A COMPARISON OF STROKE IN YOUNG AND OLDER ADULTS ADMITTED AT MUHAS ACADEMIC MEDICAL CENTRE IN TANZANIA

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By

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A Dissertation Submitted in (Partial) Fulfillment of the Requirements for the Degree of Masters of Medicine (Internal Medicine) of

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October, 2019

CERTIFICATION

The undersigned certify that, they have read and hereby recommend for examination of thesis dissertation entitled ***'A comparison of stroke in young and older adults admitted at MUHAS Academic Medical Centre in Tanzania',*** in (partial) fulfillment of the requirement for the degree of Master of Medicine (Internal Medicine) of the Muhimbili University of Health and Allied Sciences Muhimbili University of Health and Allied Sciences a dissertation entitled.

…….

Dr. Patricia Munseri

(Supervisor)

……

Date

DECLARATION AND COPYRIGHT

I, **Dr. Sarah Shali Matuja**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature_____ Date_____

ACKNOWLEDGEMENT

Luke 1:37 *'For with God nothing shall be impossible'*. In Thee I trust!

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DEDICATION

This is for Esther Gwalugano Matuja, my mother, my warrior and my heart. Although she was my true inspiration in pursuing this Master's degree, she was unable to see my graduation. All the hard work, challenges and sleepless nights encountered were worth it Mother. Rest in Peace.

To my father, my greatest mentor, Professor William Matuja, you are my Hero. This is just the beginning of many more to come. I shall carry your legacy forever! Our motto 'Sky is the Limit'.

To my siblings and relatives Mtanya, Pungu, Geoffrey, Perpetua, Godfrey, Salome, and Rebecca.

Finally, to my adorable niece, Esther Tamera Matuja, I see greatness in you. You too carry the family's legacy, lets shine!

ABSTRACT

Background: Current epidemiological evidence indicates a global rise in stroke burden among young adults mainly attributed to unique risk factors inherent to genetics and the environment. The outcomes of stroke in young adults is devastating associated with substantial morbidity and fatality jeopardizing their prime time. Furthermore, there is paucity of data on the prevalence, risk factors and 30-day outcomes of stroke among young adults in Tanzania.

Aim: To determine the prevalence of first ever stroke, describe stroke sub types, risk factors and 30 day outcomes in young adults (≤45 years) compared to older adults (>45 years).

Methodology: This cohort study consecutively recruited 369 consented first ever stroke participants (123 young vs 246 older adults) admitted at Muhas Academic Medical Center with a World Health Organization clinical criteria for stroke. Demographics, stroke sub type and stroke risk factors were captured. Stroke severity was assessed using the National Institute of Health Stroke Scale. Each participant was followed up at 24 hours, 72 hours, 7 days, 14 days to 30 days for outcomes using the Modified Rankin Scale. Stroke prevalence and risk factors in the young were compared to old adults. Kaplan Meier analysis was used to estimate 30-day survival in young and old.

Results: The prevalence of stroke in young adults was 25.4% (95% CI 21.5% - 29.3%) and in older adults 26.8% (95% CI 23.9% - 29.6%). Hemorrhagic stroke occurred in 42.3% among the young vs 27.2% in older adults p=0.005. Factors associated with stroke in the young compared to the old were: a new diagnosis of hypertension at hospital admission 26.8% vs 9.3% p<0.001, HIV infection 11.4% vs 4.9% p=0.021, use of illicit drugs 4.1% vs 0.8% p=0.044, hormonal contraception 48.5% vs 9.4% p<0.001, mitral stenosis 3.3% vs 0% p=0.012, Hypercholesteremia 31.2% vs 20.2% p=0.031 and sickle cell disease 9.7% vs 4.2% p=0.047. Majority of the participants had severe stroke and at 30 days the fatality rates were 49.1% in young vs 67.2% in older adults.

Conclusion and Recommendation: The high burden of stroke in young is coupled with very high 30-day fatality rates. Young strokes have special risk factors that should be screened and controlled so as to prevent subsequent development of stroke. There is an urgent need of integrating preventive strategies to combat stroke in young adults.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AF	Atrial Fibrillation
ADC	Apparent Diffusion Coefficient
AIDS	Acquired Immunodeficiency Syndrome
CNCDs	Chronic Non communicable Diseases
CNS	Central Nervous System
CT scan	Computed Tomography Scan
CVD	Cerebral Vascular Disease
DALYs	Disability Adjusted Life Years
DWI	Diffusion Weighted Image
FBG	Fasting Blood Glucose
HIV	Human Immunodeficiency Virus
HDL	High Density Lipoprotein cholesterol
ICH	Intra Cerebral Hemorrhage
LDL	Low Density Lipoprotein cholesterol
LVH	Left Ventricular Hypertrophy
MRS	Modified Rankin Scale
MUHAS	Muhimbili University of Health and Allied Sciences
MNH	Muhimbili National Hospital
MAMC	MUHAS Academic Medical Center
MRI	Magnetic Resonance Image
NIHSS	National Institute of Health Stroke Scale
NCD	Non-Communicable Diseases
PSS	Perceived Stress Scale
RHD	Rheumatic Heart Disease
SAH	Sub Arachnoid Hemorrhage
SCA	Sickle Cell Anemia
SCD	Sickle Cell Disease
SSA	Sub Saharan Africa

DEFINITION OF TERMS

Stroke: According to WHO, as a rapidly developing clinical signs of focal or global disturbance in cerebral function lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin (1).

First ever stroke: According to WHO, index episode of stroke that has not been preceded by a prior history of stroke (1).

Recurrent stroke: According to WHO, index stroke diagnosis is preceded by previous history of stroke (1).

Stroke in Young adults: A diagnosis of stroke occurring in an individual aged ≤45 years. This definition is adopted from different comparison stroke studies done in different settings (2) (3).

Stroke in older adults: A diagnosis of stroke occurring in an individual aged >45 years. This definition is adopted from different comparison stroke studies done in different settings (2) (3).

Modifiable risk factors for stroke: Factors that increase the likelihood of having a stroke but can be reversed, controlled or treated (4).

Hypertension: Systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg, or a patient on drug treatment for high blood pressure (5).

Diabetes mellitus: A previous diagnosis of type I or II diabetes, or a single random blood glucose reading of ≥ 11.1 mmol/l, and a fasting blood glucose reading of ≥ 7 mmol/l (6).

Large vessel disease: is a thrombotic subtype of ischemic stroke which affects either extra cranial (common and internal carotids, vertebral) or intracranial arterial system (Circle of Willis) (7).

Small vessel disease: is a thrombotic subtype of ischemic stroke which affects the cerebral arterial system particularly the penetrating vessels that arise from distal major vessels in the Circle of Willis (7).

Perceived Stress Scale: Is a psychological scale used to measure the degree to which one's situation over the past month is appraised as stressful. It is designed to detect how unpredictable, uncontrollable, and overloaded respondents find their lives (8).

Atrial Fibrillation (AF): According to the European Society of Cardiology that is based on ECG findings of irregular RR intervals and no discernible distinct P waves (9).

Fatal events: Stroke that resulted in death of a patient within 30 days (1).

Non-fatal events: A person with stroke (with or without disabilities) who survives 30 days following a stroke (1).

CHAPTER ONE

1.0 INTRODUCTION

1.1 BACKGROUND

Stroke is defined as a rapidly developing clinical signs of focal or global disturbance in cerebral function lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin (1). Globally stroke is the second most common cause of death worldwide accounting for 11.8% of all deaths after ischemic heart disease and the third most common cause of disability, 4.5% Disability Adjusted Life Years from all cause (10). Furthermore, reports have indicated an increase in stroke burden in low to middle income countries from 295.9 cases per 100,000 in 2005 to 299.6 cases per 100,000 in 2010 (11). In Tanzania the incidence of stroke was estimated at 108-316 per 100,000 and change in life style has been linked to this dramatic increase in stroke incidence (12,13).

In the past stroke commonly affected individuals aged 55 years and above and seldom affected individuals between 15 to 45 years of age (14). In high income countries a population based study showed a rise in proportion of all strokes under the age of 55 from 12.9% in 1993/1994 to 18.6% in 2005 (15). This observation has also been mirrored in Sub saharan Africa (SSA), resulting in to significant disabilities at this prime age (16). Community based studies conducted in Nigeria among stroke individuals showed a prevalence range of 5% to 12% in young adults aged 15-45 years compared to 25.6% among those aged 55 to 64 years (17,18).

Stroke in the young is of interest as young adults have special risk factors inherent to genetics and the environment. Cardiac abnormalities, Sickle Cell Disease (SCD), HIV infection and use of illicit drugs are some factors that need to be identified and adequately controlled (19–21). Different reports have indicated that young adults suffer from ischemic stroke partly related to modifiable risk factors as hypertension, smoking, obesity and dyslipidemia that contribute to atherosclerosis (20,22–24).

In Tanzania, a hospital based prospective study done in the year 2017, revealed a 30-day fatality rate following a stroke of 33.3% and factors associated with fatality were age

above 65 years, loss of consciousness, raised White Cell Count (WBC) and left sided weakness (25). Young stroke survivors were noted to have significant disabilities that had significant negative social and economic impact, justifying the need to study the magnitude, associated risk factors and 30-day outcomes of stroke in the young compared to the old.

1. 2 LITERATURE REVIEW

1.2.1 BURDEN OF STROKE IN YOUNG ADULTS

Globally the burden of stroke in young adults has increased with reports of 358.6 cases per 100,000 in 2005 to 366.9 cases per 100,000 in 2010 (11). In high income countries a population based study showed the proportion of all stokes under the age of 55 increased from 12.9% in 1993/1994 to 18.6% in 2005 (15). Likewise, a steep increase in stroke incidence among the young was noted in individuals aged 35-44 years of age with rates of 22 to 45 per 100,000 (26,27), occurring mainly among black race in the U.S (28,29). In SSA, community based studies conducted in Nigeria among young adults with stroke aged 15-45 years have shown a prevalence range of 5% to 12% compared to 25.6% among those aged 55 to 64 years (17,18). However, in Tanzania the burden of stroke in young adults remains unknown.

1.2.2 STROKE SUBTYPES

There are two main stroke subtypes; hemorrhagic and ischemic. The pathogenesis of cerebral ischemia is mainly due to cerebral vessel thrombosis, embolism or systemic hypo-perfusion, while cerebral hemorrhage is mainly due to uncontrolled elevated blood pressure that ruptures cerebral blood vessels, arteriovenous malformations, bleeding diathesis or use of illicit drugs (30,31). Globally rates of ischemic strokes are higher compared to cerebral hemorrhage 78% vs 22% respectively (32,33), this is also the case in SSA irrespective of age (2,34–38). However contrary to existing data, a retrospective study in Tanzania showed 60% of stroke patients had hemorrhage and 40% infarcts and majority of the participants were hypertensive (39). Hemorrhagic stroke subtype is usually associated with fatality rates approximately 17% in SAH, 6% ICH at 30 days and 45% at 1 year (40,41). In Tanzania, the overall 30 day fatality rate in the older population following hemorrhagic stroke was 44.3% compared to 29.5% with ischemic stroke (25).

1.2.3 STROKE SEVERITY

The National Institutes of Health Stroke Scale (NIHSS) is a frequently used tool to measure stroke severity in relation to neurological deficits, monitor treatment efficacy and predict outcomes (1,42). Other scales include the Pediatric National Institutes of Health Stroke Scale developed by modifying the adult NIHSS, European Stroke Scale designed to evaluate patients with stroke limited to the middle cerebral artery territory, Canadian Neurological Scale which is simpler to use than NIHSS but does not capture many stroke related impairment compared to NIHSS and Scandinavian Stroke Scale which is routinely used based on retrospective data of patients using medical records (43–46). The use of the NIHSS tool in Norway indicted no significant differences in stroke severity between the young and old however in India younger patients had severe stroke compared to older adults on admission (47,48). In Malawi older age was associated with severe stroke that resulted in to longer duration of hospital stay (49). However, there is limited data in Tanzania on the use of NIHSS to assess stroke severity in young adults.

