



Clinical and neuroimaging factors associated with 30-day fatality among indigenous West Africans with spontaneous intracerebral hemorrhage

Morenikeji A. Komolafe^a, Taofiki Sunmonu^b, Joshua Akinyemi^c, Fred S. Sarfo^d, Albert Akpalu^e, Kolawole Wahab^f, Reginald Obiako^g, Lukman Owolabi^h, Godwin O. Osaigbovoⁱ, Godwin Ogbale^j, Hemant K. Tiwari^k, Carolyn Jenkins^l, Daniel T. Lackland^l, Adekunle G. Fakunle^m, Ezinne Uvere^m, Onoja Akpa^c, Hamisu A. Dambatta^h, Josephine Akpalu^d, Akinola Onasanyaⁿ, Adeniji Olaleye^f, Okechukwu S. Ogah^o, Sulaiman Y. Isah^h, Micheal B. Fawale^a, Akintunde Adebawale^a, Akinkunmi P. Okekunle^c, Donna Arnett^p, Abiodun M. Adeoye^o, Atinuke M. Agunloye^j, Abiodun H. Bello^f, Adeniyi S. Aderibigbe^q, Ahmed O. Idowu^a, Ahmad A. Sanusi^a, Adebimpe Ogunmodede^a, Simon A. Balogun^r, Adedeji A. Egberongbe^b, Folorunso T. Rotimi^b, Adeyemi Fredrick^b, Andrew O. Akinnuoye^b, Folu A. Adeniyi^b, Benedict Calys-Tagoe^s, Philip Adebayo^t, Oyedunni Arulogun^m, Obiageli U. Agbogu-Ike^g, Joseph Yaria^o, Lambert Appiah^d, Philip Ibinaiye^g, Arti Singh^e, Sunday Adeniyi^e, Oladotun Olalusi^o, Aliyu Mande^h, Olayemi Balogun^g, Rufus Akinyemi^{o,u}, Bruce Ovbiagele^v, Mayowa Owolabi^{o,w,*}, on behalf of SIREN

^a Department of Medicine, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria

^b Department of Medicine, Federal Medical Centre, Owo, Ondo State, Nigeria

^c Department of Epidemiology and Medical Statistics, College of Medicine, University of Ibadan, Nigeria

^d Department of Medicine, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

^e Department of Medicine, University of Ghana Medical School, Accra, Ghana

^f Department of Medicine, University of Ilorin Teaching Hospital, Ilorin, 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 Department of Radiology, University of Ibadan, Nigeria

^k University of Alabama at Birmingham, Birmingham, AL, USA

^l Medical University of South Carolina, SC, USA

^m College of Medicine, University of Ibadan, Nigeria

ⁿ Department of Medicine, Federal Medical Centre, Abeokuta, Nigeria

^o University College Hospital, Ibadan, Nigeria

^p College of Public Health, University of Kentucky, USA

^q Department of Radiology, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria

^r Department of Surgery, Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Osun State, Nigeria

^s Department of Community Health, University of Ghana Medical School, Accra, Ghana

^t Aga-Khan University, Dar es Salaam, Tanzania

^u Federal Medical Centre, Abeokuta, Nigeria

^v Weill Institute for Neurosciences, School of Medicine, University of California, San Francisco, USA

^w Center for Genomic and Precision Medicine, College of Medicine, University of Ibadan, Nigeria

* Corresponding author at: Center for Genomic and Precision Medicine, College of Medicine, University of Ibadan, University College Hospital Ibadan and Blossom Specialist Medical Center, Ibadan, Nigeria.

E-mail address: mayowaowolabi@yahoo.com (M. Owolabi).

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ABSTRACT

Background: Spontaneous intracerebral hemorrhage (ICH) is associated with a high case fatality rate in resource-limited settings. The independent predictors of poor outcome after ICH in sub-Saharan Africa remains to be characterized in large epidemiological studies. We aimed to determine factors associated with 30-day fatality among West African patients with ICH.

Methods: The Stroke Investigative Research and Educational Network (SIREN) study is a multicentre, case-control study conducted at 15 sites in Nigeria and Ghana. Adults aged ≥ 18 years with spontaneous ICH confirmed with neuroimaging. Demographic, cardiovascular risk factors, clinical features and neuroimaging markers of severity were assessed. The independent risk factors for 30-day mortality were determined using a multivariate logistic regression analysis with an adjusted odds ratio (OR) and 95% confidence interval (CI).

