- Increased blood glucose (57)
- Patients not admitted to stroke units.

The following tests are usually done in a patient with stroke (7)

- (i) Full blood count including platelet count
- (ii) Erythrocyte sedimentation rate (ESR)
- (iii) Anticardiolipin antibody
- (iv) Serology for HIV
 - herpes simplex virus
 - toxoplasma antibodies
 - Syphilis
- (v) Blood cultures when indicated
- (vi) Coagulation studies - ant thrombin III levels
 - protein S levels
 - protein C levels
 - Prothrombin time (PT)
 - activated partial thromboplastin time (APTT)
 - bleeding time
 - clotting time
- (vii) Auto antibody studies
- (viii) Urine toxicology
- (ix) Imaging
 - Computerized axial tomography (CAT scan)
 - Magnetic resonance imaging (MRI scan)
 - Computerised tomography angiography (CTA)
 - Cerebral angiography
- (x) Echocardiography
- (xi) Electrocardiography
- (xii) Chest x-ray

(xiii) A lumbar puncture for subarachnoid haemorrhage and screen for infections

Treatment depends on whether the stroke is thromboembolic (ischaemic) or haemorrhagic. The treatment of acute ischaemic stroke includes supportive care, treatment of neurological complications, antithrombotic therapy and thrombolytic therapy (11).

Thrombolytic therapy should be started in moderate to severe ischaemic strokes in a time window of no more than 3 hours (Hackle W. Reperfusion Therapy). Recombinant Tissue type plasminogen Activator (rtPA) is a thrombolytic agent that is used. Patients must be carefully selected.

Cerebral oedema associated with ischaemic stroke is treated by means of hyperventilation and mannitol. Since hyperthermia accelerates ischaemic neuronal injury, antipyretics are indicated. The other measures in ischaemic strokes are anticoagulant therapy with heparin or Warfarin (58). Heparin prevents clot propagation by potentiating antithrombin III activity thereby inactivating thrombin, clotting factors X, XII, XI and IX. Platelet activation and vascular smooth muscle proliferation are inhibited. Warfarin inhibits vitamin K activation hence reduced activation for the vitamin K dependant clotting factors.

Heparin is commonly used but has not been shown to improve outcome (59). There are useful in atrial fibrillation, other dysrhythmias and valve lesions.

Anti platelet therapy reduces the incidence of further strokes. Aspirin has been the most widely used antiplatelet. Aspirin inhibits cyclo-oxygenase, which converts arachidonic acid to prostaglandins and thromboxanes. Overall aspirin reduces platelet aggression.

Neuroprotective therapy is advocated for in ischaemic strokes. There are agents for neuroprotection. There are designed to inhibit glutamate like lubeluzole, which benefits patients with ischaemic stroke when given within six hours. There are also non competitive inhibitors of the N-Methyl-D-aspartate (NMDA) receptor. "Based on definitive experimental results, activation of NMDA receptor can have deleterious effects on the cell where by calcium entry induces neurotoxicity and if sufficiently severe leads to neuronal cell death (58).

The NMDA receptor inhibitors, for instance aptiganel appear particularly promising when given early in the course of ischaemia (11). The others are neuroprotectants for later events in the ischaemic cascade and they are mainly free radical scavengers e.g. citicoline and neuronal membrane stabilizers like enlimomab, a late neuroprotectant monoclonal antibody against leucocyte adhesion molecules.

Calcium $2+$ influx being one of the earliest events in ischaemic cascade, indicates treatment with nimodipine (60) a calcium channel blocker. It has been shown to reduce mortality. Ebselen, a Seleno organic compound with antioxidant activities through a glutathione peroxidase like action improves the outcome of acute ischaemic strokes (61).

Blood pressure should be controlled if very high. Extreme hypotension should be avoided. Polycythaemia should be treated if present by means of venesection. The underlying condition predisposing to stroke should be sought and treated. In HIV more than other patients with stroke treating underlying disease, HIV itself and any intercurrent infection or neoplasms that may be responsible for stroke is essential (7).

