Stroke risk factors in an incident population in urban and rural Tanzania: a prospective, community-based, case-control study

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Summary

Background The burden of stroke on health systems in low-income and middle-income countries is increasing. However, high-quality data for modifiable stroke risk factors in sub-Saharan Africa are scarce, with no community-based, case-control studies previously published. We aimed to identify risk factors for stroke in an incident population from rural and urban Tanzania.

Methods Stroke cases from urban Dar-es-Salaam and the rural Hai district were recruited in a wider study of stroke incidence between June 15, 2003, and June 15, 2006. We included cases with first-ever and recurrent stroke. Community-acquired controls recruited from the background census populations of the two study regions were matched with cases for age and sex and were interviewed and assessed. Data relating to medical and social history were recorded and blood samples taken.

Findings We included 200 stroke cases (69 from Dar-es-Salaam and 131 from Hai) and 398 controls (138 from Dar-es-Salaam and 260 from Hai). Risk factors were similar at both sites, with previous cardiac event (odds ratio [OR] 7·39, 95% CI 2·42–22·53; p<0·0001), HIV infection (5·61, 2·41–13·09; p<0·0001), a high ratio of total cholesterol to HDL cholesterol (4·54, 2·49–8·28; p<0·0001), smoking (2·72, 1·49–4·96; p=0·001), and hypertension (2·14, 1·09–4·17; p=0·026) identified as significant independent risk factors for stroke. In Hai, additional risk factors of diabetes (4·04, 1·29–12·64) and low HDL cholesterol (9·84, 4·06–23·84) were also significant.

Interpretation We have identified many of the risk factors for stroke already reported for other world regions. HIV status was an independent risk factor for stroke within an antiretroviral-naive population. Clinicians should be aware of the increased risk of stroke in people with HIV, even in the absence of antiretroviral treatment.

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Introduction

The burden of stroke in sub-Saharan Africa is increasing.[1,2] Because prevention is likely to be the most effective way to reduce this burden, identification and quantification of stroke risk factors, particularly those that are modifiable, is of interest. The international, multicentre, INTERSTROKE study[3] of 3000 cases and 3000 controls from 22 countries identified ten risk factors that accounted for 90% of the risk of stroke in those countries. These risk factors were history of hypertension, current smoking, high waist-to-hip ratio, poor diet, absence of regular physical activity, diabetes mellitus, high alcohol intake, psychosocial stress and depression, cardiac causes, and apolipoprotein ratio. The study included four countries in sub-Saharan Africa: South Africa, Nigeria, Mozambique, and Uganda. History of hypertension or blood pressure higher than 160/90 mm Hg was the biggest risk factor overall and had the highest odds ratio (OR) in the 323 African cases (3·89 overall [99% CI 3·33–4·54] and 4·96 [99% CI 3·11–7·91] in African cases). However, all included patients with stroke had to present at hospital within 5 days of symptom onset and undergo a CT or MRI scan of the brain within 1 week. Such imaging facilities are unlikely to be widely available or affordable to patients in sub-Saharan Africa, and those who undergo CT scan are unlikely to be representative of the wider population of patients with incident stroke. We have previously shown that only a few patients with stroke present to hospital in sub-Saharan Africa, and, in many of the most severe cases, patients die soon after onset.[4,5]

Several studies from high-income countries have shown that black and white populations from the same region have different risk-factor profiles for stroke, with hypertension and diabetes mellitus being much more prevalent risk factors in black populations, and cardiac abnormalities and smoking more prevalent in white populations.[6,7] However, data from sub-Saharan Africa are scarce. Investigators of the Berlin–Ibadan stroke study[8] compared risk factors for hospital admissions for stroke in Berlin, Germany, with those in Ibadan, Nigeria. Hypertension was significantly more common in the Ibadan cohort, whereas smoking, high cholesterol, atherosclerosis, and cardiac abnormalities were more common in patients from Berlin. Amu and colleagues[9] assessed 80 patients with stroke and 80 controls recruited from hospital admissions in Nigeria. Hypertension, diabetes mellitus, atrial fibrillation, obesity, physical

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inactivity, and smoking were significant risk factors for stroke, whereas concentrations of serum cholesterol, alcohol consumption, and dietary habits had no increased odds of stroke for cases versus controls. These results are similar to those of Danesi and colleagues[10] in a previous hospital-based study in Lagos, Nigeria; however, findings from that study showed raised serum cholesterol and low socioeconomic class as additional risk factors.