Results: Among 964 patients with ICH, 590 (61.2%) were males with a mean age (SD) of 54.3(13.6) years and a case fatality of 34.3%. Factors associated with 30-day mortality among ICH patients include: Elevated mean National Institute of Health Stroke Scale(mNIHSS);(OR 1.06; 95% CI 1.02–1.11), aspiration pneumonia; (OR 7.17; 95% CI 2.82–18.24), ICH volume > 30 mls; OR 2.68; 95% CI 1.02–7.00) low consumption of leafy vegetables (OR 0.36; 95% CI 0.15–0.85).

Conclusion: This study identified risk and protective factors associated with 30-day mortality among West Africans with spontaneous ICH. These factors should be further investigated in other populations in Africa to enable the development of ICH mortality predictions models among indigenous Africans.

1. Introduction

Spontaneous intracerebral hemorrhage (ICH) accounts for 10%–40% of all cerebrovascular diseases worldwide with higher frequencies and case fatality rates in low-and middle-income countries (LMIC) in Asia and Africa [1]. A 30-day mortality rate of 40% for ICH has been reported and 55% of the survivors of ICH recovered with functional dependence [2,3], a finding that was corroborated by the global burden of disease study in 2010 [4].

The clinical presentation of ICH can be catastrophic. Risk stratification scores that made use of GCS, volume of bleed, hydrocephalus have been linked with mortality and functional outcome of patients with ICH have been assessed outside Africa among diverse populations [5–8]. However, some of the items in the ICH score may have poor predictive value in some populations including indigenous West Africans. For example, the cut-off value age of 80-years was found not to be applicable in a study conducted in the Democratic Republic of Congo (DRC) where ICH cases were younger and experienced a higher mortality rate [9].

In Sub-Saharan Africa, the independent predictors of poor outcome after ICH have not been characterized in large studies. Therefore, we sought to determine the clinical and neuroimaging factors associated with 30-day mortality in indigenous West Africans with ICH. This could serve as a template to conduct a study on long term outcome of patients with ICH. We hypothesized that the risk factors associated with 30-day mortality is similar to those of the other countries.

2. Methodology

2.1. Study design

It is a prospective cohort and multicenter study involving fifteen tertiary hospital sites in Nigeria and Ghana as part of the Stroke and Investigative Research Education Network (SIREN) study. The study protocol has been previously published. [10] These centers are located in both Urban and semi-rural areas. Patients were admitted in general medical wards and stroke units. Patients were managed conservatively with hyperosmolar therapy, antihypertensives and other supportive measures. Few patients had surgical intervention like hematoma evacuation, external ventriculostomy or craniectomy. None of our patients had DNR orders and withdrawal of active life support.

The Review Board (IRB) of all study sites approved the study and the patients or their legal representatives provided informed consent. The Ethical Approval for the study were obtained from all the participating centres as shown in Supplementary file I. ICH patients ($n = 964$) were prospectively studied over three years (2015–2018). They were all black

Africans.

2.2. Assessment of clinical characteristics

ICH cases included consecutive consenting adult patients aged ≥ 18 years with onset of symptoms or 'last seen without deficit' to presentation within 8 days (in unconscious or aphasic patients, consent was obtained from next of kin). Flow chart for the recruitment of patient is described in supplementary file I. Imaging analysis was done by the Consultant radiologist at each study sites with CT or MRI scan within 10 days of symptom onset. The ventricular sizes were analyzed in 200 patients who had ICH and concomitant IVH, 3rd and 4th ventricular size > 10 mm was taken as significant for hydrocephalus. [11] The patients were recruited via the medical emergency units of the participating hospitals. ICH patients were evaluated at admission with detailed clinical history, general physical / neurological examinations. Patients with extra-axial hemorrhage, subarachnoid hemorrhage, tumours, abscesses, traumatic hemorrhage, or haemorrhagic transformation of cerebral infarction were excluded. Samples for random blood glucose, lipid panels, full blood count, erythrocyte sedimentation rate (ESR), urinalysis, and serum glycated haemoglobin were obtained. Age, place of domicile, monthly income, level of education, and Glasgow Coma Scale (GCS) scores were documented. The renal function of each patient was estimated with the Modification of Diet for Renal Disease–Glomerular Filtration Rate (MDRD-GFR) equation [12]. The waist/hip ratio, body mass index (BMI), blood lipid level, platelet count, tobacco use, and dietary habits were collected at admission. Stroke severity was assessed with the aid of the National Institute of Health Stroke Scale (NIHSS) and Stroke Levy Scale (SLS) score. [13] mRS data was collected by doctors during patient visit and occasionally by phone call.

