



# Pre-Stroke Depression in Ghana and Nigeria: Prevalence, Predictors and Association With Poststroke Depression

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## Abstract

**Objectives:** Depression is a risk factor for stroke. There is a knowledge gap on the predictors of prestroke depression in stroke survivors living in low- and middle-income countries (LMICs). We estimated prevalence and predictors of prestroke depression, as well as its association with poststroke depression (PSD) in the largest study of stroke in Africa. **Methods:** We evaluated information collected as part of the Stroke Investigative Research and Education Network (SIREN) study, a multicentre, case-control study conducted at 15 sites in Ghana and Nigeria. Prestroke depression status was ascertained in stroke survivors using a validated self-report tool, while PSD was assessed using a stroke specific screening tool for depression (“HRQOLISP-E”). Independent associations were investigated using complementary log-log regression and binary logit models. **Results:** Among 1,977 participants, prestroke depression was found in 141 (7.1%). In multivariate analyses, prestroke depression was significantly associated with tachycardia (OR = 2.22, 95% CI = 1.37-3.56) and low consumption of green leafy vegetables (OR = 1.91, 95% CI = 1.12-3.24). Forty-one (29.1%) of the prestroke depression sub-sample developed PSD. However, prestroke depression was not significantly associated with PSD. **Conclusion:** The findings should energize before-the-stroke identification and prioritization of limited treatment resources in LMICs to persons with depression who have multiple, additional, risks of stroke.

## Keywords

stroke burden, stroke risk factors, mental health complications, prestroke symptoms, Sub-Saharan Africa

## Introduction

Prior depression is a risk factor for stroke,<sup>1</sup> greater stroke severity<sup>2</sup> and poststroke disability.<sup>3</sup> Recent evidence suggests that identification and antidepressant treatment of depression in persons at risk of stroke provide protection against incident stroke and improve poststroke rehabilitation outcomes including greater odds of own home versus nursing home discharge.<sup>4</sup> Better understanding of prestroke depression and its correlates should thus be of interest to poststroke rehabilitation efforts, as well as policy regarding identification and treatment of depression in the population at increased risk of stroke.<sup>5</sup>

With studies reporting estimates of between 0.4%<sup>6</sup> and 52%,<sup>7</sup> prevalence of pre-stroke depression are not well established in the global literature. Also, while a personal history of depression is widely regarded as the best predictor of future depression in the general, stroke-free, population,<sup>8</sup> the association between pre-stroke and poststroke depression (PSD) remains unclear in stroke survivors.<sup>9</sup>

The knowledge gap on the prevalence, predictors and prognostic significance of prestroke depression in survivors living

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in low- and middle-income countries (LMICs) is even more striking. First, LMICs have more than 2 thirds of the worldwide burden of stroke.<sup>10</sup> Secondly, to the best of our knowledge, the only publicly available study investigating correlates of pre-stroke depression in a LMIC<sup>11</sup> found no link with baseline demographic, clinical or lifestyle factors in 148 Turkish stroke survivors. Yet, such information is desirable in LMICs, as it could inform before-the-stroke identification and prioritization of limited treatment resources to persons with depression who have multiple, additional, risks of stroke. Notably, information on prevalence, predictors and the mechanistic link between prestroke depression and PSD in African stroke survivors is currently unavailable.

In the present study, which is based on a sample of approximately 2000 stroke survivors from Ghana and Nigeria, we aimed to: 1). Estimate prevalence and factors associated with pre-stroke depression and 2), describe the relationship between prestroke depression and PSD.

## Methods

We evaluated information collected as part of the largest study of stroke in Africa, the Stroke Investigative Research and Education Network (SIREN). The SIREN is a multicentre, case-control study conducted at 15 sites in Ghana and Nigeria. The methodology of the SIREN has been fully described.<sup>12</sup> Here we provide a brief description relevant to the objectives of the present study.

## Subjects

Participants comprised 1,977 adult ischemic or hemorrhagic survivors of a first ever stroke who were consecutively recruited within 10 days of symptoms onset. The diagnosis of stroke was confirmed based on neuro-imaging (CT or MRI)<sup>13</sup> and clinical examination criteria. Ethical approval was obtained from all SIREN study sites.<sup>12</sup>

Written informed consent was obtained from all eligible stroke survivors and/or their next of kin (spouses or adult children) after the procedure of the study was explained to them either in English or the local languages. We excluded patients with a known previous history of stroke, those who were unable to communicate reliably (usually because of severe stroke, aphasia or severe dementia), and those with current hospitalization for coronary heart disease.