We are not aware of any previous community-based, case-control studies of risk factors for stroke in sub-Saharan Africa. We did a case-control study to investigate the role of potential risk factors for stroke in an incident group of patients with stroke from an urban and rural region of Tanzania.

Methods

Study design and participants

Participants in the present study were part of a wider study of stroke incidence[4] in which patients were recruited from June 15, 2003, to June 15, 2006. The study was done at two sites: the rural Hai district in northern Tanzania, and urban Dar-es-Salaam, Tanzania's largest city and its commercial capital. The Hai district site is a region of 52 villages, with an economy based on subsistence farming, with cash crops such as coffee also grown. The Dar-es-Salaam site was chosen to be representative of the socioeconomic profile and living conditions within the city, with a mixture of planned and unplanned housing. Both sites were set up in the 1990s as Demographic Surveillance Sites (DSS) for use in the Adult Morbidity and Mortality Project (AMMP) for epidemiological monitoring by the Tanzanian government. Key results from the AMMP have been previously published.[11]

The wider incidence study used two methods of case ascertainment: the Tanzanian Stroke Incidence Project (TSIP) and verbal autopsy.[4] Our study here is based on consecutive cases recruited via TSIP who survived long enough to undergo assessment. We used the standard WHO definition of stroke and included patients with first-ever and recurrent stroke. To maximise recruitment and reduce selection bias, the TSIP study was extensively advertised within the study regions and paid for participants to attend hospital and receive treatment for the first year after stroke. A programme of awareness raising via census enumerators, local health-care workers, and community leaders was also done. Any possible cases of incident stroke were notified, via the enumerators, to clinical officer supervisors for the study as soon as possible so they could be assessed in their own homes. This prompt notification was particularly important for those making a rapid recovery from stroke. Individuals thought to have had a stroke were transferred to hospital for further investigation led by a local physician (EA or AJ).

Controls were recruited from the background census population of the Hai and Dar-es-Salaam DSS. They were identified from the census list and frequency matched to cases for age (plus or minus 3 years) and sex. A list of possible controls was produced with a random number generator. The controls were randomly assigned a preference and visited in order. If a control was unavailable or refused to participate the next person on the list was visited and so forth, until sufficient controls had been recruited. All participants were given an identification number to ensure that testing of blood samples was done anonymously.

Ethics approval for the TSIP study was obtained from the National Institute of Medical Research, Dar-es-Salaam, and from the Newcastle and North Tyneside Joint Ethics Committee, UK. Approval included blood sampling and anonymous HIV testing. Each participant provided signed informed consent. We obtained a thumbprint for participants who could not read or write, and the purpose and implications of the study were verbally explained. When patients were unable to provide consent, written assent was obtained from a close relative.

Measurement of risk factors

Cases and controls were interviewed in as similar a way as possible by members of the study team (supervised by EA or AJ) who had received specific training in the data collection process. The same proforma was used, although sections relating to the stroke itself were not completed for controls. Patients were interviewed in hospital and controls in their nearest health facility or at home. Demographic information, social history, and past medical history were recorded. Collection of accurate information about age can be difficult in sub-Saharan Africa; thus, age was calculated from birth year and confirmed with memory prompts when the year of birth was in doubt.[12] All participants underwent a medical assessment and examination. Post-stroke impairment was assessed with the modified Rankin scale.[13] Blood pressure was recorded at least 7 days after stroke to allow for the fact that blood pressure can rise during the first few days after stroke. Three measurements were taken and the average of the second and third measurement used.[14] A cutoff of greater than 160 mm Hg systolic or 90 mm Hg diastolic blood pressure, a history of hypertension, or taking of antihypertensive drugs before stroke were regarded as indicators of hypertension.[3] Smoking and drinking were categorised in a similar way to the INTERSTROKE study.[3] Current smokers were patients who had smoked tobacco in the past 12 months, including those who had quit in that period, and former smokers were those who had smoked, but not in the past year. Drinkers were categorised as never, former, moderate (<4 days per week) and heavy (≥4 days per week). Non-fasting blood samples were taken from those who consented. The collected blood samples were centrifuged, frozen, and transported back to the UK where they were analysed at North Tyneside General Hospital with an automated biochemical analyser. In accordance with the recommendations of the US National Cholesterol Education Program,[15] high serum total cholesterol was

defined as 5·18 mmol/L or greater, and low concentrations of HDL cholesterol as less than 1·04 mmol/L. Although no universally accepted cutoff exists, a high ratio of total cholesterol to HDL cholesterol was defined as 5·0 or more.

