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Predisposing factors and incidence of newly diagnosed atrial fibrillation in an urban African community: insights from the Heart of Soweto Study

Karen Sliva,1,2 Melinda Jane Carrington,2,3 Eric Klug,4 Lionel Opie,1 Geraldine Lee,2 Jocasta Ball,3 Simon Stewart2,3

ABSTRACT
Background Little is known about the incidence and clinical characteristics of newly diagnosed atrial fibrillation/flutter (AF) in urban Africans in epidemiological transition.

Methods This observational cohort study was carried out in the Chris Hani Baragwanath Hospital in Soweto South Africa. A clinical registry captured detailed clinical data on all de novo cases of AF presenting to the Cardiology Unit during the period 2006–2008.

Results Overall, 246 of 5328 cardiac cases (4.6%) presented with AF (estimated 5.6 cases/100 000 population/annum). Mean age was 59±18 years and the majority were of African descent (n=211, 86%) and/or female (n=150, 61%). Men were more than twice as likely to smoke (OR 2.88, 95% CI 1.92 to 4.04) than women, but women were twice as likely to be obese (OR 1.80, 95% CI 1.28 to 2.52) than men. Lone AF occurred in 22 (8.9%) cases, while concurrent valve disease and/or functional valvular abnormality occurred in 107 cases (44%). Overall, 171 cases (70%) presented with uncontrolled AF (ventricular rate >90 beats/min) with no sex-based differences. Common co-morbidities were any form of heart failure (56%) and rheumatic heart disease (21%). Women with AF were more likely to present with hypertensive heart failure (OR 2.37, 95% CI 1.24 to 4.54) but less likely to present with a dilated cardiomyopathy (OR 0.42, 95% CI 0.23 to 0.76) or coronary artery disease (OR 0.38, 95% CI 0.14 to 1.02) than men. Mean overall CHADS2 score (in 195 non-rheumatic cases) was 1.51±0.91 and, despite a similar age profile, women had higher scores than men (1.73±0.94 vs 1.24±0.78; p<0.0001).

Conclusions These unique data suggest that urban Africans in Soweto develop AF at a relatively young age. Conventional strategies used to manage and treat AF need to be carefully evaluated in this setting.

INTRODUCTION
Atrial fibrillation/flutter (AF) is the most common sustained arrhythmia found in high income countries, its prevalence rising exponentially with age and affecting >1 in 10 adults aged ≥75 years.1 Given ageing populations in whom cardiac risk factors and other forms of heart disease are prevalent, AF is described as the next cardiac ‘epidemic’.2 This epidemic will not be benign given that chronic AF is independently associated with substantial morbidity and mortality.3 Many population- and hospital-based surveys describe the epidemiology, antecedents and characteristics of AF in addition to its management and long-term outcomes in Western Europe3 4 and North America.5 It is unknown whether these studies can be easily translated to a low-to-middle income region, such as sub-Saharan Africa, where reported cases remain scarce. For example, in the USA, there appear to be important ethnic differences in the awareness and prevalence of AF. Compared with the rest of the population, African Americans not only have a lower prevalence of AF6 but are also less aware of the condition and its treatment.7

The Heart of Soweto Study is investigating emergent heart disease in the geographically compact townships that comprise Soweto in South Africa.8 9 Like other urban regions in sub-Saharan Africa, many Sowetans have adopted western lifestyles and are in epidemiological transition. Simultaneously, Soweto is being steadily populated by migrants from rural regions where traditional lifestyles predominate. Apart from dyslipidaemia, we have documented highly prevalent modifiable cardiovascular risk factors in Soweto usually associated with high income countries.10 As such, we have preliminary data to support the hypothesis that epidemiological transition has increased the spectrum of heart disease beyond that linked to poverty (eg, rheumatic heart disease (RHD))7 and towards non-communicable forms commonly seen in high income countries. In this study, we specifically examined the rate of clinical presentation, characteristics (including thrombo-embolic risk) and initial management of newly diagnosed cases of AF in Soweto.

METHODS
Study setting
The 5500 bed Chris Hani Baragwanath Hospital is a tertiary referral hospital that provides most specialist cardiac services and treatment for Soweto (population of 1.1 million) and surrounding communities. Applying gold standard cardiological expertise and advanced diagnostic investigations to provide definitive diagnostic and treatment services, the Cardiology Unit manages ~21000 cardiac cases per annum, its caseload representing an important ‘barometer’ of heart disease in Soweto.

