Journal of the Neurological Sciences 427 (2021) 117535

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Frequency and factors associated with post-stroke seizures in a large multicenter study in West Africa

Fred S. Sarfo [a,*], Joshua Akinyemi [b], Albert Akpalu [c], Kolawole Wahab [d], Joseph Yaria [e], Oladimeji Adebayo [e], Morenike Komolafe [f], Reginald Obiako [g], Lukman Owolabi [h], Godwin O. Osaigbovo [i], Carolyn Jenkins [j], Yaw Mensah [a], Godwin Ogbole [k], Benedict Calys-Tagoe [l], Philip Adebayo [g], Lambert Appiah [a], Arti Singh [c], Adekunle Fakunle [m], Ezinne Uvere [m], Tiwari Hemant [n], Olayemi Balogun [o], Osi Adeleye [o], Bimbo Fawale [f], Adeniyi Abdulwasiu [o], Luqman Ogunjimi [p], Onasanya Akinola [p], Oyedunni Arulogun [m], Arnette Donna [q], Okechukwu Ogah [r], Rufus Akinyemi [o,s], Bruce Ovbiagele [t], Mayowa O. Owolabi [s,u,**], on behalf of SIREN

[a] Department of Medicine, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana
[b] Department of Epidemiology and Medical Statistics, College of Medicine, University of Ibadan, Nigeria
[c] Department of Medicine, University of Ghana Medical School, Accra, Ghana
[d] Department of Medicine, University of Ilorin Teaching Hospital, Ilorin, Nigeria
[e] University College Hospital, Ibadan, Nigeria
[f] Department of Medicine, Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria
[g] Department of Medicine, Ahmadu Bello University, Zaria, Nigeria
[h] Department of Medicine, Aminu Kano Teaching Hospital, Kano, Nigeria
[i] Jos University Teaching Hospital Jos, Nigeria
[j] Medical University of South Carolina, SC, USA
[k] Department of Radiology, University of Ibadan, Nigeria
[l] Department of Community Health, University of Ghana Medical School, Accra, Ghana
[m] College of Medicine, University of Ibadan, Nigeria
[n] University of Alabama at Birmingham, Birmingham, AL, USA
[o] Federal Medical Centre, Abeokuta, Nigeria
[p] Department of Pharmacology and Therapeutics, Obafemi Awolowo College of Health Sciences, Olabisi Onabanjo University, Remo Campus, Shagamu, Ogun State, Nigeria
[q] College of Public Health, University of Kentucky, USA
[r] University College Hospital, Ibadan, Nigeria
[s] Center for Genomic and Precision Medicine, College of Medicine, University of Ibadan, Nigeria
[t] Weill Institute for Neurosciences, School of Medicine, University of California San-Francisco, USA
[u] Department of Medicine, University of Ibadan, Nigeria

ARTICLE INFO

Keywords:
Seizures
Epilepsy
Stroke types
Africa

ABSTRACT

Background: Post-stroke seizures (PSS) are associated with significant morbidity and mortality across the globe. There is a paucity of data on PSS in Africa.

Purpose: To assess the frequency and factors associated with PSS by stroke types across 15 hospitals in Nigeria and Ghana.

Methods: We analyzed data on all stroke cases recruited into the Stroke Investigative Research and Educational Network (SIREN). We included adults aged ≥18 years with radiologically confirmed ischemic stroke (IS) or intracerebral hemorrhage (ICH). PSS were defined as acute symptomatic seizures occurring at stroke onset and/or during acute hospitalization up until discharge. We used logistic regression to estimate adjusted odds ratios (aOR) with 95% Confidence Interval.

* Correspondence to: F. S. Sarfo, Department of Medicine, Kwame Nkrumah University of Science and Technology, Private Mail Bag, Kumasi, Ghana.
** Correspondence to: M. O. Owolabi, University College Hospital Ibadan and Blossom Specialist Medical Center, Ibadan, Nigeria.
E-mail addresses: stephensarfo78@gmail.com (F.S. Sarfo), mayowaowolabi@yahoo.com (M.O. Owolabi).

https://doi.org/10.1016/j.jns.2021.117535
Received 19 January 2021; Received in revised form 6 June 2021; Accepted 7 June 2021
Available online 9 June 2021

Results: Among 3344 stroke patients, 499 (14.9%) had PSS (95% CI: 13.7–16.2%). The mean duration of admission in days for those with PSS vs no PSS was 17.4 ± 28.6 vs 15.9 ± 24.7, $p = 0.72$. There were 294(14.1%) PSS among 2091 ischemic strokes and 159(17.7%) among 897 with ICH, $p = 0.01$. The factors associated with PSS occurrence were age < 50 years, aOR of 1.59 (1.08–2.33), National Institute of Health Stroke Score (NIHSS), 1.29 (1.16–1.42) for each 5 units rise and white cell count 1.07 (1.01–1.13) for each 10^3 mm^3 rise. Factors associated with PSS in ischemic were NIHSS score, aOR of 1.17 (1.04–1.31) and infarct volume of 10–30 cm^3 aOR of 2.17(1.37–3.45). Among ICH, associated factors were alcohol use 5.91 (2.11–16.55) and lobar bleeds 2.22 (1.03–4.82).

Conclusion: The burden of PSS among this sample of west Africans is substantial and may contribute to poor outcomes of stroke in this region. Further longitudinal studies are required to understand the impact on morbidity and mortality arising from PSS in Africa.

1. Introduction

Stroke is a major cause of symptomatic seizures among older adults [1–3]. It is estimated that between 5 and 15% of stroke patients develop seizures within two years of stroke onset [4]. The pathogenesis of early post-stroke seizures (PSS) following an ischemic stroke is putatively linked to a lowering of seizure threshold secondary to local ionic shifts, the release of excitotoxic neurotransmitters and the presence of global hypoperfusion with cortical hyperexcitability [2]. The mechanisms for post-stroke seizures in intracerebral hemorrhage involve direct stimulatory effects of blood degradation products on neural tissues and extracellular glutamate toxicity [7,8].

Sub-Saharan Africa is currently at the epicenter of a stroke epidemic characterized by a younger age of onset and very poor short- and long-term outcomes from mortality and post-stroke morbidity [5–14]. There are no reports from large scale multi-center studies on the burden of post-stroke seizures except a few single center studies [15–17]. Furthermore, the delineation of factors associated with occurrence of post-stroke seizures according to stroke types within the sub-Saharan African context remains to be elucidated. We therefore present data on the frequency and factors associated with post-stroke seizures by the primary stroke types from the Stroke Investigative Research and Education Networks (SIREN) study. The SIREN study is the largest study on stroke in Africa to date involving 15 sites in northern and southern belts of Nigeria and Ghana.

2. Methods

2.1. Study design

The study protocol has been previously published [18]. In brief, stroke cases were consecutively consenting adults aged ≥18 years with clinical stroke presenting within 8 days of current symptom onset or 'last seen without deficit'. We confirmed all stroke diagnosis using either CT or MRI scan typically within 10 days of symptom onset. Ethical approval was obtained from all study sites and informed consent was obtained from all subjects [18]. In unconscious or aphasic patients, consent was obtained from next of kin.

