# Prevalence and Prognostic Features of ECG Abnormalities in Acute Stroke

## Findings From the SIREN Study Among Africans

Abiodun M. Adeoye*, Okechukwu S. Ogah*, Bruce Ovbiagele†, Rufus Akinyemi‡, Vincent Shidali§, Francis Agyekum‖, Akinyemi Aje*, Oladimeji Adebayo*, Joshua O. Akinyemi*, Philip Kolo¶, Lambert Tetteh Appiah#, Henry Iheonye§, Uwanuruochi Kelechukwu**, Amusa Ganiyu††, Taiwo O. Olunuga‡, Onoja Akpa*, Ojo Olakanmi Olagoke*, Fred Stephen Sarfo#, Kolawole Wahab¶, Samuel Olowookere¶, Adekunle Fakunle*, Albert Akpalu‖, Philip B. Adebayo‡‡, Kwadwo Nkromah‖, Joseph Yaria*, Philip Ibinaiye§, Godwin Ogbole*, Aridegbe Olumayowa§§, Sulaiman Lakoh*, Benedict Calys-Tagoe‖, Paul Olowoyo‖‖, Chukwuonye Innocent**, Hemant K. Tiwari¶¶, Donna Arnett##, Osaigbovo Godwin††, Bisi Ayotunde*, Josephine Akpalu‖, Okeke Obiora**, Odo Joseph*, Adeleye Omisore***, Carolyn Jenkins††, Daniel Lackland†, Lukman Owolabi†††, Suleiman Isah†††, Abdu H. Dambatta†††, Morenikeji Komolafe***, Andrew Bock-Oruma‡‡‡, Ezinne Sylvia Melikam*, Lucius Chidiebere Imoh**, Taofiki Sunmonu§§§, Mulugeta Gebregziabher†, Oluyemisi Olabisi***, Kevin Armstrong†, Ugochukwu U. Onyeonoro**, Emmanuel Sanya¶, Atinuke M. Agunloye*, Luqman Ogunjimi*, Oyedunni Arulogun*, Temitope H. Farombi*, Olugbo Obiabo‡‡‡, Reginald Obiako§, Mayowa Owolabi*, on behalf of the SIREN Team as part of the H3Africa Consortium

*Ibadan, Nigeria; Charleston, SC, USA; Abeokuta, Nigeria; Zaria, Nigeria; Accra, Ghana; Ilorin, Nigeria; Kumasi, Ghana; Umuahia, Nigeria; Jos, Nigeria; Ogbomoso, Nigeria; Ido-Ekiti, Nigeria; Birmingham, AL, USA; Lexington, KY, USA; Ile-Ife, Nigeria; Kano, Nigeria; Ogara, Nigeria; and Owo, Nigeria*

The authors report no relationships that could be construed as a conflict of interest.

This work is supported by the National Institutes of Health and National Institute of Neurological Disorders and Stroke (Grant 1U54HG007479).

From the *University of Ibadan, Ibadan, Nigeria; †Medical University of South Carolina, Charleston, SC, USA; ‡Federal Medical Centre, Abeokuta, Nigeria; §Ahmadu Bello University, Zaria, Nigeria; ‖University of Ghana Medical School, Accra, Ghana; ¶University of Ilorin Teaching Hospital, Ilorin, Nigeria; #Komfo Anokye Teaching Hospital, Kumasi, Ghana; **Federal Medical Center, Umuahia, Nigeria; ††Jos University Teaching Hospital, Jos, Nigeria; ‡‡Ladoke Akintola University of Technology, Ogbomoso, Nigeria; §§Sacred Heart Hospital, Abeokuta, Nigeria; ‖‖Federal University Teaching Hospital, Ido-Ekiti, Nigeria; ¶¶University of Alabama at Birmingham, Birmingham, AL, USA; ##University of Kentucky at Lexington, Lexington, KY, USA; ***Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria; †††Aminu Kano Teaching Hospital, Kano, Nigeria; ‡‡‡Delta State University Teaching Hospital, Ogara, Nigeria; and §§§Federal Medical Centre, Owo, Nigeria. Correspondence: M. Owolabi (mayowaowolabi@yahoo.com).

GLOBAL HEART

VOL. ■, NO. ■, 2017
ISSN 2211-8160/$36.00.
http://dx.doi.org/10.1016/j.gheart.2017.01.002

## ABSTRACT

**Background:** Africa has a growing burden of stroke with associated high morbidity and a 3-year fatality rate of 84%. Cardiac disease contributes to stroke occurrence and outcomes, but the precise relationship of abnormalities as noted on a cheap and widely available test, the electrocardiogram (ECG), and acute stroke outcomes have not been previously characterized in Africans.

**Objectives:** The study assessed the prevalence and prognoses of various ECG abnormalities among African acute stroke patients encountered in a multisite, cross-national epidemiologic study.

**Methods:** We included 890 patients from Nigeria and Ghana with acute stroke who had 12-lead ECG recording within first 24 h of admission and stroke classified based on brain computed tomography scan or magnetic resonance imaging. Stroke severity at baseline was assessed using the Stroke Levity Scale (SLS), whereas 1-month outcome was assessed using the modified Rankin Scale (mRS).

**Results:** Patients' mean age was 58.4 ± 13.4 years, 490 were men (55%) and 400 were women (45%), 65.5% had ischemic stroke, and 85.4% had at least 1 ECG abnormality. Women were significantly more likely to have atrial fibrillation, or left ventricular hypertrophy with or without strain pattern. Compared to ischemic stroke patients, hemorrhagic stroke patients were less likely to have atrial fibrillation (1.0% vs. 6.7%; p = 0.002), but more likely to have left ventricular hypertrophy (64.4% vs. 51.4%; p = 0.004). Odds of severe disability or death at 1 month were higher with severe stroke (AOR: 2.25; 95% confidence interval: 1.44 to 3.50), or atrial enlargement (AOR: 1.45; 95% confidence interval: 1.04 to 2.02).

