Published in final edited form as:

J Neurol Sci. 2018 December 15; 395: 8–16. doi:10.1016/j.jns.2018.09.021.

Risk Factors for Stroke Occurrence in a low HIV endemic West African Country: a case-control study.

Fred Stephen Sarfo, MD, PhD, PhD^{1,2}, Ohene Opere-Sem, MD, MSc^{1,2}, Martin Agyei, MD, MSc^{1,2}, John Akassi, MD^{1,2}, Dorcas Owusu, MSc², Mayowa Owolabi, MD, DM³, and Bruce Ovbiagele, MD, MSc⁴

¹Kwame Nkrumah University of Science & Technology, Kumasi, Ghana

²Komfo Anokye Teaching Hospital, Kumasi, Ghana

³University of Ibadan, Ibadan, Nigeria

⁴Medical University of South Carolina, South Carolina, USA

Abstract

Background: HIV infection is an emerging vascular risk factor associated with stroke occurrence. The weight of evidence from sub-Saharan Africa in support of this has accrued from countries with high HIV prevalence. Our objective was to assess the contribution of HIV seropositivity to the occurrence and outcomes of stroke in a West African country with low HIV prevalence.

Methods: A case-control study design conducted at a tertiary medical center in Ghana involved in the Stroke Investigative Research & Educational Networks (SIREN) epidemiological study. Stroke cases were adults (aged ≥ 18 years) with CT or MRI confirmed stroke and stroke-free controls were age-matched and recruited from communities in the catchment areas of cases. Standard instruments were used to assess vascular and lifestyle factors and serological screening for HIV antibodies was conducted for all study participants. Stroke patients were followed for in-patient mortality outcomes. Associations between HIV, demographic and vascular risk factors and stroke occurrence and outcomes were assessed using logistic regression analysis.

Results: We enrolled 540 stroke cases and 540 control subjects with a mean ($\pm$ SD) age of 60.8 ± 15.5 years (cases) and 60.0 ± 15.5 (controls). Among stroke cases, the frequency of HIV was 12/540 (2.2%, 95% CI: 1.3% - 3.6%) versus 15/540 (2.8%, 95% CI: 1.7% - 4.6%) among stroke-free controls, $p=0.70$. However, the median (IQR) age of Persons Living with HIV (PLWH) with stroke was significantly lower at 46.5 (40 – 65.3) years versus 61.0 (50–74) years, $p=0.03$ among HIV- stroke patients. Stroke among PLWHA was predominantly hemorrhagic in 7 out of 12 cases and ischemic in 5 of 12 with notable clustering of established factors such as hypertension,

Corresponding Author: Fred Stephen Sarfo, Kwame Nkrumah University of Science & Technology, Division of Neurology, Department of Medicine, Private Mail Bag, Kumasi, Ghana, Telephone #: 233 243 448464, stephensarfo78@gmail.com.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of Interests: None to declare.

(100%), dyslipidemia, 83.3%, central obesity, 50.0%, diabetes mellitus, 33.3%, cardiac diseases, 8.3% in this group. None of the PLWH with stroke were receiving antiretroviral therapy.

Conclusion: We found no associations between HIV infection and stroke occurrence among Ghanaians. However a clustering of cardio-metabolic factors in the context of HIV may promote stroke occurrence in younger individuals.

Keywords

HIV; stroke; outcomes; risk factors; low HIV prevalence; Africa

INTRODUCTION

The burden of stroke in sub-Saharan Africa (SSA) is now among the highest in the world.¹⁻⁷ This recent secular trend is due to a sustained surge in uncontrolled rates of vascular risk factors notably hypertension, diabetes mellitus, and dyslipidemia on the continent.^{8,9} Distinctively, stroke in SSA affects a younger population^{10,11}, has a higher propensity to be hemorrhagic¹⁰⁻¹², has high early^{6,7,13-15} and long-term mortality¹⁶ and is associated with post-stroke depression¹⁷, vascular cognitive impairment¹⁸ and stigma.¹⁹ The Human Immunodeficiency Virus (HIV) has been posited as a vascular risk factor for adverse vascular events including strokes. A recent systematic review and meta-analysis involving 334,000 Persons Living with HIV (PLWH) mainly from the US and Europe compared with HIV- controls provided compelling evidence of associations between HIV and any stroke, ischemic and hemorrhagic strokes.²⁰ The HIV population has a heightened predisposition to CVD risk due to a combination of accelerated atherosclerosis from the pro-inflammatory milieu created by chronic HIV infection and the potential adverse metabolic side effects from cART medications.²¹⁻²³

In the US, a retrospective review revealed that admissions of stroke patients with concurrent HIV infection had increased by 43% over a decade.²⁴ There is however a paucity of studies that has evaluated the associations between stroke occurrence and outcomes and HIV in SSA with nearly 70% of the global burden of HIV/AIDS.²⁵ A systematic review of 17 studies involving 478 PLWHA with acute stroke in SSA identified younger age of onset of stroke, advanced HIV disease and worse outcomes among those infected with HIV compared with HIV-uninfected group.²⁶ A seminal case-control study in Malawi involving 222 acute stroke cases with 503 stroke-free controls, identified HIV as an independent risk factor for stroke occurrence in country with a high prevalence of HIV.²⁷ It however remains unknown whether these associations observed in HIV high endemicity countries would pertain in SSA countries such as Ghana where HIV prevalence is low.

We have therefore assessed the associations between HIV sero-positivity and stroke occurrence and its subtypes among 540 stroke cases compared with 540 community stroke-free controls at a tertiary medical center in Ghana involved in the Stroke Investigative Research and Educational Networks (SIREN) epidemiological study-the largest on-going study on stroke in SSA.²⁸

METHODS

Study site:

The study was conducted at the Komfo Anokye Teaching Hospital (KATH), a tertiary referral center in Kumasi, Ghana. Ghana is a low middle income country with an HIV prevalence of 2.0%.²⁹ KATH is the second largest hospital in Ghana and has a stroke unit and a dedicated neurology clinic. Approximately, 2 million people reside in Kumasi. The teaching hospital receives referrals from 5 out of 10 administrative regions of Ghana due to its central location. Ethical approval for the study was obtained from the Committee of Human Research Publication and Ethics.

Study design and study participants:

This is a case-control study. Stroke cases were consecutive consenting (in unconscious/aphasic subjects, consent from next of kin was obtained) adults aged ≥ 18 years with stroke symptoms < 8 days of current symptom onset or 'last seen without deficit' with neuroimaging confirmation with CT or MRI scan within 10 days of symptom onset. Stroke patients typically presented to hospital via the Accidents and Emergency Department where initial evaluation including cranial CT scans and treatments are commenced in consultation with the neurology team, led by FSS. Stroke patients are then transferred to a 6-bed Stroke Unit for multi-disciplinary stroke team care or the general medical ward depending on availability of beds at the stroke unit. To minimize selection and referral biases, we broadened patient recruitment by including patients admitted to hospital via the emergency room and ambulatory clinics. Furthermore, community engagement outreaches were conducted across sites periodically to sensitize members of the community and encourage stroke patients to present to hospital.

Stroke-free controls were consenting adults recruited mostly from the communities in the catchment areas of stroke cases. Stroke-free status was confirmed with the 8-item questionnaire for verifying stroke-free status (QVSFS) which had 98% negative predictive value in a validation study involving 3 major languages spoken in West Africa (Ashanti, Yoruba and Hausa).^{30–32} Controls were matched by age (± 5 years) to minimize the potential confounding effect of this variable on stroke, HIV and vascular risk factors. Community controls were recruited mainly from the suburbs of Kumasi where the Teaching Hospital is situated and from the immediately adjoining semi-urban and rural communities. Matching of controls to cases was not stratified by location of residence.