Infection with HIV was tested with an ARCHITECT HIV Ag/Ab Combo assay (Abbott Laboratories, Wiesbaden, Germany), which is a chemiluminescent microparticle immunoassay for the simultaneous qualitative detection of HIV p24 antigen and antibodies to HIV type 1 (HIV-1 group M and group O) or type 2 (HIV-2), or both. An ARCHITECT HIV Ag/Ab Combo reactive result does not distinguish between the detection of HIV-1 p24 antigen, HIV-1 antibody, or HIV-2 antibody. If the ratio of sample chemiluminescent to the cutoff (S:CO) values is 1 or greater then the sample was considered to be reactive. Each sample that tested positive was retested to check the result. CT head scan was done in stroke cases who survived long enough to undergo examination.[16] Findings of ischaemia, haemorrhagic infarct, or no evidence of stroke were classified as ischaemic stroke.

Statistical analysis

In view of the uncertainty in determination of age, pair matching was not regarded as an appropriate technique; therefore, we used frequency matching for age and sex to obtain a similar distribution for cases and controls. We analysed data as for an unmatched case-control study. The data were quantitative and obtained at a nominal, ordinal, interval, and ratio level. Data were analysed with SPSS (version 18). CIs were calculated for odds ratios (OR; categorical data) and for differences between means (continuous, normally distributed data). We used univariate logistic regression modelling to identify significant predictors of caseness before multivariable analysis. The known stroke risk factors of hypertension, smoking status, alcohol consumption, presence of diabetes mellitus, having had a previous stroke or transient ischaemic attack, and a high ratio of total cholesterol to HDL cholesterol were forced into the multivariable model and other possible predictor variables investigated via stepwise methods. We used two-tailed tests throughout. Missing values were treated as being missing completely at random.

Role of the funding source

The sponsors of this study had no role in study design, data collection, data analysis, data interpretation. or writing of the report, or in the decision to submit for publication. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

201 strokes were identified by the TSIP system (132 in Hai and 69 in Dar-es-Salaam). One case of subarachnoid haemorrhage in Hai was excluded from the present study because of the different cause of this stroke type. Cases were matched to 138 (1:2) controls in Dar-es-Salaam and 260 (1:1·98) controls in Hai. Table 1 shows the baseline characteristics of cases and controls at each site. We noted no significant difference between cases

	Cases	Controls	Difference or OR (95% CI)
Dar-es-Salaam			
n	69	138	..
Age (years)	61·7 (15·0)	61·4 (13·1)	Difference 0·3 (−3·9 to 4·5)
Men	38 (55%)	74 (54%)	OR 1·06 (0·59 to 1·89)
Tribe			
Zaramo	19 (28%)	23 (17%)	..
Ndengereko	10 (14%)	33 (24%)	..
Other	40 (58%)	82 (59)	..
Formal education			OR for no formal education versus formal education 1·21 (0·63 to 2·33)
None or illiterate	20 (29%)	39 (28%)	..
Primary education (≤8 years)	30 (43%)	63 (46%)	..
Secondary school	3 (4%)	9 (7%)	..
Tertiary education	8 (12%)	25 (18%)	..
Missing value	8 (12%)	2 (1%)	..
Pre-stroke modified Rankin scale score*†			
0–1	42 (61%)	..	..
2–3	14 (20%)	..	..
4–5	4 (6%)	..	..
Stroke type by CT scan‡			
Haemorrhage	3 (4%)	..	..
Infarct	14 (20%)	..	..
Hai			
n	131	260	..
Age (years)	68·8 (14·8)	69·4 (14·6)	Difference 0·6 (−2·5 to 3·7)
Men	69 (53%)	140 (54%)	OR 1·05 (0·69 to 1·60)
Tribe			
Zaramo	11 (8%)	3 (1%)	..
Chagga	110 (84%)	240 (92%)	..
Other	10 (8%)	17 (7%)	..
Formal education			OR for no formal education versus formal education 1·26 (0·77 to 2·06)
None or illiterate	34 (26%)	57 (22%)	..
Primary education (≤8 years)	83 (63%)	174 (67%)	..
Secondary school	6 (5%)	14 (5%)	..
Tertiary education	6 (5%)	13 (7%)	..
Missing value	2 (2%)	2 (<1)	..
Pre-stroke modified Rankin scale score*§			
0–1	95 (73%)	..	..
2–3	6 (5%)	..	..
4–5	3 (2%)	..	..
Stroke type by CT scan¶			
Haemorrhage	11 (8%)	..	..
Infarct	52 (39%)	..	..