2.2. Stroke phenotyping

Stroke diagnosis and phenotyping were based on clinical evaluation and brain neuroimaging (CT or MRI), ECG, transthoracic echocardiography, and carotid Doppler ultrasound performed according to standardized protocols (SOP) at each site. Presumed etiological sub-types of ischemic stroke were defined etiologically using the A-S-C-O-D classification into A: Atherosclerosis, S: Small-vessel occlusion, C: Cardiac pathology, O: Other causes and D: dissection [19] and intracerebral hemorrhage was classified etiologically into Structural, Medication-related, Amyloid angiopathy, Systemic/other disease, Hypertension and Undetermined causes (SMASH-U) [20].

3. Definition of terms

3.1. Post-stroke seizures

Post stroke seizures (PSS) were defined as acute symptomatic seizures occurring after an acute stroke following ILAE recommendations [21,22]. Early PSS was classified as symptomatic seizures occurring within 7 days of stroke onset while late PSS was defined as symptomatic seizures occurring after 7 days of stroke onset. For this study, seizures were diagnosed clinically and were classified as acute symptomatic PSS based on medical history from a witness (often a family member) of focal or generalized seizures at the time of presentation for admission with stroke or by clinically documented seizures during hospitalization for acute stroke. No electroencephalographic studies were performed to confirm diagnosis of seizures and we did not record seizures into focal-onset or generalized onset for the purposes of this report.

3.2. Vascular risk factors of stroke

We collected basic demographic and lifestyle data including, socio-economic status, cardiovascular risk profile, dietary patterns, routine physical activity, stress, depression, cigarette smoking, and alcohol use using a validated INTERSTROKE instrument [23]. We have reported these definitions in our previous publications [9,24].

3.3. Statistical analysis

We compared demographic and vascular risk factor data among stroke cases who reported with post-stroke seizures versus those without post-stroke seizures using Student's *t*-test for parametrically distributed continuous data and Chi-squared tests for categorical data. We assessed factors associated with post-stroke seizures among stroke cases and by stroke types (ischemic and hemorrhagic strokes) using a multivariable logistic regression model. Covariates which were included in the multivariate logistic models were selected if they achieved a *p*-value of <0.10 in bivariate analyses. Sensitivity analyses for factors associated with early PSS and late PSS were also performed. All statistical tests of hypotheses were two-sided. Statistical analyses were performed with Stata MP version 14.

4. Results

4.1. Characteristics of participants with post-stroke seizures

We enrolled 3344 patients meeting study criteria of an acute stroke. The frequency of post stroke seizures was 499 (14.9%; 95% CI: 13.7–16.2%). Among those with PSS, 382 (76.6%) had early PSS and 117 (23.4%) with late PSS. The mean age of those with post-stroke seizures of 58.3 ± 15.3 years was significantly lower than 60.2 ± 14.1 years for those without seizures, $p = 0.006$. The characteristics of those with PSS are compared with those without PSS in Table 1. Those with PSS were *less likely* to earn monthly income > $100 (49.8% vs

Table 1
Comparison of demographic and clinical characteristics of stroke cases with Post-stroke seizures versus those with no Post-stroke seizures.

