

Stroke Recurrence Rate and Risk Factors Among Stroke Survivors in Sub-Saharan Africa: A Systematic Review

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Purpose: Evidence supporting secondary stroke in sub-Saharan Africa is scarce. This study describes the incidence of stroke recurrence and associated risk factors in sub-Saharan Africa.

Methods and Materials: Scientific databases were systematically searched from January 2000 to December 2022 for population-based observational studies, case-control or cohort studies of recurrent stroke involving adults aged 18 years and above in sub-Saharan Africa (SSA). We assessed the quality of the eligible studies using the Critical Appraisal Skills Program (CASP) checklist for observational studies.

Results: Six studies met the inclusion criteria and were included in this study. Stroke recurrence rates in SSA ranged from 9.4% to 25%. Majority of the studies were conducted from Western Africa and showed that stroke recurrence rates are high within sub-Saharan Africa ranging from 2% to 25%. The known stroke risk factors such as hypertension, chronic alcohol consumption, etc., remained the leading causes of stroke recurrence. The studies reported a higher mortality rate ranging from 20.5 –23% among those with recurrent strokes compared to primary strokes.

Conclusion: This systematic review is an update and summary of the available literature on stroke recurrence within sub-Saharan Africa. Further studies are warranted to assess the outcomes and burden of stroke recurrence in SSA.

Keywords: stroke recurrence, sub-Saharan Africa, risk factors, secondary prevention, cardiovascular disease

Introduction

Stroke remained a leading cause of death and ranked the second most common disease worldwide in 2019.¹ Most literature indicates that modifiable risk factors such as hypertension, dyslipidemia, diabetes, cardiac disorders, sickle cell disease, high fat diet, sleep apnea, obesity, tobacco smoking, migraines, alcohol and drug abuse, oral contraceptive use, and lack of exercise are responsible for majority of the strokes.^{2–4}

In 2011, a global meta-analysis estimated that 11% of individuals will have a recurrence within a year of their first stroke and 26% within 5 years.⁵ Secondary stroke prevention measures such as antithrombotic, statin, and antihypertensive therapies can reduce the risk of secondary vascular events by 20% to 30%.^{6–9}

Recent studies show that nearly 30% of strokes are recurrent events, and these recurrent strokes are more likely to result in disability or death.¹⁰ In addition to premature mortality, recurrent strokes are associated with physical and cognitive disability and significant social and financial impact. In particular, patients with lacunar infarcts are 4 to 12

times more likely to be diagnosed with dementia than the average population, with recurrent lacunar strokes causing subcortical dementia^{11,12} and cardioembolic stroke is the most important predictor of mortality.¹³

Generally, the predictive and significant risk factors of stroke are well known.^{3,14} However, in Sub-Saharan Africa (SSA), risk factors for stroke recurrence are less well understood.¹⁵ Studies indicate that sub-Saharan Africa has high indices of stroke burden compared to the rest of the world.^{16–18} Estimations of the annual incidence rate of up to 316 per 100,000, with a prevalence of up to 1,460 per 100,000 and a 3-year fatality rate greater than 80%, have been made over the past decade in SSA.^{16,18–20} The majority of these strokes occur within the fourth to sixth decades of life, leading to severe family and societal implications as this impacts the socioeconomic productivity of individuals in SSA.

Understanding relevant risk factors of stroke recurrence among individuals from SSA may help develop strategies and interventions to address this burden. The aim of this systematic literature review was to identify stroke recurrence rates and risk factors for recurrent strokes identified in studies conducted in SSA over the last two decades. Findings have the potential to inform care approaches and health policy decisions.

Materials and Methods

Our investigations targeted two foci, all focused on manuscripts published from 2000 to April 2022 to ensure contemporary relevance: 1) a survey of original reports on stroke recurrence rate with emphasis from ONLY sub-Saharan Africa and 2) focus on original reports that addressed both stroke recurrence rates AND risk factors or if they included either recurrent rates or risk factors of stroke recurrence in SSA.