Ethical approval for this study was sought from the University of Witwatersrand and permission confirmed through the relevant administrative bodies at Baragwanath Hospital. The study conformed to the principles outlined in the Declaration of Helsinki.
Study cohort
There were a total of 246 cases of newly diagnosed adult patients with AF. Most cases were referred via a medical outpatient clinic (n=110 cases, 45%) or inpatient unit (n=118 cases, 48%—mostly medical wards). The remainder were directly referred from one of the 12 local primary care clinics.

Data collection
A comprehensive range of demographic and clinical data were collected at the initial visit when the diagnosis was made and when any relevant co-morbidities were identified. In general, laboratory results of standard tests performed to investigate cardiac and renal function and prescribed medications were recorded as initiated at the first assessment of the patient. AF was identified on ECG at the time of presentation or during initial assessment (eg, during an echocardiogram)—see below.

12-Lead ECG
A 12-lead ECG was performed in all patients, with specific measurements available in 4783 patients (90%) over 3 years. Very few patients arrived with a previously recorded ECG, making the distinction of new-onset, paroxysmal or permanent AF impossible. Presentation with palpitations, dizziness and/or syncope was recorded. All ECGs were interpreted by Minnesota coding by a trained cardiac nurse (with final review and determination made by SS).

Echocardiography
Detailed echocardiographic assessment of ventricular function, valvular integrity and function, and regional wall abnormalities was also performed. Specific measurements were available in all except 731 de novo cases (14%) over 3 years. All procedures were undertaken by trained operators and measurements made according to the American Society of Echocardiography guidelines.

Case definitions
We categorised all cases involving primary valve (notably RHD) or valvular dysfunction secondary to another cardiac condition using previously described criteria. The syndrome of heart failure (HF) and its various manifestations (including idiopathic dilated cardiomyopathy (CMO), ischaemic CMO and hypertensive HF) were investigated and classified according to the European Society of Cardiology guidelines and the EuroHeart Failure Survey. Specifically, right heart failure (RHF) was defined by right-sided pathology with increased jugular venous pressure and liver size, tricuspid regurgitation and/or elevated right ventricular systolic pressure (RVSP) >35 mm Hg.

Thrombo-embolic risk
The widely applied CHADS2 score was also used to estimate underlying thrombo-embolic risk in non-RHD cases. Scores range from 0 to 6 based on the presence of six medical conditions: congestive HE hypertension, above 75 years age, diabetes and history of stroke/transient ischaemic attack (TIA) (each worth 1 point, except for stroke or TIA which attracts 2 points). A CHADS2 score of 1–2 implies that the risk—benefit ratio of preventing a thrombo-embolic event relative to the risk of bleeding associated with anticoagulation treatment is clinically equivocal. A score of ≥3 indicates a higher risk of stroke and more rigorous treatment.

Statistical analyses
All study data were documented and entered into the study database (Microsoft Access) by experienced cardiac nurses. Data were verified and analysed using SPSS Statistics 17.0 (SPSS, Chicago, Illinois, USA). Normally distributed continuous data are presented as the mean±SD. Percentages are presented with 95% CIs where appropriate. Comparisons according to demographic and clinical profiles involved χ2 analyses with calculation of ORs and 95% CIs for discrete variables, and Student t test and analysis of variance (ANOVA) for normally distributed continuous variables. Multiple logistic regression analyses (entry model) were performed on age, sex, ethnic origin and risk factors to derive adjusted ORs. The rate of incident case presentations per annum of AF was calculated on an age- and sex-specific basis using the most up to date census data for the Chris Hari Baragwannah Hospital catchment area (including Soweto) with adjustment for the 3 year study period. Significance was accepted at the two-sided level of p=0.05.

RESULTS
Clinical and demographic profile
During 2006–2008, 246 of 5528 de novo cardiac cases (4.6%) presented with AF. Mean age was 59±18 years and most (n=211, 58%) were of African origin (typically of Zulu or Xhosa origin). Women predominated (n=150 cases, 61%), with 28% being of childbearing age (ie, <45 years old). The most common concurrent diagnosis was any form of HF (56%). Primary valve disease and/or valvular dysfunction secondary to another cardiac aetiology (eg, CMO) was also common (affecting 45% of cases). A primary diagnosis of valve disease was made in 71 cases (29% of the total cohort), comprising 51 cases of RHD (21%) and 20 cases of degenerative valve disease (8.1%). Of the 51 cases with RHD, 22 (43%) had mitral stenosis with a mean gradient of 10.8±4.8 mm Hg. Ten cases (20%) had mixed mitral valve disease and 12 cases (24%) had predominantly mitral regurgitation. A further 50 patients (20%) had some form of tricuspid regurgitation (30 of whom (60%) had an elevated RVSP indicative of pulmonary hypertension) and 30 patients (12%) had mitral valve regurgitation (only five cases of which were secondary to idiopathic dilated CMO). Overall, 107 cases (44%) had clinically significant valve disease/dysfunction. Less common diagnoses were coronary artery disease (16 cases—6.5% of total), type 2 diabetes (nine cases—3.7%), stroke (six cases—2.4%) and postpartum CMO (three cases—1.2%). Only 22 cases (8.9%) presented with ‘lone’ AF (ie, no other diagnoses or evidence of underlying cardiac dysfunction).