## Data Collection

**Ascertainment of prestroke depression.** Prestroke depression status was ascertained based on a self-report assessment tool adapted from the INTERSTROKE study.<sup>14</sup> The parent tool from which depression assessment was adapted is the short form fourth edition of the diagnostic and statistical manual of mental disorders Composite International Diagnostic Interview (CIDI) questionnaire for depression.<sup>15</sup> The CIDI short form has a sensitivity of 98.4% and a specificity of 72.7% in

clinical samples.<sup>15</sup> In the adapted CIDI short form depression questionnaire, respondents are asked whether, during the past 4 weeks (Instead of 12 months in the original CIDI-short form), the participant had felt sad, blue, or depressed persistently for 2 weeks or more, and if yes, further enquiries are made about a set of 7 other depression symptoms through Yes/No type questions: lose interest in things, feel tired or low on energy, gain or lose weight, trouble falling asleep, trouble concentrating, think of death, feeling worthless. Endorsement of 5 or more symptoms were defined as clinical depression.<sup>16</sup>

**Ascertainment of poststroke depression (PSD).** PSD was assessed using a stroke-specific screening tool for depression, the "HRQOLISP-E."<sup>17</sup> The tool is empirically designed from the psychoemotional domain of Health Related Quality of Life in Stroke patients (HRQOLISP-26).<sup>18</sup> HRQOLISP-E contains items corresponding to depressed mood, loss of interest in *work* and *leisure*, decreased energy or fatigability, and low self esteem/confidence. These items overlap with the symptoms described in the conceptual framework of depression in the 10th revision of the International Classification of Diseases.<sup>19</sup> HRQOLISP-E score of 20 out of a maximum of 30 demonstrates high agreement with the depression sub-scale of the Hospital Anxiety and Depression Scale (HADS-D) cutoff  $\geq 8$ . "The sensitivity and specificity rates are 77.1% and 76.6%, respectively, with posterior-test probability of 87% (95% C.I = 83%- 91%) and Cronbach's alpha = 0.939 (compared with 0.742 for the HADS-D)." Lower HRQOLISP-E scores represent more severe depression.

## Other Data Collection

The following information was obtained from all participants using a standardized questionnaire: demographic data, personal history of smoking and alcohol consumption, physical activities, medical history of hypertension, diabetes, and the use of medications for these conditions. Information on dietary patterns was obtained using the food frequency questionnaire. The severity of stroke was ascertained using the Stroke Levity Scale.<sup>20</sup> The average of 3 blood pressure (B.P) measurements was recorded. Along with the BP and pulse rates, anthropometric measurements of weight and height were also undertaken. Records of other relevant risk factors for stroke, including fasting plasma glucose and glycated hemoglobin (HbA1c) were also made.

## Definition of Risk Factors

Blood pressure measurements of  $\geq 140/90$  mmHg for up to 72 hours after stroke, a history of hypertension, or use of antihypertensive drugs before stroke or more than 72 hours after stroke were regarded as indicators of systemic hypertension. Diabetes was defined as a history of diabetes, use of drugs for diabetes, HbA1c  $>6.5\%$ , or a fasting plasma glucose concentration  $>7.0$  mmol/L measured after the

