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Low population prevalence of atrial fibrillation in rural Uganda: A community-based cross-sectional study

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ABSTRACT

Objectives: Atrial fibrillation (AF) is a major risk factor for stroke, which is the leading cause of cardiovascular mortality in sub-Saharan Africa. However, there is limited population-based epidemiological data on AF in sub-Saharan Africa. We sought to estimate the prevalence and correlates of AF in rural Uganda.
Methods: We conducted a cross-sectional study using community health fairs in 2015 targeting eight villages in rural Uganda. Study participants completed a medical history, a clinical exam, blood collection, and 12 lead electrocardiographic (ECG) screening. Of 1814 participants enrolled in a parent cohort study that includes 98% of adults residing in the geographic area, 856 attended a health fair and were included in this study. Our primary outcome was AF or atrial flutter. We modelled population prevalence of the outcome with inverse probability of treatment weighting using data collected from the full population.
Results: 856 (47.2%) adults in the area attended a health fair and were included in the analysis. Health fair attendees were older (42 vs 34 years, $P < 0.0001$), in worse self-reported health ($P < 0.0001$) and more likely to be female (62% vs 49%, $P < 0.0001$) compared with non-attendees. After applying weights, the estimated population mean age was 37.7 ± 14.9 years. 15% of the population was overweight or obese and 1.9% had left atrial enlargement on ECG. Despite this, the weighted estimate of AF was 0% (95%CI 0–0.54%).
Conclusions: AF appears less prevalent in rural Uganda than in developed countries. The explanations for this finding may be genetic, environmental or related to survivorship bias.

1. Introduction

Atrial fibrillation (AF) is a major public health concern in developed nations with clinical sequelae including heart failure, cardio-embolic stroke and cardiovascular mortality. Although data from sub-Saharan Africa are sparse, model-based estimates from the Global Burden of Disease Study suggest AF is the fastest growing cardiovascular disease in the region, their data also suggests that factors other than rheumatic heart disease are responsible for the AF burden [1]. The authors highlight the need for significant additional surveillance and detailed analysis of the mechanisms of atrial fibrillation. If corroborated by population-based data, such estimated trends in AF would be of high public health import, because its risk factors, such as alcohol, hypertension, peripheral vascular disease and tobacco use, and clinical sequelae, such as stroke, are among the highest burden non-communicable public health problems in the region [1,2].

Quality epidemiological data on AF in sub-Saharan Africa are needed to better inform burden of disease models [1]. A meta-analysis of cross-sectional studies including both clinic-based and community-based data from the U.S., Europe, and Commonwealth countries, estimated a prevalence of AF of 2.3% rising to 4.4% among those ≥65 years old [3]. Similar attempts to estimate the prevalence of AF in sub-Saharan Africa have been conducted, but these studies were commonly hospital-based and/or have been limited by selection and measurement bias [4,5]. The objective of this study was to use population-

Abbreviations: AF, atrial fibrillation; NCD, non-communicable disease; ECG, electrocardiogram; HbA1c, hemoglobin A1c; HIV, human immunodeficiency virus; LVH, left ventricular hypertrophy; BMI, body mass index; MET, metabolic equivalent of task; IPT, inverse probability of treatment.

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representative data to estimate the prevalence of electrocardiogram (ECG)-detected AF and its correlates in a rural Ugandan community.

2. Material and methods

2.1. Study design and participants

Residents of Nyakabare Parish were invited to attend free community health fairs by means of radio announcements, printed posters, church announcements and endorsements from community leaders. The health fairs were conducted daily between June 25–29, 2015 in a geographical region approximately 22 km outside of Mbarara Town in southwestern Uganda. The area is rural, the local economy is based primarily on subsistence farming, and both food and water insecurity are common [6]. Prior to the health fairs, during June 2014–May 2015, all adult residents in the parish were enumerated in a population census and invited to participate in a longitudinal cohort study. Approximately 98% (1814 of 1851) of eligible adults consented to participate and completed interviews.

2.2. Data collection

There were two primary sources of data from this study: [1] population census interviews and [2] the community health fairs. During the 2014–2015 population census, we collected demographic, social and geographical variables from virtually all Nyakabare Parish residents. Thus, we had detailed information about the whole population (including demographic, social, psychological and geographical data) eligible to attend the health fairs, whether they attended or not. During health fairs, participants completed a survey administered by trained research assistants to ascertain medical history and sociodemographic characteristics. Physical activity was assessed using the International Physical Activity Questionnaire and converted into metabolic equivalent of task (MET) minutes and divided into three categories: active, minimally active and inactive [7]. Smoking was assessed using a version of the WHO Steps Questionnaire [8].