The definition of risk factors associated with Intracerebral hemorrhage is as described elsewhere [14] and supplementary file II.

2.3. Image analysis

The diagnosis of ICH was based on the clinical history, physical examination and brain CT or MRI. The neuroimaging review identified the location and volume of the haematoma as well as the presence of associated intraventricular hemorrhage. The ellipsoid formula ($ABC/2$) for estimation of ICH haematoma volume was utilized to calculate the ICH volume [15] where A, B, and C are diameters of the three semi-axes of the haematoma. All the patients were admitted, managed and monitored over the subsequent 30 days by periodic clinical examinations.

Table 1

Summary of the socio-demographic characteristics and clinical parameters, univariate predictors of mortality and multivariate adjusted analysis.

Variable	Alive (633)	Dead (331)	Total (n = 964)	p-value	Unadjusted		Adjusted	
	n (%)	n (%)	n (%)		OR (95% C-I)	p-value	OR (95% CI)	p-value
Socio-demographic								
Age(years): mean (Sd)								
<55	343(54.2)	162(48.9)	505(52.4)	0.122	ref			
≥ 55	290(45.8)	169(51.1)	459(47.6)		1.23(0.95–1.61)	0.122	1.10(0.79–1.53)	0.559
Domicile								
Rural	45(7.1)	33(10.0)	78(8.1)	0.221	ref			
Semi-urban	183(29.1)	85(25.8)	268(27.9)		0.63(0.38–1.06)	0.084		
Urban	402(63.8)	212(64.2)	614(63.9)		0.72(0.45–1.16)	0.177		
Monthly income								
≤100 USD	276(43.8)	154(46.5)	430(44.8)	0.421	ref			
> 100 USD	354(56.2)	177(53.5)	531(55.3)		0.89(0.69–1.17)	0.421		
Education								
None	70(11.1)	58(17.6)	128(13.3)	0.05	ref			0.666
Some	561(88.9)	272(82.4)	833(86.7)		0.58(0.40–0.85)	0.005*	0.79(0.27–2.31)	
Sex								
Male	391(61.8)	199(60.1)	590(61.2)	0.618	0.93(0.71–1.23)	0.618		
Female	242(38.2)	132(39.9)	374(38.8)		ref			
Clinical								
Hypertension	615(97.6)	326(99.4)	941(98.2)	0.049	3.98(0.90–17.49)	0.068		
Dyslipidemia	490(77.8)	258(78.4)	748(78.0)	0.82	1.04(0.75–1.43)	0.82		
Cardiac disease	45(7.1)	17(5.2)	62(6.48)	0.247	0.71(0.40–1.27)	0.248		
Seizure at admission	27(4.6)	37(12.4)	64(7.2)	<0.001	2.97(1.77–4.97)	<0.001*	1.17 (0.31–4.46)	0.82
Aspiration pneumonia	70(11.8)	144(47.7)	214(23.9)	<0.001	6.82(4.87–9.55)	<0.001*	7.17 (2.82–18.24)	<0.001*
