Original Article

Prevalence, clinical profile, and stroke risk of atrial fibrillation in rural Andhra Pradesh, India (the AP-AF study)

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ABSTRACT

The burden of atrial fibrillation (AF) is increasing worldwide. It is often asymptomatic, with stroke being the first manifestation in some. AF burden in the community and the practice of stroke prophylaxis has not been studied in India. The problem might be higher in rural regions due to poor health awareness and challenges to healthcare access. This study aimed to estimate the prevalence of AF, clinical profile and stroke risk in rural India.

Methods: This is a community-based cross-sectional study done in rural Andhra Pradesh (AP). Adults from 40 villages formed the study population. We did a door-to door survey to collect information on demographics, and medical history. Electrocardiogram was recorded using a smart phone based Alivecor device. Participants diagnosed with AF underwent echocardiogram. Study cardiologists assessed the cardiovascular risk profile and collected detailed medical history.

Results: Fourteen of the 4281 individuals screened had AF (0.3%). The mean age of the sampled population was 44 ± 16.5 years with 56% women. The mean age of participants with AF was 71 ± 7.8 years; males were 71%. Except for one, all were non-valvular AF. Majority had a $CHA_2D_2S_2Vasc$ score of ≥ 2. Three had history of stroke. Two were on anticoagulant therapy but without INR monitoring.

Conclusion: The prevalence of AF is lower in this study compared to studies from the developed countries. Non-rheumatic cardiovascular risk factors were primary causes for AF. Non-adherence to stroke prophylaxis is a major threat that needs to be addressed.

1. Introduction

Atrial Fibrillation (AF) is the most common sustained heart rhythm disorder in the general population with a community prevalence of 0.5–5.5% worldwide.[1–4] Studies conducted in India have shown wide variations in AF prevalence, ranging from 0.1 to 1.6 (%).[5,6] Unfortunately, in India population-based information on AF is limited. Moreover, the available knowledge on AF and oral anticoagulation (OAC) practices are largely derived from the hospital-based studies. Till date, there are only two community-based prevalence studies on AF in India.[5,6] The first, a pilot for the present study, was an opportunistic screening of a religious conglomeration in the city of Nagpur, central India (Nagpur-AF study), which showed a prevalence of 0.19%.[5] It revealed, rheumatic heart disease (RHD) as the predominant aetiology of AF. Another notable observation from the study was, even in those with AF who suffered thromboembolic complications, the adherence to OAC was poor. The second, SMART-AF study, a systematic population-based study done in a rural area in the state of Gujarat (North-West India) showed AF prevalence of 1.6%.[6] However, the SMART-AF study did not report information on the clinical profile of participants with AF and their stroke prophylaxis.

The AF detection and stroke prophylaxis is likely to be suboptimal in rural regions compared to regions in urban India due to comparatively poor health awareness and accessibility issues.[7–9] To strategize resource allocation for primary prevention of stroke, more epidemiological studies on AF in rural areas are needed.

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Therefore, we aimed to study the prevalence of AF in the villages of Andhra Pradesh, a state in South India. In addition, we planned to assess the clinical profile of participants with AF, their stroke risk and prophylaxis against stroke.

2. Methods

2.1. Study design

The Andhra Pradesh Atrial Fibrillation (AP-AF) study was a systematic, population-based, cross-sectional study in rural AP, India, using a door-to-door survey. The study was a collaborative effort of CARE hospital, and CARE Foundation-Care Rural Health Mission (CRHM), Hyderabad. Study workflow and procedures have been detailed in our 'rationale and design' paper.[10]

2.2. Study objectives

The Primary objective of this study was to determine the prevalence of AF in adults (aged ≥18 years) sampled from a general population residing in rural AP.

The secondary objectives were: to understand the demographic profile and prevalence of cardiovascular risk factors in the population; to understand the clinical profile of participants with AF and their stroke prophylaxis.

2.3. Rationale for selection of study sites

The study was done in villages of East and West Godavari districts where CRHM runs peripheral health centres (PHCs). The PHCs are managed by qualified auxiliary nurse midwives. They have experience in conducting health camps/surveys and have a good rapport with the residents of their respective villages. For administrative convenience we chose those villages where the CRHM was operational and utilized the midwives as field investigators.

2.4. Participant inclusion and exclusion criteria

All residents of the villages, aged 18 and above were eligible for the study.

2.5. Ethical considerations

The study was done after obtaining consent from the Institutional Ethics Committee. All study procedures were done after obtaining informed consent from the participants.

2.6. Sample size and sampling strategy

A sample size of 11,021 was estimated from the Nagpur-AF pilot study. Sampling was done in two stages. In the first stage, from the 127 villages where the CRHM has public health centers, 40 villages were sampled using probability proportional to sample size method. In the second stage, participants aged ≥18 years were sampled using age and sex-stratified simple random sampling.