Literature Review and Search Strategy

Using the PICO guidelines, we set out to answer the study question below; What are the reported recurrent stroke rates and their risk factors among adults within sub-Saharan Africa?

PubMed, EMBASE, WHO Africa-African Index Medicus and Google Scholar were systematically searched for relevant articles. Gray literature sources such as ProQuest and conference registries were also searched to identify unpublished relevant articles. Reference lists of eligible studies were manually searched for additional unindexed pertinent references. The search was limited to human studies that were published from January 2000 until April 2022. Articles published in English language were considered.

Search terms used were stroke*stroke recurrence*stroke risk factors*stroke incidence*Africa*and sub-Saharan Africa; (*) was used as a wildcard to include several forms of the terms. A second search was done using EMBASE using the keywords; (“stroke recurrence” [MeSH Terms] OR “stroke recurrence rates” [All Fields]) AND (“incidence” [MeSH Terms] OR (“prevalence” [All Fields] AND “risk factors” [All Fields]) OR “stroke risk factors” [All Fields] AND (“Africa” [MeSH Terms] OR “Africa” [All Fields])).

Critical Appraisal and Assessment of Bias

All authors considered the risk of bias in the individual studies and across studies during full text reading using the Critical Appraisal Skills Program (CASP) checklist for observational studies. See [Table S1](#) for the checklist and [Table S2](#) for the critical appraisal.

Inclusion and Exclusion Criteria Considered for Selection of Studies

The search was intended to determine the distribution of research studies on stroke recurrence and risk factors in sub-Saharan Africa.²¹ Inclusion criteria were: 1) observational or experimental studies on stroke recurrence and risk factors, original research (randomized controlled trials, prospective non-randomized controlled and uncontrolled interventional studies), and publications in English.

A reference search of reviews on stroke recurrence and risk factors from SSA was used to identify additional studies potentially missed in the initial search. We excluded articles that were case reports, other literature reviews, stroke attributed to sickle cell disease and other hematological abnormalities and COVID-19, and stroke recurrence reports in children from sub-Saharan Africa.

Selection of Publications

All abstracts were prescreened for relevance by one reviewer (SNM) based on title and abstract information. Abstracts were then assessed by a three-member review team (SNM, M.K., MNK) to ensure consistent application of inclusion and exclusion criteria. Discrepancies were discussed until a consensus was reached. Once the inclusion and exclusion criteria were finalized, all abstracts were reviewed by two independent reviewers (SNM, MK) to determine suitability for further in-depth review.

Data Collection, Synthesis, and Reporting

Reviewers used a structured data extraction form modelled on other systematic reviews and recommendations.^{22,23} Reports were also assessed to see whether they included 1) stroke recurrence rates, 2) risk factors, and 3) a focus on adults.

Results

Search Findings

A total of 25 records were identified from the search of databases and indexing services. Accordingly, 19 studies were retrieved in PubMed/Medline, four from WHO Africa–African Index Medicus, and two were retrieved in Google Scholar databases. Two duplicates were removed, and titles and abstracts screened 21 articles. From this, six articles were excluded, and the retained 17 full-text articles were assessed for eligibility. Out of this, six articles were excluded for reasons such as lack of relevance and no stroke recurrence rates, and six studies were included for the final analysis (Figure 1).

Study Characteristics

The six studies included in the systematic review had 6285 participants. Out of these, a total of 3481 (55.4%) patients are reported to have suffered an initial ischemic stroke, while 1679 (26.7%) patients had a hemorrhagic stroke, while the rest were unclassified. The sample size of the included studies ranged from 100 to 3553.^{24–29} Of the total studies, the majority (5 studies) were conducted in Western Africa, with half coming from Cameroon.^{27–29} Table 1 shows the summary of the articles included in the review.