Table 1 summarises the demographic and clinical profile of patients according to sex, with some important differences being evident. While women were on average 4 years older than men, this did not reach statistical significance. However, the body mass index of women (all of African origin) was significantly elevated in comparison with men; 75% versus 40% were obese on presentation (OR 1.80, 95% CI 1.28 to 2.52). Men, however, were far more likely to have a smoking history (OR 2.88, 95% CI 1.24 to 4.54), they were less likely to present on presentation (OR 1.80, 95% CI 1.28 to 2.52). Men, however, were far more likely to have a smoking history (OR 2.88, 95% CI 1.24 to 4.54), they were less likely to present on presentation (OR 1.80, 95% CI 1.28 to 2.52). Women, however, were far more likely to have a smoking history (OR 2.88, 95% CI 1.24 to 4.54), they were less likely to present on presentation (OR 1.80, 95% CI 1.28 to 2.52). Women, however, were far more likely to have a smoking history (OR 2.88, 95% CI 1.24 to 4.54), they were less likely to present on presentation (OR 1.80, 95% CI 1.28 to 2.52). Women, however, were far more likely to have a smoking history (OR 2.88, 95% CI 1.24 to 4.54), they were less likely to present on presentation (OR 1.80, 95% CI 1.28 to 2.52).
Global burden of cardiovascular disease

Table 1  Clinical and socio-demographic profile

<table>
<thead>
<tr>
<th>All (n = 246)</th>
<th>Women (n = 150)</th>
<th>Men (n = 96)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Socio-demographic profile</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>58.8±18.2</td>
<td>60.5±18.5</td>
<td>56.2±17.4</td>
</tr>
<tr>
<td>African descent</td>
<td>211 (86%)</td>
<td>135 (90%)</td>
<td>76 (79%)</td>
</tr>
<tr>
<td>Median (IQR) years in Soweto</td>
<td>46.0 (35.0–55.0)</td>
<td>45.5 (37.3–55.0)</td>
<td>46.0</td>
</tr>
<tr>
<td><strong>Risk factor profile</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of smoking</td>
<td>116 (47%)</td>
<td>46 (31%)</td>
<td>70 (73%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>148 (60%)</td>
<td>96 (65%)</td>
<td>52 (54%)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.7±6.5</td>
<td>29.4±6.7</td>
<td>24.6±5.0</td>
</tr>
<tr>
<td>Serum cholesterol (mmol/l)</td>
<td>4.0±1.2</td>
<td>4.0±1.2</td>
<td>3.9±1.3</td>
</tr>
<tr>
<td>Multiple cardiac risk factors</td>
<td>106 (43%)</td>
<td>69 (46%)</td>
<td>37 (39%)</td>
</tr>
<tr>
<td>History of alcohol intake</td>
<td>119 (48%)</td>
<td>48 (32%)</td>
<td>71 (74%)</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA class II or III</td>
<td>171 (70%)</td>
<td>109 (73%)</td>
<td>62 (65%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>136 (55%)</td>
<td>93 (62%)</td>
<td>43 (45%)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>145 (59%)</td>
<td>96 (64%)</td>
<td>49 (51%)</td>
</tr>
<tr>
<td>Heart rate/min</td>
<td>82±21</td>
<td>83±20</td>
<td>81±21</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>127±25</td>
<td>130±24</td>
<td>125±26</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>74±15</td>
<td>75±13</td>
<td>72±15</td>
</tr>
<tr>
<td>Estimated GFR</td>
<td>80±31</td>
<td>76±29</td>
<td>85±34</td>
</tr>
<tr>
<td>Probable aetiology of AF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lone AF</td>
<td>22 (8.9%)</td>
<td>16 (11%)</td>
<td>6 (6.3%)</td>
</tr>
<tr>
<td>Valvular AF</td>
<td>107 (43%)</td>
<td>65 (43%)</td>
<td>42 (44%)</td>
</tr>
<tr>
<td>Concurrent disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive HF</td>
<td>47 (19%)</td>
<td>37 (25%)</td>
<td>10 (10%)</td>
</tr>
<tr>
<td>Idiopathic dilated CMO</td>
<td>38 (15%)</td>
<td>15 (10%)</td>
<td>23 (24%)</td>
</tr>
<tr>
<td>All HF</td>
<td>138 (56%)</td>
<td>87 (58%)</td>
<td>51 (53%)</td>
</tr>
<tr>
<td>Rheumatic heart disease</td>
<td>51 (21%)</td>
<td>33 (22%)</td>
<td>18 (19%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>16 (6.5%)</td>
<td>6 (4.0%)</td>
<td>10 (10%)</td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>51±16</td>
<td>53±16</td>
<td>48±16</td>
</tr>
<tr>
<td>LVSD (LVEF&lt;45%)</td>
<td>76 (35%)</td>
<td>35 (27%)</td>
<td>41 (47%)</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>48±10</td>
<td>45±11</td>
<td>51±8</td>
</tr>
<tr>
<td>RVSP&gt;35 mm Hg</td>
<td>35±11</td>
<td>34±11</td>
<td>38±10</td>
</tr>
</tbody>
</table>