In patients with internal carotid stenosis where the lumen narrows by more than 70%, theres need for internal carotid endarterectomy. General management in

haemorrhagic strokes is as for cerebral infarction. Mannitol, hyperventilation and head elevation may decrease elevated intracranial pressure.

Antiplatelet drugs and anticoagulation are contraindicated in haemorrhagic strokes. Physiotherapy does help in restoring function of the affected limbs.

STUDIES DONE

No study has been done on stroke in the young adults in Zambia. There are very little data on incidence, prevalence or outcome of stroke in the African setting. That many young people are affected doesn't seem to be explained by meningovascular neurosyphilis or abnormal titers of coagulation factors nor haemoglobinopathies. Often no specific cause or risk factors is found (4).

In Central and Southern Africa there are three studies which have discussed stroke in young adults and two of which associated strokes in such age groups with HIV.

In a study in Durban, KwaZulu Natal, South Africa (62), race and endemic disease both appeared to be important determinations of stroke in the young adults. HIV associated stroke was highest in the otherwise unknown aetiological Trial of Org 10172 in acute stroke (Toast Category). Several clinical and autopsy studies have suggested increased incidence of strokes in HIV infected persons.

A retrospective case controlled study in the Durban Stroke Data Bank (DSDB) found that 16% of all strokes in young black Africans occurred in association with HIV. The incidence rate here paralleled that of the young black population at large meaning there was no significant overall incidence rate of stroke in association with HIV.

Compared to strokes in an age-sex matched HIV-seronegative control population, the cryptogenic stroke was more common in the HIV infected population (63).

In a study to determine the clinical syndromes, aetiopathogenesis and prognostic factors in a prospectively evaluated multi-ethnic young stroke population, most young patients were grouped into non atherogenic and non cardiac causes with a definite or probable cause found in 94%. The non atherogenic strokes were mostly prothrombotic states, infection associated and dissection (64).

The other African countries where stroke studies are documented are Tanzania and Nigeria. In Tanzania, as in other Sub Saharan African countries, HIV 1 seroprevalence which may be associated with various neurological deficits including hemiplegia is high (65).

A retrospective study was done to characterize the pattern of stroke in a specialist center in Nigeria's Federal capital territory over a 5-year period. 27% were classified as having stroke in the young i.e. less than 45 years. Hypertension was found to be the single most important contribution factor-causing stroke in young Nigerians (66). Stroke in very young Nigerians is uncommon and has been related to sickle cell disease, cervical trauma and cocaine abuse.

The role of HIV has not been widely studied in Nigerian stroke subjects (56). World over strokes appear infrequently in young adults before the age of 45. In a neuroepidemiological survey in Sicily it was established stroke in young is unknown. Its prevalence increases in an age related fashion (66).

Reports on intracerebral haemorrhages are rare (67) and ischaemic stroke, are infrequent in young adults (68). In a study in the L'Aquila district, Central Italy,

aimed at evaluating the incidence and prognosis of first ever strokes in the young and to make direct comparisons with patients in the older age groups it was found that stroke patients less than 45 years had a disproportionate cumulative high prevalence of subarachnoid haemorrhage and intracerebral haemorrhage with respect to older patients mainly due to aneurysms and arteriovenous malformations. The 30-day case fatality rate was lower (11.2%). Patients more than 45 years had a case fatality of 25%. Highest mortality was with intracerebral haemorrhage whereas most severe disability was with cerebral infarction. Young patients accounted for as much as 70% of the years of potential life lost because of stroke (69).

At the University Teaching Hospital, the largest and main referral hospital there are several patients who present with a diagnosis of stroke in the young. In 2001 according to the medical records office there were 69 patients in total who had cerebrovascular disease and of these 34 were of the age group 15 to 45 years. The following year for the first six months there were 14 out of 34 cases of strokes. No study had been done on the aetiology of these strokes at UTH hence the justification for the study.