**Table 1.** Prestroke Depression and SIREN Study Participants Characteristics.

Variables	Overall sample, n(%) N = 1977	No depression, n(%) N = 1836	Depression, n (%) N = 141	Test statistics	p-value
Age, years				4.48	0.106
≤45	298(15.0)	276(15.0)	22(15.6)		
45-65	1092(55.2)	1004(54.7)	88(62.4)		
>65	587(29.7)	556(30.3)	31(22.0)		
Mean (SD)	58.6 (12.5)	57.0(14.04)	57.0(12.50)	1.46	0.145
Female gender	863(43.6)	794(43.2)	69(48.9)	1.78	0.182
Education				1.37	0.712
None	344(17.4)	321(17.5)	23(16.3)		
Primary	372(18.8)	347(18.9)	25(17.7)		
Secondary	533(27.0)	489(26.7)	44(31.2)		
Higher	726(36.8)	677(36.9)	49(34.8)		
Occupation				1.58	0.813
Skilled/professional	505(27.0)	467(27.0)	38(27.9)		
Semi-skilled	322(17.2)	296(17.1)	26(19.1)		
Manual	612(32.8)	568(32.8)	44(32.4)		
Retired	324(17.3)	305(17.6)	19(6.6)		
Others	105(5.6)	96(5.5)	9(6.6)		
Monthly income <100 USD	871(44.5)	817(45.0)	54(38.3)	2.36	0.125
Stroke severity				9.10	0.011
Mild	492(24.8)	462(25.1)	30(21.3)		
Moderate	777(39.2)	705(38.3)	72(51.1)		
Severe	712(35.9)	673(36.6)	39(27.7)		
Smoking (Ever)	181(9.3)	161(8.9)	20(14.3)	4.40	0.036
Pulse < 60/min (Bradycardia)	29(1.5)	27(1.5)	2(1.4)	0.00	0.963
Pulse >100/min (Tachycardia)	166(8.8)	144(8.2)	22(16.7)	10.83	0.001
BMI >30 kg/m <sup>2</sup>	337(20.9)	307(20.6)	30(25.9)	1.84	0.175
Hypertension	1869(95.4)	1734(95.3)	135(95.7)	0.05	0.82
Diabetes mellitus	746(38.1)	688(37.8)	58(41.1)	0.60	0.438
Diet					
Low fish	1703(93.1)	1574(92.7)	129(98.5)	6.33	0.012
Low vegetables	1400(76.6)	1287(75.8)	113(87.6)	9.38	0.002
Low fruits	1608(88.0)	1493(87.9)	115(88.5)	0.03	0.857
Alcohol (Ever)	559 (30.2)	531 (29.3)	58 (41.4)	9.41	0.009
Physical activity	1839(95.9)	1709(96.0)	130(94.2)	1.06	0.303

SIREN = Stroke Investigative Research and Education Network

post-acute phase. Obesity was defined in participants as a body mass index of  $\geq 30$  kg/m<sup>2</sup>. Tachycardia was defined as a resting pulse rate of  $\geq 100$  bpm, while pulse rates of  $< 60$  bpm were classified as bradycardia. Individuals were considered physically active if they were regularly involved in moderate exercise (walking, cycling, or gardening) pre-stroke. Regular intake of fish, green leafy vegetables and fruits was defined as intake of at least one serving of the respective food items per month. Alcohol users were categorized into current, former or never users of any alcoholic drink. Similarly, smoking status was defined as current, former and never smokers of a tobacco product.

### Statistical Analyses

We summarized pre-stroke depression, PSD, socio-demographic, and vascular risk factor variables using frequency and percentage

while mean and standard deviation (SD) were calculated for age and other continuous variables.

To explore factors associated with pre-stroke depression and PSD, Chi square and t-test was conducted for categorical and continuous variables, respectively. Due to the relatively small sample of survivors with pre-stroke depression in the present study, complementary log-log regression model<sup>21</sup> was fitted to quantify the effect of associated risk factor variables. Conversely, a binary logit model was fitted to explore variables associated with PSD.

The unadjusted and adjusted odds ratio (OR) and their 95% Confidence Intervals (95% CI) estimated from complementary log-log regression and binary logit models are presented. Only variables with p-values  $< 0.1$  were entered into multivariable analyses. Model fitness was assessed using residual analysis and goodness of fit tests. All analyses were conducted using Stata MP version 14.0.<sup>22</sup> Values of  $p < 0.05$  were considered significant.

**Table 2.** Results of Multivariate Complementary Log-Log Regression Showing Predictors of Prestroke Depression in Ghana and Nigeria.

Variables	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	P-value (adjusted)
Smoking			0.221
Never	Reference	Reference	
<b>Ever</b>	1.66(1.03-2.66)	1.40(0.82-2.42)	
Pulse rate			0.001*
60-100/Min (Normal)	Reference	Reference	
<b>&gt;100/Min (Tachycardia)</b>	2.14(1.36-3.39)	2.22(1.37-3.56)	
Fish diet			0.067
Regular	Reference	Reference	
<b>Low</b>	4.92(1.22-19.90)	3.70(0.91-15.03)	
Vegetable diet			0.017*
Regular	Reference	Reference	
<b>Low</b>	2.21(1.31-3.73)	1.91(1.12-3.24)	
Current alcohol use			0.066
No	Reference	Reference	
<b>Yes</b>	1.57(1.04-2.37)	1.51(0.95-2.39)	
Ever alcohol use			0.078
Yes	Reference	Reference	
<b>No</b>	1.80(1.17-2.78)	1.58(0.97-2.58)	

\*p&lt;0.05

## Results

### Subject Characteristics

There were 1,118 males and 853 females in the study sample (Table 1). Their mean age was  $58.6 \pm 12.5$  years. Over 82% of the participants had at least 6 years of formal education.