Data are mean (SD) or n (%), unless otherwise indicated. OR=odds ratio. *0=no symptoms, 1=minor symptoms not interfering with lifestyle, 2=some restriction of lifestyle, 3=significant restriction in lifestyle or prevention of independent existence, or both, 4=symptoms clearly prevent independent existence, 5=totally dependent requiring constant attention, 6=deceased.[13] †Nine missing values. ‡52 missing values. §27 missing values. ¶68 missing values.

Table 1: **Baseline characteristics**

	Cases	Controls	OR (95% CI)
Dar-es-Salaam			
n	69	138	..
Hypertension			3·33 (1·46–7·57)
Yes	55/63 (87%)	93 (67%)	..
No	8/63 (13%)	45 (33%)	..
Missing value	6	..	..
Smoking status			Non *vs* former or current 5·96 (2·96–11·98)
Non-smoker	18/53 (34%)	95/126 (75%)	..
Former smoker	21/53 (40%)	14/126 (11%)	..
Current	14/53 (26%)	17/126 (14%)	..
Missing value	16	12	..
Alcohol consumption			Never, former or moderate *vs* heavy 0·79 (0·20–3·08)
Former or never	49/62 (79%)	102/132 (77%)	..
Moderate	10/62 (16%)	22/132 (17%)	..
Heavy	3/62 (5%)	8/132 (6%)	..
Missing value	7	6	..
Diabetes mellitus			2·76 (0·89–8·58)
Yes	7/62 (11)	6/136 (4%)	..
No	55/62 (89%)	130/136 (96%)	..
Missing value	7	2	..
Atheroma risk factors*†	9/59 (15%)	10/136 (7%)	2·27 (0·87–5·91)
Missing value	10	2	..
Previous stroke, myocardial infarction, or transient ischaemic attack*			4·45 (1·42–13·90)
Yes	9/62 (14%)	5/136 (4%)	..
No	53/62 (86%)	131/136 (96%)	..
Missing value	7	2	..
Asthma	7/58 (12%)	7/136 (5%)	2·53 (0·84–7·57)
Missing value	7	2	..
Blood serum samples			
High total cholesterol	28/54 (52%)	42/103 (41%)	1·56 (0·81–3·03)
Missing value	15	35	..
Low HDL cholesterol	42/53 (79%)	66/103 (64%)	2·14 (0·98–4·65)
Missing value	16	35	..
High ratio of total to HDL cholesterol ratio	41/53 (77%)	45/103 (44%)	4·40 (2·08–9·34)
Missing value	16	35	..
HIV seropositive	14/30 (47%)	10/58 (17%)	4·20 (1·56–11·30)
Missing value	39	80	..
Hai			
n	131	260	..
Hypertension			1·80 (1·04–3·10)
Yes	88/109 (81%)	182 (70%)	..
No	21/109 (19%)	78 (30%)	..
Missing value	22	..	..
Smoking			Non *vs* former or current 2·69 (1·62–4·49)
Non-smoker	25/109 (23%)	113/254 (44%)	..
Former smoker	67/109 (62%)	78/254 (31%)	..
Current	17/109 (15%)	63/254 (25%)	..
Missing value	22	6	..