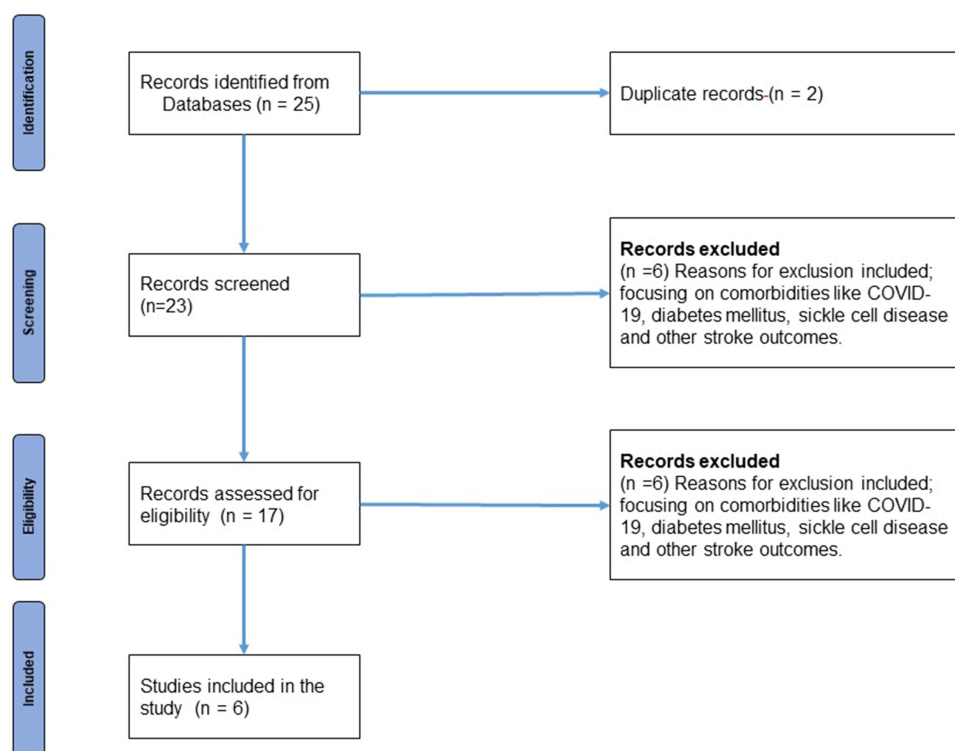


Figure 1 Papers screened.

Table I Summary of the Articles Included in the Review

Lead Author, Year, and Country	Study Design	Sample Size	Reported Incidence of Stroke Recurrence	Reported Mortality Rates	Time Interval Between Strokes
Akpalu A et al 2022 Ghana ²⁵	Multi-center case control study	3553	335(9.4%)	In patient mortality rate was 20.5% among those with recurrent strokes compared to 21.4 in first time strokes.	NA
Dabilgou A, A et al 2021 Burkina Faso ²⁴	Cross-sectional observational study	266	44 (16.4%)	No mortality rates reported	The mean interval time between initial and second stroke was 24 ± 24.34 months, ranges (3 months–10 years). The majority of patients (59.5%) had their stroke after 12 months. This time was 5.85 years between second stroke and third stroke.
Walker RW et al 2013 Tanzania ²⁶	Case control study	201	4 (1.99%)	No mortality rates reported	NA
Mbonda, PC Cameroon 2021 ²⁹	Retrospective study Cross sectional prospective study	528	75 (14.20%)	23% deaths occurred among those with recurrent strokes	The time between the first stroke and recurrence was 1 to 2 years in 37.8% of patients, more than 3 years in 28.4% of patients, and 14.9% of patients had recurrence within six months of the first stroke
Kamgang, J Cameroon 2021 ²⁷	Case control study Retrieved data from patient records at a hospital	100	25(25%)	No mortality rates	The median time from the index stroke event to the second stroke was 16.0 (95% CI = 3.36–28.64) months in right-handed patients, 19.0 (95% CI = 3.76–34.25) months in patients with heart failure, and 15.0 (95% CI = 0.78–29.22) months in patients with hypertension.
Lekoubou, A et al Cameroon 2017 ²⁸	Retrospective study Admission and discharge registries, and patient files for the period 1999–2012	1678	243 (14.5%) had recurrent stroke	20.6% deaths occurred among those with recurrent strokes 95% CI (1.43 (1.03–1.99) compared to deaths among first ever strokes. Known risk factors like diabetes mellitus, history of hypertension did not alter the association between recurrent stroke and death.	NA