Variable	All Stroke type			Ischemic Stroke			Intracerebral hemorrhage		
	No Post-stroke seizures	Post-stroke seizures	P-value	No Post-stroke seizures	Post-stroke seizures	P-value	No Post-stroke seizures	Post-stroke seizures	P-value
	N = 2845	*n* = 499		*N* = 1797	*n* = 294		*N* = 738	*n* = 159	
Country, Ghana, n (%)	974 (34.2)	161 (32.3)	0.391	582 (32.4)	86 (29.3)	0.285	371 (50.3)	72 (45.3)	0.254
Gender, Male, n (%)	1578 (55.5)	292 (58.5)	0.208	939 (52.3)	159 (54.1)	0.567	463 (62.7)	109 (68.6)	0.166
Age, mean ± SD	60.2 ± 14.1	58.3 ± 15.3	**0.006**	62.4 ± 13.8	61.3 ± 15.0	0.195	54.7 ± 13.2	51.7 ± 13.7	**0.010**
<30	37 (1.3)	18 (3.6)	**0.001**	20 (1.1)	14 (4.8)	**<0.001**	10 (1.4)	4 (2.5)	**0.017**
30–49	584 (20.6)	117 (23.5)		285 (15.9)	39 (13.3)		241 (32.7)	71 (44.7)	
50–69	1433 (50.4)	232 (46.7)		894 (49.8)	143 (48.6)		383 (51.9)	67 (42.1)	
≥ 70	787 (27.7)	130 (26.2)		596 (33.2)	98 (33.3)		104 (14.1)	17 (10.7)	
Domicile									
Rural, n (%)	272 (9.6)	40 (8.1)	0.508	176 (9.8)	23 (7.8)	0.288	63 (8.6)	14 (8.9)	0.832
Semi-urban, n (%)	828 (29.2)	152 (30.6)		516 (28.8)	96 (32.7)		208 (28.3)	41 (26.0)	
Urban, n (%)	1735 (61.2)	305 (61.4)		1101 (61.4)	175 (59.5)		463 (63.1)	103 (65.2)	
Monthly Income >$100, n (%)	1551 (54.9)	247 (49.8)	**0.036**	989 (55.5)	150 (51.0)	0.153	418 (56.8)	81 (51.9)	0.266
Education, (some) n (%)	2310 (81.4)	405 (81.2)	0.890	1417 (79.1)	226 (76.9)	0.382	640 (86.8)	138 (86.8)	0.988
Hypertension, n (%)	2739 (96.3)	462 (92.6)	**<0.001**	1721 (95.8)	264 (89.8)	**<0.001**	725 (98.4)	155 (97.5)	0.443
Dyslipidemia, n (%)	2402 (84.4)	402 (81.1)	0.059	1570 (87.4)	253 (86.4)	0.628	588 (79.7)	117 (73.6)	0.089
Diabetes, n (%)	1068 (37.6)	205 (41.2)	0.126	740 (41.2)	133 (45.2)	0.191	209 (28.4)	46 (28.9)	0.885
Cardiac Disease, n (%)	352 (12.4)	43 (8.7)	**0.017**	266 (14.8)	32 (10.9)	0.076	54 (7.3)	9 (5.7)	0.456
HDL-Cholesterol, mg/dl, mean ± SD	47.7 ± 19.3	48.7 ± 20.3	0.316	46.4 ± 18.4	45.4 ± 17.9	0.457	52.1 ± 20.5	55.3 ± 22.9	0.100
HDL-Cholesterol ≤18.54 mg/dl, n (%)	78 (2.7)	12 (2.4)	0.668	48 (2.7)	10 (3.4)	0.480	17 (2.3)	2 (1.3)	0.406
LDL-Cholesterol, mg/dl, mean ± SD	121.8 ± 51.1	116.1 ± 53.3	**0.039**	121.6 ± 50.8	116.1 ± 53.5	0.131	127.8 ± 51.5	120.9 ± 53.9	0.160
LDL-Cholesterol ≥61.2 mg/dl, n (%)	2203 (90.6)	338 (86.2)	**0.007**	1393 (90.4)	202 (87.1)	0.116	626 (93.3)	119 (88.8)	0.071
LDL/HDL ratio, mean ± SD	3.0 ± 1.9	2.7 ± 1.7	**0.034**	3.0 ± 1.9	2.9 ± 1.8	0.433	2.8 ± 2.0	2.5 ± 1.5	0.089
LDL/HDL ratio > 2.96, n (%)	925 (38.4)	130 (33.4)	0.063	607 (39.7)	88 (38.3)	0.683	235 (35.4)	36 (26.9)	0.057
LDL/HDL ratio by thirds:									
≤ 2.00, n (%)	760 (31.5)	143 (36.8)	0.079	456 (29.8)	79 (34.4)	0.351	226 (34.0)	53 (39.6)	0.159
2.01–2.96, n (%)	726 (30.1)	116 (29.8)		466 (30.5)	63 (27.4)		203 (30.6)	45 (33.6)	
≥ 2.97, n (%)	926 (38.4)	130 (33.4)		608 (39.7)	88 (38.3)		235 (35.4)	36 (26.9)	
Total Cholesterol, mmol/l, mean ± SD	192.0 ± 57.7	186.3 ± 58.4	0.065	191.3 ± 57.9	183.3 ± 58.9	0.051	200.0 ± 57.5	196.3 ± 57.5	0.496
Total Cholesterol ≥93.6 mg/dl, n (%)	2415 (98.0)	383 (96.0)	**0.014**	1536 (98.1)	224 (95.7)	**0.022**	666 (98.2)	133 (97.1)	0.376
Triglyceride, mg/dl, mean ± SD	126.2 ± 83.9	120.9 ± 71.6	0.231	130.1 ± 85.5	122.3 ± 67.2	0.185	122.4 ± 84.2	122.2 ± 81.2	0.978
Triglyceride ≥30.6 mg/dl, n (%)	2447 (99.5)	395 (99.5)	0.950	1559 (99.7)	234 (100.0)	0.439	668 (99.0)	134 (99.3)	0.751
Waist-to-hip Ratio, mean ± SD	0.9 ± 0.1	0.9 ± 0.1	0.217	0.9 ± 0.1	0.9 ± 0.1	0.105	0.9 ± 0.1	0.9 ± 0.1	0.473
Waist-to-hip Ratio raised, n (%)	2207 (83.0)	387 (82.7)	0.883	1420 (84.5)	236 (86.1)	0.493	552 (79.9)	120 (79.0)	0.795
Waist-to-hip Ratio by thirds:									
≤ 0.90, n (%)	703 (26.4)	118 (25.2)	0.294	426 (25.3)	61 (22.3)	0.055	202 (29.2)	42 (27.6)	0.772
0.91–0.96, n (%)	941 (35.4)	183 (39.1)		591 (35.2)	117 (42.7)		251 (36.3)	53 (34.9)	
≥0.97+, n (%)	1017 (38.2)	167 (35.7)		664 (39.5)	96 (35.0)		238 (34.4)	57 (37.5)	
WHR**, Lowest vs highest thirds, n (%)	1017 (59.1)	167 (58.6)	0.866	664 (60.9)	96 (61.2)	0.956	238 (54.1)	57 (57.6)	0.529
WHR**, 1st vs 2nd + 3rd thirds, n (%)	1958 (73.6)	350 (74.8)	0.585	1255 (74.7)	213 (77.7)	0.274	489 (70.8)	110 (72.4)	0.693
BMI*** (kg/m2), mean ± SD	26.8 ± 5.3	26.7 ± 5.6	0.867	26.9 ± 5.4	26.5 ± 5.2	0.230	26.3 ± 4.9	27.2 ± 6.3	0.066
BMI*** > 30 kg/m^2, n (%)	491 (21.3)	87 (21.9)	0.812	332 (22.5)	55 (23.0)	0.867	103 (17.6)	22 (18.2)	0.880
Physical Activity (some activity), n (%)	2658 (95.1)	460 (95.0)	0.957	1680 (95.2)	271 (94.4)	0.553	699 (95.6)	149 (96.1)	0.777
Tobacco use in past 12 months, n (%)	102 (3.7)	20 (4.1)	0.620	54 (3.1)	7 (2.5)	0.581	41 (5.6)	12 (7.6)	0.331
Tobacco (any use), n (%)	272 (9.6)	51 (10.4)	0.616	170 (9.5)	33 (11.4)	0.325	81 (11.0)	16 (10.2)	0.758
Alcohol (current user), n (%)	478 (16.9)	91 (18.4)	0.397	262 (14.6)	34 (11.7)	0.181	182 (24.8)	49 (31.0)	0.104
Alcohol (any use), n (%)	926 (32.7)	172 (34.8)	0.350	545 (30.5)	88 (30.2)	0.943	311 (42.3)	70 (44.3)	0.646
Alcohol use categories:									
Never Use, n (%)	1908 (76.5)	322 (74.9)	0.129	1245 (78.4)	203 (81.2)	0.442	424 (68.2)	88 (62.9)	**0.020**
Ever Low Use, n (%)	521 (20.9)	89 (20.7)		308 (19.4)	44 (17.6)		172 (27.7)	38 (27.1)	
Ever High Use, n (%)	66 (2.7)	19 (4.4)		35 (2.2)	3 (1.2)		26 (4.2)	14 (10.0)	
Stress, n (%)	525 (19.9)	101 (22.7)	0.178	321 (19.3)	59 (22.4)	0.234	156 (22.8)	30 (20.8)	0.606
Depression, n (%)	203 (7.3)	40 (8.3)	0.479	130 (7.5)	25 (8.7)	0.451	60 (8.3)	11 (7.1)	0.595
Family history of CVD, n (%)	1096 (38.5)	169 (33.9)	**0.048**	689 (38.3)	102 (34.7)	0.232	328 (44.4)	57 (35.9)	**0.047**
Adding salt at table, n (%)	188 (6.8)	45 (9.5)	**0.035**	109 (6.3)	20 (7.3)	0.529	65 (9.0)	19 (12.4)	0.193
Adding salt at table categories:									
Never/rarely, n (%)	1913 (69.4)	334 (70.8)	**0.029**	1230 (70.8)	191 (69.5)	0.803	481 (66.6)	116 (75.8)	**0.002**
Occasionally, n (%)	655 (23.8)	93 (19.7)		399 (23.0)	64 (23.3)		176 (24.4)	18 (11.8)	

(*continued on next page*)

Table 1 (*continued*)