Stroke Phenotyping:

Stroke phenotyping was based on clinical evaluation and brain neuroimaging with Computerized tomography, electrocardiography (ECG), transthoracic echocardiography, and carotid Doppler ultrasound performed according to standards of practice (SOP). Ischemic stroke was typed into etiological sub-types using the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria³³ and clinically using the Oxfordshire Community Stroke Project (OCSP) criteria³⁴. Intracerebral hemorrhage was classified etiologically into Structural, Medication-related, Amyloid angiopathy, Systemic/other disease, Hypertension and Undetermined causes (SMASH-U)³⁵.

Data collection:

Basic demographic, socioeconomic and lifestyle data including cigarette smoking, and alcohol use as well as cardiovascular risk profile were collected. Blood samples for HbA1c and early morning samples after overnight fast in cases (post-acute phase when fasting is feasible) and controls for blood glucose, and lipid profile [total cholesterol (TC), Low Density Lipoprotein-cholesterol (LDL-C), High Density Lipoprotein-cholesterol (HDL-C) and triglyceride (TG)] were obtained by study nurses.

Definition of risk factors

- Hypertension: Blood pressure (average of three measurements used) was recorded at baseline and daily for 7 days or until death. A cutoff of 140/90 mmHg for up to 72 hours after stroke, a history of hypertension, or use of antihypertensive drugs before stroke or >72 hours after stroke were regarded as indicators of hypertension. Definition of hypertension in controls was self-reported history of hypertension or use of antihypertensive drugs or average BP at first clinical encounter 140/90mmHg.³⁶
- Diabetes mellitus was defined based on history of diabetes mellitus, use of medications for DM, an HbA1c >6.5% or a fasting blood glucose (FBG) levels > 7.0mmol/l at first encounter in controls or measured after the post-acute phase in cases due to the known acute transient elevation of glucose as a stress response after stroke.³⁷
- Dyslipidemia was defined as TC ≥5.2mmol/L, HDL-C <1.03mmol/l, TG ≥1.7mmol/l or LDL-C ≥3.4mmol/l according to NCEP guidelines³⁸ or use of statin prior to stroke onset.
- Cardiac disease was defined after evaluation by study cardiologists based on history or current diagnosis of atrial fibrillation, cardiomyopathy, heart failure, ischemic heart disease, rheumatic heart disease, and valvular heart diseases.
- Obesity: We assessed both waist circumference and body-mass index. Subjects were classified individually either using the WHO guidelines using cutoffs of 94cm (men) and 80cm (women) for waist circumference or 30kg/m² for BMI (Obesity).³⁹
- Alcohol use was categorized into current users (users of any form of alcoholic drinks) or never/former drinker while alcohol intake was categorized as low drinkers (1–2 drinks per day for female and 1–3 drinks per day for male) and high drinker (>2 drinks per day for female and >3 drinks per day for male. 1 drink or 1 unit of alcohol = 8g of alcohol).³⁶
- Smoking status was defined as current smoker (individuals who smoked any tobacco in the past 12 months) or never/former smoker.³⁶
- Stroke outcome on discharge from hospital was assessed as alive or dead.

Serological testing for HIV:

HIV-1 and 2 antibody testing was done using the First Response® HIV-1/2 test (Premier Medical Corporation Limited, India) and the Genscreen® ULTRA HIV Ag-Ab Assay (Bio-Rad, France) at the Komfo Anokye Teaching Hospital. All cases and controls were tested for HIV.

Statistical Analysis

We compared means and medians of continuous variables using the Student's t-test and the Mann-Whitney's U-test respectively. Proportions were compared using Chi-squared test or the Fischer's exact test. Associations between vascular risk factors, demographic factors and HIV status and two outcome variables namely stroke occurrence and stroke mortality were assessed in a multivariate logistic regression analyses. Factors included in these models namely age, male gender, urban residence, highest educational attainment, household income dichotomized as >100USD versus <100USD, presence of hypertension, diabetes mellitus, dyslipidemia, central obesity, cigarette smoking, alcohol use, heart disease and HIV sero-positivity were selected based on their known associations with stroke occurrence and outcomes. In bivariate analysis, factors that attained a p-value of <0.05 were included in the multivariable model with two-tailed p-values <0.05 considered statistically significant. Statistical analysis was performed using SPSS version 19 and GraphPad Prism version 7.

RESULTS

Demographic and clinic characteristics:

There were 540 stroke cases and 540 control subjects with a mean ($\pm$ SD) age of 60.8 ± 15.5 years (cases) and 60.0 ± 15.5 (controls) respectively but there was a female preponderance in the control compared with cases. Differences in socio-demographic indicators such as location of residence, marital status, educational level, monthly income, and employment status were present between the two groups (Table 1). Comparing cases with controls, 91.6% versus 58.0% had hypertension ($p<0.0001$), 80.4% versus 70.6% had dyslipidemia ($p=0.0002$), 38.1% versus 6.1% had diabetes mellitus ($p<0.0001$), and 3.5% versus 0.6% had cardiac disease ($p=0.0006$). Both current use of alcohol and cigarette smoking were significantly higher among cases than controls. The mean ($\pm$ SD) waist circumference of stroke cases of 95.0 ± 16.5 cm was significantly higher than 88.6 ± 12.7 cm among controls, $p<0.0001$.

Stroke type information was available for 535 cases of which 318 (59.4%) were ischemic and 217 (40.6%) were hemorrhagic. Etiologic subtypes of ischemic stroke included small vessel stroke - 34.6%, cardio-embolic stroke- 27.6%, large-vessel atherosclerosis- 26.0%, undetermined causes- 11.1% and other determined causes- 0.6%. Hemorrhagic strokes were predominantly caused by hypertension –84.8%, structural lesions (including intracerebral aneurysms and arteriovenous malformations) –10.6%, undetermined – 2.3%, cerebral amyloid angiopathy –1.8% and systemic diseases – 0.5%.

HIV Sero-prevalence and stroke occurrence:

Among stroke cases, the frequency of HIV was 12/540 (2.2%, 95% CI: 1.3% - 3.6%) versus 15/540 (2.8%, 95% CI: 1.7% - 4.6%) among stroke-free controls, $p=0.70$. Among stroke cases, HIV serotypes were type 1 in 10/12, type 1 and 2 in 1/12 and type 2 in 1/12 while among stroke free controls, HIV type 1 was found in 10/15, type 1 and 2 in 1/15 and type 2 in 4/15. (Table 1). None of the PLWH were aware of their sero-status and therefore were not receiving antiretroviral therapy.

The median (IQR) age of PLWH with stroke was significantly lower at 46.5 (40 – 65.3) years versus 61.0 (50–74) years, $p=0.03$. The proportion of PLWH with stroke under 50 years was therefore significantly higher at 58.3% versus 24.4% among HIV sero-negative stroke cases, $p=0.01$. However, among stroke free controls, there were no significant age differences between the PLWH and HIV-negative participants. (Table 2). There were also a significantly higher proportion of HIV-negative stroke cases who were married 65.2% compared with 33.3% among PLWH with stroke, $p=0.004$. Prevailing vascular risk factors among PLWH with stroke in decreasing order of frequency were hypertension, 100%, dyslipidemia, 83.3%, central obesity, 50.0%, diabetes mellitus, 33.3%, cardiac diseases, 8.3% and cigarette smoking 0.0%. There were no significant differences in risk factor profile between PLWH and negative stroke cases (Table 2), except for a higher diastolic BP among PLWH with stroke. Hemorrhagic strokes 7/12 (58.3) were non-significantly commoner among PLWH with stroke than ischemic strokes 5/12 (41.7%).