Pyrexia(malaria)	231(36.5)	121(36.6)	352(36.5)	0.884	1.01(0.77–1.34)	0.938		
Neuroimaging characteristics ICH volume								
<30	386(73.1)	121(36.6)	546(67.7)	<0.001	ref		ref	
≥ 30	142(26.9)	118(42.5)	260(32.3)		2.00(1.48–2.72)	<0.001*	2.68(1.02–7.00)	0.044
Location of lesion								
Deep/non-lobar	455(77.0)	261(82.1)	716(78.8)	0.074	ref			
Lobar	136(23.0)	57(17.9)	193(21.2)		0.73(0.52–1.03)	0.074		
Internal capsule	77(12.2)	30(9.1)	107(11.1)	0.146	0.72(0.46–1.12)	0.147		
Brainstem(medulla)	1(0.2)	0(0.0)	1(0.10)	0.469				
Cerebellar	31(4.9)	0(0.0)	45(4.7)	0.641	0.86(0.45–1.64)	0.641		
GCS score								
14–15	67(52.8)	13(17.8)	80(40.0)	<0.001	Ref			
9–13	38(29.9)	13(17.8)	60(30.0)		3.0(1.35–6.59)	0.007		
≤8	22(17.3)	38.52.1	60(30.0)		8.90(4.03–19.67)	<0.001*		
Intraventricular hemorrhage IVH+	182(34.5)	155(55.8)	337(41.8)	<0.001	2.4(1.78–3.22)	<0.001*	0.79(0.35–1.78)	0.557
Hydrocephalus								
Lateral ventricle size(mm)								
0–5	106(86.2)	83(74.8)	189(80.8)	0.086				
6–10	13(10.6)	83(74.8)	35(15.0)					
>10	4(3.3)	6(5.4)	10(4.3)					
3rd ventricle size(mm)								
0–5	63(100.0)	75(97.4)	138(98.6)	0.198				
6–10	0(0.0)	2(2.6)	2(1.4)					
>10								
4th ventricle								
0–5	46(100)	56(100.0)	102(100.0)					
6–10								
>10								
IVH without hydrocephalus								
Infratentorial origin	52(9.9)	33(11.8)	85(10.6)	0.374	1.23(0.78–1.96)	0.375		
Other variables and lab parameters MNIHSS score								
Not severe (≤15)	354(62.2)	50(17.7)	404(47.4)	<0.001	ref		ref	
Severe (>15)	215(37.8)	233(82.3)	448(52.6)		5.1(3.71–7.01)	<0.001*	1.06(1.02–1.11)	0.007
SLS total score: mean (Sd)	6.48(4.29)	3.32(3.09)	5.41(4.19)	<0.001				
0–5 (severe)	275(44.4)	256(80.3)	531(56.6)		15.01 (7.20–31.28)	<0.001*		
6–10 (moderate)	216(34.8)	55(17.2)	531(56.6)		4.11(1.90–8.90)	<0.001*		
11–15(mild)	129(20.8)	8(2.5)	531(56.6)		Ref			
Systolic BP	165.81 (31.43)	176.82 (33.29)	169.59(32.49)	<0.001				
<140	136(21.5)	44(13.1)	180(18.7)	0.002	ref			
≥ 140	497(78.5)	287(86.7)	784(81.3)		1.78(1.23–2.58)	0.002	2.58(0.68–9.81)	0.163
Diastolic BP	100.73 (18.41)	106.0 (20.8)	102.5 (19.4)	0.0001				
<90	158(25.0)	64(19.3)	222(23.0)	0.049	ref			
≥ 90	475(75.0)	267(80.7)	742(77.0)		1.39(1.00–1.92)	0.049	0.82(0.26–2.61)	0.737
BMI								
<30	414(80.5)	209(81.9)	623(81.0)	0.637	ref			