Variable	All Stroke type			Ischemic Stroke			Intracerebral hemorrhage		
	No Post-stroke seizures	Post-stroke seizures	P-value	No Post-stroke seizures	Post-stroke seizures	P-value	No Post-stroke seizures	Post-stroke seizures	P-value
	N = 2845	*n* = 499		*N* = 1797	*n* = 294		*N* = 738	*n* = 159	
Very often, n (%)	188 (6.8)	45 (9.5)		109 (6.3)	20 (7.3)		65 (9.0)	19 (12.4)	
Green vegetable consumption, n (%)	1940 (73.4)	329 (74.1)	0.758	1222 (73.6)	193 (75.4)	0.547	504 (72.3)	101 (69.2)	0.445
Whole grains consumption, n (%)	2225 (83.5)	375 (84.1)	0.743	1399 (83.8)	215 (83.3)	0.859	588 (83.8)	125 (86.2)	0.462
Legumes consumption, n (%)	1791 (67.7)	299 (68.0)	0.912	1117 (67.5)	170 (66.9)	0.848	477 (68.1)	99 (69.2)	0.781
Fruit consumption, n (%)	2259 (85.3)	374 (83.9)	0.447	1410 (84.9)	217 (83.8)	0.630	587 (84.1)	118 (81.9)	0.524
Sugar consumption or otherwise, (%)	771 (29.6)	145 (33.3)	0.122	474 (29.0)	77 (30.7)	0.580	216 (31.2)	54 (37.8)	0.125
Meat consumption or otherwise, (%)	2285 (85.6)	381 (85.0)	0.752	1409 (84.4)	214 (82.6)	0.474	603 (85.4)	128 (87.7)	0.476
Fish consumption or otherwise, (%)	2474 (93.1)	393 (88.5)	**0.001**	1532 (92.1)	225 (87.6)	**0.014**	663 (94.2)	131 (90.3)	0.088
Serum sodium	137.6 ± 9.1	138.2 ± 11.6	0.278	137.5 ± 8.6	137.8 ± 13.4	0.642	137.9 ± 10.3	139.2 ± 9.2	0.241
White blood cell count, mean ± SD	16.9 ± 2.9	21. 5 ± 3.6	**0.017**	17.1 ± 3.0	19.3 ± 3.0	0.420	16.1 ± 2.7	23.8 ± 4.3	**0.015**
NIHSS score, mean ± SD	12.7 ± 8.6	15.2 ± 9.3	**<0.001**	12.1 ± 8.3	14.3 ± 9.2	**<0.001**	14.3 ± 8.8	16.7 ± 9.3	**0.008**
Location of lesions									
Lobar							149 (20.2)	57 (35.9)	**<0.001**
Non-lobar							589 (79.8)	102 (64.2)	
Volume of lesions									
≤10cm^3	1414 (64.5)	203 (50.6)	**<0.001**	1109 (74.0)	158 (62.7)		298 (43.6)	44 (29.9)	
10.1-30 cm^3	452 (20.6)	109 (27.2)		209 (14.0)	53 (21.0)	**0.001**	240 (35.1)	56 (38.1)	**0.003**
> 30cm^3	326 (14.9)	89 (22.2)		180 (12.0)	41 (16.3)		146 (21.4)	47 (32.0)	
Duration of admission in days, mean ± SD	15.9 ± 24.7	17.4 ± 28.6	0.716	15.9 ± 24.9	19.1 ± 35.4	0.819	15.0 ± 22.8	14.0 ± 13.3	0.529

NIHSS – National Institute of Health Stroke Score.

54.9%), to be hypertensive (92.6% vs 96.3%), to have cardiac disease (8.7% vs 12.4%) and to consume fish regularly (88.5% vs 93.1). However, the white cell count and National Institute of Health Stroke Score were significantly higher among those with post-stroke seizures than those without. Also 22.2% with post-stroke seizure had a lesion volume of >30cm^3 compared with 14.9% among those without seizures. The mean duration of admission days for those with PSS vs no PSS was 17.4 ± 28.6 vs 15.9 ± 24.7, $p = 0.72$. (Table 1).

4.2. Characteristics of participants with post-stroke seizures by stroke type

There were 294 (14.1%) post-stroke seizures found among 2091 patients with ischemic stroke and 159 (17.7%) among 897 with intracerebral hemorrhage, $p = 0.01$. Data on stroke type information were missing for 356 participants. Among 1864 patients with Oxfordshire Community Stroke Project (OCSP) classification data, 778 (41.7%) had LACI, 635 (34.1%) had PACI, 268 (14.4%) had TACI and 183 (9.8%) had POCI. Proportions with post-stroke seizures by OCSP classification of ischemic strokes were 18.7% for those with TACI, 16.9% for POCI, 14.1% for LACI and 11.8% among those with PACI ($p = 0.039$), Fig. 1A.

Among 1386 ischemic stroke patients with data on etiology, 54.5% had small vessel occlusion (SVO), 26.3% had large artery atherosclerotic disease (LAA), 16.1% had cardio-embolic stroke (CE) and 3.1% had other causes. In decreasing order, 17.3% with LAA, 14.4% with SVO, 13.4% with CE and 7.0% with other causes, respectively had post-stroke seizures, $p = 0.23$, by chi-squared test for trend (Fig. 1B). Among 801 patients with ICH, 90.8% had hypertensive ICH, 4.0% had structural lesions, 2.7% had undetermined causes, 1.5% had cerebral amyloid associated bleeds, and 0.5% each had either medication-related or systemic disease-related bleeds. The frequencies of post-stroke seizure occurrence by etiology of ICH in decreasing order were 50.0% for those with medication-related ICH, 41.7% in amyloid-related bleeds, 18.2% in bleeds of undetermined causes, 17.5% in hypertensive-related bleeds and 9.4% with structural lesions such as aneurysms and AV malformations, $p = 0.09$ (Fig. 2). Data on ICH stroke subtype information were missing for 96 participants.

4.3. Factors associated with occurrence of post-stroke seizures

In Table 2, we show 12 potential factors associated with occurrence of post-stroke seizures overall in bivariate analysis. Upon adjusting for potential confounders, the adjusted odds ratio (95% CI) of three factors which remained independently associated with post-stroke seizures were: age < 50 years 1.59 (1.08–2.33), NIHSS score at presentation 1.29 (1.16–1.42) for each 5 units rise and white cell count 1.07 (1.01–1.13) for each 10^3 mm^3 rise. Two factors were independently associated with post-stroke seizures among those with ischemic stroke were NIHSS score and lesion volume of >30cm^3 (see Table 3). Among patients with ICH, post-stroke seizures were associated with alcohol use 5.91 (2.11–16.55) and lobar bleeds 2.22 (1.03–4.82) (Table 4). Factors associated with early PSS were stroke severity and white blood count (Table S1 in supplementary information). Late-onset PSS was associated with stroke severity as shown in supplementary information Table S2.