Comparisons between PLWH with stroke and stroke-free controls as well as PLWH without stroke versus HIV-negative stroke-free controls are shown in Table 2. With the exception of a higher frequency of diabetes mellitus of 4/12 (33.3%) versus 0/15 (0.0%) among PLWH with stroke and HIV-positive stroke-free controls respectively, $p=0.02$, there were no significant differences between the two groups with respect to frequency of vascular risk factors.

Risk factors for stroke:

Factors significantly associated with stroke occurrence included hypertension, diabetes mellitus, heart diseases, cigarette smoking, and alcohol use. Socio-demographic factors associated with stroke occurrence were urban residence, and higher income of >100USD per month. Unadjusted and adjusted odds ratio, 95%CI and p-values associated with these factors are shown in Table 3. HIV sero-positivity was not associated with stroke occurrence, unadjusted OR (95% CI) of 0.80 (0.37–1.73), $p=0.57$. Limiting the analysis to participants under 50 years, unadjusted OR (95% CI) of HIV and stroke was 1.06 (0.36–3.09).

Predictors stroke mortality outcomes:

There were 134 (24.8%, 95% CI: 21.4 – 28.6%) in-patient deaths; 1 occurred among PLWH with stroke and 133 among the HIV negative stroke cases, $p=0.31$. The mortality reported in the PLWH was a hemorrhagic stroke. Overall, those who died were significantly older than survivors and more likely to reside in rural settings. Participants who died compared with those who survived were less likely to have hypertension 86.6% versus 94.3%, $p=0.004$, less likely to have elevated LDL-cholesterol 44.0% versus 56.2%, $p=0.01$, more likely to have

low HDL-cholesterol 36.6% versus 26.4%, $p=0.02$ and hypertriglyceridemia 30.6% versus 21.1%, $p=0.03$. Furthermore, large-vessel atherosclerotic strokes were more likely to die than other stroke subtypes. Other differences between the two groups are shown in Table 4. In a multivariate logistic regression model, factors independently associated with stroke mortality with their adjusted OR (95% CI) are stroke severity 1.42 (1.29–1.57) for each 5-points increase on the National Institute of Health Stroke Scale, use of antihypertensive therapy after stroke was protective with adjusted OR of 0.39 (0.19 – 0.81) and hypertriglyceridemia, 1.68 (1.02 – 2.07). HIV sero-positivity was not significantly associated with stroke-related mortality, unadjusted OR (95% CI) of 0.27 (0.03 – 2.09), $p=0.21$ (Table 5).

DISCUSSION

This is one of the largest studies with a case-control design to evaluate in a systematic fashion the associations between stroke occurrence and outcomes in relation to HIV sero-prevalence in a low HIV endemic West African country. We found a low frequency of HIV among stroke patients overall and no associations between HIV sero-positivity and stroke occurrence or adverse outcomes after stroke. Notably, PLWH with stroke were significantly younger but also had traditional vascular risk factors such as hypertension, dyslipidemia and diabetes mellitus as predispositions for stroke occurrence. Furthermore, hemorrhagic stroke was the more frequent stroke type among PLWH than ischemic strokes but this was not statistically different from the HIV sero-negative stroke cases.

A similar prior study conducted in Malawi²⁷, with a national HIV prevalence of 10.3%, identified HIV to be independently associated with stroke occurrence unlike the present study which was conducted in Ghana with a national HIV prevalence of 1.8%. Also, although untreated HIV was associated with increased risk of stroke, a much higher risk of stroke occurrence within the first 6 months after initiation of antiretroviral therapy likely attributable to Immune Reconstitution Inflammatory Syndrome (IRIS) was observed.²⁷ However in our study, none of the stroke patients identified with HIV infection were aware of their diagnosis and hence were not receiving ART. Similar to the Malawian study, we observed that compared with the HIV-negative stroke cases, PLWH with stroke were significantly younger with a mean age of 51 years but this is higher than the 43 years reported in two cohorts from the US^{21,24}, 33.4 years in South Africa⁴⁰, or 40 years in Malawi⁴¹. However the median age of 46.5 (IQR:40.0–65.3) among PLWH with stroke in the present study falls within the range of age distribution from previous studies conducted at our medical center where median age of a large cohort PLWHA enrolled for antiretroviral therapy was 38 (IQR: 14–77).^{42–45} Importantly, all stroke patients with HIV co-infection in the present study had hypertension in addition to a cluster of other risk factors such as dyslipidemia and diabetes which in concert would orchestrate the occurrence vascular events. There is however a suggestion that HIV sero-positivity and stroke co-occurrence may be coincidental particularly in low-and-middle income countries with low HIV prevalence and rising burden of non-communicable diseases.⁴⁶

Mechanistically, HIV-associated vasculopathy⁴⁶ caused directly or indirectly by HIV, may invoke vascular perturbations including accelerated atherosclerosis, vasculitis, stenosis and

aneurysm formation, which in the setting of established vascular risk factors such as hypertension and dyslipidemia would promote the occurrence of vascular events such as stroke. We however found a higher proportion of hemorrhagic strokes among HIV positive stroke patients than ischemic strokes. This is in contrast with previous studies in SSA and from the US where ischemic strokes were the predominant stroke type among HIV infected patients with stroke.^{21, 24,40,41,47,48} However, a pre-ART era population-based study in Baltimore, US reported nearly equal proportions of ischemic infarctions and intracerebral hemorrhage⁴⁹ similar to our study where all HIV infections identified were ART-naive. An elegant systematic review and meta-analysis of 44 prospective cohorts including 334,417 HIV+ individuals from the US and Europe compared with HIV negative controls provided compelling evidence of independent associations between HIV positivity and both ischemic and hemorrhagic strokes.²⁰ It is important to emphasize here that among young West Africans below 50 years, hemorrhagic stroke has outstripped ischemic strokes although hospital-referral bias for hemorrhagic strokes cannot be entirely ruled out.⁵⁰ Given that PLWH with stroke were relatively younger than HIV negative stroke patients, it is conceivable that the factors driving the higher burden of hemorrhagic strokes among West Africans could be driving the higher frequency of intracerebral hemorrhage. Hypertension prevalence in Ghanaian adults has reached epidemic proportions with estimated prevalence of up to 48%⁵¹, similar to 37% in Nigeria⁵², 40% in Burkina Faso⁵³ and 42% in Niger⁵⁴ based on West African studies conducted before 2010. Furthermore, blood pressure control among patients with hypertension in this region is severely challenged.⁵⁵ Expectedly, hypertension was causally associated with 6 out of 7 hemorrhagic strokes while etiology for ischemic stroke was sparsely distributed between lacunar, cardio-embolic, large-vessel and undetermined using the TOAST classification. However, the etiologic subtypes of both ischemic and hemorrhagic strokes among PLWH with stroke were not significantly different from the HIV negative group. We did not observe excess mortality in PLWH with stroke in concordance with a previous study from Malawi.⁵⁶

We do acknowledge the limitation of small sample size of PLWH with stroke would have a bearing on stroke type and sub-type data as well as outcomes in our study. Larger multi-center collaborative efforts would be needed to provide further granular resolution on the impact of HIV to stroke type and sub-type occurrence in the West African sub-region and ultimately at the continental level. Data on WHO clinical stage, CD4 T-cell counts and HIV viral loads were not collected as part of the SIREN study to help enrich and explore for associations between these key variables and characteristics of stroke among the PLWH. Furthermore, while HBA1c was measured for stroke cases to ascertain diabetes status to avoid post-stroke glycemic excursions, the stroke free controls were mainly assessed using fasting blood glucose. In addition, we matched cases and controls by age and not by sex nor location of residence as some authors suggest that the validity of case-control studies which is contingent on selecting controls independently of risk factor status could be compromised by matching⁵⁷. Due to the imbalances in matching of demographic characteristics of cases and controls, such as gender and location of residence we employed unconditional logistic regression models.⁵⁸ In addition, because cases were recruited from hospitals, the potential for selection bias for recruiting severe stroke cases, in particular hemorrhagic stroke exist. Finally, causal relationships between HIV sero-status and stroke occurrence and outcomes

are difficult to establish in a case-control study. However, this sub-study from the on-going SIREN study is one of the largest to date and neuro-radiologically confirmed stroke type information was available for >95% of all stroke cases. In addition, etiologic information on stroke subtypes were explored in a detailed and comprehensive manner.