Participants also underwent short clinical examinations and blood sampling to assess height, weight, blood pressure, creatinine, hemoglobin A1c (HbA1c, Siemens DCA Vantage, Munich, Germany), serum lipids, and human immunodeficiency virus (HIV) rapid antibody testing based on the 2010 Ugandan National HIV Testing Guidelines algorithm. Lastly, the patients underwent a 10-second seated ECG recording using a portable ECG machine (CardioCard Digital ECG Box with CardioCard software, Nasiff Associates, New York, USA).

2.3. ECG interpretation

ECGs were interpreted by a board-certified cardiac electrophysiologist (AA) using a standardised interpretation sheet with 89 possible itemized categories. ECG left atrial enlargement was defined as either a biphasic P-wave in lead V1 with a large negative deflection (>0.1 mV) or prolongation of the P-wave duration to >0.12 s with a widely notched appearance [9]. ECG left ventricular hypertrophy (LVH) was defined using the Sokolow-Lyon criteria of the S wave in V1 or V2 and an R wave in V5 or V6 ≥ 3.5 mV [10]. Atrial fibrillation was defined as the presence of fibrillatory waves associated with an irregular ventricular response. Atrial flutter was defined as the presence of rapid flutter waves [11]. Left bundle branch block was defined as a QRS duration of >0.12 s with a wide slurred R wave in leads I, aVL, V5 and V6, and absent Q waves in leads I, V5 and V6. A Q wave myocardial infarction was defined per the ACC/AHA definition [12].

2.4. Statistical analysis

We described our sample using both standard descriptive techniques of the health fair sample and weighted population estimates. For unweighted characteristics, continuous data are presented as mean ± SD or median with interquartile range (IQR), depending on their distribution. Normality was assessed visually with the use of histograms. Categorical data are expressed as a percentage with frequency with missing data recorded as missing.

To estimate weighted population characteristics and outcomes, we constructed sampling weights using inverse probability of treatment (IPT) weighting. We first estimated propensity to participate in the health fair using a logistic regression model that included variables which we expected to determine participation: sex, age, marital status, educational attainment, household asset wealth, village of residence, distance from the health fair, difference between the altitude of the household residence and the altitude of the health fair, heavy alcohol use, self-reported HIV status, self-reported overall health, social network size, index of social participation, food insecurity, and water insecurity. The inverse of the predicted conditional probabilities of health fair attendance were applied as IPT weights [13]. The IPT weights enabled population estimates to be generated from the health fair data. We assessed the accuracy of this method using variables that were not included in the IPT model for which we had values for the whole population (as shown in Supplementary Table 2). We also assessed the sensitivity of the model to extreme weights using trimming at the 95th/5th percentiles (as shown in Supplementary Table 4).

We generated population-representative estimates of risk factors and ECG findings applying the sampling weight technique described above. Our primary outcome of interest was the prevalence of AF. Most proportions are presented with logit-transformed confidence intervals and survey design incorporated via Taylor linearization. However, this approach cannot estimate confidence intervals if the sample proportion is 0%, as it was for some of our outcomes. For such variables, we approximated the confidence interval by calculating Wilson confidence intervals, and then multiplying the upper bound by the design factor from a similar outcome (left bundle branch block). We were unable to conduct our pre-planned regression modelling to identify AF correlates due to zero cells in our primary outcome. All analyses were performed using Stata version 14 (StataCorp LP, College Station, Texas).

2.5. Ethical considerations

All study procedures were approved by the institutional review committees of the Mbarara University of Science and Technology and Partners Healthcare. Consistent with national guidelines, we also obtained clearance for the study from the Ugandan National Council of Science and Technology and from the Research Secretariat in the Office of the Ugandan President. All participants gave written informed consent to participate.

3. Results

Of the 1814 adults included in the Nyakabare parish census, 856 (47.3%) presented to one of the five health fairs. The sample consisted of 320 (37.5%) men, the mean age was 42.3 ± 17.5 years, and the mean BMI was 24.7 ± 5.1 kg/m^2 as shown in Table 1. There were 105 (12.3%) participants aged <25 years old and 127 (14.8%) aged >65 years old. Forty participants (4.7%) had a positive HIV test result. Four-hundred-and-six (47.4%) had completed at least primary education. Comparing health fair attendees to those in the census who did not attend, women were more likely to attend than men ($P < 0.0001$, Supplementary Table 1). Health fair attendees were older ($P < 0.0001$) and more likely to report bad or very bad overall health ($P < 0.0001$), but were similar in household asset wealth ($P = 0.3$) and village location ($P = 0.1$). Twenty-eight (3.3%) participants had missing ECG data, but were similar in other characteristics as the rest of the sample (Supplementary Table 3).