Quality of Studies

All the studies included were either prospective observational cohort studies (2 studies), retrospective registry studies (2 studies) or case–control studies (3 studies). One study had an initial retrospective part and a cross-sectional part. The mean age at index stroke ranged from 29.6 to 66.5 years. The adapted Newcastle–Ottawa Scale (NOS) ratings for three studies ranged from a low of 6 to a high of 8. One study had a sample size of only 100,²⁷ two studies had between 200 and 300 study participants,^{18,24} and the rest had more than 500 study participants.^{25,28}

The Reported Prevalence of Stroke Recurrence

The reported prevalence of stroke recurrence in the studies was 14.2%, 14.5% and 25% in studies conducted in Cameroon by Mbonda et al, Lekoubou et al and Kamgang, respectively.^{27–29} In a study from Burkina Faso by Dabilgou et al, forty-four patients were hospitalized due to recurrent stroke of which 13.9% were admitted for a second stroke, while 2.6% were admitted for a third stroke.²⁴ While in Ghana and Nigeria, 9.4% had recurrent strokes,²⁵ and in a community study in Tanzania, 1.99% had stroke recurrence.¹⁸

The mean interval between the index and second stroke was 24 ± 24.34 months (3 months – 10 years); 1–2 years in 37.8%, >3 years in 28.4% and 14.9% within six months; 16.0 months (95% CI = 3.36–28.64).²⁴ Most of the patients had their strokes after 12 months.²⁴

Recurrent Stroke According to Subtypes

In all the reported studies, stroke diagnosis was based on clinical evaluation and brain C.T. neuroimaging. The etiological subtypes of strokes were defined using the A-S-C-O-D classification as A – Atherosclerosis, S – Small vessel occlusion, C-cardiac pathology, O – Other causes and D – dissection.³⁰ One study utilized the ASCOD classification for ischemic strokes,²⁹ while another used both the ASCOD classification for ischemic strokes, and Structural, Medication-related, Amyloid angiopathy, Systemic/other diseases, Hypertension and Undetermined causes (SMASH-U) was used for hemorrhagic strokes.^{25,31} Ischemic strokes were the commonest in all studies, ranging from 43.6% to 81%, while 9% to 20.1% were hemorrhagic; one study reported that 40.7% were unclassified.²⁸ Most ischemic strokes were within the MCA territory, while most hemorrhagic strokes were in the temporal-parietal region.

Risk Factors and Predictors for Stroke Recurrence

Risk factors associated with stroke recurrence were reported in 5 studies.^{24,25,27–29} Four studies reported using odds ratios for some known risk factors,^{25–27,29} while 2 reported with percentages.^{24,28} See Table 2 showing weighted risk factors for stroke recurrence in SSA. A history of hypertension or untreated hypertension was the most common vascular risk factor for recurrent strokes, ranging from 81.8%; to 90.7% in all the studies except for one study which described stroke risk factors for incident strokes. Stroke recurrence was also associated with current alcohol consumption in 3 studies, ranging between 10.51% and 45.5%. The other two studies did not report alcohol consumption among recurrent stroke patients. Three studies reported that patients with recurrent strokes were less likely to consume tobacco or smoke than those with incident strokes. None of the studies reported that tobacco smoking or consumption was associated with recurrent strokes.