(continued on next page)

Table 1 (continued)

Variable	Alive (633)	Dead (331)	Total (n = 964)	p-value	Unadjusted	Adjusted		
Socio-demographic	n (%)	n (%)	n (%)		OR (95% C-I)	p-value	OR (95% CI)	p-value
≥ 30	100(19.5)	46(18.0)	146(18.9)		0.91(0.62–1.34)	0.637		
Waist-hip- ratio								
< 0.9	182(30.8)	86(27.6)	268(29.7)	0.592	ref			
0.91–0.96	209(35.4)	114(36.5)	323(35.8)		1.15(0.82–1.63)	0.413		
≥ 0.97	200(33.8)	112(35.9)	312(34.6)		1.19(0.84–1.67)	0.335		
Random blood sugar eGFR (mls/min)	7.73(3.45)	8.62(3.20)	7.99(3.39)	0.006	1.08(1.02–1.14)	0.01	1.08(0.97–1.21)	0.154
< 60	132(31.0)	90(40.5)	222(34.3)	0.002	2.07(1.36–3.16)	0.001	2.20(0.81–5.95)	0.12
60–90	148(34.7)	84(37.8)	232(35.8)		1.73(1.13–2.63)	0.011	1.47(0.55–3.97)	0.446
>90	146(34.3)	48(21.6)	194(29.9)		ref			
Low HDL(<0.78 mmol/l)	165(29.7)	91(31.4)	256(30.3)	0.62	1.08(0.79–1.47)	0.62		
High LDL (≥ 4.53 mmol/l)	228(41.2)	117(40.5)	345(41.0)	0.835	0.97(0.73–1.29)	0.835		
LDL/LDL ratio								
≤2	205(37.4)	93(32.3)	298(35.7)	0.313	ref			
2.01–2.96	161(29.4)	88(30.6)	249(29.8)		1.2(0.84–1.72)	0.306		
≥ 2.97	182(33.2)	107(37.2)	289(34.6)		1.29(0.92–1.82)	0.138		
High total cholesterol (≥ 6.5 mmol/l)	246(43.9)	133(45.9)	379(44.5)	0.576	1.08(0.82–1.44)	0.576		
High triglyceride (≥ 1.73 mmol/l)	131(23.4)	78(26.9)	209(24.6)	0.261	1.2(0.87–1.67)	0.261		
Etiology of ICH								
Macrovascular (AVM,Aneurysm)	44(7.0)	21(6.3)	65(6.7)	0.721	0.91(0.53–1.55)	0.721		
Anticoagulant use	5(0.8)	3(0.9)	8(0.3)	0.85	1.15(0.27–4.84)	0.85		
Cerebral amyloid angiopathy	11(1.7)	8(2.4)	19(2.0)	0.471	1.40(0.56–3.52)	0.473		
Systemic diseases	20(3.16)	6(1.8)	26(2.7)	0.22	0.57(0.23–1.42)	0.226		
Hypertensive arteriopathy	459(72.5)	235(71.0)	694(72.0)	0.619	0.93(0.69–1.25)	0.619		
Time of onset to admission(days)								
1–3	451(77.4)	257(84.3)	708(9.3)	0.05	Ref			
4–7	93(16.0)	35(11.5)	128(14.4)		0.66(0.43–1.00)	0.052		
>7	39(6.7)	13(4.3)	52(5.9)		0.58(0.31–1.12)	0.104		
Duration of admission								
< 10	232(45.4)	189(65.6)	421(53.0)	0.001	Ref			
10–20	185(36.2)	55(19.1)	240(30.0)		0.36(0.26–0.52)	<0.001*	0.55(0.23–1.33)	0.185
>20	94(18.40)	44(15.3)	138(17.3)		0.57(0.38–0.86)	0.008	0.55(0.16–1.90)	0.346
Lifestyle								
Tobacco use								
Never	570(90.8)	296(90.2)	866(90.6)	0.794	Ref			
Ever	58(9.2)	32(9.8)	90(9.4)		1.06 (0.67–1.67)	0.794		
Alcohol use								
Never	393(62.6)	205(62.7)	598(62.6)	0.973	ref			
Current/former	235(37.4)	122(37.3)	357(37.4)		0.99(0.75–1.31)	0.973		
Leafy vegetables consumption	436(72.9)	182(61.4)	618(68.4)	<0.001	0.55(0.41–0.74)	<0.001*	0.36(0.15–0.85)	0.02
Legume's consumption	424(70.1)	186(61.4)	610(67.2)	0.008	0.68(0.51–0.91)	0.009*	0.96(0.40–2.30)	0.925
Grains consumption	527(86.9)	260(84.7)	787(86.2)	0.347	0.83(0.56–1.23)	0.347		
Sugar consumption	160(27.2)	111(36.4)	271(30.4)	0.005	1.53(1.14–2.06)	0.005*	1.72(0.63–4.70)	0.289
Fish consumption	572(94.4)	284(92.8)	856(93.9)	0.348	0.77(0.44–1.34)	0.349		
Meat consumption	524(86.3)	277(89.6)	801(87.5)	0.152	1.37(0.89–2.11)	0.153		
Added salt at the table								
Not often	561(90.8)	286(89.9)	847(90.5)	0.678	ref			
Very often	57(9.2)	32(10.1)	89(9.5)		1.37(0.89–2.11)	0.678		

2.4. Data collection and statistical analysis

Data were collected using a standardized case report form across all sites. Demographic and lifestyle data, such as socioeconomic status, dietary patterns, and cardiovascular risk profile, were collected. Validated instruments were used to assess physical inactivity, stress, depression, cigarette smoking, and alcohol use. The investigation results and imaging data were also documented. Differences in the distribution of categorical variables by gender and survival status were assessed using the Fisher's Chi-square test. Independent-sample *t*-tests were employed for continuous variables associated with survival status. Variables with *p* values <0.05 were entered subsequently into the multiple logistic regression model, and results were expressed as odds ratio (OR) with a 95% confidence interval (CI).

3. Results

3.1. Clinical characteristics

Sociodemographic characteristics, clinical parameters and lifestyle pattern of the patients are summarized in Table 1. Male ICH patients had

a higher prevalence of obesity (BMI > 30 kg/m²) than female ICH patients (*p* < 0.05), while abdominal obesity was also more common in males than females. Also, dyslipidaemia, tobacco use, alcohol intake, higher educational level attainment, and higher monthly income were more common in male ICH patients than females. Mortality rate was 34.3%. There was no statistical significance in patient who had medical decompression and surgical decompression in this study *P* > 0.05. There were no significant gender differences in other clinical and neuroimaging characteristics.