5. Discussion

In this large multi-center study across 15 hospitals in Ghana and Nigeria, we found the frequency of post-stroke seizures to be 14.9% (95% CI of 13.7–16.2%). The frequency of post-stroke seizures was significantly higher among those with spontaneous intracerebral hemorrhage at 17.7% compared with 14.1% among those with ischemic strokes. The prevalence of post-stroke seizures in the present study was quite high and is comparable with a figure of 17.9% (14.6–21.8%) found in an Indian study [25]. Otherwise, most of the previous studies have reported much lower prevalence of post-stroke seizures ranging from 3.0% in Taiwan [26], 3.9% to 6.3% from three Italian studies [27–29], 4.2% in Denmark [30], 4.1% from the US [31], 8.9% from an international collaborative study involving tertiary medical centers in Canada, Australia, Israel and Italy [32] and one study from Egypt reported 9.3% [15]. While differences in study designs and cohort characteristics may underlie these differences in prevalence observed across studies, a key reason could be differences in the time window for defining early post-stroke seizures which has varied between 1 and 30 days in various

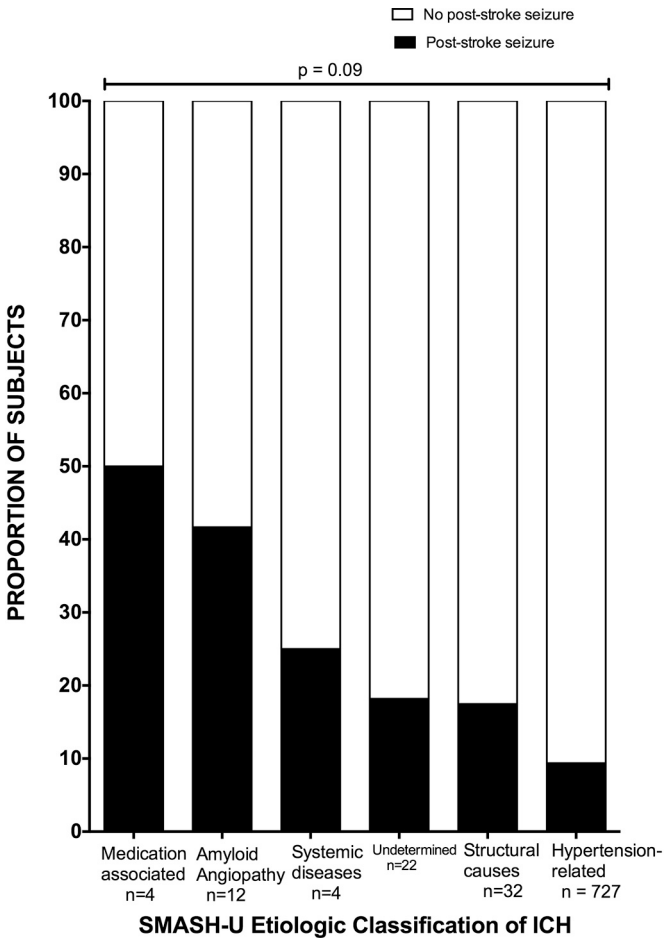

Fig. 1. Frequency distribution of post-stroke seizures by etiology of Intracerebral hemorrhage in West Africa.

studies. In our study, the observation window for identifying PSS was within the period of stroke onset until discharge from hospital or death. The average duration of hospitalization for those with PSS of 17 days was not significantly different from a mean of 16 days for those without PSS. Admittedly, there is potential for the differential duration of hospitalization to influence our ability to identify PSS. For instance, those with mild stroke might have be discharged earlier than those with severe stroke and therefore less likely to have seizures identified. However, we did not find a significant association between duration of hospitalization and risk of PSS.

Intracerebral hemorrhage, cerebral infarction with hemorrhagic transformation, stroke severity and alcoholism are factors associated with early post-stroke seizures from meta-analytic data [33]. Late-onset seizures were associated with cortical involvement and stroke severity [33]. In our study, stroke severity was independently associated with post-stroke seizure with each 5 units rise in the NIHSS score corresponding to a 29% higher odd of seizures (95% CI: 16–42%). Acute stroke patients <50 years old had a 59% higher odds of a post-stroke seizures than those who were older. This higher proclivity for post-stroke seizures occurrence among young west Africans may be explained by the relative preponderance of intracerebral hemorrhage in this age group [9,34]. In sensitivity analyses, the odds ratio of post-stroke seizure among those <50 years with ICH was 1.82 (95% CI: 0.94–3.51) compared with 1.12 (0.69–1.82) among those with ischemic stroke. Leukocytosis was also independently associated in a graded manner with post-stroke seizures, with 7% higher odds for each 10^3 rise in white blood cell count at presentation. It is uncertain whether leukocytosis is simply a marker of stroke severity [35], is a result of post-

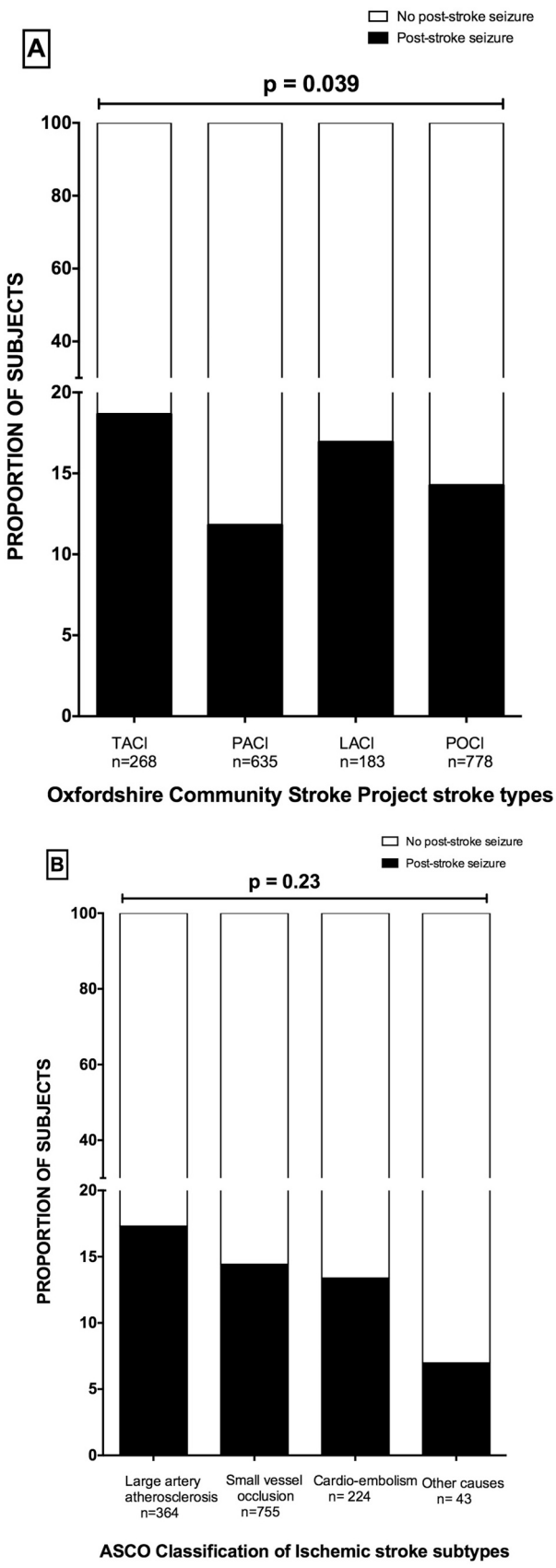

Fig. 2. Frequency distribution of post-stroke seizures by etiology of Ischemic Stroke in West Africa. (1A) by Oxfordshire Community Stroke Project classification; (1B) by ASCO classification.