3.1. Weighted population estimates of atrial fibrillation risk factors

Using IPT weights, the entire population was defined by a mean age of 37.7 ± 14.9 years, BMI 24.4 ± 4.5 kg/m^2, 2.1% with diabetes, 8.7% with hypertension, 3.9% with self-report of a prior myocardial infarct or heart failure and 3.1% with a prior stroke (Table 1). Almost 30% of the population had consumed alcohol within the past year, of which 17% met criteria for binge drinking (≥6 drinks in one occasion). Approximately one quarter (26.4%) were former or current smokers. The majority (75.3%) had high levels of physical activity.

3.2. ECG findings

In weighted estimates, approximately two-thirds of the population had a normal ECG (67.7%, 95% CI 62.4 to 72.6, Table 2). ECG-defined left atrial enlargement was found in 1.9% (95% CI 1.2 to 3.2) and left ventricular hypertrophy in 1.1% (95% CI 0.6 to 1.9). Despite this, there were no cases of atrial fibrillation or atrial flutter detected (0%, 95% CI 0% to 0.54%). Trimmed weight estimates at the 95th/5th percentiles were similar to the untrimmed estimates (Supplementary Table 4).

4. Discussion

In this cross-sectional, population-based study in rural Uganda, we found a 0% prevalence of AF or atrial flutter using single-point 12 lead ECG screening. By applying weights derived from whole-population data to account for self-selection into health fair participation, we obtained a population estimate of AF prevalence with an upper bound confidence interval of approximately 0.5%. These findings are unexpected given the prevalence of multiple established AF risk factors in this cohort, including obesity, hypertension, left atrial enlargement and ischemic heart disease/heart failure [14–17]. Our results contrast with a large meta-analysis of 30 studies—all from developed countries—that used similar single-point screening to estimate the

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Table 1
Cohort of subjects completing a resting electrocardiogram at a community health fair and population characteristics.

Characteristic	Unweighted study sample ($N = 856$)	Population weighted estimates
Age	42.3 ± 17.5 years	37.7 ± 14.9 years
<30 years old	24.5% ($n = 210$)	37.8%
30–39 years old	23.0% ($n = 197$)	20.7%
40–49 years old	20.0% ($n = 171$)	16.4%
50–59 years old	13.6% ($n = 116$)	11.1%
60–69 years old	7.7% ($n = 66$)	5.6%
>70 years old	11.2% ($n = 96$)	8.4%
Male sex	37.5% ($n = 320$)	49.3%
Body mass index	24.7 ± 5.1 kg/m^2	24.4 ± 4.5 kg/m^2
History of renal disease	1.9% ($n = 16$)	1.4%
Creatinine (μmol/L)	62.8 ± 15.0	63.6 ± 14.1
Diabetes mellitus	3.4% ($n = 29$)	2.1%
HbA1c	5.3 ± 0.9	5.2 ± 0.6
Hypertension	11.6% ($n = 99$)	8.7%
Systolic blood pressure (mm Hg)	125 ± 22	122 ± 18
Diastolic blood pressure (mm Hg)	80 ± 13	78 ± 12
Hyperlipidemia	2.7% ($n = 23$)	1.7%
Total Cholesterol (mmol/L)	4.2 ± 1.1	4.1 ± 1.0
High density lipoproteins (mmol/L)	1.1 ± 0.4	1.1 ± 0.4
Prior AMI or heart failure	5.6% ($n = 48$)	3.9%
Prior stroke	2.7% ($n = 23$)	3.1%
History of COPD	0.8% ($n = 7$)	0.7%
Former smokers	19.7% ($n = 168$)	14.9%
Current smokers	10.9% ($n = 93$)	11.5%
Lifetime consumption of alcohol		
Never	40.0% ($n = 342$)	42.3%
>5 years ago	20.1% ($n = 172$)	17.2%
1–5 years ago	9.4% ($n = 80$)	11.3%
<1 year ago	30.6% ($n = 262$)	29.2%
HIV Seropositive	4.7% ($n = 40$)	4.2%
IPAQ physical activity category		
Inactive	12.0% ($n = 102$)	10.7%
Minimally active	11.6% ($n = 99$)	13.6%
Active	76.1% ($n = 652$)	75.7%
Educational attainment		
None	18.4% ($n = 158$)	13.0%
Some primary education	34.2% ($n = 293$)	26.2%
Complete primary education	23.6% ($n = 202$)	22.5%
Primary and more	23.8% ($n = 204$)	38.3%

HbA1c – Hemoglobin A1C, AMI – Acute myocardial infarction, COPD – Chronic obstructive pulmonary disease, HIV – Human Immunodeficiency Virus, IPAQ – International Physical Activity Questionnaire.

prevalence of AF in the all-ages adult population to be 2.3% (95% CI 2.2 to 2.4). Importantly, our unweighted sample had 127 participants ≥65 years old. Our results are pertinent to public health programmers in sub-Saharan Africa, which suffers a dearth of non-communicable disease epidemiological data that can be used to inform health policy [1].