3.2. Univariate predictors of mortality

The details of the clinical and neuroimaging factors in the patients with ICH that were associated with 30-day fatality are as highlighted in Table 1.

3.3. Multivariate adjusted analysis

The four factors identified to be associated with 30-day mortality in patients with ICH (*p* < 0.05) with adjusted odds ratio (95% CI) were: elevated National Institute of Health Stroke Scale(NIHSS)(OR 1.06; 95%

CI 1.02–1.11), presence of aspiration pneumonitis; (OR 7.17; 95% CI 2.82–18.24), ICH volume > 30mls; (OR 2.68; 95% CI 1.02–7.00) and low consumption of leafy vegetables (OR 0.36; 95% CI 0.15–0.85) as shown in Table 1 while age, monthly income, level of education, SLS score, mRS score, presence of systemic hypertension and obesity (BMI and Waist/hip ratio), the presence of cardiac disease, pyrexia, location of lesions, presence of intraventricular hemorrhage, and origin of the hemorrhage were not associated with mortality in patients with ICH ($p > 0.05$). This is as highlighted as in Table 1 and on forest plot in Fig. 1.

4. Discussion

Mean age of the patients was 53.4 years which is lower than the mean age from the “Reasons for Geographic and Racial Difference in Stroke – REGARDS” study and other cross-cultural studies [4,13,16,17] The lower average lifespan of West Africans could explain this. The 30-day mortality rate in this study was 34%, similar to that of a previous Central African study that reported a mortality rate of 35% [9]. Some other international studies showed variable mortality rates in their studies ranging from 25% to 52%. [18–20] This disparity could be related to the time of presentation and level of health care delivery. In our settings, many patients were unable to pay for ICH care as stroke care in West Africa is by out-of-pocket payment and many of them might have died at home because of this reason.

Gender and age were not related to outcome in our study which is consistent with other studies. [18,21]

Large hematoma volume was associated with 30-day mortality in our study which is consistent with other studies. [18,22,23] Large hematoma volume predisposes patients to cerebral oedema and raised ICP which could have worsened the outcome. Our study reported a bleeding volume of >30 ml which is similar to an earlier study. [24] Some authors quoted ICH volume of 40 mls and 60mls as cut-off points. [25,26] The variation in these studies could be related to the location of the hemorrhage and presence or absence of surgical intervention. The latest American heart Association guideline recommends that minimally invasive hematoma evacuation for supratentorial bleed of >20-30mls volume along with GCS of 5–12 can help reduce mortality when compared to medical management alone. [27] Intratentorial location has been linked with a high 30-day mortality. [22–24] This was not

reflected in our study probably because few patients presented with infratentorial bleed with a possibility that others could have died at home. Intraventricular hemorrhage has been reported as a predictor of 30-day mortality [18,28] Our study reported IVH in about 42% of patients and but this was not a predictor of mortality possibly because it wasn’t associated with obstructive hydrocephalus. [29]

Aspiration pneumonitis is a common complication in the unconscious patient with ICH [14,30]. The factors responsible for predisposition to aspiration pneumonitis could be pre-hospital or intra-hospital. In our setting, many patients aspirate as a result of loss of consciousness and wrong first aid measures administered such as herbal drugs or fluids in the community before being transported to the hospital [31]. Our study showed that the presence of aspiration pneumonitis in patients with ICH is associated with an increased death rate and this aligns with findings in some previous studies. [14,31,32].

Elevated mean NIHSS score was predictive of 30 day mortality in our study similar to other reports. [33,34] A NIHSS score of 15 at admission was used in our study while Cheung et al. 2003 used a cutoff point of 20 to predict 30 day mortality and long term outcome. [34] GCS wasn’t evaluated further in our study because it shared co-linearity with NIHSS. Although low GCS has been recognized as a predictor of 30 day outcome, [22,28,35] NIHSS is preferred to GCS because it has a wider spectrum in accessing neurological dysfunction. [36,37] More studies need to be carried out on the functional outcome of ICH using GCS and NIHSS.

Hypertension is recognized as the most common cause arterio-sclerosis (a common form of SVD), which is, in turn, the most common cause of ICH in the SIREN study occurring in 80.9% of cases [14]. In this study, there was no association between systemic hypertension and 30-day mortality in patients with ICH which is in contrast with previous studies [38,39]. However, high blood pressure following ICH could also be a manifestation of raised intracranial pressure.

Patients who had consumed dietary fibers (leafy vegetables, fruits, and grains) regularly were shown to have a lower risk of development of ICH and decreased death which is consistent with an earlier report. [40] The antioxidant and blood pressure lowering effect of these dietary fibers have protective effect against cerebrovascular accident. [41]

The reasons for some of these findings would need to be explored in further large controlled clinical trials in the future.