RESEARCH HYPOTHESIS

HIV is causal either directly or indirectly to most of the strokes in the young adults.

GENERAL OBJECTIVE

To study the relationship of HIV with strokes in the young adults coming to UTH.

SPECIFIC OBJECTIVES

1. To establish the incidence of strokes in the young.
2. To determine the aetiology in general of strokes in the young.



3. To look at the magnitude of risk factors in the patients who present with stroke in the young.
4. To study the clinical associations of these strokes.
5. To determine the outcome of these strokes over a short-term period i.e. over a month and to do a monthly fatality rate.
6. A possible comparison of the clinical presentation, laboratory finding and histopathological picture on autopsy.

CHAPTER TWO

RESEARCH METHODOLOGY

STUDY DESIGN

A prospective cross sectional study involving sixty patients was carried out over a period of 6 months.

STUDY SETTING

The study patients were recruited at the University Teaching Hospital (UTH) from three sites namely the medical admission ward (MAW), medical wards and the general clinic.

STUDY POPULATION

Included in the study were patients 15 to 45 years of age. Patients with stroke outside the age bracket were excluded. Those to participate in the study signed a consent form. Patients who declined to take part in the study were also excluded. Only patients having stroke for the first time were considered for the study. Patients already on antiretroviral therapy were excluded.

SAMPLE SIZE

Sample size was conveniently chosen. The sample size was 30 patients with stroke and 30 without stroke and an HIV test was done on all the 60 patients.

METHODS

The patients fitting the criteria were subjected to a basic clinical examination. The history was taken and patient examined. Counselling was done for retroviral disease. A number of tests were done including an HIV test. The other tests done were: -

1. MPS
2. ECG
3. Echo
4. RPR/VDRL
5. RBS
6. FBC/ESR/DC/sickling
7. Liver and renal function tests
8. CSF-Microscopy, biochemistry, culture
9. CD4
10. Clotting profile

A computed tomography scan (CT scan) was done on some of the patients. The limiting factor was the cost of the CT scan. The same goes for DNA studies. Some of the patients who unfortunately died during follow up were to have a post mortem done the possibility of which depended on the consent from the relatives.

The patients were reviewed on a monthly basis to determine the outcome of the strokes and were on treatment depending on the outcome of the results of the above investigations.

DATA ANALYSIS

The data was analysed by means of a computer. EPI INFO 6 programme was used with the help of a statistician. Tables were used to present the findings.

ETHICAL CONSIDERATIONS

Ethical approval was sought and granted from the Research Ethics Committee of the University of Zambia. Informed and signed consents were obtained from the subjects. Merits and demerits of participating in the research were explained to the subjects.

CHAPTER THREE- RESULTS

Sixty patients were prospectively studied over a period of six months to determine the relationship between HIV and strokes in the young adults.

Table 1 sex distribution for patients

SEX	Freq	Percent	Cum.
F	36	60.0%	60.0%
M	24	40.0%	100.0%
Total	60	100.0%	

Thirty patients with stroke and thirty without stroke were enrolled in the study and table 1 shows the sex distribution.

Table 2 Age distribution for the study and control groups

	Age range 15-25	26-45
Control	10	20
Stroke group	8	22

The median age for the study patients was 29 years

Table 3 ECHO results for the study and control groups

	Normal	Abnormal
Control	30	0
Stroke group	26	3

Of the abnormal echo results, one was a two mitral stenosis and one dilated cardiomyopathy .

Table 4. HIV Status for those with stroke

HIV	Freq	Percent	Cum.
Neg	5	16.7%	16.7%
Pos	25	83.3%	100.0%
Total	30	100.0%	

The results in table 4 show that 25 (83.3% patients of those with stroke were HIV infected.