Our findings contribute significantly to an important and emerging public health issue regarding the impact of HIV to stroke occurrence in LMICs. Clinicians in LMICs where both HIV and stroke burden are high and rapidly rising should give consideration to the inclusion of HIV screening for all acute stroke patients, particularly those below 50 years. This approach would help identify patients with undiagnosed HIV for appropriate treatment of HIV to be instituted in addition essential care for acute stroke. In conclusion, we have demonstrated that in a low HIV endemic country, HIV is not independently associated with stroke occurrence. While the association between HIV and stroke is indisputable, perhaps a much larger sample size may be required to demonstrate effect in regions with lower prevalence. However a clustering of cardio-metabolic factors in the context of HIV may promote stroke occurrence in younger individuals in sub-Saharan Africa.

Acknowledgements:

Grant R21 TW010479–01 from the National Institute of Health and U54 HG007479 from NIH (NHGRI, -NINDS). We are also grateful to Mr. Nathaniel Adusei Mensah and Michael Ampofo for helping with data cleaning.

REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics-2015 update: a report from the American Heart Association. *Circulation* 2015 127;131(4):e29–322. [PubMed: 25520374]
2. WHO. The top ten causes of death. <http://www.who.int/mediacentre/factsheets/fs310/en/> 2017; Available at: URL: <http://www.who.int/mediacentre/factsheets/fs310/en/>.
3. Seshadri S, Wolf PA. Lifetime risk of stroke and dementia: current concepts, and estimates from the Framingham Study. *Lancet Neurol* 2007 12;6(12):1106–14. [PubMed: 18031707]
4. Walker R, Whiting D, Unwin N, Mugusi F, Swai M. Stroke incidence in rural and urban Tanzania: a prospective, community-based study. *Lancet Neurology* 2010;9:786–92. [PubMed: 20609629]
5. Ezejimofor MC, Uthman OA, Maduka O, et al. Stroke survivors in Nigeria: A door-to-door prevalence survey from the Niger Delta region. *J Neurol Sci* 2017 1 15;372:262–9. [PubMed: 28017225]
6. Sarfo FS, Awuah DO, Nkyi C, Akassi J, Opare-Sem OK, Ovbiagele B. Recent patterns and predictors of neurological mortality among hospitalized patients in Central Ghana. *J Neurol Sci*. 2016; 363:217–224. [PubMed: 27000253]
7. Sarfo FS, Akassi J, Awuah D, Adamu S, Nkyi C, Owolabi M, Ovbiagele B. Trends in Stroke admission & mortality rates from 1983 to 2013 in Central Ghana. *J Neurol Sci*. 2015; 357(1–2): 240–5. [PubMed: 26293417]
8. NCD Risk factor Collaboration (NCD-RisC). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet*. 2017;389(10064):37–55. [PubMed: 27863813]
9. Owolabi MO, Akarolo-Anthony S, Akinyemi R, et al. The burden of stroke in Africa: a glance at the present and a glimpse into the future. *Cardiovasc J Afr* 2015 3;26(2 Suppl 1):S27–S38. [PubMed: 25962945]
10. Feigin VL, Roth GA, Naghavi M, et al. Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol* 2016;15(9):913–924. [PubMed: 27291521]

11. O'Donnell MJ, Chin SL, Rangarajan S, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *Lancet* 2016;388(10046):761–75. [PubMed: 27431356]
12. Owolabi M, Sarfo FS, Akinyemi R, Gebregziabher M, Akpa O, Akpalu A, et al. Dominant risk factors for stroke among West Africans: findings from the SIREN large multisite study. *Lancet Global Health* 2018;6(4): e436–e446. [PubMed: 29496511]
13. Walker RW, Jusabani A, Aris E, et al. Post-stroke case fatality within an incident population in rural Tanzania. *J Neurol Neurosurg Psychiatry* 2011;82(9):1001–5. [PubMed: 21386108]
14. Danesi MA, Okubadejo NU, Ojini FI, Ojo OO. Incidence and 30-day case fatality rate of first-ever stroke in urban Nigeria: the prospective community based Epidemiology of Stroke in Lagos (EPISIL) phase II results. *J Neurol Sci* 2013; 331:43–7. [PubMed: 23726277]
15. Gomes J, Damasceno A, Carrilho C, et al. Determinants of early case-fatality among stroke patients in Maputo, Mozambique and impact of in-hospital complications. *Int J Stroke* 2013; 8 (Suppl. 100):69–75. [PubMed: 23331721]
16. Sarfo FS, Akassi J, Kyem G, Adamu S, Awuah D, Kantanks OS, et al. Long-term outcomes of Stroke in a Ghanaian Outpatient Clinic. *J Stroke Cerebrovasc Dis.* 2018;27(3):1090–1099. [PubMed: 29275059]
17. Sarfo FS, Jenkins C, Singh A, Owolabi M, Ojagbemi A, Adusei N, Saulson R, Ovbiagele B. Post-stroke depression in Ghana: characteristics and correlates. *J Neurol Sci* 2017;379:261–265. [PubMed: 28716256]
18. Sarfo FS, Akassi J, Adamu S, Obese V, Ovbiagele B. Burden and predictors of vascular cognitive impairment among long-term Ghanaian stroke survivors. *J Stroke Cerebrovasc Dis.* 2017;26(11): 2553–2562.
19. Sarfo FS, Nichols M, Qanungo S, Teklehaimanot A, Singh A, Mensah N, et al. Stroke-related stigma among West Africans: Patterns and predictors. *J Neurol Sci* 2017;375: 270–274. [PubMed: 28320146]
20. Gutierrez J, Albuquerque ALA, Falzon L. HIV infection as vascular risk: a systematic review of the literature and meta-analysis. *PLoS ONE* 2017;12(5): e0176686. [PubMed: 28493892]
21. Oritz G, Koch S, Romano JG, Forteza AM, Rabinstein AA. Mechanisms of ischemic stroke in HIV-infected patients. *Neurology* 2007;68 (16): 1257–61. [PubMed: 17438215]
22. Depairon M, Chessex S, Sudre P, Rodondi N, Doser N, Chave JP, et al. Premature atherosclerosis in HIV-infected individuals-focus on protease inhibitor therapy. *AIDS* 2001; 15(3): 329–34. [PubMed: 11273212]
23. Jerico C, Knobel H, Calvo N, Sorli ML, Guelar A, Gimeno-Bayon JL, et al. Sub-clinical carotid atherosclerosis in HIV-infected patients: role of combination antiretroviral therapy. *Stroke* 2006; 37(3):812–7. [PubMed: 16439699]
24. Ovbiagele B, Nath A. Increasing incidence of ischemic stroke in patients with HIV infection. *Neurology* 2011; 76(5):444–50. [PubMed: 21248273]
25. UNAIDS. 2015 Epidemiological slides – How AIDS Changed Everything report; 2015.
26. Abdallah A, Chang JL, O'Carroll CB, Musubire A, Chow FC, Wilson AL, et al. Stroke in Human Immunodeficiency Virus-infected individuals in Sub-Saharan Africa (SSA): a systematic review. *J Stroke Cerebrovasc Dis* 2018; 27(7): 1828–1836. [PubMed: 29628338]
27. Benjamin LA, Corbett EL, Connor MD, Mzinganjira H, Kampondeni S, Choko A, et al. HIV, antiretroviral treatment, hypertension, and stroke in Malawian adults: a case-control study. *Neurology* 2016.
28. Akpalu A, Sarfo FS, Ovbiagele B, et al. Phenotyping stroke in sub-Saharan Africa: Stroke Investigative Research and Education Network (SIREN) Phenomics protocol. *Neuroepidemiology* 2015;45(2):73–82. [PubMed: 26304844]
29. Ghana AIDS Commission. Ghana National HIV and AIDS Strategic Plan 2016–2020. Accra: GAC; 2016.
30. Sarfo F, Gebregziabher M, Ovbiagele B, et al. Multilingual validation of the Questionnaire for verifying stroke-free status in West Africa. *Stroke* 2016;47(1):167–172. [PubMed: 26578660]