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and controls in age, sex, or education. We attempted to interview cases as soon as possible after incident stroke, but a few were not identified as having had a stroke until visited by a health-care worker or key informant some months later. Nevertheless, 114 (57%) cases were seen within 28 days of stroke, only 17 (8%) cases were interviewed at more than 6 months after stroke. The median time from incident stroke to assessment interview was 19 days (range 0–252). For the groups who were seen at 28 days or more after stroke and those seen at less than 28 days, we noted no significant difference in rates of hypertension (OR 1·82, 95% CI 0·75–4·42) or ratio of total cholesterol to HDL cholesterol (1·99, 0·91–4·36).

Some cases and controls refused to have blood samples taken or blood samples could not be taken for other reasons—eg, the participant had died before a blood sample could be obtained or were unavailable at the time of testing. However, for the entire study population of 598 individuals, when we made comparisons between the 410 (69%) individuals who did have blood samples taken and the 188 (31%) who did not, we noted no significant differences in age (mean 65·8 [SD 15·2] *vs* 68·2 [13·7] years, 95% CI for difference –0·1 to 4·8) or sex (226 [55%] *vs* 95 [51%] men, 95% CI for difference –4·4 to 12·8). In 11 (5%) cases for whom the HIV result was borderline positive (S:CO value range 1–9) the sample was too insufficient to allow a repeat sample. However, in all patients for whom the test could be repeated, the initial result was confirmed.

Table 2 shows results of the univariate analysis. The findings show that risk factors were similar at both sites, with HIV status, hypertension, smoking status, previous cardiac event, and a high ratio of total to HDL cholesterol level being significantly associated with caseness at both sites (table 2). In Hai, additional risk factors of diabetes and low HDL cholesterol were also significant (table 2). Diabetes was associated with increased risk in Dar-es-Salaam, albeit not significantly (table 2). Of 25 stroke cases with HIV infection, 16 (64%) were men, whereas of 77 cases without HIV infection, 39 (51%) were men (95% CI for difference in proportions –8·5 to 35·2). The mean age of stroke cases that had HIV infection was 63·2 years (SD 16·5) versus 67·4 years (17·6) for cases without HIV infection (95% CI –12·0 to 3·6). HIV status was not significantly associated with stroke subtype. At both sites, of the 56 (9%) participants with a blood result and a CT scan within 15 days of stroke, two (15%) of 13 with HIV had haemorrhagic stroke, and 11 had ischaemic stroke. By comparison, five (12%) of 43 without HIV had a haemorrhagic stroke and 38 had an ischaemic stroke (χ^2_1=0·129, p=0·720). No participant identified as being HIV positive was previously diagnosed; therefore, none was receiving antiretroviral therapy.

The risk-factor profile was similar across both sites; therefore, for multivariable analysis, we combined data from both sites and constructed a logistic regression

model (table 3). The analysis was based on data for 92 cases and 220 controls. High total cholesterol to HDL cholesterol ratio, being a current or former smoker, HIV infection, hypertension, and a previous cardiac event were all independent predictors of stroke; however, we recorded no association between stroke and alcohol consumption or a diagnosis of diabetes mellitus (table 3). The adjusted odds of someone with HIV infection having a stroke were more than five times that of someone without HIV (table 3).

Discussion

This report is the first published community-based, case-control study to identify HIV infection as a risk factor for stroke with prospective case-ascertainment.[17] Our data suggest that, aside from this risk factor, the stroke risk-factor profile of this east-African population is similar to that shown for other world regions.[3] Hypertension, diabetes, smoking, cholesterol, and previous cardiac events have been cited by other investigators as risk factors for stroke in sub-Saharan Africa and elsewhere.[3,9,10] Hypertension is extremely common in this population and is generally undiagnosed and untreated.[18] Nevertheless, in this resource-poor setting, this disorder is one of the most easily treatable risk factors. Identification of people with hypertension at a community level need not involve expensive equipment or highly skilled personnel, and treatment is relatively inexpensive.