**Conclusions:** About 4 in 5 acute stroke patients in this African cohort had evidence of a baseline ECG abnormality, but presence of any atrial enlargement was the only independent ECG predictor of death or disability.

Stroke is a common neurologic condition in all regions of the world. Of the 14.1 million people who died of cardiovascular diseases (CVD) in 2012 in the world, stroke accounted for 6.7 million deaths [1]. Many people who suffer acute stroke have underlying CVD such as hypertension, atrial fibrillation, and ischemic heart disease [2].

These underlying CVD are associated with several pre-existing electrocardiographic (ECG) anomalies such as rhythm and conduction abnormalities, and left ventricular hypertrophy (LVH) with or without St-T wave changes.

However, several researchers have postulated the existence of a brain-heart axis whereby structural brain lesions by themselves result in electrocardiographic changes [3]. The precise mechanism that leads to the development of these ECG changes is still uncertain, though increasing evidence suggests that it is mainly due to autonomic nervous system dysregulation [3,4]. Whereas some authors attribute these ECG changes in acute stroke to underlying CVD, others have demonstrated their presence in acute stroke patients without underlying CVD [5,6].

Irrespective of pre-existing cardiac diseases or not, observing an abnormal ECG in an acute stroke patients more than doubled their mortality rate at 6 months [5] and these abnormal ECG changes have not been shown to be perfect predictive tool for stroke subtypes [6,7]. Although cardiac arrhythmia, such as atrial fibrillation, and LVH have been linked with the occurrence and prognosis of acute stroke, the prognostic value of repolarization changes commonly seen after stroke such as ST-segment depression as well as T-wave and U-wave abnormalities still remains unclear [8,9].

Despite the common occurrence of stroke in Africa, there is sparse data on the prevalence and prognostic significance of ECG abnormalities in acute stroke in the region. In addition, there is inadequate data on the contributions of cardiac arrhythmias, conduction abnormalities, LVH, QTc prolongation, and QRS prolongation on 1-month case fatality in acute stroke especially in the African context. Understanding these interactions will help develop interventions to reduce the morbidity and mortality associated with acute stroke.

We investigated the prevalence of specific baseline ECG abnormalities in Africans with acute stroke and their prognostic effect on severe disability or death at 1-month after stroke.

## METHODS

### Study design

Design of the SIREN (Stroke Investigative Research And Education Network) study has been described elsewhere [10]. It is a multicenter case-control study involving several sites in Nigeria and Ghana, which has been running since August 2014. Ethical approval was obtained from the institutional ethical committees of all study sites and written informed consent was obtained from all subjects.

Cases included consecutively consenting adults (18 years of age or older) with first clinical stroke within 8 days of current symptom onset, or "last seen without deficit" with cranial computer tomography or magnetic resonance imaging scan performed to confirm diagnosis within 10 days of symptom onset. We excluded those with stroke mimics, primary subarachnoid hemorrhage and previous strokes that were not radiologically ascertained. Stroke severity was assessed at baseline using the Stroke Levity Scale (SLS) [11]. One-month outcome was assessed using the modified Rankin scale (mRS) [11]. Other clinical and laboratory information were obtained according to the SIREN protocol [10].

### Electrocardiography

A standard (resting) 12-lead ECG was performed in each subject using a commercially available ECG machine at 25 mm/s and 1 mV/cm calibration. All the 12-lead ECGs were obtained within 24 h after the onset of stroke. The ECG tracings were independently analyzed by the cardiologists who were unaware of the details of the clinical status of the patients. Abnormalities obtained from the ECGs were defined according to standard criteria as shown in Table 1 [12,13]. Left ventricular hypertrophy was diagnosed using the following criteria: Sokolow-Lyon voltage (sum of the amplitudes of S-wave in V1 and R-wave in V5 or V6 $\geq$3.5 mV), sex-specific Cornell voltage (sum of the amplitudes of S-wave in V3 and R-wave in aVL of 2.0 mV in women and of 2.8 mV in men). Cornell's product (CP) was calculated as the product of Cornell voltage times QRS duration. Repolarization abnormalities in leads V5 or V6 indicated typical strain when there was down-sloping convex ST segment with an inverted asymmetrical T-wave opposite to the QRS axis [14,15]. QT interval was determined using the tangent method [16]. The measured QT interval was corrected for heart rate using the Bazett's formula. Prolonged QT interval was considered present when the QTc was >450 ms and >440 ms in women and men, respectively. Presence of other St-T wave changes were documented according to standard criteria [12]. ECG definitions of criteria are in Table 1.

### Data management and analysis

Quantitative variables were summarized using mean $\pm$ SD for normally distributed and median for asymmetric variables. Frequency and percentage was computed for categorical variables. To investigate the statistical significance of the difference in continuous variables according to sex and stroke type, independent samples Student t test was used. For categorical variables, the chi-square test for the comparison of proportions was used.

Total mRS scores of 0 to 3 and 4 to 6 were categorized as good and poor, respectively. Association among selected demographic, clinical characteristics, and ECG findings was investigated at bivariate and multivariate levels. For bivariate analysis, chi square test was used while binary logistic regression was used for multivariate. Criteria for inclusion of variables in the logistic regression model was a p value <0.05 in the bivariate or previous report in literature or basic demographic factors (age and sex). Goodness of fit was assessed using the Hosmer-Lemeshow test.