31. Sarfo FS, Adu Gyamfi R, Adamu S, Sarfo-Kantanka O, Owolabi M, Ovbiagele B. Administration of a pictorial questionnaire to screen for stroke among patients with hypertension or diabetes in rural Ghana. *J Neurol Sci* 2017;373:289–294. [PubMed: 28131208]
32. Sarfo FS, Gebregziabher M, Ovbiagele B, Akinyemi R, Owolabi L, Obiako R, et al. Validation of the 8-item questionnaire for verifying stroke free status with and without pictograms in three West African languages. *eNeurologicalSci.* 2016; 3:75–79. [PubMed: 27148595]
33. Kolominsky-Rabas PL, Weber M, Gefeller O, Neundoefer B, Heuschmann PU. Epidemiology of ischemic stroke subtypes according to TOAST criteria: incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study. *Stroke* 2001; 32(12):2735–40. [PubMed: 11739965]
34. Banford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet* 1991; 337(8756):1521–6. [PubMed: 1675378]
35. Meretoja A, Strbian D, Putaala J, et al. SMASH-U: a proposal for etiologic classification of intracerebral hemorrhage. *Stroke* 2012;43(10):2592–7. [PubMed: 22858729]
36. O'Donnell M, Xavier D, Diener C, et al. Rationale and design of INTERSTROKE: a global case-control study of risk factors for stroke. *Neuroepidemiology* 2010; 35(1):36–44. [PubMed: 20389123]
37. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med.* 1998;15(7):539–53. [PubMed: 9686693]
38. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of high blood cholesterol in adults (Adult treatment panel). Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high cholesterol in adults (Adult Treatment Panel III). *Circulation* 2002;106:3143–21. [PubMed: 12485966]
39. World Health Organization. Waist circumference and waist-hip ratio. Report of a WHO expert consultation. 2008 Last assessed on 27/05/2017 at http://www.who.int/nutrition/publications/obesity/WHO_report_waistcircumference_and_waisthip_ratio/en/.
40. Tipping B, de Villiers L, Wainwright H, Candy S, Bryer A. Stroke in patients with human immunodeficiency virus infection. *J Neurol Neurosurg Psychiatr.* 2007;78:1320–1324.
41. Heikinheimo T, Chimbayo D, Kumwenda JJ, Kampondeni S, Allain TJ. Stroke outcomes in Malawi, a country with high prevalence of HIV: a prospective follow-up study. *PLoS One.* 2012;7:e33765. [PubMed: 22479439]
42. Sarfo FS, Sarfo MA, Norman B, Phillips R, Bedu-Addo G, Chadwick D. Risk of deaths, AIDS-defining and non-AIDS defining events among Ghanaians on long-term combination antiretroviral therapy. *PLoS One.* 2014;9(10):e111400. [PubMed: 25340766]
43. Sarfo FS, Sarfo MA, Norman B, Phillips R, Chadwick D. Incidence and determinants of nevirapine and efavirenz-related skin rashes in West Africans: nevirapine's epitaph? *PLoS One.* 2014;9(4):e94854. [PubMed: 24728406]
44. Sarfo FS, Sarfo MA, Chadwick D. Incidence and risk factors for neuropsychiatric events among Ghanaian HIV patients on long-term non-nucleoside reverse transcriptase inhibitor-based therapy. *eNeurologicalSci.* 2016;3:21–25. [PubMed: 29430531]
45. Sarfo FS, Bibby DF, Schwab U, Appiah LT, Clark DA, Collini P, et al. Inadvertent non-nucleoside reverse transcriptase inhibitor (NNRTI)-based antiretroviral therapy in dual HIV-1/2 and HIV-2 seropositive West Africans: a retrospective study. *J Antimicrob Chemother.* 2009;64(3):667–9 [PubMed: 19549668]
46. Benjamin LA, Bryer A, Emsley HCA, Khoo S, Solomon T, Connor MD. HIV infection and stroke: current perspectives and future directions. *Lancet Neurol.* 2012;11(10):878–890. [PubMed: 22995692]
47. Tipping B, de Villiers L, Candy S, Wainwright H. Stroke caused by human immunodeficiency virus-associated intracranial large-vessel aneurysmal vasculopathy. *Arch Neurol.* 2006;63:1640–1642. [PubMed: 17101835]

48. Mochan A, Modi M, Modi G. Protein S deficiency in HIV associated ischaemic stroke: an epiphenomenon of HIV infection. *J Neurol Neurosurg Psychiatr.* 2005;76:1455–1456.
49. Cole JW, Pinto AN, Hebel JR. Acquired immunodeficiency syndrome and the risk of stroke. *Stroke.* 2004;35:51–56. [PubMed: 14684782]
50. Sarfo FS, Ovbiagele B, Gebregziabher M, Wahab K, Akinyemi R, Akpalu A, et al. Stroke Among Young West Africans: evidence from the SIREN, Large Multisite case-control study. *Stroke.* 2018;49(5):1116–1122. [PubMed: 29618553]
51. Bosu WK. Epidemic of hypertension in Ghana: a systematic review. *BMC Public Health.* 2010;10:418. [PubMed: 20626917]
52. Adedoyin RA, Mbada CE, Balogun MO, Martins T, Adebayo RA, Akintomide A, et al. Prevalence and pattern of hypertension in a semiurban community in Nigeria. *Eur J Cardiovasc Prev Rehabil.* 2008 12; 15(6):683–7. [PubMed: 19177626]
53. Niakara A, Fournet F, Gary J, Harang M, Nébié LV, Salem G. Hypertension, urbanization, social and spatial disparities: a cross-sectional population-based survey in a West African urban environment (Ouagadougou, Burkina Faso). *Trans R Soc Trop Med Hyg.* 2007 11; 101(11):1136–42. [PubMed: 17706257]
54. World Health Organization. STEPS Fact Sheet. Brazzaville: WHO AFRO; 2008.
55. Sarfo FS, Mobula LM, Burnham G, Ansong D, Plange-Rhule J, Sarfo-Kantanka O, et al. Factors associated uncontrolled blood pressure among Ghanaians: Evidence from a multicenter hospital-based study. *PLoS One.* 2018;13(3):e0193494. [PubMed: 29554106]
56. Heikinheimo T, Chimbayo D, Kumwenda JJ, Kampodeni S, Allain TJ. Stroke outcomes in Malawi, a country with high prevalence of HIV: A prospective follow-up study. *PLoS ONE.* 2012; 7(3): e33765. [PubMed: 22479439]
57. Rose S, van der Laan MJ. Why match? Investigating matched case-control study designs with causal effect estimation. *Int J Biostat* 2009;5:1.
58. Kuo CL, Duan Y, Grady J. Unconditional or conditional logistic regression for age-matched case-control data? *Front Public Health.* 2018;6:57. [PubMed: 29552553]

Highlights

- To assess the impact of HIV on stroke occurrence in a low HIV endemic West African country
- 540 adult stroke cases age-matched to 540 stroke free controls
- HIV prevalence in stroke cases was 2.2% vs 2.8% among controls
- Stroke patients with HIV were much younger than stroke cases without HIV

Table 1.