Diabetes mellitus was associated with recurrent strokes in two studies,^{25,28} while three studies reported that diabetes mellitus was not associated with stroke recurrence.^{24,27,29} Though one study noted that casual blood glucose was statistically associated with recurrence.²⁷

Other factors reported as independent factors for stroke recurrence were female sex and non-compliance with therapy after the first stroke, right-handedness, congestive heart disease, gout, facial palsy, dysarthria and²⁷ dyslipidemia,^{25,29} however, one study noted no associations with medication adherence to various risk factors.²⁷

One study reported congestive heart failure OR, 3.45 95% CI = 1.16–10.28; gout OR, 4.44; 95% CI = 1.09–18.09; dyslipidemia adj OR, 2.78; 95% CI = 1.25–6.18; family history of CVD adj OR, 2.1; 95% CI = 1.1–4.2 as risk factors for recurrent strokes.²⁷ Another study reported older age as a risk factor; patients with recurrent strokes were older, with

Table 2 Weighted Risk Factors for Stroke Recurrence in SSA Studies. Odds Ratio; 95% (Confidence Interval)

Study	Hypertension	Alcohol Abuse/Excessive Consumption	Diabetes Mellitus	Medication non-Adherence	Older Age	History of Stroke
Akpalu et al ²⁵ *	50.73; (6.55–392.7); p<0.001	NA	4.04 (2.12–7.69); p<0.001	NA	2.10 (0.37–11.96); P=0.399	2.12 (1.07–4.21); p=0.031
Kamgang et al ²⁷	1.40 (0.50–3.97)	2.26 (0.89–5.77)	2.21 (0.89–5.77)	NA	NA	NA
Walker et al ²⁶	2.14 (1.09–4.17); p=0.026	1.62 (0.69–3.78); p=0.268	1.38 (0.35–5.39); p=0.644	NA	NA	7.39 (2.42–22.53); p<0.0001
Mbonda et al ²⁹	2.68 (1.4756–4.8692); p=0.001	NA	0.973 (0.421–2.251); p=0.95	0.399 (0.160–0.992); P=0.042	NA	NA
Lekoubou et al ²⁸	NA	NA	NA	NA	NA	NA
Dabilgou A et al ²⁴	NA	NA	NA	NA	NA	NA

Notes: *Study reported adjusted Odds Ratio(OR), while others reported unadjusted OR.

a median age of 65.0 years.²⁸ Atrial fibrillation (A.F.) was also reported as an independent risk factor for stroke recurrence.²⁸

Stroke Mortality Among Stroke Recurrence Patients

Stroke mortality is reported in three studies ranging from 20.5% to 23%.^{25,28,29} In general, mortality was higher for patients with recurrent stroke than those with incident strokes in these studies. Akpalu et al reported an in-patient mortality of 20.5% among those with recurrent strokes compared to 21.4% of those with first-time strokes.²⁵ Lekoubou et al reported that 14.5% of participants with recurrent stroke died and stroke recurrence increased the risk of death by 43% after adjustment for age, sex, and residency.²⁸ The known risk factors such as diabetes, history of hypertension, Glasgow coma scale and time to admission did not alter the association. In this study, the in-hospital mortality rate was 20.6%, which was higher than that of participants with first-ever stroke (19.6%). Mbonda et al reported a 23% death rate among those with stroke recurrence;²⁹ other studies did not report mortality rates.^{18,24,27}

Discussion

This review had three significant findings: (1) Stroke recurrence rates are high within sub-Saharan Africa; (2) the known stroke risk factors remain the main associated factors for stroke recurrence; (3) mortality associated with stroke recurrence is high compared to primary strokes.