### Prestroke Depression

A total of 141 (7.1%) stroke survivors had prestroke depression. Rates of prestroke depression were higher among women (8.0%) than among men (6.4%). Table 1 also contains the risk factors for prestroke depression investigated in the present study.

In Table 2, tachycardia (OR = 2.22, 95% CI = 1.37-3.56) and low consumption of green leafy vegetables (OR = 1.91, 95% CI = 1.12-3.24) were independently associated with prestroke depression.

### Association of Prestroke Depression With PSD Symptoms

Five hundred and twelve (25.9%) participants had PSD symptoms. Greater stroke severity and low consumption of green leafy vegetables were the main independent correlates of PSD symptoms (Table 3).

Forty-one (29.1%) of the 141 survivors with prestroke depression had PSD symptoms. There was no statistically significant association between prestroke depression and PSD symptoms (Table 3).

## Discussion

In this large sample of Africans assessed within 10 days of surviving a first ever stroke, we found a prevalence of 7.1%

for depression occurring in the 4 weeks preceding the stroke. Prestroke depression was independently associated with tachycardia and low consumption of green leafy vegetables. Approximately 29.1% of survivors with prestroke depression developed PSD symptoms. However, there was no significant association between prestroke depression and PSD symptoms. The rate of PSD symptoms (25.9%) in this population was 3 times the prevalence of prestroke depression.

Rates of prestroke depression are not well established in the global literature, and prior studies, recently reviewed by Taylor-Rowan and Colleagues (2019),<sup>9</sup> have often reported widely varying rates. Our finding of 7.1% prevalence for prestroke depression in the present study is lower, but not substantially out of the global pooled average range of 7.4–15.2 estimated in a meta-analysis of studies relying on self-report evaluations similar to those of the present study.<sup>7,9,23</sup>

Our result for prevalence of prestroke depression also overlaps within 95% CI (5.9-8.3) of the 7.8% prevalence estimated for depression in a large representative sample of older adult Africans.<sup>24</sup> Ostensibly, this finding of overlapping rates of depression in the older adult population and a selected cohort at definite risk of stroke may be surprising given the fact that depression is a risk factor for stroke.<sup>1</sup> However, our results are in keeping with those of many previous studies suggesting that the prevalence of prestroke depression mirrors those of depression in the general adult population.<sup>9,23</sup>

The present study found significant associations between prestroke depression and 2 important indices of high cardiovascular risk profile and stroke (low vegetable diet and tachycardia).<sup>25</sup> However, given that in our previous study,<sup>16</sup> depression was not found to be among the topmost risk factors for stroke in Ghana and Nigeria, it would appear, at least in our study population, that the risk of stroke in persons with

**Table 3.** Association of Poststroke Depression With Prestroke Depression and SIREN Study Participants Characteristics.

Variables	Overall sample, n(%) N = 1977	No depression, n(%) N = 1465	Depression, n(%) N = 512	Test statistics	p-value
Prestroke depression	141(7.12)	100(6.8)	41(8.0)	0.80	0.371
Age, years				11.52	0.003
≤45	298(15.1)	230(15.7)	68(13.3)		
45-65	1092(55.2)	830(56.7)	262(51.2)		
>65	587(29.7)	405(27.7)	182(35.6)		
Mean (SD)	58.6(13.9)	58.04(13.82)	60.34(14.15)	-3.21	0.001
Female gender	863(43.6)	615(41.9)	248(48.3)	6.43	0.011
Education				5.46	0.141
None	344(17.4)	242(16.5)	102(19.9)		
Primary	372(18.8)	271(18.5)	101(19.7)		
Secondary	533(27.0)	393(26.9)	140(27.3)		
Higher	726(36.8)	557(38.1)	169(33.0)		
Occupation				5.39	0.250
Skilled/professional	505(27.0)	377(27.4)	128(25.9)		
Semi-skilled	322(17.2)	244(17.8)	78(15.8)		
Manual	612(32.8)	447(32.5)	165(33.4)		
Retired	324(17.3)	238(17.3)	86(17.4)		
Others	105(5.6)	68(5.0)	37(7.4)		
Monthly income <100 USD	871(44.5)	635(43.8)	236(46.6)	1.18	0.277
Stroke severity				94.21	<0.001
Mild	492(24.8)	432(29.4)	60(11.7)		
Moderate	777(39.2)	587(40.0)	190(37.0)		
Severe	712(35.9)	449(30.6)	263(51.3)		
Smoking (ever)	181(9.3)	149(10.4)	32(6.4)	7.03	0.008
Pulse rate < 60/Min (Bradycardia)	29(1.5)	22(1.5)	7(1.4)	0.05	0.828
Pulse rate >100/Min (Tachycardia)	166(8.8)	120(8.7)	46(9.4)	0.22	0.636
Obesity (BMI > 30 kg/m <sup>2</sup> )	337(20.9)	264(21.9)	73(18.0)	2.76	0.096
Hypertension	1869(95.4)	1375(94.8)	494(97.1)	4.47	0.035
Diabetes mellitus	746(38.1)	550(37.9)	196(38.6)	0.07	0.787
Diet					
Low fish	1703(93.1)	1255(93.0)	448(93.5)	0.18	0.675
Low vegetables	1400(76.6)	1058(78.5)	342(71.3)	10.34	0.001
Low fruits	1608(88.0)	1193(88.2)	415(87.4)	0.22	0.642
Alcohol					
Former	334(17.1)	264(18.3)	70(13.8)	6.82	0.033
Current	255(13.1)	194(13.4)	61(12.0)		
Never	1362(69.8)	986(68.3)	376(74.2)		
Physical activity	1839(95.9)	1364(95.9)	475(95.8)	0.02	0.881