Prior studies of AF in sub-Saharan Africa have typically been based on samples of hospitalized patients, which limit generalizability or promote selection bias. For example, participants in inpatient studies from the region are more likely to be of higher socioeconomic status relative to the general population and are selected for medical comorbidity [4,5]. Shavadia et al. retrospectively analysed private hospital admissions in Nairobi, Kenya, and observed a combined prevalence of 0.7% for AF or atrial flutter [4]; 60% of these patients had either persistent or permanent AF and thus, would likely have been detected by single-point screening in a study design such as ours. Notably, a disproportionate fraction of participants in this study were not of African background. Additionally, the mean age of those with AF was 67 years old, and the most common predisposing factors to AF were hypertension, diabetes and heart failure. Similarly, in South Africa, Sliwa et al. examined presentations to a cardiology unit to explore the characteristics of AF [5]. Of 5328 cardiac cases with a mean age of 59, only 4.6% presented with AF. This estimate is lower than expected given that the study sample was restricted to cardiac cases from a specialist medical center. In this sample, they found a high rate of primary valve disease, affecting 29% of cases. Only one study of AF from sub-Saharan Africa has been community-based, and this study from Tanzania reported a similarly low prevalence of AF (0.67%) among 2232 study participants over 70 years old (mean age 77.9 years old) [18]. This estimate is much lower than has been reported among similar age groups elsewhere globally [3,18].

Table 2
Electrocardiogram findings.

ECG finding	Study sample estimates ($N = 828$)	Weighted population estimate [95% CI]
Normal ECG	65.8% $n = 564$	67.7% [62.4 to 72.6]
Left atrial enlargement	2.3% $n = 20$	1.9% [1.2 to 3.2]
Left ventricular hypertrophy	1.6% $n = 14$	1.1% [0.6 to 1.9]
Left bundle branch block	0.7% $n = 6$	0.7% [0.3 to 1.8]
Q wave myocardial infarction	1.2% $n = 10$	0.8% [0.4 to 1.5]
Atrial flutter	0% $n = 0$	0% [0 to 0.54[a]]
Atrial fibrillation	0% $n = 0$	0% [0 to 0.54[a]]

ECG – electrocardiogram.
[a] Confidence intervals for population estimates of atrial flutter and atrial fibrillation were determined using the design effect from left bundle branch block (1.184), which was selected based on its similar proportion and pathophysiology with atrial tachycardias.

These data, in combination with our findings, suggest that the prevalence of AF in sub-Saharan Africa is lower than in high-income countries and challenge modelling estimates suggesting that AF might be of much greater impact in the region than in higher-income settings. The 2010 Global Burden of Disease Study hypothesized that AF, alongside peripheral vascular disease, was the fastest growing cardiovascular disease in sub-Saharan Africa [1]. However, GBD estimates lack population-based prevalence data and mainly rely on risk factor modelling from South Africa to derive estimates [19]. Thus, the GBD investigators have called for additional studies like ours to improve population estimates of cardiovascular disease [1].

We propose several possible explanations for the low prevalence of AF observed. First, genetic predisposition to AF might differ in this population. Although there are multiple genetic mutations that have been identified as risk factors for AF in those of European and Asian ancestry [20], similar studies are lacking from the African population. Determining whether such mutations are prevalent among persons in sub-Saharan Africa or whether unique genotypes are potentially protective against AF are important areas for future investigation. The SIGNAL study is currently mapping the human genome in sub-Saharan African populations and intends to describe genetic determinants of arrhythmia in this population [21]. Interestingly, among African-Americans of mixed ancestry, for every 10% increase in genetic European ancestry, there is a 13% higher risk of incident AF, which supports a protective effect of African ancestry [22].