Odds ratio [95% CI]

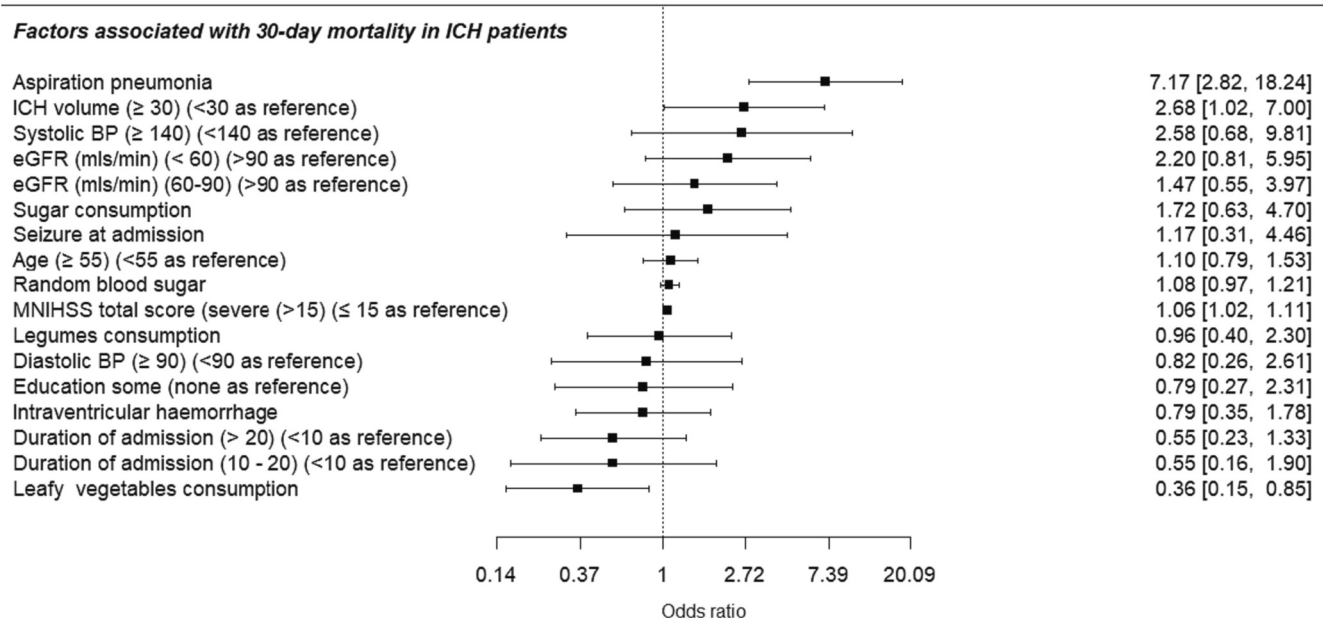


Fig. 1. Forest plot of the factors associated with 30-day mortality in ICH patients.

5. Strengths, limitations, and future directions

Some of the strengths of the study include the inclusion of multiple centers across Nigeria and Ghana which is an assessment of the representativeness of the sample, A relatively large sample size. Serial imaging to determine haematoma expansion, midline shift, effacement of sulci or brain ventricles were not done for the patients. Other detailed neuroimaging procedures such as angiography could not be done to evaluate the patients due to the non-availability of prerequisite equipments for these procedures in some of the study sites. Also, the rate of risk factors such haematoma expansion, peri-hematoma oedema, oedema extension volume, and oedema extension distance could not be determined because of the same reasons. Treatment modalities such as ICU admission, ventilation support and surgical interventions that could affect 30-day mortality in ICH could not be fully evaluated in this study due to the lack of dedicated stroke units and facilities for acute care in some of the centres that recruited patients. The dietary history obtained from family members may not be accurate as some of the patients were aphasic or comatose. There is a potential for bias and a possibility of spurious association with diet given that there is poor reliability of dietary history. The assertion that reduced consumption of leafy vegetable in association with poor outcome in ICH can be confounded by other socio-economic or lifestyle factors associated with a healthy diet.

Patients with severe ICH might also have been missed because of early mortality in communities. More males than females were recruited for the study and this could have confounded the findings of this work. In the near future, SIREN can develop more refined efforts to address the critically unanswered questions found in this study.