Table 5. HIV Status for those without stroke

HIV	Freq	Percent	Cum.
Neg	14	46.7%	46.7%
Pos	16	53.3%	100.0%
Total	30	100.0%	

The table above shows 16 (53.3%) of the control group were HIV infected.

Table 6. ECG results for all patients

	Normal	Abnormal
Control	30	0
Stroke group	30	2

The two abnormal ECGS showed Right axis deviation and right ventricular Hypertrophy. The other had a generalized micro voltage.

Blood slide results were negative for malaria. RPR was non reactive for all the patients. Random blood sugar was within normal limits. Liver function tests and urea, electrolytes and creatinine were normal.

CSF for all the 30 stroke patients showed no growth although 12 patients had elevated proteins with normal sugar. The clotting profile was normal. FBC in the study group showed normochromic normocytic anaemia in 19 patients. ESR was raised in all except 7 stroke and 11 non stroke patients. Sickling test was negative in all patients.

Table 7 clinical features of 30 stroke patients

Symptom/sign	Total (%)	
Motor weakness	30	(100)
Wt loss	23	(76)
Headache	16	(53)
Fits	5	(17)
Fever	20	(67)
Diarrhoea	18	(60)
Cough	19	(32)
Rash	17	(56)
Oral thrush	21	(70)
Impaired vision	16	(53)
Abdominal distension	4	(13)
Vomiting	10	(33)
Confusion	13	(43)
Papilloedema	8	(27)
H.Zoster scar	15	(50)
Neck stiffness	4	(13)
Aphasia	6	(20)
Cranial nerve palsies	28	(93)

The clinical features were vast as can be seen from table 7

Table 8 clinical features of 30 patients without strokes

Symptom/sign	Total	(%)
Motor weakness	0	(0)
Wt loss	21	(70)
Headache	4	(13)
Fits	7	(23)
Fever	8	(27)
Diarrhoea	14	(47)
Cough	7	(23)
Rash	11	(37)
Oral thrush	10	(33)
Impaired vision	4	(13)
Abdominal distension	6	(20)
Vomiting	17	(57)
Confusion	10	(33)
Papilloedema	5	(17)
H.Zoster scar	3	(10)
Neck stiffness	12	(40)
Aphasia	8	(27)
Cranial nerve palsies	13	(22)

The clinical features were vast as can be seen from table 8

CHAPTER FOUR

DISCUSSION

This study was conducted at the University Teaching Hospital to find out the relationship of strokes in young adults with Aids.

During this study which was conducted over a period of six months, it has been demonstrated that majority of the young adults present with strokes at the mean age of 29. This age group unfortunately happens to be the peak of the reproductive age group of our society.

The HIV seroprevalence in the stroke age group at 83% compared to 53% in the control group. This clearly demonstrates that the HIV infection increases the risk of strokes in young adults and what remains to be demonstrated is whether it is the opportunistic infections or HIV vasculitis that is responsible for this phenomenon. Several studies done elsewhere, have shown that some of the strokes in HIV may be due to neurotoxin products of the virus itself and cytokine abnormality secondary to immunodysregulation (33) and the virally induced interleukin 1 and tumor necrosis factor have been implicated. The fact that there was more HIV infection in the group does not exclude the possibility of the stroke being secondary to other pathogens such as cerebral cystercercosis, malaria, brain abscess, tuberculous meningitis, Cryptococcal meningitis, Cytomegalovirus infection, encephalitis and parasitic infections (35,36,39, 40), Interestingly, none of the patients seen in this study had a RPR test or hypoglycaemia. This may suggest that complications of syphilis are not often seen as the cause of strokes in this age group. HIV and syphilis may be found in the same patient and as neurosyphilis may form a gamma leading to strokes; it is an important cause of focal signs in the young. Neurosyphilis presents as a stroke in 23% of the patients and it is relatively young adults who are affected and mostly the middle cerebral artery (37)

The ECG abnormality was seen in 2 patients with strokes and these had demonstrable mitral stenosis and one dilated cardiomyopathy on ECHO. No emboli or vegetation were reported but this seems to be a significant finding as some of the strokes in young adults, are likely to be from emboli from the heart. It is therefore important that a good physical examination to exclude abnormalities be performed in all young adults with strokes.