1.2.4 RISK FACTORS FOR STROKE

Risk factors for stroke are grouped into either modifiable or non-modifiable. A large INTERSTROKE study looking into worldwide (including low to middle income countries) stroke risk factors showed hypertension as a major risk factor accounting for 34.6%, increased waist- hip ratio 26.5%, current smoking 18.9%, diabetes mellitus 5%, stress 4.6% and alcohol 3.8% commonly observed in the elderly (50). Another study found the most common vascular risk factors for stroke in young adults were dyslipidemia (60%), smoking (44%), and hypertension (39%) (51). However, the distribution of risk factors may vary across countries and some regions have other unique risk factors such as HIV vasculitis (52). In Tanzania the main risk factors for stroke in a population that mainly comprised of older adults with a mean age 60 years in urban area were: hypertension (87%), increased hip to waist ratio 77%, HIV infection (47%), smoking (26%) and previous cardiac disease (14%) (53).

1.2.4.1 HYPERTENSION

Hypertension is a common risk factor for stroke (4,50). It aggravates atherosclerosis by inducing complex vascular micro aneurysm formation, lipohyalinosis and micro atheroma resulting into rupture or occlusion of the vessel leading to ICH or ischemia respectively (54). Globally, hypertension accounts for more than 50% of all strokes across all age groups (2,38). In high income states, one study found higher rates of hypertension among stroke patients in older adults compared to the young 55.1% vs 18.5% respectively (3). The burden of hypertension is also mirrored in SSA where it is observed that 45% of all stroke cases could have been prevented by blood pressure control (55,56). In Tanzania hypertension is an established risk factor for stroke (OR 2.14, 95% CI 1.09–4.17; p=0·026) and has contributed to 75% of all stroke deaths (57–59). However, the burden of hypertension in young adults with stroke in Tanzania is unknown.

1.2.4.2 HIV INFECTION

HIV causes vasculopathy resulting into stroke, however the risk increases if there is an underlying secondary infection (53). Anti-Retro Viral's (ARVs) have significantly improved the life expectancy of HIV infected patients allowing the patients to be exposed to conventional risk factors (60). Globally 1 to 5% of HIV infected patients develop stroke with an incidence of 5.27 per 1,000 person-years compared to incidence of 3.75 per 1,000 person-years in a HIV-negative cohort particularly in low to middle income countries (19). Approximately 16% of strokes that occur in young adults are attributed to HIV infection and 90% are ischemic (61,62). A study in Malawi showed 42% of strokes in individuals aged 45 years or below was attributed to HIV infection (63). In Tanzania the prevalence of HIV associated stroke was 20% (64). In this study those in the age group between 45 to 54 years had a prevalence of 28.9% compared to 13.3% for those above 64 years (64).

1.2.4.3 HYPERLIPIDEMA

Hypercholesterolemia is an important modifiable risk factor for coronary and cerebral vascular disease (65). It promotes vessel atherosclerosis leading to athero-thrombotic or cardio embolic stroke events (65). There is a positive relation between total cholesterol and LDL cholesterol in the development of extra cranial carotid atherosclerosis (66). A hospital based study in India found high rates of hyperlipidemia in young (≤50 years) compared to older (>50 years) adults 33.4% vs 22.4% respectively (67). High cholesterol levels accounts for 29% of ischemic strokes in SSA among individuals aged 30 years and above (68). In Tanzania a high total cholesterol to HDL ratio is an independent risk factor for stroke regardless of age category (OR 9.84, 95% CI 4.06–23.84; p=<0.0001) (60). Therefore, there is a need to study the extent of dyslipidemia with particular reference to younger stroke patients.

1.2.4.4 DIABETES MELLITUS

Diabetes Mellitus (DM) increases susceptibility to atherosclerosis either alone or in combination with other atherogenic risk factors such as hypertension, obesity, and dyslipidemia (69). Both type 1 and 2 DM have been associated with stroke development however most ischemic strokes are linked with type 2 DM (70). A hospital based comparison study by Park et al among young and older adults with stroke showed that a greater proportion of older adults had diabetes 25.5% vs 7.8% in young respectively (3). In Tanzania DM has been identified as an independent risk factor for stroke in rural areas (OR 4.04, 95% CI 1.29–12.64) (57). However, data is lacking on the burden of DM in young adults with stroke.

1.2.4.5 ATRIAL FIBRILLATION (AF)

AF is a precursor for stroke associated with aging and the risk doubles each year after the age of 55 (4). AF leads to uncoordinated contraction and stasis most marked at the left atrial appendage (71). This causes increased concentrations of fibrinogen, D-dimer, and von Willebrand factor, which are indicative of prothrombotic states and a dislodgement of thrombus leads to cerebral infarct (71). Globally, the burden of AF as a source of cardio-embolism is 23% in high income states and 7% in SSA including Tanzania (50). The risk of AF cardio embolism in Sagrat hospital in Barcelona was higher in the elderly aged >85 years compared to individuals aged <65 years with prevalence of 36% and

14.6% respectively (71). Information on AF in young as compared to older adults with stroke is lacking in our setting.

1.2.4.6 RHEUMATIC HEART DISEASE (RHD)

RHD is by far the most important form of acquired heart disease in children and young adults living in developing countries (72). The predominant valvular lesions include mitral regurgitation under 20 years, Mitral Stenosis in the third decade and multivalvular disease in older adults (73). Mitral Stenosis has a 30% risk of systemic thromboembolism leading to stroke and the risk of recurrence is as high 60% in the first year (74,75). Ischemic stroke burden from RHD is as low as 1% to 2% in high income states and up to 8% in low to middle income countries commonly observed in younger adults (76,77). In low to middle income countries like Tanzania where the burden of RHD is high it is an important risk factor for stroke in young adults that warrants studying (56,78)

1.2.4.7 SMOKING

Cigarette smoking increases the burden of ischemic stroke by altering lipid metabolism leading to increased levels of LDL thus favoring atherosclerosis (79). In high income states smoking is an important risk factor for stroke in young adults (3,80). One study showed a higher proportion of younger adults with stroke had a history of smoking compared to older adults 57% vs 40.1% respectively (3). In SSA smoking is a modifiable risk factor for stroke and its cessation is associated with reduction in stroke risk across gender, race, and age (57,59,81). In Tanzania a cross sectional population based study done in urban areas showed a smoking prevalence of 27.1% (95% CI 20.8% to 33.2%) in males and 5% (95% CI 2.8% to 7.2%) in females, highest in the age group between 35 to 54 years (82). Furthermore, a large community based study in Tanzania identified smoking as an independent risk factor for stroke (OR 2.72, 95% CI 1.49–4.96; p=0·001) (57). There is lack of information on the effect of cigarette smoking among younger adults with stroke.

1.2.4.8 ALCOHOL CONSUMPTION

Alcohol causes cardiac arrhythmias, myocardial dysfunction and promotes platelet aggregation leading to cerebral hypo-perfusion and alterations in brain metabolism (83). Studies in high income countries have shown a greater proportion of alcohol consumption among young adults with stroke as compared to older adults 53.1% vs 29.7% respectively (3). A study done in Northern Tanzania showed a prevalence of alcohol consumption was highest among male college students (70.4%, 95% CI: 54.8–74.2) and about 20.1% of males and 9.2% of females had hazardous drinking habits (84). Interestingly, stroke studies in SSA including Tanzania have shown no significant association between alcohol use and risk of developing stroke (60,85). Possible reasons being recalling retrospective events or behaviors can lead to bias and subjectivity of the given data especially on factors that might have some social stigma (60).

1.2.4.9 DRUGS

1.2.4.9.1 ILLICIT DRUG USE

The main drugs that are implicated with stroke are cocaine, amphetamines, heroine, phencyclidine, cannabis and lysergic acid diethylamide (86). Proposed mechanisms include hypertensive surges, vasospasm, enhanced platelet aggregation, cerebral vasculitis, accelerated atherosclerosis, and cardio embolism (86). Drug abuse is the most predisposing risk factor for stroke among individuals less than 35 years, (86,87). In the US a study by Sloan et al among individuals aged 15 to 44 years, 4.7% had a previous drug history as a probable risk for ischemic stroke (88). In SSA factors predisposing to high rates of drug abuse include widespread poverty, poor education, unemployment and political instabilities (89). In Tanzania 5 to 12% of adolescents and youth are involved in drug abuse with drugs like cannabis and khat, and 2.1% have a history of injecting themselves with heroin (90,91). It is therefore, of interest to study the proportion of young adults with a history of drug abuse as a probable risk factor for stroke.

1.2.4.9.2 ORAL CONTRACEPTIVES

Estrogen containing oral contraceptives at doses of greater than 50µg have been associated with a higher risk for thromboembolism by inducing hypercoagulable states leading to stroke (92). However, other studies have also implicated the newer low dose containing estrogen contraceptives as a potential risk for stroke (93). In high income states the use of oral contraceptives has been largely restricted to women who are free from cardiovascular diseases (92). Despite the wide spread use of different family planning methods many countries in SSA lag in the adoption of the modern methods. In some parts of Tanzania about 10.6% use injectables, 6.7% of women are known to use pills and 0.6% use intra uterine devices as a means of family planning (94). The contribution of hormonal contraception as a risk for stroke in young adults is not well studied in our setting.

1.2.4.10 SICKLE CELL DISEASE (SCD)

SCD confers an increased risk for both stroke subtypes and this has been demonstrated in multiple case series in high income countries with an increase in first ever strokes in African Americans aged less than 35 years (21,95). In Tanzania the prevalence of Sickle cell trait is 13% and it is estimated that more than 50% of patients will die before reaching adulthood due to complications (96). Furthermore, a cross sectional study done in Northern Tanzania in children below 15 years showed 16.9% of patients admitted had a previous history of stroke with no data in adults above 18 years (97). Other studies in SSA reveal a stroke prevalence of 6.67% of in individuals aged < 35 years with SCD (98).

1.2.5 STROKE OUTCOMES

Despite the decline in stroke fatality over the past two decades seen in high income states, the fatality rates and disability is still high in low to middle income countries (32). In high income states the 30-day fatality is less than 15% (99). This reduction is attributed to availability of neurovascular interventions and multidisciplinary stroke units (99). However, in SSA including Tanzania, stroke fatality is usually highest within the first 30 days with rates ranging from 26% to 33% (25,100,101).

In high income states known predictors for 30-day fatality include severe stroke, older age above 60 years, male gender, level of consciousness score less than 7, presence of fever, Atrial Fibrillation, and radiological findings such as size of the cerebral lesion as grade 3 with either hematoma volume more than 60mls in hemorrhagic stroke or involvement of more than 1 lobe (lesion size more than 7.5 cm diameter) in ischemic stroke (102–104). In Tanzania, a prospective study that recruited all participants with stroke showed that the predictors for 30 days fatality included age of 65 years and above, loss of consciousness, raised total leucocyte count, hyperglycemia and left sided weakness (25).

1.3 PROBLEM STATEMENT

The rise in non-communicable diseases such as Diabetes Mellitus and hypertension in low to middle income countries does not seem to spare young individuals less than 45 years, ultimately posing a consequent risk for development of stroke in this population (20).

Based on a pilot study at MUHAS Academic Medical Center between March and May 2018, we observed an increase in stroke admissions ranging from 50 to 60 monthly admissions compared to an average of 40 admissions in 2017. Furthermore, young adults aged ≤45 years were observed to comprise more than a quarter of the stroke admissions. This is alarming as the age group is unique and a prime time. Succumbing a stroke at a younger age has negative implications at both family and national levels as this age group is the nation's task force.

Efforts to limit and reverse the burden of stroke would thus require acquisition of adequate information on risk factors affecting this young population. Unique risk factors such as HIV infection, rheumatic heart disease and sickle cell disease which are common in low to middle income countries like Tanzania further increase the likelihood of stroke in young adults.

Furthermore, existing data in Tanzania on the burden of stroke, risk factors and outcomes have mainly focused in the older population with limited data in the young.