Comparison of stroke cases and stroke-free controls

Characteristic	Stroke cases N= 540	Stroke free controls N= 540	P-value
Age, mean $\pm$ SD	60.8 $\pm$ 15.5	60.0 $\pm$ 15.5	0.40
Female gender	247 (45.7)	331 (61.3)	<0.0001
Location of residence			<0.0001
Urban	285 (52.8)	416 (77.0)	
Semi-urban	196 (36.3)	51 (9.4)	
Rural	55 (10.2)	27 (5.0)	
No data available	4 (0.7)	46 (8.5)	
Marital Status			<0.0001
Married/co-habiting	348 (65.0)	289 (53.9)	
Single/never married	25 (4.7)	38 (7.1)	
Divorced/separated	54 (10.1)	41 (7.6)	
widow	108 (20.2)	168 (31.3)	
Educational level			<0.0001
None	132 (24.6)	165 (30.6)	
Primary	111 (20.7)	155 (28.7)	
Secondary	214 (39.9)	153 (28.3)	
Tertiary	79 (14.7)	67 (12.4)	
Monthly income per month			<0.0001
0–100 USD	272 (50.8)	329 (62.0)	
101–250 USD	187 (35.0)	110 (20.8)	
251–500 USD	51 (9.5)	55 (10.4)	
>501 USD	25 (4.7)	36 (6.8)	
Employment status			<0.0001
Skilled employment	265 (49.5)	352 (68.8)	
Manual worker	122 (22.8)	70 (13.7)	
Retired	113 (21.1)	30 (5.9)	
Unemployed	35 (6.6)	60 (11.7)	
Vascular risk factors			
Systolic BP (mmHg), mean $\pm$ SD	152.1 $\pm$ 30.1	143.0 $\pm$ 24.8	<0.0001
Diastolic BP (mmHg), mean $\pm$ SD	91.9 $\pm$ 19.6	85.4 $\pm$ 15.0	<0.0001
Hypertension, n (%)	495 (91.6)	313 (58.0)	<0.0001
Total cholesterol (mmol/L), mean $\pm$ SD	5.4 $\pm$ 1.5	5.5 $\pm$ 1.3	0.17
Total cholesterol >5.2mmol/L, n (%)	299 (55.7)	312 (57.8)	0.49
LDL-cholesterol (mmol/L), mean $\pm$ SD	3.5 $\pm$ 1.4	3.6 $\pm$ 1.3	0.35
LDL-Cholesterol 3.4mmol/l, n (%)	285 (53.3)	266 (49.4)	0.20
HDL-cholesterol (mmol/L), mean $\pm$ SD	1.3 $\pm$ 0.6	1.4 $\pm$ 0.4	0.003
HDL-cholesterol 1.03mmol/l, n (%)	155 (29.0)	80 (14.8)	<0.0001
Triglyceride (mmol/L), mean $\pm$ SD	1.4 $\pm$ 0.8	1.2 $\pm$ 0.6	0.009
Triglyceride 1.7mmol/l, n (%)	126 (23.5)	90 (16.7)	0.006

Characteristic	Stroke cases N= 540	Stroke free controls N= 540	P-value
Dyslipidemia, n (%)	431 (80.4)	381 (70.6)	0.0002
Diabetes mellitus, n (%)	204 (38.1)	33 (6.1)	<0.0001
Alcohol use			<0.0001
Current user	92 (17.0)	63 (11.7)	
Former user	140 (25.9)	87 (16.1)	
Never used	292 (54.1)	389 (72.0)	
No response	16 (3.0)	1 (0.2)	
Cigarette smoking			<0.0001
Current smoker	14 (2.6)	1 (0.2)	
Former smoker	43 (8.0)	22 (4.1)	
Never smoked	467 (86.4)	515 (95.4)	
No response	16 (3.0)	2 (0.4)	
Waist circumference (cm), mean $\pm$ SD	95.0 $\pm$ 16.5	88.6 $\pm$ 12.7	<0.0001
Raised waist circumference, n (%)	183 (40.3)	199 (37.1)	0.31
Cardiac disease, n (%)	19 (3.5)	3 (0.6)	0.0006
HIV sero-positive, n (%)	12 (2.2)	15 (2.8)	0.70
HIV sero-types, n			
HIV-1, n	10	10	
HIV-1 and 2, n	1	1	
HIV-2, n	1	4	

Table 2.
Comparison of demographic and clinical characteristics of HIV seropositive stroke cases and seronegative cases

Characteristic	HIV seropositive Stroke cases N=12	HIV seronegative Stroke cases N=528	HIV sero-positive Stroke-free controls N=15	HIV sero-negative Stroke-free controls N=525	P-value A vs B	P-value A vs C	P-value C vs D
Age, mean $\pm$ SD	51.3 $\pm$ 15.5	61.0 $\pm$ 15.4	54.9 $\pm$ 13.9	60.1 $\pm$ 15.6	0.03	0.54	0.20
Age, median (IQR)	46.5 (40–65.3)	61.0 (50–74.0)	51.0 (45.0–66.0)	60.0 (49.0–71.0)	0.03	0.46	0.18
Age <50 years, n (%)	7 (58.3)	129 (24.4)	6 (40.0)	136 (25.9)	0.01	0.34	0.22
Female gender, n (%)	5 (41.7)	241 (45.6)	11 (73.3)	320 (61.0)	1.00	0.10	0.33
Location of residence					0.22	0.04	0.43
Urban	6 (50.0)	279 (52.8)	13 (92.9)	403 (84.0)			
Semi-urban	3 (25.0)	193 (36.6)	0 (0.0)	51 (10.6)			
Rural	3 (25.0)	52 (9.8)	1 (7.1)	26 (5.4)			
Marital Status					0.004	0.07	0.43
Married/co-habiting	4 (33.3)	344 (65.2)	8 (57.1)	281 (53.7)			
Single/never married	3 (25.0)	22 (4.2)	0 (0.0)	38 (7.3)			
Divorced/separated	2 (16.7)	51 (9.7)	0 (0.0)	41 (7.8)			
widow	3 (25.0)	105 (19.9)	6 (42.9)	163 (31.2)			
Educational level					0.22	0.61	0.74
None	5 (41.7)	127 (24.2)	4 (26.7)	160 (30.5)			
Primary	4 (33.3)	107 (20.4)	4 (26.7)	151 (28.8)			
Secondary	2 (16.7)	212 (40.5)	6 (40.0)	147 (28.1)			
Tertiary	1 (8.3)	78 (14.9)	1 (6.6)	66 (12.6)			
Monthly income					0.80	0.10	0.18
0–100 USD	6 (50.0)	266 (51.0)	12 (85.7)	317 (61.4)			
101–250 USD	5 (41.7)	182 (34.9)	1 (7.1)	109 (21.2)			
251–500+ USD	1 (8.3)	74 (14.1)	1 (7.1)	90 (17.4)			
Employment status					0.28	0.09	0.52
Skilled employment	5 (41.7)	261 (49.7)	10 (66.7)	342 (68.8)			
Manual worker	5 (41.7)	118 (22.5)	1 (6.7)	69 (13.9)			
Retired/unemployed	2 (16.6)	146 (27.8)	4 (26.6)	86 (17.3)			