It was observed in this study that, all patients in this study had CD4 below 200 except one. The majority of the patients had CD4 between 150-200 and this may be a contributing factor to the plethora of clinical features seen. In other ways, the strokes seen in this control tended to occur in AIDS patients. However, fundoscopic examination of those patients did not reveal any abnormalities such as Toxoplasmosis or indeed cytomegalovirus infection. On the other contrary, there was one CT abnormality of which toxoplasmosis was suspected. The diagnosis of whether or not a stroke has occurred is straightforward if there is a clear history of sudden onset of focal brain dysfunction or if the symptoms were first noticed when the patient was walking especially if the patient is aged over 50 and has vascular risk factors or disorders. Most of the history of stroke patients in the developed world is usually clear-cut and likelihood of a CT scan showing anything other than an infarction or haemorrhage is under 5%. However, in the developing Countries, patients may not give clear histories and CT scans are not widely available and therefore it becomes important to include causes other than infections in the differential diagnosis. Routine laboratory tests should therefore include fasting blood sugar, lipid concentrations and immunological tests for syphilis.

A CT is essential for the definite diagnosis of stroke subtype (cerebral infarction or haemorrhage) as well as for identifying the site of the lesion and determining the extent of the disease. Unfortunately, CT scanners are expensive and in developing countries, most of the patients cannot afford them and they are only

found in bigger hospitals. Where scans are not widely available, haemorrhage can be distinguished from infarction with 90% accuracy using the Siriraj stroke score. This score is based on weights given to each of five clinical variables (level of consciousness, diastolic blood pressure, headache, vomiting and atheroma markers). It is very useful for developing Countries but each country should adapt it for local use because the prevalence of hemorrhagic strokes differs from Country to Country. Where Scans are not widely available as in our case, they should be limited to cases in which the diagnosis is uncertain, the source of the disease is atypical, the stroke is in the cerebellum or thalamus or the patient is young. The scan can also be used in situations where it is intended to give anticoagulation therapy.

Using the current screening tests for infections in patients with strokes, it is not possible to diagnose any infections causes except for syphilis and HIV infection. The clinical spectrum though vast either indicated to a past or present history of HIV related opportunistic infection. Motor weakness was of course present in all stroke patients as opposed to the control group and weight loss was slightly more in the stroke group than the control group (76% and 70%). The most striking difference between the two age groups was the presence of headache and fever in the stroke group, which was evidently more than the control group. This may suggest an infectious bigger. The presence of oral thrush was also more in the stroke than the control group.

The history in the stroke group pointed more towards HIV defining illnesses than in the control group. However both groups did seem to show some papilloedema. The stroke group as would be expected had more cranial nerve palsies and few patients had neck stiffness.

Almost all patients had anemia of chronic ill health. The major obstacle in this study was due to lack of a CT within 24hours of the appeared accruing. Most of

the patients in the first place appeared 2-3 days after the stroke had occurred and major reason given for this was lack of transport for the paralysed patients. Most of the patients had to find their own means to the hospital.

CHAPTER 5

CONCLUDING REMARKS AND RECOMMENDATIONS

This study has shown that strokes in the young are an important cause of admission to the Medical wards of the University teaching hospital.

There appears to be a strong association between HIV and strokes seen in young adults as 83.3% of patients who presented with a diagnosis of stroke in young adults had a positive HIV test.

The prevalence of HIV in the medical wards is still high as the matched control group of patients without strokes had a seroprevalence of 55.3%.

Syphilis and other infections do not appear to be important causes of strokes in this age group though there was one patient with suspected toxoplasmosis in the study group with strokes.

Cardiovascular disorders are important risk factors for strokes in the young age group and therefore it is important to perform a complete physical examination to exclude them.