Data are presented as a mean±SD or proportions. Height and weight data were used to calculate body mass index.

AF, atrial fibrillation/flutter; BP, blood pressure; CMO, cardiomyopathy; GFR, glomerular filtration rate—calculated using the Modification of Diet in Renal Disease abbreviated formula (estimated GFR (eGFR) ml/min/1.73 m²≈186.3 × (serum creatinine mg/dl)−1.154 × (age)−0.742 female sex) (1.21 if black African) using serum creatinine concentrations (μmol/l) converted to mg/dl. Renal dysfunction defined as eGFR <60 ml/min/1.73 m² (moderate to severe renal impairment); HF, heart failure; LVESD, left ventricular end diameter at systole; LVEF, left ventricular ejection fraction (specific values recorded in 219 cases); LVESD, left ventricular end diameter at systole; LVEDD, left ventricular diameter at systole; NS, non-significant; NYHA, New York Heart Association; RVSP, right ventricular systolic pressure (specific values recorded in 56 cases).

vs 1.24±0.78; <0.0001). ANOVA revealed no difference in mean scores in all age groups except those aged >75 years in whom an age-related point was added (p=0.01 for the comparison between the youngest and oldest age groups).

Rate of case presentation

The estimated rate of AF case presentations was 5.6 per 100 000 per annum. Figure 1 shows the number of cases per age decade and the corresponding rate of presentation relative to the adult population. As expected, there was a steep increase in case presentations with age. There was <1 case per 100 000 for those aged 15–24 years compared with close to 50 cases per 100 000 for those aged ≥75 years. After the age of 25 years, significantly more women presented with AF compared with men (ranging from 46% to 77% in each age group), with the peak incidence rate for men occurring in the 55–64 year age group.

Pharmacotherapy

Table 2 summarises initially prescribed pharmacotherapy. At the time of data capture, a total of 122 cases (50%) were already prescribed antiplatelet or antithrombotic treatment. Similarly, a total of 104 cases (42%) were prescribed agents with rate or rhythm control properties. Of these, 68 patients (predominantly those prescribed digoxin) were receiving an antiplatelet or antithrombotic agent.

DISCUSSION

To the best of our knowledge, this is the largest prospective study of AF in sub-Saharan Africa and the first to provide an estimated rate of incident case presentations of AF in this region. A contemporary report from Cameroon is the only study to provide (some) comparable data. It provides important insights (pending more definitive studies) into the causes and potential consequence of AF in sub-Saharan Africa. We found a surprisingly large number of cases for this region, characterised by a broad range of contributory cardiovascular conditions in a relatively young cohort. With a predominance of women, there were important sex-based differences in potential causative factors and underlying disease states (including valve disease). Significantly, AF seems to present throughout the life course, with a relatively large number of cases (38%) presenting before 50 years of age.

Consistent with previous reports, HF was highly prevalent in this cohort. Put another way, AF occurred in only 6.6% of all 2593 HF cases within the entire study cohort. In the EuroHeart Failure Survey, one-third of patients with HF had AF prior to hospitalisation and 9% were diagnosed with new-onset AF during that admission. The prognostic influence of AF in patients with HF remains controversial. A recent meta-analysis of 16 studies reported a twofold increase in mortality associated with AF in those with preserved or impaired systolic function. Unfortunately, we are unable to determine the exact causes of AF in our patients with HF. We also do not have detailed data on alcohol consumption. Consistent with the overall Heart of Soweto HF cohort, pulmonary hypertension occurred in >10% of cases. In the Cameroon cohort, 64 (45%) and 100 (58%) of 141 patients with AF were concurrently diagnosed with pulmonary hypertension and HF, respectively. With few reports examining pulmonary pathology in HF cases overall, it is imperative that this be considered in future research focusing on AF and HF in sub-Saharan Africa.