Characteristic	HIV seropositive Stroke cases N=12	HIV seronegative Stroke cases N=528	HIV sero-positive Stroke-free controls N=15	HIV sero-negative Stroke-free controls N=525	P-value A vs B	P-value A vs C	P-value C vs D
Vascular risk factors							
Systolic BP (mmHg), median (IQR)	164.5 (140.81–180.8)	149.0 (130.0–170.0)	137.0 (125.0–158.0)	141.0 (124.0–158.0)	0.09	0.04	0.75
Diastolic BP (mmHg), median (IQR)	100.5 (87.8–107.8)	90.0 (80.0–100.0)	90.0 (73.0–96.0)	84.0 (75.0–93.0)	0.03	0.06	0.55
Hypertension, n (%)	12 (100.0)	483 (91.5)	9 (60.0)	304 (57.9)	0.29	0.19	0.24
Total cholesterol (mmol/L), mean ± SD	5.5 ± 1.6	5.4 ± 1.5	5.2 ± 0.8	5.5 ± 1.3	0.84	0.58	0.37
Total cholesterol >5.2mmol/L, n (%)	7 (58.3)	292	9 (60.0)	303 (57.7)	0.83	0.93	0.23
LDL-cholesterol (mmol/L), mean ± SD	3.7 ± 1.4	3.5 ± 1.4	3.2 ± 0.8	3.6 ± 1.3	0.77	0.36	0.27
LDL-Cholesterol 3.4mmol/L, n (%)	7 (58.3)	278 (55.3)	5 (33.3)	261 (49.7)	0.72	0.19	0.58
HDL-cholesterol (mmol/L), mean ± SD	1.4 ± 0.6	1.3 ± 0.6	1.5 ± 0.5	1.4 ± 0.4	0.53	0.85	0.65
HDL-cholesterol 1.03mmol/L, n (%)	2 (16.7)	153 (29.0)	3 (20.0)	77 (14.7)	0.52	0.82	0.32
Triglyceride (mmol/L), mean ± SD	1.2 ± 0.6	1.4 ± 0.8	1.2 ± 0.6	1.2 ± 0.6	0.57	0.95	0.84
Triglyceride 1.7mmol/L, n (%)	4 (33.3)	122 (23.1)	2 (13.3)	88 (16.8)	0.42	0.21	0.99
Dyslipidemia, n (%)	10 (83.3)	421 (79.7)	12 (80.0)	369 (70.3)	0.80	0.82	0.42
Diabetes mellitus, n (%)	4 (33.3)	200 (37.9)	0 (0.0)	33 (6.3)	0.72	0.02	0.32
Alcohol use					0.60	0.08	0.24
Current user	3 (25.0)	89 (17.4)	0 (0.0)	63 (12.0)			
Former user	4 (33.3)	136 (26.5)	4 (26.7)	83 (15.8)			
Never used	5 (41.7)	287 (56.1)	11 (73.3)	378 (72.2)	0.82	0.25	0.71
Cigarette smoking							
Current smoker	0 (0.0)	16 (3.1)	0 (0.0)	1 (0.2)			
Former smoker	1 (8.3)	40 (7.8)	0 (0.0)	22 (4.2)			
Never smoked	11 (91.7)	456 (89.1)	15 (100.0)	500 (95.6)			
Waist circumference (cm), mean ± SD	94.3 ± 13.9	95.0 ± 16.5	88.9 ± 9.3	88.6 ± 12.7	0.88	0.24	0.95
Raised waist circumference, n (%)	6 (50.0)	177/442 (38.5)	7 (46.7)	192 (36.6)	0.49	0.74	0.42
Cardiac disease, n (%)	1 (8.3)	18 (3.4)	0 (0.0)	3 (0.6)	0.36	0.25	0.77
Stroke type					0.21	--	--
Ischemic type	5 (41.7)	313 (59.8)	N/A	N/A			
Hemorrhagic type	7 (58.3)	210 (40.2)					
Ischemic stroke sub-types (TOAST)					0.96	--	--
			N/A	N/A			

Characteristic	HIV seropositive Stroke cases N=12	HIV seronegative Stroke cases N=528	HIV sero-positive Stroke-free controls N=15	HIV sero-negative Stroke-free controls N=525	P-value A vs B	P-value A vs C	P-value C vs D
Large-vessel atherosclerosis	1 (20.0)	81 (26.1)			0.76		
Cardio-embolic	1 (20.0)	86 (27.7)			0.70		
Small vessel disease	2 (40.0)	107 (34.5)			0.80		
Other determined causes	0 (0.0)	2 (0.6)			0.88		
Undetermined causes	1 (20.0)	34 (11.0)			0.52		
Ischemic stroke sub-types (OCSP)			N/A	N/A	0.04	--	--
Total Anterior Circulation Stroke (TACI)	0 (0.0)	71 (24.0)					
Partial Anterior Circulation Stroke (PACI)	1 (20.0)	110 (37.2)					
Lacunar Stroke (LACI)	2 (40.0)	93 (31.4)					
Posterior Circulation Stroke (POCI)	2 (40.0)	22 (7.4)					
Hemorrhagic subtypes			N/A	N/A		--	--
Hypertensive	6 (85.7)	178 (84.8)			0.95		
Structural [#]	1 (14.3)	22 (10.5)			0.75		
Medications-associated	0 (0.0)	0 (0.0)			N/A		
Cerebral amyloid	0 (0.0)	4 (1.9)			0.71		
Systemic	0 (0.0)	1 (0.5)			0.85		
Undetermined	0 (0.0)	5 (2.4)			0.68		
Died as in-patient, n (%)	1 (8.3)	133 (25.2)	N/A	N/A	0.31	--	--

[#] Structural includes aneurysms and Arterio-venous malformations.

Table 3.

Factors associated with stroke occurrence among Ghanaians

Risk Factor[§]	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age, each 10-year rise	1.03 (0.96–1.12)	0.40	--	--
Male gender	1.87 (1.46–2.38)	<0.0001	1.43 (0.99–2.05)	0.06
Urban residence	0.21 (0.16–0.28)	<0.0001	0.19 (0.13–0.27)	<0.0001
No education	0.74 (0.57–0.97)	0.03	1.13 (0.76–1.68)	0.56
Household income >100USD	1.58 (1.24–2.02)	0.0002	1.55 (1.11–2.17)	0.01
Hypertension	8.56 (5.96–12.30)	<0.0001	7.98 (5.24–12.17)	<0.0001
Diabetes mellitus	9.44 (6.37–13.98)	<0.0001	8.68 (5.50–13.71)	<0.0001
Dyslipidemia	1.71 (1.29–2.27)	0.0002	1.27 (0.88–1.83)	0.19
Central obesity	1.14 (0.88–1.47)	0.31	--	--
Cigarette smoking	2.67 (1.62–4.41)	0.0001	1.93 (1.00–3.69)	0.05
Alcohol use	1.91 (1.36–2.68)	0.0002	1.58 (1.02–2.47)	0.04
Heart disease	6.58 (1.94–22.36)	0.0025	13.97 (1.74–112.11)	0.01
HIV sero-positivity	0.80 (0.37–1.73)	0.57	--	--

[§]**Risk factors:** Age was specified as a continuous variable; gender: female gender was referent group; location of residence: urban residence was compared with residence in rural/semi-urban location as referent group; educational attainment was dichotomized into no formal education versus some education (primary, secondary or tertiary); Household income was dichotomized into monthly income >100 US Dollars vs <100USD. Vascular or Life style factors included hypertension (yes or no), diabetes mellitus (yes or no), dyslipidemia (yes or no), central obesity based on waist circumference cut-offs (yes or no); current cigarette smoking (yes or no); alcohol use was dichotomized as current alcohol versus former/never used; Cardiac diseases included history or current diagnosis of atrial fibrillation, cardiomyopathy, heart failure, ischemic heart disease, rheumatic heart disease, and valvular heart diseases (yes or no); HIV sero-positivity (yes or no).