Majority of the patients presenting with strokes have a past or present history suggestive of chronic ill health secondary to retroviral disease. Almost all the patients have anemia of chronic ill health at admission.

Most patients with strokes report late at medical admission such that a timely intervention even if CT scans were readily available would be difficult to undertake.

As most of the stroke patients were young adults at the peak of their professional and reproductive years, it is important to prevent strokes rather than wait till they have occurred. Prevention of stroke is now feasible and applicable throughout the world. At the fundamental level, education of the public is critical. It involves the development of health behaviours, maintenance of body weight, cessation or avoidance of smoking, avoidance of heavy alcohol use and early detection and control of the other risk factors like hypertension, atrial fibrillation, diabetes mellitus and increased cholesterol levels.

HIV also could be considered a risk factor for stroke as has been demonstrated in this study and therefore early diagnosis and treatment would inevitably lead to a reduction in the morbidity and mortality associated with strokes in young adults. HIV prevention programmes will in a way help in the control of strokes. Counseling and testing for HIV must be enhanced in patients who are young who present with stroke.

Although aspirin (ASA) has been shown to be effective for secondary stroke prevention but not primary, there will be need to consider ASA administration in all HIV patients without medical contraindications.

CT scans on all patients with stroke must be routinely done and an autopsy study must be conducted to find out the exact pathology in young people with strokes.

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APPENDIX 1

CONSENT FORM

I, _____ of _____ give consent to participate in the study entitled 'Stroke in the Young Adults'. The study purpose and implications of the study have been explained to me.

I agree to submit blood for HIV testing and the results obtained will be confidential.

I have a right to withdraw from the study anytime without having my medical care being compromised.

Signature of participant : _____

Signature of Principal Investigator : _____

Date : _____

APPENDIX II

CLINICAL PROFILE

1. Study Number _____
2. Initials _____
3. Sex _____ Age: _____
4. Marital Status _____
5. Profession _____
7. Address _____
8. Level of Education _____
9. Monthly Income _____
10. Religion _____
11. Date of Presentation _____
12. Symptoms
 - (i) _____
 - (ii) _____
 - (iii) _____
13. Do you have/have you had any of the following? If yes elaborate
 - (i) SCD _____
 - (ii) Hypertension _____
 - (iii) Heart disease _____
 - (iv) DM _____
 - (v) Syphilis _____
 - (vi) Tuberculosis _____
 - (vii) Bleeding Disorder _____
 - (viii) Epilepsy _____
 - (ix) Migraine _____
 - (x) Miscarriage _____
 - (xi) DVT _____

- (xii) Cysticercosis _____
- (xiii) Joint Pains with Rashes _____
- (xiv) Fever _____

14. Are you currently taking

- (i) Oral contraceptives
- (ii) Alcohol heavily

15. Do you smoke, if yes what do you smoke and how do you describe your smoking

16. Physical Findings

- (i) Consicous (Y, N)
- (ii) Orientation
- (iii) Talking/Aphasia
- (iv) Pupil size
- (v) Neck stiffness
- (vi) BP
- (vii) Pulse
- (viii) Cranial nerve palsies (N, Y)

If yes, which one

- (ix) Limb
 - (a) Motor

Orientation

Physique

Tone

Power

Reflexes

Babinsk

Clonus

(b) Sensory

CVS (Normal/abnormal)

(x) Fundoscopy

(xi) Respiratory system (Normal/abnormal)

(xii) Gastrointestinal system + hepatobilliary

APPENDIX III

RESULTS

- 1

(a) Study Number
- (b) Age
- (c) Sex
2.

HIV Test

+ve

-ve
3.

RPR

+ve

-ve
4.

RBS Normal?

Yes

No,

If No Specify
5.

Hb
6.

ESR
7.

Platelet
17.

Sickling test
18.

ECG
19.

Echo
20.

CT Scan
21.

Post mortem results