Data from our community-based antiretroviral-naive cohort suggest that HIV positivity is a significant independent risk factor for stroke (panel). Although increasing evidence exists for a link between HIV and stroke, definitive data have been scarce.[17,22–25] Research has been complicated by the use of antiretroviral therapy to treat people with HIV, some forms of which have been linked to an increased risk of cardiovascular disease.[26] Even in the absence of medication, although HIV infection can be a direct cause of vasculopathy, it is more likely to be associated with an increased risk of stroke when combined with a secondary infection.[23,27] HIV-infected patients with stroke are generally thought to have a more varied presentation than those without HIV infection.[28]

Most previous studies of HIV and stroke have used a retrospective, exposed and non-exposed cohorts design to compare people with and without HIV infection and investigate stroke incidence within the groups.[24,29] The strongest evidence comes from a retrospective, hospital-based, case-control study done between 1990 and 1994, in Atlanta, GA, USA.[23] The investigators reviewed post-stroke hospital admissions in 113 patients aged 19–44 years and the same number of controls (admissions with status asthmaticus) in whom HIV status was known. The researchers noted that stroke cases were significantly more likely (OR 2·3, 95% CI 1·0–5·3) to be HIV positive than were controls, after adjustment for confounding variables. However, the generalisability of these results to the wider population is limited by the

	Cases	Controls	OR (95% CI)
(Continued from previous page)			
Alcohol			Never, former or moderate *vs* heavy 1·53 (0·84–2·77)
Former or never	47/109 (43%)	103/259 (40%)	..
Moderate	41/109 (38%)	121/259 (47%)	..
Heavy	21/109 (19%)	35/259 (13%)	..
Missing value	22	1	..
Diabetes			4·04 (1·29–12·64)
Yes	8/109 (7%)	5/260 (2%)	..
No	101/109 (93%)	255/260 (98%)	..
Missing value	22	..	..
Atheroma risk factors*†			1·21 (0·50–2·91)
Yes	8/109 (7%)	16/260 (6%)	..
No	101/109 (93%)	244/260 (94)	..
Missing value	22		..
Previous stroke, myocardial infarction or transient ischaemic attack*			9·14 (3·77–22·14)
Yes	22/109 (20%)	7/260 (3%)	..
No	87/109 (80%)	253/260 (97%)	..
Missing value	22	..	..
Asthma	3/109 (3%)	11/260 (4%)	0·64 (0·18–2·34)
Missing value	22	..	..
Blood serum samples			
High total cholesterol	26/76 (34%)	60/177 (34%)	1·01 (0·58–1·79)
Missing value	55	83	..
Low HDL cholesterol	70/76 (92%)	96/177 (54%)	9·84 (4·06–23·84)
Missing value	55	83	..
High ratio of total to HDL cholesterol ratio	52/76 (68%)	67/177 (38%)	3·56 (2·01–6·30)
Missing value	55	83	..
HIV seropositive	11/72 (15%)	5/174 (3%)	6·10 (2·04–18·26)
Missing value	59	86	..

Data are n or n/N (%), unless otherwise indicated. OR=odds ratio. *Presence of one or more of these factors was recorded as "yes". †Angina, diabetes, or intermittent claudication.

***Table 2*: Univariate analysis of stroke risk factors**

	OR (95% CI)	p value
Previous transient ischaemic attack or stroke	7·39 (2·42–22·53)	<0·0001
HIV seropositive	5·61 (2·41–13·09)	<0·0001
High ratio of total cholesterol to HDL cholesterol	4·54 (2·49–8·28)	<0·0001
Current or former smoker	2·72 (1·49–4·96)	0·001
Hypertension	2·14 (1·09–4·17)	0·026
Diabetes mellitus	1·38 (0·35–5·39)	0·644
Alcohol consumption		
Non-drinker*	1	0·700
Former drinker	1·05 (0·43–2·56)	0·916
Moderate drinker	0·96 (0·45–2·02)	0·912
Heavy drinker	1·62 (0·69–3·78)	0·268
Constant†	0·04	<0·0001

Based on data for 92 cases and 220 controls. OR=odds ratio. *Reference category. †The y intercept in a hypothetical schematic representation of our model.