Second, persons in low-income settings in sub-Saharan Africa are exposed to markedly different environmental exposures, many of which are observable in the present study, compared with persons in high-income countries. Rates of physical activity were extremely high in our study, with 75.3% of the population classified active. However, it should be noted that, in high-income countries, AF follows a U-shaped pattern in relation to physical activity, with athletes experiencing higher rates of AF compared to those with moderate physical activity [15]. Additionally, our measured prevalence of smoking and binge drinking were lower than those measured in United States general populations [23,24]. Despite these differences, there are numerous environmental factors that could theoretically predispose persons in sub-Saharan Africa to a higher risk of AF, such as higher rates of untreated hypertension, diabetes mellitus and rheumatic valvular disease [25–27]. Notably, our estimated prevalence of left atrial enlargement was 1.9%, and would be expected to increase the risk of AF.

Another potential explanation for a lower detected prevalence of AF in sub-Saharan African populations is survivorship bias. In a prospective cohort of adults with AF in Cameroon, 29.5% died at a mean follow-up of

318 days. Additionally, 12.5% suffered a stroke and 26.1% presented with severe heart failure [28]. These poor outcome rates are markedly higher than those observed in a similar longitudinal cohort study in Europe, in which only 5.7% of patients died and 0.9% suffered a stroke or transient ischemic attack at 1 year [29]. Survivorship bias might be particularly present in rural populations, where barriers to emergency cardiac care are significant. These data suggest that patients with AF in sub-Saharan Africa might potentially die or suffer debilitating strokes, thereby leading to under-estimate of disease burden from cross sectional, community-based studies.

Given the low prevalence of AF in our study, in combination with the high existing burden of other non-communicable disease and limited resources, it is reasonable to consider how our data should be interpreted to inform public health strategies in the region. These data might suggest that AF is less of a priority in this population than previously considered. However, the population in sub-Saharan Africa >65 years old is expected to grow from 40.6 million currently to 150.5 million by the year 2050, which has significant potential to alter AF epidemiology [30]. Moreover, because health outcomes among people with AF in sub-Saharan Africa appear worse, continued attention to AF despite its low prevalence may be warranted [28]. AF management appears suboptimal in studies from sub-Saharan Africa, with substantial evidence of both overtreatment and undertreatment. For example, in the above-mentioned Cameroonian cohort, only one-third of patients who warranted anticoagulation based on $CHADS_2$ stroke risk score were receiving anticoagulation therapy. Conversely, more than one-fifth of participants who did not require anticoagulation were receiving it [28]. Interventions to increase awareness and management of AF—combined with increased access to direct oral anticoagulants not requiring monitoring may offer a simple, feasible, and cost-effective method of stroke prevention in these settings [31]. For these reasons, continued careful monitoring of the emergence of AF is arguably warranted, until such time that our findings are corroborated in other populations and older age groups.

We acknowledge limitations in our work. First, not all Nyakabare Parish residents presented to a health fair, which may have subjected our estimates to selection bias. This may have been, in part, due to the symptomatology of AF itself (e.g., fatigue and dyspnoea). We leveraged census data from the whole population to generate reliable population-estimates using IPT weighting. Because parish residents who did not attend the health fair were more likely to report better health and be younger than those who did attend, it is unlikely that a whole-population sample would have significantly increased our low estimates – rather the opposite may have been true. Second, single-point ECG screening can be limited in detecting paroxysmal AF. Future studies should use continuous single lead ECG monitors to improve detection rates. Third, our study included all adult participants. Whilst the sample contained 127 participants over the age of 65, the mean age is still younger than that typically seen in the AF population. However, prior African studies recruiting only older participants have demonstrated a similarly low AF prevalence [4]. Lastly, it is challenging to obtain a validated health history in areas with poor diagnostic capacity, lack of electronic health records, and low health literacy. We attempted to offset this limitation by using clinical examination and direct collection of clinical and biomarker data to measure AF risk factors.

Future studies should focus on larger sample sizes, household-based sampling, and follow-up to corroborate our findings and estimate the long-term risk of AF in sub-Saharan Africa. Addition of echocardiography to a similar cohort may better assess the risk of AF by measuring chamber enlargement and/or valvular disease. Increased attention to the genetics, risk factors, and outcomes of AF in sub-Saharan African populations will also be helpful for understanding the epidemiology of AF, and populating risk-prediction models, such as the $CHADS_2$-VASc score, which still require regional validation.

5. Conclusion

In a community-based, adult population in rural Uganda, we estimated a population prevalence of AF below 0.54% based on single-point ECG screening, a low prevalence compared to investigators studying AF in developed countries. Future studies should seek to confirm whether our findings replicate in other populations and consider the optimal public health response to cardiovascular conditions in the region.

Conflict of interest

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

Acknowledgements and affiliations

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Appendix A. Supplementary data

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