1.4 RATIONALE

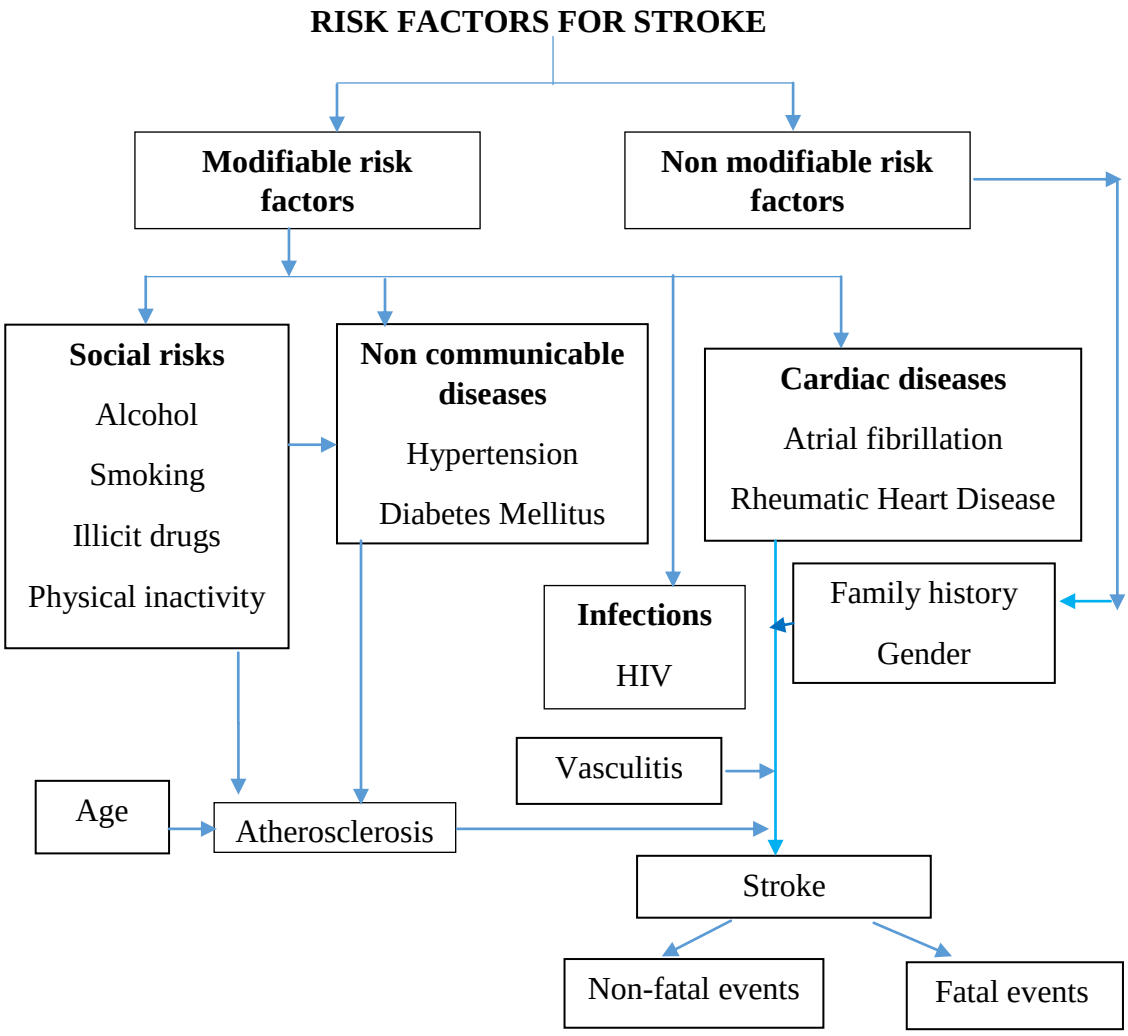
Hypertension and diabetes mellitus are the known conventional risk factors for stroke however young adults in a low income setting have additional unique risk factors that predisposes them to stroke. Identifying factors that predisposes to stroke is paramount important as this offers an opportunity for prevention for this special group of individuals who are the nation's task force.

Likewise, the 30-day post stroke outcomes in young adults will provide insight on the extent of morbidity and fatality that will help develop preventive strategies in an integrated manner.

1.5 CONCEPTUAL FRAME WORK

Figure 1 illustrates modifiable and non-modifiable risk factors for stroke. These factors cause chronic inflammation either from atherosclerosis or vasculitis. Aging also causes vulnerability of the blood vessels via atherosclerosis further exacerbating the risk for stroke. The ultimate outcomes include fatal or non-fatal events.

Figure 1: Conceptual framework



1.6 RESEARCH QUESTIONS

i. Is there a difference in prevalence of stroke in the young aged ≤45 years compared to older adults age >45 years admitted at MUHAS Academic Medical Center medical wards?
ii. What is the commonest stroke subtype among young adults (age ≤45 years)?
iii. Are the modifiable and non-modifiable risk factors for stroke in young adults (age ≤45 years) similar to those observed in older adults (age >45 years)?
iv. Are the 30-days post stroke outcomes in young adults (age ≤45 years) similar to those observed in older adults (age >45 years)?

1.7 OBJECTIVES

1.7.1 BROAD OBJECTIVE

To determine the prevalence of first ever stroke, characterize stroke sub types, describe the associated risk factors and 30-day post stroke outcomes in younger and older adults.

1.7.2 SPECIFIC OBJECTIVES

i. To determine the prevalence of first ever stroke among adults aged ≤45 years admitted at MAMC medical wards.

ii. To describe the stroke sub-types among young adults (age ≤45 years) as compared to older adults (age >45 years).

iii. To describe modifiable and non-modifiable stroke risk factors in the young (age ≤45 years) as compared to older adults (age >45 years).

iv. To describe the outcomes (death or disability) at 30 days' post stroke among adults age ≤45 years as compared to adults age >45 years.

CHAPTER TWO

2.0 METHODOLOGY

2.1 STUDY DESIGN

A cohort study.

2.2 STUDY AREA

The study was conducted at MAMC medical wards in Tanzania. MAMC is a tertiary referral hospital that offers super specialized medical care to all specialties, in the capital city of Dar es Salaam. It receives referral patients from both public and private hospitals from all over the country. Patients who attend MAMC are either health insured, pay out of pocket or of public category. It has a hospital bed capacity of 571, 108 of these are allocated for medical inpatients. It also admits all medical patients including those with neurological disorders such as stroke. Approximately 70-80% of all admissions at MAMC medical wards are stroke patients. MAMC has the capacity to cater for all stroke patients in terms of investigations from neuro imaging to laboratory work up with definitive management plan.

2.3 STUDY DURATION

Study participants were recruited for a period of 8 months from 5th June 2018 to 26th January 2019. Each participant was thereafter followed up for study outcomes at 24 hours, 72 hours, 7 days, 14 days and 30 days.

2.4 STUDY POPULATION

All patients with WHO clinical diagnosis of stroke admitted at MAMC medical wards.

2.5 INCLUSION CRITERIA

- All patients with WHO clinical diagnosis of stroke

2.6 EXCLUSION CRITERIA

- Patients unable to obtain consent
- Recurrent stroke

2.7 SAMPLE SIZE

To determine the minimal sample size required the following formula for comparing two unequal proportions was used (105).

$$n_A = [P_A(1-P_A) + P_B(1-P_B)]\,[z_{1-\alpha/2} + z_{1-\beta}]^2$$

$$\kappa \qquad\qquad P_A - P_B$$

Where n_A is the sample size in group A, α/2 is the critical value of the Normal distribution at α/2 (for a confidence level of 95%, α is 0.05 and the critical value is 1.96), β is type II error and 1- β is the power (for a power of 80%, β is 0.2 and the critical value is 0.84), κ is the matching ratio (n_A / n_B). P_A and P_B are expected sample proportions of the two groups.

For this study:

n_A = Sample size of stroke in older adults (>45 years)

n_B = Sample size of stroke in younger adults (≤45 years).

κ = 2 (this matching ratio was obtained based on a previous pilot study done at MAMC which showed the ratio of admitted stroke patients who were old compared to young adults was an average of 2:1 each month).

P_A = 0.21 is the proportion of older adults (>45 years) with stroke who were current smokers in Malawi (106).

P_B = 0.10 is the expected proportion of younger adults (≤45 years) with stroke who are current smokers.

Therefore, the sample size for n_A was 224 patients and n_B was 112 patients adding 10% lost to follow up in each group gives 246 older adults with stroke and 123 younger adults making an overall sample size of **N= 369 participants.**

2.8 SAMPLING TECHNIQUE AND STUDY PROCEDURES

- Consecutive patients with clinical diagnosis of first ever stroke admitted at MAMC medical wards, were recruited after obtaining written informed consent from either the patient or the next of Kin (for patients unable to give consent). The recruitment process took a period of 7 months.

- The prevalence of first ever stroke by age was determined by including all first ever stroke patients over total admissions in medical ward, categorized and grouped by age that is ≤45 years and >45 years.

2.9 DATA COLLECTION

2.9.1. Participant Interview

- An interviewer based questionnaire was administered by the Principal investigator to each study participant or next of Kin for those participants who were unable to communicate due to stroke related disabilities. The questionnaire captured demographic information such date of birth, gender, residency, marital status, possession of health insurance and contact details.

- Other information collected included: risk factors for NCDs such as:

    - Smoking that was categorized as, current smokers (smoked within the last 12 months) vs former smokers (last time smoked was more than 12 months ago), alcohol consumption, current drinkers (alcohol consumption within the last 12 months) vs former drinkers (last alcohol consumed was more than 12 months ago) the type of alcohol and duration of alcohol consumption as adapted from a former large stroke study in Tanzania (57).

    - Drug history collected included use of: anti-hypertensive, anti-diabetic medications, ARV, hormonal contraception (in females) and illicit drugs.

    - Past medical history of hypertension, diabetes mellitus, cardiac disease, cardiac surgeries, HIV infection, recent active cancer (within the last 6 months).

- Family history of hypertension, diabetes and sudden death.

- Evaluation of other modifiable risk factors included:

  - The level of physical activity which was assessed using the short form version of The International Physical Activity Questionnaire. It is structured to provide total scores using summation of duration (minutes) and frequencies (days) in the 3 main domains. A total score of >3000 MET- min/week was regarded as vigorous intensity, 600 – 2900 MET-min/week as moderate intensity and <600 MET- min/week as light intensity physical activity (107) (108). Appendix 5.

  - Stress levels which was assessed using the Cohen Perceived Stress scale. It consists of 10 questions that ask about feelings and thoughts during the last month. It provides a summation of the total score for each question, a score of 0 – 13 regarded as low stress, 14 – 26 moderate stress and 27 – 40 as high stress (8). Appendix 6.

2.9.2 Clinical Examination

2.9.2.1 Blood pressure measurement:

- Blood pressure (BP) measurement was taken in supine position using a standardized digital BP machine brand AD Medical Inc. Three BP measurements spaced 1-2 minutes apart were taken from the unaffected arm to minimize the effects of changes in tone from hemiplegic side (109).

- An average of three measurements was recorded as systolic and diastolic BP by the first and fifth Korotkoff sounds respectively and the average blood pressure was used for analysis (110). A SBP ≥140 mmHg or DBP ≥90 was regarded as hypertension.

2.9.2.2 Anthropometric measurement:

- Waist measurements was performed using a tape measure at the mid-point between the lower margin of the last palpable rib and upper border of the anterior iliac crest (111).
- Hip circumference was measured using a tape measure while arms on the sides taken around the widest portion of the hips and waist-hip ratio was interpreted per WHO guidelines in males the ratio of ≥0.90 and females ≥0.85 was regarded as substantially increased (111).

2.9.2.3 Other physical examinations:

- The radial pulse of the unaffected limb was examined for pulse rate and rhythm that was recorded for one minute to detected for presence of an irregular pulse (arrhythmia).
- Auscultation over the carotid vessels on either side of the neck and auscultation of the precordium for a mid-diastolic murmur using the bell of the stethoscope in the left lateral position to assess for carotid artery stenosis and mitral stenosis respectively.

2.9.3 Laboratory investigations

- Venous blood was collected aseptically from the cubital fossae. Approximately 15mls of blood was collected: 5mls was collected for lipid profile using red topped vacutainers, 5mls was collected for CBC and 5mls for sickling test using purple topped vacutainers.
- Blood samples were analyzed at MUHAS GENETICS Laboratory using machine model A15 BIO- SYSTEMS SN. 831052588 and HEMOLYZER 3 PRO SN. 480235 for lipid profile and CBC respectively. Cut offs for total cholesterol >240mg/dl was regarded as hypercholesteremia, Triglycerides >200mg/dl as hypertriglyceridemia, LDL >129mg/dl as elevated and HDL <35mg/dl as reduced levels. For CBC Total white cell count >11.6, 000 was regarded as leukocytosis, hemoglobin of <13.2 g/dl in males and <11.5g/dl in females as anemia, hemoglobin of >17.3 g/dl in males and >15.1 g/dl in females as increased, platelets >450,000 as thrombocytosis and <150, 000 as thrombocytopenia.