SIREN = Stroke Investigative Research and Education Network

depression may be partly explained by the presence of other cardiovascular risk factors including tachycardia and poor diet. This finding is important in the context of stroke risk factors among Africans, and may enhance early identification of persons with depression who are at additionally increased risk of stroke. Such persons may be prioritized for stroke risk reduction management, including antidepressant treatment, which may be protective against incident stroke and enhance rehabilitation outcomes.<sup>4</sup>

Similar to many previous studies,<sup>6,9</sup> the prevalence of PSD symptoms in this population was several times that of prestroke depression. This may suggest that PSD do not necessarily represent a recurrence or worsening of pre-existing depression. Prior evidence<sup>26,27</sup> asserts that PSD is a unique disorder with distinct biological underpinnings from depression in the

general population. Given the foregoing, we were not surprised by our finding that prestroke depression in the present study was not significantly associated with PSD symptoms.

We note that similar to the present study, several studies<sup>9,28</sup> in the global literature did not find a statistical link between prestroke depression and PSD. Yet, some studies<sup>9,27</sup> report significant association between the 2 emotional disorders. It is well feasible that our failure to find a significant relationship between prestroke depression and PSD in the present study is due to the relatively small number of participants with pre-stroke depression. This situation may have resulted in loss of the required statistical power to detect a theoretical association between prestroke depression and PSD.

Our study has other limitations which, together, may have resulted in an underestimation of the prevalence of prestroke

depression. First, we excluded persons with coronary heart disease and those who were unable to communicate reliably because of severe stroke, aphasia or dementia. We note that this strategy might have precluded recruitment of persons representing the diversity of acute stroke survivors, thus affecting generalization of our findings. Second, we assessed patients for prestroke depression within 10 days of stroke. It is feasible that the burden of florid stroke symptoms, including altered level of consciousness, motor, and cognitive disturbances may have affected understanding and accurate self-reporting of prestroke mental health symptoms. Conversely, self-report is among the most common methods of ascertaining prestroke depression in the global literature.<sup>9</sup> Our assessment of PSD within 10 days of stroke may also have been too early for the substantive mechanism<sup>26</sup> underlying the poststroke emotional disorder to have fully evolve in some of the participants. A major strength is that, to the best of our knowledge, the present study presents the first insight into the predictors of prestroke depression in stroke survivors living in LMICs. Our large sample size, spread across 15 sites in 2 geographically expansive West-African countries, is representative of approximately one-third of the population of Sub-saharan Africa.

To conclude, we have found that the prevalence of prestroke depression in this African sample overlaps with those of the general older adult population. It is linked to low consumption of green leafy vegetables and tachycardia, 2 important indices of high cardiovascular risk profile and stroke. Prestroke depression also appears to be a distinct phenomenon from PSD in this population, with results showing no statistical association between the two. The finding from the present study are important to energize early identification of persons with depression who have additional multiple risks of stroke. Such persons may be prioritized for stroke risk reduction management. Future studies may wish to investigate the relationship between prestroke and, not only acute stage PSD, but longitudinal change in the trajectory of depression in the medium- and long-term periods after stroke.

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