Table 2
Multivariable logistic regression analysis for factors associated Post-stroke seizures.

	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age < 50 years	1.33 (1.07–1.66)	**0.009**	1.46 (0.98–2.16	0.060
Income <100$	1.23 (1.01–1.48)	**0.036**	1.06 (0.75–1.51)	0.735
Hypertension	0.48 (0.32–0.71)	**<0.001**	0.66 (0.28–1.55)	0.339
Dyslipidemia	0.79 (0.62–1.01)	0.059	0.82 (0.49–1.38)	0.455
Cardiac disease	0.67 (0.48–0.93)	**0.018**	0.95 (0.52–1.74)	0.870
Family history of CVD	0.82 (0.67–0.99)	**0.048**	0.95 (0.67–135)	0.771
Salt (very often)	1.44 (1.02–2.02)	**0.036**	1.51 (0.90–2.52)	0.118
Fish consumption	0.57 (0.41–0.79)	**0.001**	0.73 (0.38–1.37)	0.322
Hemorrhagic stroke vs ischemic stroke as referent	1.32 (1.07–1.62)	**0.011**	1.14 (0.76–1.70)	0.521
NIHSS score as a continuous variable per each 5 units higher	1.16 (1.09–1.24)	**<0.001**	1.29 (1.16–1.42)	**<0.001**
White blood cell count continuous variable	1.04 (1.01–1.08)	**0.022**	1.06 (1.01–1.12)	**0.039**
Volume of lesions				
≤10cm^3	1.00		1.00	
10.1-30 cm^3	1.68 (1.30–2.17)	**<0.001**	1.33 (0.87–2.04)	0.192
> 30cm^3	1.90 (1.44–2.51)	**<0.001**	1.03 (0.61–1.72)	0.924
Duration of admission for stroke in days	1.00 (0.98–1.01	0.259	1.00 (0.99–1.01)	0.309

Table 3
Multivariable logistic regression analysis for factors associated Post-stroke seizures among patients with ischemic strokes.

	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age < 50	1.07 (0.78–1.48)	0.662	–	
Hypertension	0.39 (0.25–0.60)	**<0.001**	0.60 (0.26–1.38)	0.230
Cardiac disease	0.70 (0.48–1.04)	0.078	0.84 (0.47–1.47)	0.536
Total cholesterol (continuous)	1.00 (0.99–1.00)	**0.051**	1.00 (0.99–1.00)	0.385
WHR (tertiles)				
0.91–0.96, n (%)	1.38 (0.99–1.93)	0.057	1.59 (0.96–2.66)	0.073
≥0.97+, n (%)	1.01 (0.72–1.42)	0.956	1.24 (0.73–2.12)	0.428
Fish consumption	0.60 (0.40–0.91)	**0.015**	0.65 (0.33–1.25)	0.198
NIHSS, each 5 units higher	1.15 (1.06–1.25)	**0.001**	1.21 (1.08–1.37)	**0.001**
Lesion volume				
<10.0 cm^3	1.00		1.00	
10.1 - 30cm^3	1.78 (1.26–2.51)	**0.001**	1.90 (1.16–3.11)	**0.010**
>30 cm^3	1.60 (1.10–2.33)	**0.015**	1.05 (0.57–1.96)	0.872
Duration of admission for stroke in days	1.00 (0.99–1.01)	0.082	1.00 (0.99–1.01)	0.266

convulsive leukocytosis or reflective of infections occurring after PSS such as aspiration pneumonitis. It is tempting to speculate that disruption of the blood brain barrier and invasion of leukocytes into the site of cerebral injury after a stroke may incite abnormal neuronal firing.

Table 4
Multivariable logistic regression analysis for factors associated Post-stroke seizures among patients with intracerebral hemorrhage.

	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age < 50	1.73 (1.22–2.45)	0.002	1.82 (0.93–3.55)	0.080
Dyslipidemia	0.71 (0.48–1.06)	0.091	0.99 (0.41–2.36)	0.979
BMI (continuous)	1.03 (1.00–1.07)	0.069	0.96 (0.88–1.03)	0.266
Alcohol use (Ever High use)	2.59 (1.30–5.17)	0.007	5.79 (1.99–16.89)	**0.001**
White blood count	1.07 (1.01–1.14)	0.018	1.02 (0.89–1.17)	0.770
NIHSS each 5 units higher	1.16 (1.04–1.30)	0.009	1.19 (0.98–1.45)	0.066
Lobar bleed	2.21 (1.52–3.20)	<0.001	2.23 (1.02–4.87)	**0.044**
Lesion volume				
<10.0 cm^3	1.00		1.00	
10.1 - 30cm^3	1.58 (1.03–2.43)	0.037	1.34 (0.61–2.96)	0.464
>30.0 cm^3	2.18 (1.38–3.44)	0.001	1.70 (0.69–4.22)	0.251
SMASH-U				
Amyloid angiopathy	12.08 (2.05–71.11)	0.006	7.43 (0.20–280.28)	0.279
Others (referent)	1.00			
Duration of admission for stroke in days	0.99 (0.98–1.01)	0.632	1.00 (0.99–1.01)	0.676

Indeed, cerebral inflammation is a prime etiological factor for ictogenesis and epileptogenesis via alterations in ionic channel sensitivity, neurotransmitter uptake and glia-associated modulation of the extracellular electrical milieu as elegantly reviewed by Shimada et al. [36]

There were also differences in risk factor profile for post-stroke seizure by stroke type. We observed among patients with intracerebral hemorrhage that alcohol use and lobar bleeds were significantly associated with post-stroke seizures. However, while binge drinking may predispose to ICH with attendant PSS, alcohol withdrawal seizures after ICH in alcoholic may conversely predispose to PSS. Thus an assessment of serum alcohol levels or specific questions to patients/relatives may help distinguish between these two possible causes of PSS among alcohol users with ICH for clinical management purposes. It is intriguing to note that, unlike the situation in high-income countries, we found a low frequency of medication-related ICH, perhaps as a consequence of low utilization rates of these pharmacological agents for primary or secondary CVD risk reduction in our settings [37,38]. Among ischemic strokes however, stroke severity and larger infarct volumes presented a higher risk for occurrence of seizures. This observation aligns with the higher frequency of seizures among those with total anterior circulation infarcts using the OCSP classification observed in our study and found by others [39]. Furthermore, those with large artery atherosclerotic disease with its tendency to cause larger territorial infarcts had the highest frequency of seizures among ischemic stroke clinical sub-types. A surprisingly high proportion (≈14%) of ischemic stroke subjects with small vessel occlusive disease had post-stroke seizures. This observation requires further studies because a significant majority of lacunar infarcts occur in the basal ganglia, an area with lower predilection for seizure generation. Further on-going analysis may throw more light on the unique determinants of seizures occurrence in the context of basal ganglionic bleeds and lacunar strokes in the African context.