- Blood analysis for sickling test was done at Central Pathology Laboratory using a chemical reducing agent sodium metabisulphite. The slides were viewed using Olympus microscope brand CX31. Results were recorded as positive or negative and for all tests performed quality control samples were used.
- Finger prick samples for RBG was done on the day of study enrollment, a diagnosis by DM was based on at least a random blood glucose reading of ≥ 11.1 mmol/l, and or a fasting blood glucose reading of ≥ 7 mmol/l (112). HIV testing was also done using SD Bioline HIV test kits and those who tested positive were confirmed using Unigold. In case of indeterminate results ELISA was used as part of Provider Initiated Testing and Counseling services (113).

2.9.4 Brain Imaging

- Brain imaging by either a non-contrast CT scan model GE Healthcare Optima CT660 SE, or MRI model GE SIGNA CREATOR 1.5 TESLA depending on availability to classify stroke to specific sub-types (Ischemic vs hemorrhagic). The Principal investigator interpreted the images under supervision of a Radiologist. For non-contrast brain CT scan, infarction was defined as a hypo dense (low density) lesion occupying a vascular territory with some brain swelling and hemorrhage as a hyper dense (white) lesion. For MRI infarction was defined as an area of T1 iso/hypointensity, high T2/Flair signal intensity with High DWI and low ADC values. Hemorrhage was defined as an area of variable T1/T2 signal based on age of stroke and a dark signal area in T2 sequence (114).

2.9.5 Echocardiogram

- The Principal investigator under supervision of a Cardiologist performed trans thoracic echocardiography using GE Medical Systems Model No. 19 ECHO machine. ECHOs were performed on all study participants in supine and left lateral position. Evidence of LVH was defined according to the European Society of Cardiology/American Society of Echocardiography as a measure of severity of septal thickness in 4 chamber view at mid-septum in end diastole.

Mid septal diameter of 11 – 13mm in male's and 10 – 12 mm in females was defined as mild LVH, 14 – 16 mm in male's and 13 – 15 mm in females as Moderate LVH and ≥17 mm in male's and ≥16 mm in females as severe LVH (115).

- The size of the left atrium in m-mode during end systole was measured and quantified according to the European Society of Cardiology/American Society of Echocardiography a diameter >4.0cm in males and >3.8cm in females was regarded as LA enlargement (115).
- Presence of mitral stenosis was assessed and degree of stenosis was defined using the mitral valve area and mean mitral valve pressure gradient. Mitral valve area >1.5cm^2 and mean pressure gradient of <5mmHg was defined as mild MS, mitral valve area of 1.0 – 1.5 cm^2 and Mean mitral valve pressure gradient of 5 to 10mmHg as moderate MS and mitrale valve area <1.0cm^2 with a Mean mitral valve pressure gradient >10mmHg as severe MS (116). Left atria thrombus and vegetations were also assessed and recorded in specific CRFs.

2.9.6 Electrocardiogram

- The Principal Investigator performed and interpreted a 12 lead ECG in all study participants under supervision of a Cardiologist using Bionet, model Cardio7. A diagnosis of Atrial fibrillation was defined According to the European Society of Cardiology as the presence of irregular RR intervals and no discernible distinct P waves (9).

2.9.7 Outcomes

- Acute stroke severity was assessed on the day of study enrollment using the National Institute of Health Stroke Scale, which objectively quantifies stroke on neurological examination. A score of 1 – 4 was defined as minor stroke, 5 – 15 moderate stroke, 15 – 20 moderate to severe and 21 – 42 severe stroke (1). Appendix 7.
- The Modified Rankin Scale was used to measure the degree of disability post stroke at 24 hours, 72 hours, 7days, 14 days and at 30 days from the date of study participant enrollment. It has a minimum score of 0 – no symptoms, 1 – no

significant disability and highest score of 6 – dead (1). Appendix 13. The main outcomes were either death or survival with disabilities.

2.10 DATA PROCESSING AND ANALYSIS

Data was entered and analyzed using SPSS version 20.0. The prevalence of stroke by age was presented as proportions with 95% confidence intervals. Continuous variables were summarized and presented as means and Standard Deviation (SD) or medians with Interquartile Range (IQR). Differences in proportion of stroke by age were compared using Chi square test. Differences in risk factors including clinical characteristics, laboratory parameters, ECG and ECHO findings were summarized as proportions and computed for differences using Chi square test/Fisher's exact test. Kaplan Meier analysis was applied to compare survival probabilities and survival curves to 30 days by age. A p value of <0.05 was used to denote statistical significance.

2.11. ETHICAL APPROVAL

Ethical clearance was obtained from research and publication committee of MUHAS. Permission to conduct the study was obtained from MAMC administration. Written informed consent was obtained from all study participants or next of Kin. All data collected was stored in files that are securely stored and electronic data password protected to maintain confidentiality. All enrolled participants received standard care as per MAMC guidelines. Participants and next of Kin were counseled by the PI on life style modification for secondary prevention. All HIV infected participants were counseled and referred to Care and Treatment Clinic for further management.

2.12 DATA DISSEMINATION

A soft copy of the dissertation will be available through the MUHAS Repository. A manuscript will also be prepared for publication in a peer reviewed journal.

CHAPTER THREE

3.0 RESULTS

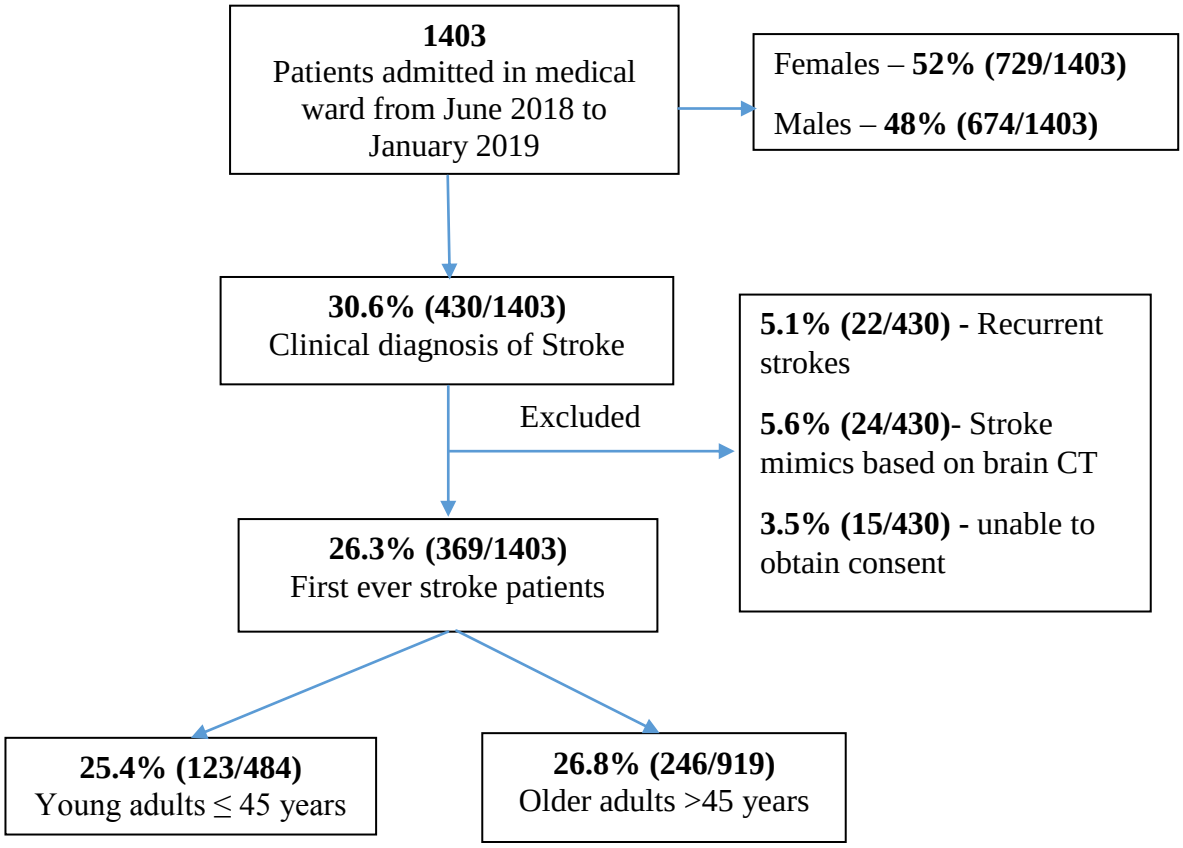
3.1 The Prevalence of first ever stroke at MAMC medical wards between June 2018 to January 2019.

There were a total of 1,403 admissions in the medical ward from 5th June 2018 to 26th January 2019, 484 admissions were aged ≤ 45 years and 919 admissions were aged > 45 years summarized in Figure 2. The prevalence of stroke among medical admissions at MAMC was 30.6% (430/1403). Out of the 430 patients admitted with stroke we excluded; 5.1% (22/430) who had recurrent stroke, 5.6% (24/430) stroke mimics and 3.5% (15/430) who were unable to give consent. The total number of study participants enrolled was 369.

The prevalence of stroke among participants aged ≤ 45 years (young) was 25.4% (123/484) (95% CI 21.5% - 29.3%) and participants >45 years (old) was 26.8% (246/919) (95% CI 23.9% - 29.6%). Majority of the study participants, 49.6% (183/369) were observed to arrive at the hospital between day 2 – 6 from symptom onset.

Figure 2: Consort chart

The Prevalence of first ever stroke at MAMC medical wards between June 2018 to January 2019.



3.2 Demographic characteristics of the first ever stroke participants (N=369)

Table 1 summarizes the demographic characteristics of the study participants. The overall mean age of the participants was 57.4 ± 16 years. The mean age for young and older adults was 39.4 ± 5.2 years and 66.4 ± 11.3 years respectively.

Females accounted for 55.8% (206/369) of the study participants with no difference in sex distribution between the two groups p=0.882 and 44.7% (55/123) vs 43.9% (108/246) were males in young and older adults respectively.

More of the young stroke participants were not married 27.6% (34/123) compared to older adults 0.8% (2/246) p=<0.001. Less than one third of the study participants were

insured with no differences between the two groups 30.1% (37/123) in young vs 26.4% (65/246) older adults p=0.459. The young were more likely to be current alcohol consumers compared to older adults 18.7% (23/123) vs 10.2% (24/246) respectively p=0.022.

Table 1: Demographic characteristics of the first ever stroke participants (N=369)

	Age groups			
	≤ 45 years n=123	> 45 years n=246	Total N= 369	p value
Female	68 (55.3%)	138 (56.1%)	206 (55.8%)	0.882
Marital status				
Ever Married	89 (72.4%)	244 (99.2%)	333 (90.2%)	**<0.001**
Never Married	34 (27.6%)	2 (0.8%)	36 (9.8%)	
Residence				
Dar-es-salaam	92 (74.8%)	195 (79.3%)	287 (77.8%)	0.33
Insurance	37 (30.1%)	65 (26.4%)	102 (27.6%)	0.459
Alcohol				
Ever	28 (22.8%)	45 (18.3%)	73 (19.8%)	0.309
Never	95 (77.2%)	201 (81.7%)	296 (80.2%)	
Current	23 (18.7%)	25 (10.2%)	48 (13%)	**0.022**
Smoking				
Ever	8 (6.5%)	17 (6.9%)	25 (6.8%)	0.884
Never	115 (93.5%)	229 (93.1%)	344 (93.2%)	
Current	3 (2.4%)	12 (4.9%)	15 (4.1%)	0.263

3.3 A comparison of stroke sub-type by brain imaging in young and older adults

Brain imaging was performed in 91.9% (339/369) of the study participants. For those who did not complete brain imaging, 66.7% (20/30) died prior to completion, 20% (6/30) were unable to afford and 13.3% (4/30) were unable to complete due to technical malfunction of the CT.

Distribution of the stroke subtype is summarized in figure 3, Ischemic subtype occurred in 55.8% (189/339), hemorrhagic subtype in 32.2% (109/339), and mixed ischemia and hemorrhagic in 1.8% (6/339).

There were 10.3% (35/339) participants who had a normal brain CT scan. Their median time was 1 day, Interquartile Range IQR (1,2) from first symptom to imaging. Similar, for those with ischemic stroke their median time was 1 day IQR (1,2). Table 2 summarizes the stroke subtypes by age. Younger adults were more likely to have hemorrhagic stroke compared to older adults 42.3% (47/111) vs 27.2% (62/228) respectively p=0.005.