6. Conclusions

The identified predictive factors for mortality in this study were low GCS score at presentation, aspiration pneumonia, ICH volume and low consumption of leafy vegetables. Further studies are required to develop better predictive models for mortality among sub-Saharan African patients with ICH. These will help with early identification of patients with ICH at high risk of mortality so that prompt actions will be taken to reduce mortality.

Disclosures

The authors have no disclosures.

CRediT authorship contribution statement

Morenikeji A. Komolafe: Conceptualization, Data curation, Investigation, Supervision, Writing – original draft. **Taofiki Sunmonu:** Conceptualization, Data curation, Writing – original draft. **Joshua Akinyemi:** Formal analysis, Investigation, Methodology. **Fred S. Sarfo:** Data curation, Investigation, Writing – review & editing. **Albert Akpalu:** Data curation, Investigation, Writing – review & editing. **Kolawole Wahab:** Data curation, Investigation, Writing – review & editing. **Reginald Obiako:** Data curation, Investigation, Writing – review & editing. **Lukman Owolabi:** Data curation, Investigation, Writing – review & editing. **Godwin O. Osaigbovo:** Formal analysis, Investigation, Writing – review & editing. **Godwin Ogbole:** Investigation, Writing – review & editing. **Hemant K. Tiwari:** Investigation, Writing – review & editing. **Carolyn Jenkins:** Investigation, Writing – review & editing. **Daniel T. Lackland:** Investigation, Writing – review & editing. **Adekunle G. Fakunle:** Investigation, Writing – review & editing, Data curation. **Ezinne Uvere:** Data curation, Writing – review & editing. **Onoja Akpa:** Formal analysis, Investigation, Writing – review & editing. **Hamisu A. Dambatta:** Data curation, Writing – review & editing. **Josephine Akpalu:** Data curation, Writing – review & editing. **Akinola Onasanya:** Data curation, Writing – review & editing. **Adeniji Olaleye:** Data curation, Writing – review & editing. **Okechukwu S. Ogah:**

Investigation, Writing – review & editing. **Sulaiman Y. Isah:** Data curation, Writing – review & editing. **Micheal B. Fawale:** Data curation, Writing – review & editing. **Akintunde Adebawale:** Data curation, Writing – review & editing. **Akinkunmi P. Okekunle:** Data curation, Writing – review & editing. **Donna Arnett:** Investigation, Writing – review & editing. **Abiodun M. Adeoye:** Investigation, Writing – review & editing. **Atinuke M. Agunloye:** Investigation, Writing – review & editing. **Abiodun H. Bello:** Data curation, Writing – review & editing. **Ahmed O. Idowu:** Data curation, Writing – review & editing. **Ahmad A. Sanusi:** Data curation, Writing – review & editing. **Adebimpe Ogunmodede:** Investigation, Writing – review & editing. **Simon A. Balogun:** Data curation, Writing – review & editing. **Adedeji A. Egberongbe:** Data curation, Writing – review & editing. **Folorunso T. Rotimi:** Data curation, Writing – review & editing. **Adeyemi Fredrick:** Data curation, Writing – review & editing. **Andrew O. Akinnuoye:** Data curation, Writing – review & editing. **Folu A. Adeniyi:** Data curation, Writing – review & editing. **Benedict Calys-Tagoe:** Data curation, Writing – review & editing. **Philip Adebayo:** Investigation, Writing – review & editing. **Oyedunni Arulogun:** Investigation, Writing – review & editing. **Obiageli U. Agbogu-Ike:** Data curation, Writing – review & editing. **Joseph Yaria:** Data curation, Writing – review & editing. **Lambert Appiah:** Data curation, Writing – review & editing. **Philip Ibinaiye:** Investigation, Writing – review & editing. **Arti Singh:** Data curation, Writing – review & editing. **Sunday Adeniyi:** Data curation, Writing – review & editing. **Oladotun Olalusi:** Data curation, Writing – review & editing. **Aliyu Mande:** Data curation, Writing – review & editing. **Olayemi Balogun:** Data curation, Writing – review & editing. **Rufus Akinyemi:** Data curation, Investigation, Methodology, Writing – review & editing. **Bruce Ovbiagele:** Data curation, Investigation, Methodology, Writing – review & editing, Funding acquisition. **Mayowa Owolabi:** Data curation, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that there are no conflicts of interests with the article. The article was written according to recommendation from International Committee of Medical Journals Editors.

Data availability

The primary data used in this article are made available as supplementary files and Tables All data submitted have complied with Institutional Ethical Review Board requirements and applicable government regulations.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jns.2023.122848>.

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