***Table 3*: Multivariable logistic regression models of stroke risk factors**

Panel: **Research in context**

Systematic review

We did not do a specific systematic review of the scientific literature before undertaking this study. However, our study team was aware of the extremely scarce previous data for stroke risk factors in sub-Saharan Africa; therefore, a formal systematic review would be unlikely to yield any additional insight. On the basis of the existing literature, and of findings from previous studies done by members of our study team,[5,19–21] we recognised that an important unanswered question was: what are the risk factors for stroke in sub-Saharan Africa? RW has conducted previous research on stroke in Tanzania, from which key findings have been published.[5,19]

Interpretation

Our study adds substantially to the existing knowledge of stroke risk factors in sub-Saharan Africa. This report is the first published community-based, case-control study of HIV infection as a risk factor for stroke with prospective case-ascertainment. The role of the risk factors investigated seems to be similar to those reported in other world regions. Our data for the role of HIV infection are unique and provide new insight into the interplay between two medical problems that are a major burden on health-care services in the region. Clinicians should be aware of the increased risk of stroke in people with HIV, even in the absence of antiretroviral treatment.

young age of the patients, the retrospective nature of the data examined, and by the hospital setting. Only few data are from sub-Saharan Africa, and much of it is descriptive in nature.[22,30] Patel and colleagues[31] recorded no difference in tests for cardiovascular disease between 293 HIV-infected and non-infected participants aged 15–44 years in KwaZulu-Natal, South Africa. These findings support those of a previous study in KwaZulu-Natal by Hoffmann and colleagues,[32] which showed no increase in rates of HIV infection in 1298 stroke cases versus the general population.

Our estimate of the prevalence of diabetes and other comorbidities could be an underestimate. Data were based on self-report, which is particularly unreliable in view of low rates of diagnosis. Unfortunately, we were unable to obtain reliable data for obesity, psychosocial stress, depression, and physical activity or diet. Although height and weight were recorded for all controls, many cases could not be weighed with the equipment available because of post-stroke disability. We were unable to assess the effect of physical exercise or diet as risk factors on stroke. In Hai, most people work as farmers, whereas in Dar-es-Salaam, people lead more westernised working lifestyles. Opportunities to make active choices about diet and exercise are often scarce in both settings. We accept that data relating to some risk factors, such as tobacco and alcohol consumption, can be somewhat subjective. Retrospective recall of events and behaviours that preceded the event being investigated is often difficult and can lead to bias, especially when questions are asked about factors that might have some social stigma. However, this limitation is one of all case-control studies and could only be overcome by collection of prospective data from an extremely large community cohort.

For several participants we were unable to obtain a blood sample. Although this shortcoming was often due to early post-stroke mortality, a few individuals were unwilling to consent to a blood sample being taken. We did our best to increase the number of participants willing to consent to blood samples being taken by enlisting the help of village elders and village heads. Although the restricted dataset could affect the generalisability of some of our data, this limitation would have been present in many other communities in sub-Saharan Africa, and, in view of the similarity in age and sex distribution of those who had blood samples taken and those who did not, any resulting bias is likely to be small. Results for the individuals in whom HIV test results were borderline positive and insufficient blood remained to repeat the test are presented as analysed. We have no reason to believe that this method could have resulted in systematic bias. All tests that were repeated confirmed the original test result. Although cholesterol concentrations can vary after stroke, we noted no significant difference in ratio of total cholesterol to HDL cholesterol levels between those seen within 28 days of stroke and those not. This minor variability in cholesterol concentrations after stroke has been noted by other investigators.[33] We treated all missing values as being missing completely at random. We could have used methods of imputation; however, this technique would have skewed our data unnecessarily and the most pragmatic approach was to present the raw data as collected.

Finally, we acknowledge that our findings are based on patients who survived long enough to be identified, interviewed, and assessed by the TSIP investigators, and that those identified only after death (by verbal autopsy) might have had a different cause of stroke, and thus a different risk-factor profile. Only with identification of a large community-based cohort, and with follow-up to see which individuals went on to have a stroke, could information about those who died rapidly after stroke be obtained. Such a study is likely to prove logistically difficult in a setting such as sub-Saharan Africa where migration into, out of, and within communities is often undocumented.

Our study identified many of the risk factors for stroke already shown for other world regions. Despite the acknowledged limitations of our study, our data for HIV status are unique, especially in view of the fact that all participants were antiretroviral therapy naive. Our study provides evidence of a link between HIV infection and stroke in the absence of secondary complications due to the side-effects of medication.

Contributors

RWW, NU, FM, MS, and GA designed the study. RWW and WKG did the literature search and the data analysis. EA, AJ, and MS collected the data. All authors interpreted the results and wrote the report.

Conflicts of interest

We declare that we have no conflicts of interest.

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