Figure 3: Brain imaging among the first ever stroke participants (N=339)

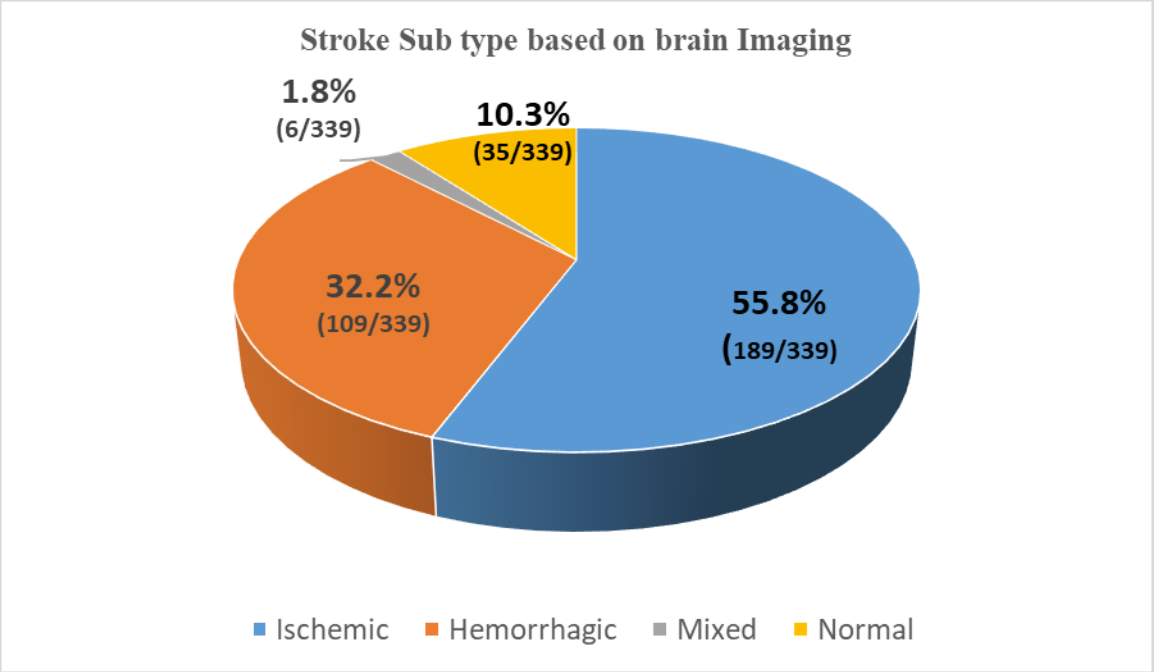


Table 2: A comparison of stroke subtype by brain imaging among the young and older adults

	Age groups			
CT findings	≤ 45 years	> 45 years	Total	p value
Missing	12 (9.8%)	18 (7.3%)	30 (8.1)	
	***n = 111**	***n = 228**	***N = 339**	
Ischemic	51 (45.9%)	138 (60.5%)	189 (55.8%)	**0.011**
Hemorrhagic	47 (42.3%)	62 (27.2%)	109 (32.2%)	**0.005**
Mixed lesions	0 (0.0%)	6 (2.6%)	6 (1.8%)	0.085
Normal scans	13 (11.7%)	22 (9.6%)	35 (10.3%)	0.558
Vessel involvement	***n= 51**	***n= 144**	***N=195**	
Major vessel disease	21 (41.2%)	80 (55.6%)	101 (51.8%)	0.077
Small vessel disease	21 (41.2%)	48 (33.3%)	69 (35.4%)	0.314
Mixed vessel disease	9 (17.6%)	16 (11.1%)	25 (12.8%)	0.23
Hemorrhagic subtype	***n= 47**	***n= 68**	***N= 115**	
Intracerebral	42 (89.4%)	67 (98.5%)	109 (94.8%)	**0.041**
Intraventricular	2 (4.3%)	0 (0.0%)	2 (1.7%)	0.165
Subarachnoid	3 (6.4%)	1 (1.5%)	4 (3.5%)	0.303

***n-**Total number of participants in each age groups, ***N-**Sum of total participants in young and old.

3.4 Comparison of risk factors among the young and older adults with stroke

Table 3 summarizes the risk factors for stroke among the young as compared to the old. Among the study participants, 77.2% (285/369) had a prior history of hypertension and only 41.4% (118/285) of the known hypertensives were on treatment.

Young adults were less likely to have a prior of hypertension compared to the old 63.5% (78/123) vs 84.1% (207/246) $p<0.001$. A prior history of HIV infection was more prevalent in the young 9.8% (12/123) vs 2.8% (7/246) compared to older adults $p=0.005$ and 94.7% (18/19) of the HIV infected were on ARVs.

Young females were more likely to be on hormonal contraception 48.5% (33/68) compared to the old 9.4% (13/138) $p<0.001$. The young were more likely to use illicit drugs 4.1% (5/123) compared to the older adults 0.8% (2/246) $p=0.044$.

Table 3: A comparison of stroke risk factors among the young and older adults

	Age groups			
	≤ 45 years n=123	> 45 years n=246	Total N=369	p value
Modifiable risk factors				
Known hypertensive	78 (63.4%)	207 (84.1%)	285 (77.2%)	**<0.001**
On treatment	30 (38.5%)	88 (42.5%)	118 (41.4%)	0.536
Known Diabetics	17 (13.8%)	47 (19.1%)	64 (17.3%)	0.206
On treatment	11 (64.7%)	20 (42.6%)	31 (48.4%)	0.117
Known HIV infected	12 (9.8%)	7 (2.8%)	19 (5.1%)	**0.005**
On treatment	11 (91.7%)	7 (100%)	18 (94.7%)	1
Hormonal contraception	33 (48.5%)	13 (9.4%)	46 (22.3%)	**<0.001**
Illicit drug use	5 (4.1%)	2 (0.8%)	7 (1.9%)	**0.044**
Cardiac disease	7 (5.7%)	9 (3.7%)	16 (4.3%)	0.366
Cardiac surgery	0 (0.0%)	1 (0.4%)	1 (0.3%)	1
Recent cancer	0 (0.0%)	3 (1.2%)	3 (0.8%)	0.554
Physical activity	***n= 28**	***n= 25**	***N= 53**	
Light intensity	3 (10.7%)	6 (24%)	9 (17%)	0.278
Moderate intensity	18 (64.3%)	17 (68%)	35 (66%)	0.776
Vigorous intensity	7 (25%)	2 (8%)	9 (17%)	0.148
Perceived stress	***n= 27**	***n= 22**	***N= 49**	
Low stress	16 (59.3%)	11 (50%)	27 (55.1%)	0.517
Moderate stress	10 (37%)	11 (50%)	21 (42.9%)	0.362
High stress	1 (3.7%)	0 (0%)	1 (2%)	1
Non modifiable risks				
Family Hx of HTN	42 (34.1%)	83 (33.7%)	125(33.9%)	0.938
Family Hx of diabetes	11 (8.9%)	33 (13.4%)	44 (11.9%)	0.211
Sudden death	8 (6.5%)	11 (4.5%)	19 (5.1%)	0.405

***n**-Total number of participants in each age groups, ***N**-Sum of total participants in young and old.

3.5 A comparison of clinical characteristics among young and older adults with stroke

Table 4 summarizes the clinical characteristics among the young and old participants with stroke. Severe stroke was observed in 56.1% (207/369) of the study participants. However, the young were likely to have a moderate stroke compared to old 35.8% (44/123) vs 24.4% (60/369) respectively p=0.022.

A new diagnosis of hypertension was common in the young 26.8% (33/123) compared to the old 9.3% (23/246) p<0.001. Likewise, mid diastolic murmurs (mitral stenosis) was common among the young 3.3% (4/123) compared to 0% (0/246) in old, Fisher's exact test=0.012.

Young adults were less likely compared to the old to have an irregular pulse (arrhythmia) 2.4% (3/123) vs 10.2% (25/246) respectively p=0.008, or have carotid bruits (carotid stenosis) 0% (0/123) vs 3.7% (9/246) respectively Fisher's exact test=0.032.

Table 4: A comparison of clinical characteristics among young and older adults with stroke

	Age groups			
	≤ 45 years n=123	> 45 years n=246	Total N=369	p value
Stroke severity				
Minor	7 (5.7%)	7 (2.8%)	14 (3.8%)	0.246
Moderate	44 (35.8%)	60 (24.4%)	104 (28.2%)	**0.022**
Moderate-severe	18 (14.6%)	26 (10.6%)	44 (11.9%)	0.256
Severe	54 (43.9%)	153 (62.2%)	207 (56.1%)	**0.001**
New hypertension	33 (26.8%)	23 (9.3%)	56 (15.2%)	**<0.001**
Irregular pulse	3 (2.4%)	25 (10.2%)	28 (7.6%)	**0.008**
Hyperthermia	24 (19.5%)	53 (21.5%)	77 (20.9%)	0.651
Mid diastolic murmur	4 (3.3%)	0 (0%)	4 (1.1%)	**0.012**
Carotid bruit	0 (0%)	9 (3.7%)	9 (2.4%)	**0.032**
Increased Waist-Hip ratio	95 (77.2%)	197 (80.1%)	292 (79.1%)	0.526

3.6 A comparison of laboratory parameters of stroke participants in young and older adults

Table 5 summarizes the laboratory parameters of the stroke participants by age group. Hypercholesteremia was prevalent in the young 31.2% (34/109) compared to the old 20.2% (40/198) p=0.031 with a higher proportion of the young having increased LDL compared to old 27.7% (28/101) vs 16.4% (29/177) respectively p=0.024. Likewise, young as compared to the old were more likely to have Sickle Cell Disease 9.7% (11/113) vs 4.2% (9/214) respectively p=0.047 and thrombocytosis 16.9% (12/71) vs 5.6% (8/144) respectively p=0.007.

Table 5: A comparison of Laboratory parameters of the stroke participants in young and older adults

	Age groups			
	≤ 45 years n=123	> 45 years n=246	Total N=369	p value
New DM	2 (1.6%)	1 (0.4%)	3 (0.81%)	0.259
Hyperglycemia	13 (10.6%)	22 (8.9%)	35 (9.5%)	0.615
New HIV	2 (1.6%)	5 (2%)	7 (1.9%)	1
Dyslipidemia	***n= 109**	***n=198**	***N=307**	
Hypercholesteremia	34 (31.2%)	40 (20.2%)	74 (24.1%)	**0.031**
Missing	14 (11.4%)	48 (19.5%)	62 (16.8%)	
	***n=107**	***n=191**	***N=298**	
Hypertriglyceremia	8 (7.5%)	17 (8.9%)	25 (8.4%)	0.671
Missing	16 (13%)	55 (22.4%)	71 (19.2%)	
	***n=101**	***n=177**	***N=278**	
Increased LDL	28 (27.7%)	29 (16.4%)	57 (20.5%)	**0.024**
Missing	22 (17.9%)	69 (28%)	91 (24.7%)	
	***n=109**	***n=196**	***N=305**	
Decreased HDL	20 (18.3%)	42 (21.4%)	62 (20.3%)	0.522
Missing	14 (11.4%)	50 (20.3%)	64 (17.3%)	
Sickling	***n= 113**	***n= 214**	***N= 327**	
Positive	11 (9.7%)	9 (4.2%)	20 (6.1%)	**0.047**
Missing	10 (8.1%)	32 (13.0%)	42 (11.4%)	
CBC	***n= 71**	***n= 144**	***N= 215**	
Leukocytosis	17 (23.9%)	49 (34%)	66 (30.7%)	0.132
Hemoglobin				
Anemia	36 (50.7%)	68 (47.2%)	104 (48.4%)	0.631
High	11 (15.5%)	12 (8.3%)	23 (10.7%)	0.11
Thrombocytopenia	14 (19.7%)	37 (25.7%)	51 (23.7%)	0.333
Thrombocytosis	12 (16.9%)	8 (5.6%)	20 (9.3%)	**0.007**
Missing	52 (42.3%)	102 (41.5%)	154 (41.7%)	

LDL- Low Density Lipoprotein, HDL- High Density Lipoproteins, CBC- Complete Blood Count, ***n**-Total number of participants in each age groups, ***N**-Sum of total participants in young and old.