This review found that hypertension, current alcohol consumption, diabetes mellitus, female gender, non-adherent to treatment after incident stroke, and cardiac causes (congestive heart failure and atrial fibrillation) were independent risk factors of recurrent stroke. These findings are similar to the conclusions drawn from the INTERSTROKE study, which was a landmark case-control study which confirmed that nine modifiable risk factors account for nearly 90% of the population's attributable risk for stroke in all regions of the world, including SSA such as hypertension, diabetes mellitus, poor diet, physical inactivity, unfavorable psychosocial factors, alcohol abuse and cardiac diseases.³

Of the top 4 risk factors for stroke identified in this sample of studies, 3 are potentially modifiable, hypertension, medication non-adherence and alcohol use. Hypertension is a major modifiable driver of the stroke burden and recurrent strokes in SSA. Nearly half of the people in Africa aged 25 years and above are estimated to be hypertensive, which constitutes the highest burden of hypertension in the world, according to the WHO, and about half were not receiving treatment after diagnosis.²⁹

Adherence to medications that can reduce stroke recurrence has potential to reduce stroke recurrent. Lack of adherence to medications for hypertension and regularly attending stroke follow-up clinics have been reported to lead to high levels of uncontrolled blood pressure levels in stroke survivors.²⁹ Reasons for non-adherence reported are lack of knowledge about hypertension being a chronic condition, costs for medications and lack of physical assistance to reach health care facilities and alcohol abuse.^{32,33} Poor knowledge among stroke survivors has been reported; nearly 42% of the stroke survivors or their caretakers in one study were unaware that stroke could recur.³⁴ This lack of knowledge leads to delays in timely health-seeking in stroke recurrences and adherence to medications. The utilization of recurrent stroke prophylaxis and adherence to statins, antiplatelets, antihypertensives, attendance to follow up clinics and physiotherapy services have been reported. Patient and caregiver education needs to be emphasized, including counselling stroke patients and their caretakers on adverse outcomes of stroke-like recurrence and death.

Use of substances is another potentially modifiable factor in recurrent stroke risk. Alcohol usage among stroke survivors was reported to be associated with stroke recurrence in three studies. Earlier studies from high-income countries reported that nearly half of stroke survivors with a history of heavy alcohol use had a recurrent brain infarction within 5 years compared with 22% of those without heavy alcohol use.^{35,36} However, this may be due to incident stroke survivors who use/abused alcohol before their strokes ceasing drinking alcohol after developing a debilitating disease. In contrast, for others, stroke could have been associated with mental health issues like depression that precipitated increased alcohol consumption and stroke recurrences. Few studies have explored the role of alcohol and stroke recurrences in sub-Saharan Africa.

Two studies have reported that diabetes mellitus was associated with recurrent stroke, while one reported casual high blood sugar levels.^{25,27,28} This is consistent with these studies from elsewhere which have reported a significant association between diabetes mellitus and stroke recurrence.^{37,38}

Limitations

While this systematic review provides an update on available data on recurrent strokes in sub-Saharan Africa, we note possible limitations in our review. First, we may be subject to publication bias as only the electronic databases and references were considered for this review. Secondly, other limitations pertain to the quality of the evidence provided by the included studies. Thirdly, most of the publications were conducted from single hospital studies in urban centers; therefore, generalizability to rural settings or whole countries may be limited. Therefore, national, or regional prospective observational studies on stroke recurrence in sub-Saharan African countries are still needed. Three of the studies (half our article sample) were from Cameroon, a west African country and the preponderance of data from a single country might skew the findings. The lack of data from many African countries is also a limitation and highlights the urgent need to establish systems of routine and reliable data monitoring across this continent. Another limitation was the selection bias as we included only papers in English language.

Conclusion

This systematic review is an update and summary of the available literature on stroke recurrence within sub-Saharan Africa. Stroke recurrence and mortality rates remain unacceptably high among stroke survivors in sub-Saharan Africa. Further studies are warranted to assess the outcomes and burden of stroke recurrence and escalation of secondary prevention measures in SSA.

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Disclosure

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