Table 4.

Comparison of characteristics of participants who died versus stroke survivors

Characteristic	Alive at discharge (n=402)	Dead at discharge (n=134)	P-value
Age, mean $\pm$ SD	59.5 $\pm$ 15.6	64.5 $\pm$ 14.6	0.001
Male gender, n (%)	213 (53.0)	76 (56.7)	0.45
Location of residence			0.03
Urban	223 (55.5)	62 (46.3)	
Semi-urban	145 (36.1)	51 (38.1)	
Rural	34 (8.4)	21 (15.6)	
Educational level			0.007
None	91 (22.6)	41 (30.6)	
Primary	94 (23.4)	17 (12.7)	
Secondary	165 (41.0)	49 (36.6)	
Tertiary	52 (13.0)	27 (20.1)	
Monthly income per month			0.35
0–100 USD	202 (50.2)	70 (52.2)	
101–250 USD	145 (36.1)	42 (31.3)	
251–500 USD	39 (9.7)	12 (9.0)	
>501 USD	16 (4.0)	10 (7.5)	
HIV Sero-positivity	11 (2.7)	1 (0.7)	0.18
Vascular risk factors			
Systolic BP (mmHg), median (IQR)	153.0 $\pm$ 29.7	149.3 $\pm$ 31.3	0.22
Diastolic BP (mmHg), median (IQR)	93.1 $\pm$ 19.7	88.0 $\pm$ 18.7	0.01
Hypertension, n (%)	379 (94.3)	116 (86.6)	0.004
Total cholesterol (mmol/L), mean $\pm$ SD	5.5 $\pm$ 1.5	5.2 $\pm$ 1.7	0.07
Total cholesterol >5.2mmol/L, n (%)	232 (57.7)	67 (50.0)	0.12
LDL-cholesterol (mmol/L), mean $\pm$ SD	3.6 $\pm$ 1.3	3.2 $\pm$ 1.5	0.02
LDL-Cholesterol 3.4mmol/l, n (%)	226 (56.2)	59 (44.0)	0.01
HDL-cholesterol (mmol/L), mean $\pm$ SD	1.4 $\pm$ 0.5	1.3 $\pm$ 0.6	0.12
HDL-cholesterol 1.03mmol/l, n (%)	106 (26.4)	49 (36.6)	0.02
Triglyceride (mmol/L), mean $\pm$ SD	1.3 $\pm$ 0.7	1.5 $\pm$ 1.1	0.003
Triglyceride 1.7mmol/l, n (%)	85 (21.1)	41 (30.6)	0.03
Dyslipidemia, n (%)	322 (80.0)	109 (81.3)	0.75
Diabetes mellitus, n (%)	151 (37.6)	53 (39.6)	0.68
Alcohol use			0.19
Current user	90 (22.3)	28 (20.9)	
Former user	78 (19.4)	36 (26.9)	
Never used	223 (55.5)	69 (51.5)	
No data	11 (2.8)	1 (0.7)	
Cigarette smoking			0.47
Current smoker	13 (3.2)	3 (2.2)	
Former smoker	29 (7.2)	12 (9.0)	

Characteristic	Alive at discharge (n=402)	Dead at discharge (n=134)	P-value
Never smoked	346 (86.1)	118 (88.1)	
No data	11 (2.7)	1 (0.7)	
Waist circumference (cm), mean $\pm$ SD	95.2 $\pm$ 16.1	94.4 $\pm$ 17.5	0.64
Raised waist circumference, n (%)	140 (34.8)	43 (32.1)	0.56
Cardiac disease, n (%)	16 (4.0)	3 (2.2)	0.35
Stroke type			0.99
Ischemic type	239 (59.4)	79 (59.4)	
Hemorrhagic type	163 (40.6)	54 (40.6)	
Ischemic stroke sub-types			0.17
Large-vessel atherosclerosis	53 (22.2)	29 (36.3)	0.01
Cardio-embolic	65 (27.2)	21 (26.3)	0.87
Small vessel disease	87 (36.4)	21 (26.3)	0.10
Other determined causes	2 (0.8)	0 (0.0)	0.41
Undetermined causes	28 (11.7)	7 (8.8)	0.46
No data	4 (1.7)	2 (2.5)	
Hemorrhagic subtypes			0.18
Hypertensive	137 (84.0)	48 (88.9)	0.38
Structural	20 (12.3)	3 (5.5)	0.16
Medications-associated	0 (0.0)	0 (0.0)	--
Cerebral amyloid	1 (0.6)	2 (3.7)	0.09
Systemic	0 (0.0)	0 (0.0)	--
Undetermined	5 (3.1)	1 (19)	0.64
NIHSS, mean $\pm$ SD	14.6 $\pm$ 9.9	23.9 $\pm$ 11.9	<0.0001

Table 5.

Factors associated with Stroke mortality

Factor*	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
HIV sero-positivity	0.27 (0.03–2.09)	0.21	--	--
Age, each 10 year higher	1.21 (1.05–1.37)	0.004	1.12 (0.97–1.29)	0.11
NIHSS, each 5 units higher	1.45 (1.32–1.60)	<0.0001	1.42 (1.29–1.57)	<0.0001
Use of antihypertensive medicines after stroke	0.39 (0.20–0.75)	0.005	0.39 (0.19–0.81)	0.01
Diabetes mellitus	1.09 (0.73–1.62)	0.68	--	--
High LDL-cholesterol	0.61 (0.41–0.91)	0.02	0.67 (0.43–1.05)	0.08
Low HDL-cholesterol	1.60 (1.06–2.43)	0.03	1.29 (0.81–2.07)	0.28
High triglyceride	1.64 (1.06–2.55)	0.03	1.68 (1.02–2.74)	0.04
Hemorrhagic stroke	0.99 (0.66–1.47)	0.96	--	--
Rural residence	2.01 (1.12–3.60)	0.02	1.45 (0.75–2.81)	0.27
No education	0.66 (0.43–1.03)	0.07	--	--

NIHSS= National Institute of Health Stroke Scale; LDL=Low Density Lipoprotein; HDL = High Density Lipoprotein

* **Risk factors:** HIV sero-positivity (yes or no); Age was specified as a continuous variable; gender: female gender was referent group; Stroke severity assessed using the NIHSS scale specified as a continuous variable; Use of antihypertensive classes after stroke was compared with no documented use of antihypertensive medications; High LDL-cholesterol was dichotomized into a cut-off 3.4mmol/l compared with <3.4mmol/l; Low HDL-cholesterol was dichotomized into a cut-off 1.03mmol/l compared with >1.03mmol/l; High triglyceride was specified as serum triglyceride 1.7mmol/l; Hemorrhagic stroke was compared with ischemic stroke (as referent group); residence: urban residence was compared with residence in rural/semi-urban location as referent group; educational attainment was dichotomized into no formal education versus some education (primary, secondary or tertiary).