3.7 A comparison of ECG and ECHO findings of the stroke participants in young and older adults

Table 6 compares ECG and ECHO findings among the stroke participants by age groups. Mild Mitral Stenosis was detected in only 4% (4/100) of the study participants in the young compared to 0% (0/191) in the old Fisher's exact test=0.013. The mean mitral valve area was 2.77±0.68 cm^2 and mean mitral valve pressure gradient was 4.95±0.24 mmHg. The young were less likely to have LVH compared to old 76% (76/100) vs 90.6% (173/191) respectively p=0.001.

Table 6: A comparison of ECG and ECHO findings of the stroke participants in young and older adults

		Age groups			
		≤ 45 years	> 45 years	Total	p value
ECG		***n= 99**	***n= 201**	***N= 300**	
	AF	3 (3%)	18 (9%)	21 (7%)	0.059
		***n=96**	***n=183**	***N=279**	
	P- mitrale	16 (16.7%)	45 (24.6%)	61 (21.9%)	0.128
Missing		24 (19.5%)	45 (18.3%)	69 (18.7%)	
ECHO		***n= 100**	***n= 191**	***N= 291**	
	LA enlargement	14 (14%)	31 (16.2%)	45 (15.5%)	0.617
	LA thrombus	1 (1%)	0 (0%)	1 (0.3%)	0.344
	MS	4 (4%)	0 (0%)	4 (1.4%)	**0.013**
	LVH	76 (76%)	173 (90.6%)	249 (85.6%)	**0.001**
	Mild	19 (19%)	44 (23%)	63 (21.6%)	0.427
	Moderate	32 (32%)	46 (24.1%)	78 (26.8%)	0.148
	Severe	25 (25%)	83 (43.5%)	108 (37.1%)	**0.002**
Missing		23 (18.7%)	55 (22.4%)	78 (21.1%)	

AF-Atrial Fibrillation, LA- Left Atrium, MS- Mitral Stenosis, LVH- Left Ventricular Hypertrophy, ***n**-Total number of participants in each age groups, ***N**-Sum of total participants in young and old.

Outcomes of stroke in young and older adults

The overall fatality at 30 days was 61.3% (215/351) among the study participants. Fatality rates in young adults were 49.1% (57/116) vs 67.2% (158/235) in older adults. There were 4.9% (18/369) lost to follow up during the entire study period, 5.7% (7/123) young and 4.5% (11/246) older adults p=0.608.

The overall median survival time for all study participants was 13 days. Using Kaplan Meier survival analysis shown in Figure 4, younger adults were more likely to survive (HR:1.52, 95% CI 1.12 – 2.03) compared to older adults (HR:0.66, 95% CI 0.49 – 0.88).

Table 7 summarizes the disability at 30 days among survivors using the Modified Rankin Scale. Young adults were more likely to have slight disability compared to older adults 16.9% (10/59) vs 6.5% (5/77) respectively p=0.038.

Figure 4: Kaplan Meier curve of 30-day survival by age

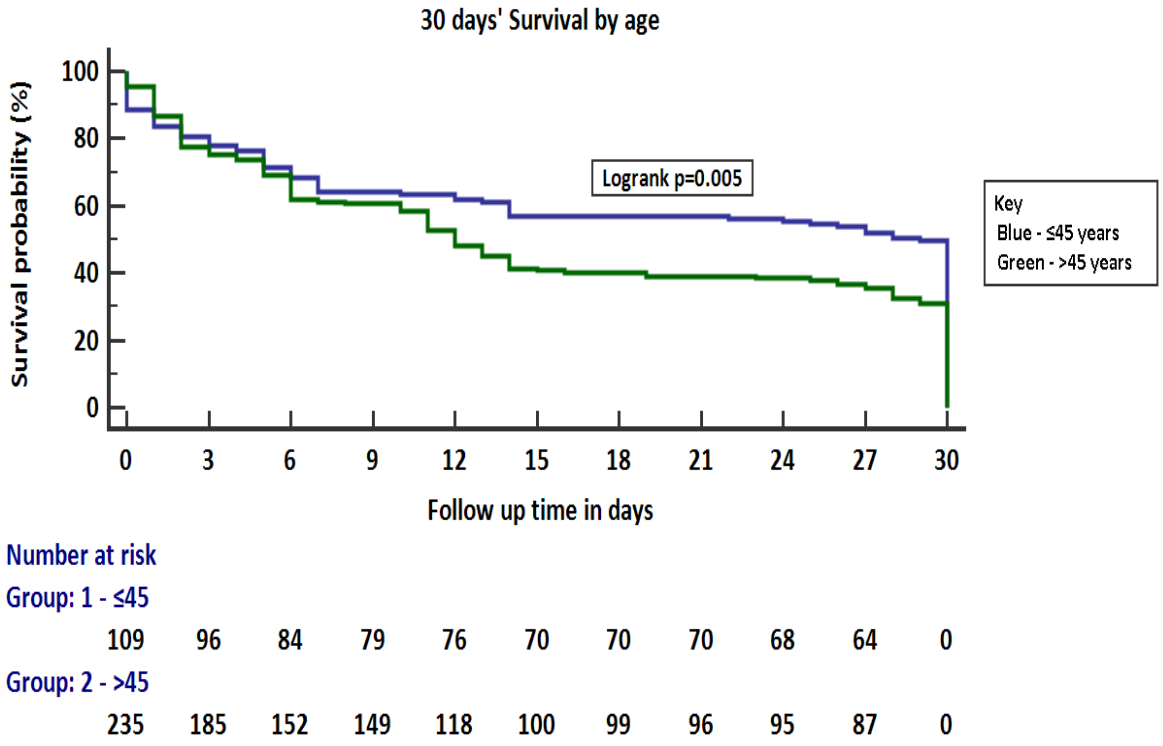


Table 7: 30-day Disability post stroke in young and older adults

	Age groups			
	≤ 45 years	> 45 years	Total	p value
Modified Rankin Scale				
	***n= 59**	***n= 77**	***N= 136**	
Severe disability	15 (25.4%)	26 (33.8%)	41 (30.1%)	0.47
Moderate to severe disability	16 (27.1%)	27 (35.1%)	43 (31.6%)	0.516
Moderate disability	16 (27.1)%)	17 (22.1%)	33 (24.3%)	0.358
Slight disability	10 (16.9%)	5 (6.5%)	15 (11%)	**0.038**
No significant disability	2 (3.4%)	2 (2.6%)	4 (2.9%)	1

***n-**Total number of participants in each age groups, ***N-**Sum of total participants in young and old.

CHAPTER FOUR

4.0 DISCUSSION

This was a cohort study among participants admitted with first ever stroke at MAMC medical wards in Dar es Salaam, Tanzania. This study looked in to the prevalence of first ever stroke, the associated factors and 30 day outcomes in young adults (≤ 45 years) compared to the old (>45 years).

4.1 Prevalence and risk factors for stroke in young adults

In this study, the prevalence of first ever stroke in young adults admitted at MAMC medical wards was similar to that observed in older adults 25.4% vs 26.8% respectively. This prevalence observed was much higher compared to previous studies in SSA (17,18). A study done in Nigeria decades ago showed a prevalence in the young of 12.3% while a more recent study in the same country the stroke prevalence was 5.4% in participants aged 35 to 44 years and 25.6% among participants aged 55 to 64 years (17,18). However, both studies were community based compared to ours which may account for their lower prevalence. Our findings are in keeping with a 2017 report from the Global Burden of Disease which stated that stroke should no longer be regarded as a disease of the old as it has the same potential of affecting the young (10). In our setting this raises great concerns as approximately 50% of the total population in Tanzania consists of individuals between 15 to 54 years (117). Developing a stroke at this age has both social and economic repercussions, as young citizens make up majority of the nation's workforce. Therefore, the initial key steps in addressing the current changes in stroke trends involves first raising awareness that stroke is no longer solely a disease of the old. Second, there is an urgent need of integrating preventive strategies to fight against stroke.

The rise in the burden of stroke among young adults is mainly factored by rapid transitioning of risk factors which were previously thought to be uncommon in this population (118). Our study describes specific risk factors mainly observed in young adults such as hypertension, use of drugs, dyslipidemia, HIV infection, SCD and RHD.

Hypertension accounted for more than 90% of all stroke admissions and more than one quarter of the young participants with stroke had a new diagnosis of hypertension. Of note, more than half of the participants with a previous history of hypertension were not

on treatment. Our findings indicate that hypertension is the single most important risk factor for stroke in young adults similar to other hospital based cross sectional studies (67,119). However, these high rates of new hypertension observed in younger adults should be interpreted with caution due to the initial blood pressure surge that occurs as a result of physiological auto regulatory mechanisms following an acute stroke (120). Nonetheless, it is quite alarming that young adults were unaware of their blood pressure status until hospital admission and for those with a previous diagnosis of hypertension more than half were not on treatment. These findings signal the need for efforts to promote awareness of regular blood pressure screening for early diagnosis and treatment of hypertension in the young.

The higher rates of hemorrhagic strokes observed in younger adults could likely be as a result of hypertension since it was the major risk factor observed. Different reports have identified hypertension in conjunction with the use of illicit drugs as a common etiology of hemorrhagic stroke in young adults, including a hospital based cross sectional case control study done in India in keeping with our findings (67,86,121). The sympathomimetic effects of illicit drugs transiently raises blood pressure with the risk of causing spontaneous cerebral bleeds (86). This indicates the need of developing health education programs targeting the young generation on the potential side effects of illicit drugs.

Younger females with stroke were more likely to be on hormonal contraception compared to older females in keeping in with a study in the US by Petit et al (92). This is of concern because women in Tanzania are now becoming exposed to different family planning methods ranging from the use of oral pills to injectables (94). Estrogen containing contraception have shown to induce hypercoagulable states thus increasing the like hood of cerebral vascular events especially in combination with other comorbidities (93). Therefore, there is a need for healthcare providers to be well educated on different family planning methods and tailoring the available options based on patient's preexisting illnesses.

A significant proportion of young adults with stroke had dyslipidemia. This was also mirrored in other hospital based comparison and prospective cohort studies which have

linked the association of dyslipidemia and stroke in young adults (51,67,122). The high rates of deranged lipids seen in the young population is linked to changes in lifestyle factors observed such as alcohol consumption although this study did not look into the daily quantity of alcohol consumed. Other risk factors such as smoking, diabetes, and physical inactivity observed in this study could have been contributory factors to stroke development in their own or in combination with hypertension by further exacerbating the likelihood of dyslipidemia. These factors are also independent risk factors for stroke as seen in other studies (60).

More of the young stroke participants were infected with HIV compared to the older counterparts. This is similar to previous reports in Tanzania (64,123,124). In this study, 90% of the HIV infected participants were on ARVs. It will be of interest to study if stroke among HIV infected individuals is due to immune responses to the virus or due to use of ARV as some of the protease inhibitors are known to cause dyslipidemia that predisposes to stroke (125). ARVs are known to prolong survival, increased survival exposes patients to the conventional stroke risk factors (53,60,125).

Sickle Cell Disease was observed as a risk factor among the young stroke participants in this study. Sickle cell has been reported as a risk factor in several studies in high and low to middle income countries where highest stroke rates were observed in individuals below 35 years of age (21,95). Despite the fact that this study did not look into specific sickle cell genotypes, this study highlights the need for regular follow up of patients with SCD to prevent cerebrovascular complications. The use of drugs like hydroxyurea have been proven beneficial in primary prevention of stroke in SCD (126).

Rheumatic Mitral stenosis was an exclusive risk factor for stroke in the young similar to what was observed in India by Kumbha et al (127). Mitral stenosis coupled with atrial fibrillation causes blood stasis and thrombus formation in the left atrium with subsequent brain embolism in young individuals (74,75). These findings stress the need for prevention of rheumatic heart disease, regular screening of youth for rheumatic heart disease and provision of definitive treatment and anti-coagulant prophylaxis to prevent thrombus formation (128).

4.2 Outcomes of stroke in young adults

There was a high 30-day fatality rate of 61.3% among all the study participants, (49.1% in young vs 67.2% in old) which is twice to what has been reported previously in hospital based studies done in Tanzania and Uganda (25,100). The fatality rates among stroke patients in a tertiary hospital in Dar es Salaam in year 2017 was 33.3%, the highest was among individuals aged >65 years (25). According to WHO 2017 reports, stroke deaths in Tanzania reached 4.61% (age adjusted Death rate of 76.58 per 100,000) of the total deaths and ranks 6th in the cause of death with limited data in young adults (129). Given the overall life expectancy of a Tanzanian is 66.3 years, it is of great tragedy to have years of life lost at this young age (130). Our study provides insight on the early disastrous stroke aftermath in young adults who are the main bread winners at the family level and builders of the nation's economy.