Despite many similarities, our cohort was on average 8 years younger than the Cameroon cohort. This was reflected in lower thrombo-embolic risk (CHADS2 scores were half those

seen in clinical trials) and a large disparity in a past history of stroke (2.4% vs 17.4% in Cameroon). Many algorithms have been proposed to calculate the subsequent stroke in AF (including the CHADS2). However, none has been validated for RHD. During 1 year follow-up of 88 patients in Cameroon, nearly 50% died and 16% of survivors experienced a non-lethal embolic stroke. We have no data with which to compare this, but low prevalence of a previous or newly diagnosed embolic stroke is still noteworthy given that cases are unlikely to be missed. Historically, thrombotic strokes accounted for only 10% of stroke cases, with a far greater prevalence (50–60%) of embolic strokes secondary to RHD, prosthetic valves and infective endocarditis at Baragwanath Hospital, intracranial haemorrhage being the most common form (40–50% of cases) of stroke presentation. Significantly, younger patients suffering from haemorrhagic strokes diagnosed via CT scans are often not referred to a cardiology centre in South Africa. The relatively low thrombo-embolic risk profile of this cohort has implications for delineating risk and applying cost-effective management of AF in Africa. Unfortunately, INR (international normalised ratio) measurements for those prescribed warfarin are costly, and access to clinics for rural patients is problematic. While new agents such as dabigatran offer antithrombotic effects without therapeutic monitoring, their affordability in the sub-Saharan context is problematic. A practical compromise would be the use of aspirin and or clopidogrel (both being optimal), recognising their clinical inferiority to warfarin. Likewise, lenient ventricular rate control is as good as strict control and the key is reasonable control by β-blockade. Digoxin treatment remains problematic given the need for regular and potentially expensive therapeutic monitoring.

Overall, the lack of data from predominantly younger patients from different ethnic groups in Africa has important clinical and public health implications. For potentially childbearing women with AF (28% of women), management of anticoagulation during and after pregnancy is challenging. With RHD still prevalent (especially in African women), it is important to note that AF is a strong predictor of unfavourable clinical outcomes and re-stenosis after percutaneous mitral balloon valvotomy. Carefully conducted outcome studies are therefore urgently needed to allow appropriate risk assessment and management in African patients. Depending on their cost, the availability of new antiarrhythmic and antithrombotic modalities that offer better risk—benefit ratios may have particular advantages in similar low-to-middle income countries with limited resources. Finally, the predominance of AF in women compared with reports from high income countries and, indeed China, where more men develop AF, requires comment. Recent attention has focused on the independent risk of developing AF with increasing weight, with a consistent twofold to threefold increased likelihood of AF in obese individuals being reported. However, reflective of the pattern of obesity in Soweto, 73% versus 40% of women and men in this cohort were obese. These data are consistent with studies linking weight (rather than gender per se) to an increased risk of developing AF.
Global burden of cardiovascular disease

Our study has a number of limitations. We only included those fortunate (or sick) enough to receive specialist hospital care. Consequently, patients often had advanced forms of heart disease, and these data undoubtedly exclude those suffering from milder forms of cardiovascular disease or asymptomatic AF in the community as well as non-cardiac cases in hospital; this is particularly relevant when interpreting the estimated rate of case presentations. Moreover, as a clinical registry, we did not systematically validate diagnostic data, but (wherever possible) we have adhered to the relevant STROBE guidelines.30

In summary, these data have important clinical and public health implications for sub-Saharan Africa, the wider African continent, and other parts of the developing world in epidemiological transition. In high income countries, AF presents typically in older individuals and is rapidly becoming the next cardiac epidemic within ageing populations. In Soweto, AF appears to affect individuals at a younger age (particularly women) and is likely to rise with greater levels of obesity and hypertension linked to epidemiological transition. Much of the clinical management of AF in high income countries, therefore, may not readily apply in this context. More studies are undoubtedly required to better understand the epidemiology, detection and management of AF in sub-Saharan Africa.

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Competing interests None.

Ethics approval This study was conducted with the approval of the University of Witwatersrand.

Provenance and peer review Not commissioned; externally peer reviewed.

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