5.1. Implications

Given that approximately 15% of patients presenting with acute stroke for hospitalization have concomitant seizures, there is the need

for a heightened index for suspicion by clinicians for its screening and identification to treatment. International guidelines from the US and Europe do not recommend primary or secondary anti-epileptic drug (AED) treatment for prophylaxis for post-stroke acute symptomatic seizures although in clinical practice clinicians often do so. The use of carbamazepine and phenytoin is rife but more recent studies support the use of levetiracetam, lamotrigine and gabapentine for treatment of post-stroke seizures [40–42]. A clearer resolution of the potential role of short or longer-term use of AEDs in the management of post-stroke seizures remains to be resolved. Prospective studies are also urgently required to assess the impact of post-stroke seizures on short- and long-term outcomes of strokes, in particular the subsequent risk of development of post-stroke epilepsy in this region. A recent study from Ghana among 1101 stroke survivors reported a post-stroke epilepsy prevalence of 11.4% with male sex, cortical infarcts, elevate blood pressure as predictive factors while antihypertensive use was protective against post-stroke epilepsy [43]. This finding perhaps highlights the need for prediction models for personalized care for post-stroke seizure management.

5.2. Limitations

This study is limited by non-confirmation of clinically reported seizures with electroencephalographic studies and detailed evaluation of potential causes of seizures in the acute stroke setting. The burden of pre-stroke epilepsy risk among our study population was not ascertained as was documentation of seizures types (focal vs generalized), number of seizures (recurrent or single), and types of seizure treatments offered. None of patients in this series had thrombolytic therapy which has been shown to be associated with PSS at a frequency of 1 in every 15 ischemic stroke patients receiving reperfusion treatment [44]. Varying proportions of the study participants did not have data on stroke type or subtypes and had to be excluded from secondary data analysis. Finally, causal associations between seizures and stroke cannot be drawn due to the cross-sectional design of the study.

5.3. Conclusion

The burden of post-stroke seizures among this sample of west Africans is substantial and may contribute to poor outcomes of stroke in this region. Further longitudinal studies are required to understand the impact on morbidity and mortality arising from post-stroke seizures in Africa.

Funding

The SIREN (Stroke Investigative Research and Education Networks) and SIBS Genomics studies were funded by the National Institutes of Health grant U54 HG007479 and R01NS107900 under the H3Africa initiative.

Declaration of Competing Interest

All authors have no conflicts to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2021.117535.

References

[1] W.A. Hauser, J.F. Annegers, L.T. Kurland, Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984, Epilepsia 34 (1993) 453–468.
[2] I.E. Silverman, L. Restrepo, G.C. Mathews, Poste stroke seizures, Arch. Neurol. 59 (2002) 195–201.
[3] G. Wang, H. Jia, C. Chen, S. Lang, X. Liu, C. Xia, et al., Analysis of risk factors for first seizure after stroke in Chinese patients, Biomed. Res. Int. (2013) 702–871.
[4] S.T. Herman, Early post-stroke seizures: is it time for prospective treatment trials? Neurology 7 (2011) 776–778.
[5] R. Walker, D. Whiting, N. Unwin, F. Mugusi, M. Swai, Stroke incidence in rural and urban Tanzania: a prospective, community-based study, Lancet Neurol. 9 (2010) 786–792.
[6] M.C. Ezejimofor, O.A. Uthman, O. Maduka, et al., Stroke survivors in Nigeria: a door-to-door prevalence survey from the Niger Delta region, J. Neurol. Sci. 372 (2017 January 15) 262–269.
[7] F.S. Sarfo, D.O. Awuah, C. Nkyi, J. Akassi, O.K. Opare-Sem, B. Ovbiagele, Recent patterns and predictors of neurological mortality among hospitalized patients in Central Ghana, J. Neurol. Sci. 363 (2016) 217–224.
[8] R.W. Walker, A. Jusabani, E. Aris, et al., Post-stroke case fatality within an incident population in rural Tanzania, J. Neurol. Neurosurg. Psychiatry 82 (9) (2011) 1001–1005.
[9] F.S. Sarfo, B. Ovbiagele, M. Gebregziabher, K. Wahab, R. Akinyemi, A. Akpalu, et al., Stroke among young West Africans: evidence from the SIREN (Stroke Investigative Research and Educational Network) large multisite case-control study, Stroke. 49 (5) (2018 May) 1116–1122.
[10] A. Akpalu, M. Gebregziabher, B. Ovbiagele, F. Sarfo, H. Iheonye, R. Akinyemi, et al., Differential impact of risk factors on stroke occurrence among men versus women in West Africa, Stroke. 50 (4) (2019 Apr) 820–827.
[11] F.S. Sarfo, M. Nichols, S. Qanungo, A. Teklehaimanot, A. Singh, N. Mensah, et al., Stroke-related stigma among West Africans: patterns and predictors, J. Neurol. Sci. 375 (2017) 270–274.
[12] F.S. Sarfo, C. Jenkins, A. Singh, M. Owolabi, A. Ojagbemi, N. Adusei, et al., Post-stroke depression in Ghana: characteristics and correlates, J. Neurol. Sci. 379 (2017) 261–265.
[13] F.S. Sarfo, M. Agbenorku, S. Adamu, V. Obese, P. Berchie, B. Ovbiagele, PINGS Study investigators. The dynamics of poststroke depression among Ghanaians, J. Neurol. Sci. 405 (2019 Oct 15) 116410.
[14] F.S. Sarfo, J. Akassi, S. Adamu, V. Obese, B. Ovbiagele, Burden and predictors of poststroke cognitive impairment in a sample of Ghanaian stroke survivors, J. Stroke Cerebrovasc. Dis. 26 (11) (2017) 2553–2562.
[15] N. Shehta, R.M. Fahmi, B.M. Ramadan, E.M. Emad, A.F. Elsaid, Early post-stroke seizures in a sample of Egyptian patients with first-ever stroke, Neurol. India 66 (2018) 1031–1035.
[16] C. Napon, A. Dabilgou, J. Kyelem, J. Kabore, Post-stroke epilepsy in Burkina Faso (West Africa), J. Neurol. Sci. 368 (2016 Sep 15) 47–48.
[17] I.F. Aiwansoba, O.W. Chukwuyem, Early post-acute stroke seizures: clinical profile and outcome in a Nigerian stroke unit, Ann. Afr. Med. 13 (1) (2014 Jan-Mar) 11–15.
[18] A. Akpalu, F.S. Sarfo, B. Ovbiagele, R. Akinyemi, M. Gebregziabher, R. Obiako, et al., Phenotyping stroke in sub-Saharan Africa: Stroke Investigative Research and Education Network (SIREN) Phenomics protocol, Neuroepidemiology 45 (2015) 73–82.
[19] P. Amarenco, J. Bogousslavsky, L.R. Caplan, G.A. Donnan, M.G. Hennerici, New approach to stroke subtyping: the A-S-C-O (phenotypic) classification of stroke, Cerebrovasc. Dis. 27 (2009) 502–508.
[20] A. Meretoja, D. Strbian, J. Putaala, S. Curtze, E. Haapaniemi, S. Mustanoja, et al., SMASH-U: a proposal for etiologic classification of intracerebral hemorrhage, Stroke 43 (2012) 2592–2597.
[21] M. Holtkamp, E. Beghi, F. Benninger, R. Kalviainen, R. Rocamora, H. Christensen, et al., European Stroke Organisation. European Stroke Organisation guidelines for the management of post-stroke seizures and epilepsy, Eur. Stroke J. 2 (2017) 103–115.
[22] R.A. Fisher, C. Acevedo, A. Arzimanoglou, A. Bogacz, J.H. Cross, C.E. Elger, et al., ILAE official report: a practical clinical definition of epilepsy, Epilepsia 55 (2014) 475–482.
[23] M. O'Donnell, D. Xavier, C. Diener, R. Sacco, L. Lisheng, H. Zhang, et al., Rationale and design of INTERSTROKE: a global case-control study of risk factors for stroke, Neuroepidemiology 35 (2010) 36–44.
[24] M.O. Owolabi, F. Sarfo, R. Akinyemi, M. Gebregziabher, O. Akpa, A. Akpalu, et al., Dominant modifiable risk factors for stroke in Ghana and Nigeria (SIREN): a case-control study, Lancet Glob. Health 6 (4) (2018) e436–e446.
[25] R.P. Goswami, P.S. Karmakar, A. Ghosh, Early seizures in first-ever acute stroke patients in India: incidence, predictive factors and impact on early outcome, Eur. J. Neurol. 19 (2012) 1361–1366.
[26] H.C. Liao, S.H. Chen, C.D. Yang, Y.W. Chen, Clinical profile and outcomes of early seizures in Asian patients with acute intracerebral hemorrhage, J. Acute. Med. 9 (4) (2019) 172–177.
[27] A. Pezzini, M. Grassi, E. Del Zotto, A. Giossi, I. Volonghi, P. Costa, Complications of acute stroke and the occurrence of early seizures, Cerebrovasc. Dis. 35 (2013) 444–450.
[28] A. Alberti, M. Paciaroni, V. Caso, M. Venti, F. Palmerini, G. Agnelli, Early seizures in patients with acute stroke: frequency, predictive factors and effect on clinical outcome, Vasc. Health Risk Manag. 4 (2008) 715–720.
[29] E. Beghi, R.D. Alessandro, S. Beretta, D. Consoli, V. Crespi, L. Delaj, Incidence and predictors of acute symptomatic seizures after stroke, Neurology. 77 (2011) 1785–1793.
[30] J. Reith, H.S. Jorgensen, H. Nakayama, H.O. Raaschou, T.S. Olsen, Seizures in acute stroke: predictors and prognostic significance. The Copenhagen stroke study, Stroke 28 (1997) 1585–1589.
[31] D. Labovitz, W.A. Hauser, R.L. Sacco, Prevalence and predictors of early seizures and status epilepticus after first stroke, Neurology 57 (2001) 200–206.