The high fatality rates observed in this study may be attributed to severe stroke among the study participants and delays in seeking medical care from symptom onset, similar to other studies (3,49). More than half of the admitted stroke participants had severe stroke regardless of age category and there was delay in hospital admission as approximately 50% arrived at the hospital between day 2 to 6 after stroke symptoms. Stroke is a medical emergency and delays leave little room for any neuro-vascular based interventions (intravenous thrombolytics or mechanical clot retrieval therapies) as there are specific criteria's that need to be fulfilled in order for the therapies to be offered (131). This ultimately leaves providers with few options limited to conservative management which is inferior compared to endovascular therapies in survival outcomes (132).

Though this study indicates a better 30-day disability status in young compared to the old this does not merely mean full recovery and ability to resume duty thus impacting on decline in family and nation's economy drop. It probably reflects the need for unique rehabilitation facilities and goals compared to the older counterparts to facilitate rapid recovery. Our study only looked into early post stroke outcomes, it would be of interest to study the long term outcomes of stroke in younger adults and different secondary preventive measures undertaken.

CHAPTER FIVE

5.0 STRENGTHS OF THE STUDY

This was the first study conducted at MAMC medical wards in Tanzania addressing the burden of stroke in young adults, risk factors and 30 days' outcomes. The National Institute of Health Stroke Scale is readily used in other settings for grading acute stroke severity. This study successful utilized this tool for grading stroke severity and has been linked to the 30-day fatality.

5.1 STUDY LIMITATIONS

We used data from a single tertiary hospital center so the results will not likely reflect the general population statistics and some participants had missing data leading to limitations in studying the specific variables. Therefore, these factors may affect the validity of the findings.

A few number of the study participants (10.3%) had normal brain CT scans who had arrived within 24 hours from symptom onset. This underestimates the proportion of ischemic stroke sub type.

CHAPTER SIX

6.0 CONCLUSION

Stroke in the young is as common as the old leading to a social and economic consequences. The risk factors for young strokes include: hypertension, dyslipidemia, HIV infection, use of drugs, SCD and RHD. The 30-day post stroke outcomes are associated with significant fatality rates in young adults who are the core nation's taskforce.

6.1 RECOMMENDATIONS

6.1.1 The initial key steps in addressing the current changes in stroke trends involves first raising awareness that stroke can occur to anyone and at any age debunking the previous myths of the disease of the older population.

6.1.2 Promoting primary preventive strategies for early strokes such as early screening and provision of treatment to control hypertension, dyslipidemia, HIV infection, Sickle Cell Disease and Rheumatic mitral stenosis to all young adults ≥18 years.

6.1.3 Health education on the potential adverse effects on the use of illicit drugs and hormonal contraception.

6.1.4 Future research on the possible factors associated with 30-day fatality of stroke in young adults.

6.1.5 Further research to address the possible etiologies of hypertension in young strokes.

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APPENDICES

APPENDIX 1: INFORMED CONSENT -ENGLISH VERSION

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

Consent to participate in the study titled stroke in young adults admitted at MAMC medical wards in Tanzania, a comparison with stroke in older adults.

Greetings: I am Dr. Sarah S Matuja, a postgraduate student doing research titled stroke in young adults admitted at MAMC medical wards in Tanzania, a comparison with stroke in older adults.

Purpose of the study: To determine the prevalence of first ever stroke, characterize stroke sub types, describe the associated risk factors and 30 day outcomes in younger adults as compared to the old.

What participation involved: If you agree to participate in this study, your medical information will be used for research purpose-but will not be linked to you directly.

Confidentiality: All information collected will be entered into a computer with identification numbers only, no names included.

Risk: We expect no harm to happen to you during the course of this study.

Right to withdrawal: Taking part in this study is completely voluntary and refusal to participate or withdrawal will not involve penalty or loss of any benefits to which you are entitled.

Benefits: The results from this study will be used as evidence based information for proposing routine screening of modifiable risk factors in the young and old who are potentially at an increased risk to develop NCDs such as stroke with poor outcomes.

Approval: This study has sought approval from proper and informed authorities.

Who to contact: If you have any questions regarding this study, feel free to contact me, the investigator, Dr. Sarah S Matuja, MUHAS, PO BOX 65001, Dar-es-Salaam, Tanzania.

Mobile phone +255 685 264 336. E mail: dr.matujajunior@gmail.com

If you have any questions concerning your right as a participant, you may contact Dr. Patricia Munseri, supervisor of the study, MUHAS, PO Box 65000, Dar es salaam, Tanzania.

Mobile phone +255 744 562 784. E mail: pmunseri@yahoo.com

Do you agree; Patient/Relative Yes/No …….

I' …… have read the consent form, my questions have been answered and I agree to participate in this study.

Signature: Participant/Relatives……...

Signature of investigator……

Date of signed consent…….

Do you also agree to test for HIV for the benefit of good patient care and as one of the risks for developing stroke; Yes/No .....

I' …… have read the consent form and my questions have been answered and I agree to be tested for HIV.

Signature: Participant/Relatives……...

Signature of investigator……

Date of signed consent…….

**Participant does not agree to test for HIV but would like to proceed with testing other parameters

I' …… have read the consent form and my questions have been answered.

Signature: Participant/Relatives……...

Signature of investigator……

Date of signed consent…….

APPENDIX 2: INFORMED CONSENT – SWAHILI VERSION

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

Ruhusa ya kushiriki utafiti kuhusu ugonjwa wa kiharusi miongoni mwa vijana wakubwa na watu wazima kwenye hospitali ya taifa MAMC Tanzania.

Mimi naitwa Dr. Sarah S Matuja ni mwanafunzi wa udhamili chuo kikuu cha tiba Muhimbili. Ninafanya utafiti kuangalia ugonjwa wa kiharusi miongoni mwa vijana wakubwa na watu wazima kwenye hospitali ya taifa MAMC Tanzania.

Dhumuni la utafiti huu: Kujua wingi wa ugonjwa wa kiharusi miongoni mwa vijana na watu wazima na kuona kama kuna tofauti katika viashiria vya ugonjwa huu na matokeo yao siku 30 baada ya kupata kiharusi.

Ushiriki: Kama unakubali kushiriki huu utafiti, taarifa zako za matibabu zitatumika kwenye utafiti huu peke yake.

Usiri: Taarifa zote za uchunguzi zitaingizwa kwenye kompyuta na nambari ya utambulisho; jina halitanukuliwa.

Madhara: Tunategemea kwamba hakuna madhara yoyote yatokanayo na utafiti huu.

Haki ya kujitoa kwenye utafiti: Kushiriki katika utafiti huu ni hiari na kutokubali kushiriki au kujitoa hautaadhibiwa au kupoteza haki yako ya matibabu.

Kutokea kwa madhara: Tunategemea kwamba hakuna madhara yoyote yatokanayo na utafiti huu. Hata hivyo kama madhara ya mwili yakitokea kutokana na utafiti huu utatibiwa kilingana na kanuni na taratibu za matibabu ya Tanzania.

Faida za kushiriki kwenye utafiti: Kama utakubali kushiriki kwenye utafiti huu, faida utakazopata ni pamoja na kuonwa na kufuatiliwa kwa ukaribu na daktari anayefanya utafiti.Tunatumaini kwamba taarifa zinazopatikana zitawanufaisha wengine pia.

Kwa mawasiliano zaidi: Kama una maswali kuhusu utafiti huu uwe huru kuwasiliana na mtafiti, Dr. Sarah S Matuja, Chuo kikuu cha afya na tiba Muhimbili, P.O Box 65001,

Simu +255 685 264 336, barua pepe: dr.matujajunior@gmail.com
Kama una swali kuhusu haki yako kama mshiriki wasiliana na Dr. Patricia Munseri, msimamizi wa utafiti.
P.O Box 65001, simu +255 744 562 784, barua pepe: pmunseri@yahoo.com
Je, umekubali kushiriki? Ndio/Hapana…….

Mimi ……Nimesoma maelezo na kuyaelewa vizuri, na nimekubali kushiriki kwenye utafiti huu.

Sahihi ya mshiriki/ndugu ……

Sahihi ya mtafiti …….

Tarehe ……..…

Je, umekubali kushiriki na kupimwa virusi vya ukimwi kuboresha tiba? Ndio/Hapana
…….
Mimi …… Nimesoma maelezo na kuyaelewa vizuri, na nimekubali kupimwa virusi vya ukimwi.
Sahihi ya mshiriki/ndugu ……
Sahihi ya mtafiti …….
**Mshiriki hajakubali kupimwa virusi vya ukimwi lakini angependa kupimwa vipimo vingine …….
Mimi …… Nimesoma maelezo na kuyaelewa vizuri, na nimekubali kushiriki kwenye utafiti huu.
Sahihi ya mshiriki ……
Sahihi ya mtafiti …….
Tarehe ……

APPENDIX 3: CASE REPORT FORM DEMOGRAPHIC INFORMATION PATIENT'S IDENTIFICATION

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

- ✓ Questionnaire No. .....
- ✓ Registration No. .....
- ✓ Patient's initials .....
- ✓ Date of study enrollment .....
- ✓ Date of Admission .....
- ✓ Date of Birth .....
- ✓ Gender Male ☐ Female ☐
- ✓ Physical address .....
- ✓ Marital status

  Ever married ☐ Never married/single ☐

- ✓ Possession of health insurance

  Yes ☐ No ☐

- ✓ Mobile numbers

  Patient's mobile number .....

  Next of Kin's mobile number .....

  Close Relative mobile number .....

Patients' details

- ✓ Firm .....
- ✓ Room no. .....
- ✓ Bed no. .....

APPENDIX 4: CASE REPORT FORM STROKE RISK FACTORS

(Tick were appropriate) **Answered by the Patient or Relative**

1. Have you ever been diagnosed for hypertension?

   Yes ☐ No ☐ I don't know ☐

   ***If No or I don't know, skip to question 3.**

2. If yes, are you on any anti-hypertensive medications?

   Yes ☐ No ☐

3. Any family history of hypertension?

   Yes ☐ No ☐ I don't know ☐

4. Have you ever been diagnosed for diabetes?

   Yes ☐ No ☐ I don't know ☐

   ***If No or I don't know, skip to question 6.**

5. If yes, are you on any oral hypoglycemic drugs or insulin injections?

   Yes ☐ No ☐

6. Any family history of diabetes?

   Yes ☐ No ☐ I don't know ☐

7. Any history of hormonal contraception? **(For a Female patient)**

   Yes ☐ No ☐

8. Any history of illicit drug use?

   Yes ☐ No ☐

9. Any previous history of stroke?

   Yes ☐ No ☐

10. Any history of cardiac diseases?

Yes ☐ No ☐ I don't know ☐

If Yes, specify .....

11. Any history of cardiac related surgeries (valvular replacement)?

Yes ☐ No ☐

12. Any history of sudden death in the family **(not trauma related)?**

Yes ☐ No ☐ I don't know ☐

13. Any history of current or recent active cancer?

Yes ☐ No ☐ I don't know ☐

14. Are you HIV infected?

Yes ☐ No ☐ I don't know **(Never tested)** ☐

***If No or I don't know, skip to question 16.**

15. If yes, are you on any ARVs?

Yes ☐ No ☐ I don't know ☐

16. Are you a cigarette smoker?

Yes ☐ No ☐ I don't know ☐

***If No please skip to question 20.**

17. If yes, are you a current smoker? **(smoked within last 12 months)**

Yes ☐ No ☐ I don't know ☐

18. Years smoked …….

19. Cigarettes per day ……

20. Do you drink alcohol?

Yes ☐ No ☐ I don't know ☐

***If No please skip to question 24.**

21. If yes, are you a current drinker? (last drunk within 12 months)

Yes ☐ No ☐ I don't know ☐

22. Which kind? (tick were appropriate)

Wine ☐

Beer ☐

Local brew ☐

Spirits ☐

For how many years? ……

APPENDIX 5: CASE REPORT FORM INTERNATIONAL PHYSICAL ACTIVITY

24. INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person.

Think about all the **VIGOROUS** activities that you did in the **last 7 days**. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **VIGOROUS** physical activities **LIKE HEAVY LIFTING, DIGGING, AEROBICS, OR FAST BICYCLING?**

_____ days per week

**** If No vigorous physical activities **Skip to question 3**

2. How much time did you usually spend doing **VIGOROUS** physical activities on one of those days?

_____ hours per day

_____ minutes per day

Don't know/Not sure _____

Think about all the **MODERATE** activities that you did in the **last 7 days**. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **MODERATE** physical activities **LIKE CARRYING LIGHT LOADS, BICYCLING AT A REGULAR PACE, OR DOUBLES TENNIS?** **** Do not include walking!!

_____ days per week

No moderate physical activities **Skip to question 5**

4. How much time did you usually spend doing **MODERATE** physical activities on one of those days?

____ hours per day

_____ minutes per day

Don't know/Not sure _____

Think about the time you spent **WALKING** in the **last 7 days**. This includes **AT WORK AND AT HOME, WALKING TO TRAVEL FROM PLACE TO PLACE, AND ANY OTHER WALKING THAT YOU HAVE DONE SOLELY FOR RECREATION, SPORT, EXERCISE, OR LEISURE.**

5. During the **last 7 days**, on how many days did you **WALK** for at least 10 minutes at a time?

_____ days per week

6. How much time did you usually spend **walking** on one of those days?

_____ hours per day

_____ minutes per day

Don't know/Not sure _____

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002

** Incase the physical assessment scale is not completed, state reason .....

APPENDIX 6: CASE REPORT FORM PERCEIVED STRESS SCALE

25. KIPIMO CHA MFADHAIKO (PERCEIVED STRESS SCALE)

Maswali haya yanaulizia kuhusu hisia na fikra zako katika kipindi cha mwezi moja na yapo kwenye mfumo wa kipimo cha mizani. Kwa kila swali, unatakiwa kuzungushia jibu lako kuhusu namna ambavyo ulijisikia au kufikiria yapo kwenye kipimo cha mizani.

Jina lako_____

Tarehe_____

Umri wako_____

0=Kamwe 1= Nadra (mara **1 kwa mwezi) 2= Wakati mwingine (**mara **2 kwa mwezi) 3=Mara kwa mara (**mara **2 kwa wiki) 4= Kila wakati (**zaidi ya mara **3 kwa wiki)**

MASWALI

1. Katika kipindi cha mwezi moja uliopita, ni mara ngapi umekosa furaha kwa jambo lililotokea bila kutarajia? 0 1 2 3 4
2. Katika kipindi cha mwezi uliopita, ni mara ngapi umehisi umeshindwa kukabili mambo muhimu katika maisha yako? 0 1 2 3 4
3. Katika kipindi cha mwezi uliopita, ni mara ngapi umepata hofu na mfadhaiko?
   0 1 2 3 4
4. Katika kipindi cha mwezi uliopita, ni mara ngapi umejiamini juu ya uwezo wako wa kumudu matatizo yako binafsi? 0 1 2 3 4
5. Katika kipindi cha mwezi uliopita, ni mara ngapi umehisi kuwa vitu vinaenda kama unavyotaka? 0 1 2 3 4
6. Katika kipindi cha mwezi uliopita, ni mara ngapi umejikuta umeshindwa kumudu mambo yote kama ulivyopangilia? 0 1 2 3 4
7. Katika kipindi cha mwezi uliopita, ni mara ngapi umeweza kukabili hali ya maudhi kwenye maisha yako? 0 1 2 3 4
8. Katika kipindi cha mwezi uliopita, ni mara ngapi umejihisi kuwaunaweza kumudu vitu?
   0 1 2 3 4

9. Katika kipindi cha mwezi uliopita, ni mara ngapi umekasirishwa kwa sababu ya vitu ambavyo vipo nje ya uwezo wako? 0 1 2 3 4
10. Katika kipindi cha mwezi uliopita, ni mara ngapi umehisi kuwa changamoto zikiongezeka kwa kiwango cha kushindwa kuzikabili? 0 1 2 3 4

Tick were appropriate

1. Low Stress **Scores 0- 13** ☐
2. Moderate Stress **Scores 14-26** ☐
3. High Perceived Stress **Scores 27-40** ☐

*****Note: Reverse the scores for Questions 4,5,7 and 8 in this manner:

Response of 0= score 4, Response of 1= Score 3, Response of 2= Score 2, Response of 3= Score 1 and Response of 4= Score 0

******Incase PSS not completed state reason .....**

APPENDIX 7: STROKE SEVERITY

26. National Institute of Health Stroke Scale NIHSS

Instructions	Scale definition	Score
1a. Level of consciousness: The investigator must choose a response 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, and 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 stupors patients who do not comprehend the questions	0 = **Answers** both questions correctly. 1 = **Answers** one question correctly. 2 = **Answers** neither question correctly.	

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.		
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 him or her (pantomime), and the result scored (ie, follows	0 = **Performs** both tasks correctly. 1 = **Performs** one task correctly. 2 = **Performs** neither task correctly.	

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.		
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	0 = **Normal.** 1 = **Partial gaze palsy;** gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present. 2 = **Forced deviation,** or total gaze paresis not overcome by the oculocephalic maneuver.	

investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.		
3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat, as appropriate. Patients may 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	0 = **No visual loss.** 1 = **Partial hemianopia.** 2 = **Complete hemianopia.** 3 = **Bilateral hemianopia** (blind including cortical blindness).	

a 1, and the results are used to respond to item 11.		
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 barriers obscure the face, these should be removed to the extent possible.	0 = **Normal** symmetrical movements. 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).	
5. Motor arm: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine). Drift is scored if the arm falls before 10 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each	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	

limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	against gravity. 3 = **No effort against gravity;** limb falls. 4 = **No movement.** UN = **Amputation** or joint fusion, explain: _____ **5a. Left arm** **5b. Right arm**	
6. Motor leg: The limb is placed in the appropriate position: hold the leg at 30 degrees (always tested supine). Drift is scored if the leg falls 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 leg. Only in the case of amputation or joint fusion at the hip, the examiner should record the score as untestable (UN),	0 = **No drift;** leg holds 30-degree 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.** UN = **Amputation** or joint	

and clearly write the explanation for this choice.	fusion, explain: _____ **6a. Left leg** **6b. Right leg**	
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, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice. In case of blindness, test by having the patient touch nose from extended arm position.	0 = **Absent.** 1 = **Present in one limb.** 2 = **Present in two limbs.** UN = **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 sensory loss," 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 brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in a coma (item 1a=3) are automatically 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 of 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. For this scale item, 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 a coma (item 1a=3) will automatically score 3 on this item. The examiner must choose a score for the patient with stupor or limited cooperation, but a	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 materials difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content 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	

score of 3 should be used only if the patient is mute and follows no one-step commands.	response. 3 = **Mute, global aphasia;** no usable speech or auditory comprehension.	
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 barriers to producing speech, the examiner should record the score as untestable (UN), and clearly write an explanation for this choice. Do not tell the patient why he or she is being tested	1 = **Mild-to-moderate dysarthria;** patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = **Severe dysarthria;** 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. UN = **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	0 = **No abnormality.** 1 = **Visual, tactile, auditory, spatial, or personal inattention** or extinction to bilateral simultaneous stimulation in	

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 anosognosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.	one of the sensory modalities. 2 = **Profound hemi-inattention or extinction to more than one modality;** does not recognize own hand or orients to only one side of space.	

Tick were appropriate

1. No stroke symptoms **Score 0** ☐
2. Minor stroke **Scores 1- 4** ☐
3. Moderate stroke **Scores 5-15** ☐
4. Moderate to severe stroke **Scores 16-20** ☐
5. Severe stroke **Scores 21- 42** ☐

****** Incase NIHSS not completed state reason .....**

APPENDIX 8: CASE REPORT FORM ON CLINICAL CHARACTERISTICS

(Tick were appropriate)

- ✓ Blood pressure

Time (hours)	1st Reading	2nd reading	3rd reading	Average
0 hours				

- ✓ Pulse rate ..... b/min
  - o Rhythm .....
  - o Heart rate ..... b/min
  - o Pulse deficit ..... b/min
- ✓ Temperature ..... ^{0} C
- ✓ Carotid bruit - 1. Yes ☐ 2. No ☐
- ✓ Mid diastolic Murmur auscultated- 1. Yes ☐ 2. No ☐

******Incase this section is not completed state reason**

.....

- ✓ Height ..... meters Weight ..... Kgs
  - o BMI ..... Kg/m^2
- ✓ Waist circumference ..... cm
- ✓ Hip circumference ..... cm
- ✓ Waist-hip ratio .....

***Incase weight/height not completed indicate reason .....**

APPENDIX 9: CASE REPORT FORM ON LABORATORY INVESTIGATIONS

(Tick were appropriate)

Lab work up

- ✓ RBG ..... mmol/l FBG ..... mmol/l
- ✓ HIV Test 1. Reactive ☐ 2. Non-reactive ☐ 3. Indeterminate ☐
- ✓ Sickling Test 1. Positive ☐ 2. Negative ☐
- ✓ Lipid Profile

  Total Cholesterol .....mg/dl

  LDL ..... mg/dl

  HDL ..... mg/dl

  TGA ..... mg/dl

******Incase the lipids are not completed state reason**

.....

- ✓ Complete Blood Count

  Total WBC ..... $*10^9$/L

  Hemoglobin ..... g/dl

  Platelet count ..... $*10^9$/L

******Incase the CBC is not completed state reason**

.....

APPENDIX 10: ECG- CASE REPORT FORM

Heart rate:	..... beats/min	
Rhythm:	☐ Regular ☐ Irregular	Sinus rhythm, Yes ☐ No ☐
P wave: (Lead II and V1)	☐ Present ☐ Absent	☐ Normal ☐ P mitrale wave

******Incase ECG is not done state reason .....**

APPENDIX 11: ECHO- CASE REPORT FORM

Quantification of LVH- Severity of Septal Thickness using 2 D 4 chamber view.

- ✓ Mean Diastolic septal thickness ..... mm
- ✓ Mitral Stenosis Present ☐ Absent ☐
  - o If present, Mitral valve area ..... cm^2
  - o Mean Mitral Valve Pressure Gradient ..... mmHg
- ✓ LA size ..... cm
- ✓ Lt Atrial Thrombus Present ☐ Absent ☐
  - o If present, size of the thrombus ..... cm
- ✓ Vegetation on the Mitral valve Present ☐ Absent ☐
  - o If present, size of the vegetation ..... cm

******Incase ECHO is not done state reason .....**

APPENDIX 12: CASE REPORT FORM STROKE SUBTYPE

Name of patient..... MRN .....

Date of symptoms .....

Date of CT scan .....

- ✓ CT findings:
  - Normal CT scan ☐
  - Abnormal
    - Ischemic sub type ☐
    - Hemorrhagic sub type ☐
      - Intra cerebral ☐
      - Intraventricular ☐
      - SAH ☐
    - Age of stroke
      - New - Acute ☐
      - Old - Chronic ☐
  - Anatomical site
    - Frontal Rt ☐ Lt ☐ Both ☐
    - Parietal Rt ☐ Lt ☐ Both ☐
    - Temporal Rt ☐ Lt ☐ Both ☐
    - Occipital Rt ☐ Lt ☐ Both ☐
    - Basal ganglia Rt ☐ Lt ☐ Both ☐
    - Other specify .....
  - Vascular territory involved
    - Large vessel
      - ACA Rt ☐ Lt ☐ Both ☐
      - MCA Rt ☐ Lt ☐ Both ☐
      - PCA Rt ☐ Lt ☐ Both ☐
    - Small vessel Rt ☐ Lt ☐ Both ☐
- ✓ Other findings, specify .....

******Incase CT SCAN not done state reasons .....**

APPENDIX 13: CASE REPORT FORM ON STROKE OUTCOMES

(Tick were appropriate) **Answered by the Patient or Relative**

- ✓ **Modified Rankin Scale used at 24 hours, 72 hours, day 7, day 14 and 30 days' post stroke.**

Score	Interpretation
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities
3	Moderate disability. Requires some help, but able to walk unassisted
4	Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent
6	Dead

Date of Death .....

Date of Discharge .....

- ✓ On rehabilitation therapy? 1. Yes ☐ 2 No ☐

  If Yes, Home/hospital based, specify .....