[32] C.F. Bladin, A.V. Alexandrov, A. Bellavance, N. Bornstein, B. Chamber, R. Cote, et al., Seizures after stroke: a prospective multicenter study, Arch. Neurol. 57 (2000) 1617–1622.
[33] C. Zhang, X. Wang, Y. Wang, J.G. Zhang, W. Hu, M. Ge, et al., Risk factors for post-stroke seizures: a systematic review and meta-analysis, Epilepsy Res. 108 (10) (2014) 1806–1816.
[34] F.S. Sarfo, B. Ovbiagele, M. Gebregziabher, O. Akpa, A. Akpalu, K. Wahab, et al., Unraveling the risk factors for spontaneous intracerebral hemorrhage among West Africans, Neurology. 94 (10) (2020 Mar 10) e998–e1012.
[35] P. Welsh, M. Barber, P. Langhorne, A. Rumley, G.D. Lowe, D.J. Stott, Associations of inflammatory and haemostatic biomarkers with poor outcome in acute ischaemic stroke, Cerebrovasc. Dis. 27 (3) (2009) 247–253.
[36] T. Shimada, T. Takemiya, H. Sugiura, K. Yamagata, Role of inflammatory mediators in pathogenesis of epilepsy. Role of Inflammatory Mediators in the Pathogenesis of Epilepsy, Mediat. Inflamm. 2014 (2014), 901902, 8 pages.
[37] F.S. Sarfo, S. Adamu, V. Obese, M. Agbenorku, P.A. Opare-Addo, B. Ovbiagele, Atherosclerotic event risk and risk reduction therapies among Ghanaian hemorrhagic stroke survivors, J. Neurol. Sci. 424 (2021) 117389.
[38] F.S. Sarfo, B. Ovbiagele, J. Akassi, G. Kyem, Baseline prescription and one-year persistence of secondary prevention drugs after an index stroke in Central Ghana, eNeurologicalSci. 6 (2017) 68–73.
[39] J. Burn, M. Dennis, J. Bamford, P. Sandercock, D. Wade, C. Warlow, Epileptic seizures after a first stroke: the Oxfordshire Community Stroke Project, BMJ. 315 (7122) (1997) 1582–1587.
[40] L. Sykes, E. Wood, J. Kwan, Antiepileptic drugs for the primary and secondary prevention of seizures after stroke, Cochrane Database Syst. Rev. 1 (2014), CD005398.
[41] S.P. Singh, R. Sankaraneni, A.R. Antony, Evidence-based guidelines for the management of epilepsy, Neurol. India 65 (Suppl S1) (2017) 6–11.
[42] T. Glauser, E. Ben-Menachem, B. Bourgeios, A. Cnaan, C. Guerriro, R. Kalviainen, et al., ILAE Subcommission on AED guidelines. Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes, Epilepsia 54 (2013) 551–563.
[43] F.S. Sarfo, J. Akassi, V. Obese, S. Adamu, M. Agbenorku, B. Ovbiagele, Prevalence and predictors of post-stroke epilepsy among Ghanaian stroke survivors, J. Neurol. Sci. 418 (2020) 117138.
[44] A. Lekoubou, J. Fox, P. Ssentongo, Incidence and association of reperfusion therapies with poststroke seizures. A systematic review and meta-analysis, Stroke. 51 (2020) 2715–2723.