2.7. Study procedures

The study was carried out in two stages. In stage I, the field investigators visited the houses of the participants to carry out study procedures: informed consent, anthropometric measurements, blood pressure (BP) measurement, sampling for Fasting Blood Sugar (FBS), and record a single lead ECG. Blood pressure and FBS were measured using automated digital monitoring devices. ECG was obtained using a hand-held ECG device, Kardia Mobile (Alivecor, Inc., Mountain View, CA, United States) paired with Kardia App installed on mobile tablets. Field investigators administered the study questionnaire and recorded responses on the Redcap App installed on their mobile tablets.[11] The questionnaire captured socio-economic information of the participants, medical history, risk factors for cardiovascular diseases, history of AF and medications. Collected data was transferred to the server hosted at CARE Foundation for remote access by the study cardiologists. The ECGs were uploaded on to CARE-ICT (Information and Communication Technology) platform for study cardiologists' access. All ECG recordings were interpreted by two cardiologists at CARE Hospital independently.

The participants diagnosed to have AF on ECG in Stage I were included in Stage II of the study which was arranged in a local hospital on a pre-specified date. Study cardiologists administered AF-specific questionnaire to the participants and did two-dimensional echocardiography and colour Doppler imaging to evaluate any structural or functional changes in the heart suggestive of aetiology and/or consequences of AF.

2.8. Statistical analysis

Continuous variables are presented as mean with standard deviation and categorical variables as frequency with percentages. The prevalence of AF was calculated as the total number of participants diagnosed with AF divided by the total number of participants surveyed. Prevalence is reported as the percentage of study participants diagnosed with AF. The prevalence was also calculated for different groups categorized by age and sex and reported with 95% confidence interval. Analysis was conducted in R (R version 3.6.1).[12]

3. Results

The Socio-economic characteristics of the study population are given in Table 1 and cardiovascular risk profile in Table 2. Fourteen of the 4281 individuals screened had AF (0.3%). The mean age of the sampled population was 44 ± 16.5 years with 56% women. Elderly(≥60 years) comprised 21% of the study population. The mean age of participants with AF was 71 ± 7.8 years; males were 71%. Except for one, all were non-valvular AF. Majority had a $CHA_2D_2S_2Vasc$ score of ≥2. Three had history of stroke. Two were on anticoagulant therapy but without INR monitoring.

3.1. Prevalence of AF, socio-economic profile, and clinical characteristics of participants with AF

The overall prevalence of AF was 0.32% (95% CI: 0.17%–0.54%). Prevalence of AF in the elderly (>60 years) was 1.5% (0.8%–2.5%). Of the 14 participants (10 men: 4 women) found to have AF, two were known cases. All AF cases were above 50 years with a mean age of 71 ± 7.8 years. The prevalence was 0.52% (0.25%–0.95%) in men and 0.17% (0.05%–0.43%) in women. Age and sex stratified prevalence of AF is shown in Table 3.

All participants with AF were from poor socio-economic background. Hypertension was the most common risk factor (six participants). Diabetes and RHD were present in one participant each. There was no history of thyroid abnormality, chronic obstructive lung disease or ischemic heart disease in any. Eight participants had history of smoking. Two were current smokers and two alcohol abusers.

Table 1
Socio-economic characteristics of the study participants.

Variables	Frequency (percentage)
Educational level ($n = 3835$)	
No formal education	1559 (40.6%)
Primary education	790 (20.5%)
Middle and High school	845 (22%)
Intermediate/equivalent	368 (9.5%)
College education	173 (4.5%)
Marital status ($n = 4032$)	
Unmarried	435 (11%)
Married	3217 (80%)
Divorced/separated	57 (1%)
Widowed	323 (8%)
Occupation ($n = 3714$)	
Student	180 (4.8%)
Unemployed	128 (3.4%)
Homemaker	1667 (44.9%)
Agricultural labourer	1478 (39.8%)
Government employee	43 (1.2%)
Employed in private enterprises	196 (5.3%)
Retired	22 (0.6%)
Average monthly income of the participants in Indian rupees ($n = 3911$)	
Financially dependent	861 (22%)
$\leq$5000	1616 (41.3%)
5001-10,000	1013 (25.9%)
10,001–20,000	314 (8%)
20,001–50,000	91 (2.3)
50,001-1,00,000	9 (0.2%)
>1,00,000	7 (0.2%)

Abbreviations: SD, Standard Deviation.

Table 2
Cardiovascular risk profile of the study population.

Risk factors	Frequency
Dyslipidemia[13]	69 (1.6%)
Cardiac disease or H/O cardiac surgery	35 (0.8%)
Current smokers	311 (7.3%)
Alcohol abusers[a]	245 (5.7%)
Diabetes Mellitus	461 (10.8%)
Systemic Hypertension	836 (19.5%)
Obesity ($n = 4033$)	439 (10.9%)

[a] A person who "can no longer control their use of alcohol, compulsively abuse alcohol despite its negative ramifications, and/or experience emotional distress when they are not drinking.".[14]

3.2. Transthoracic echocardiographic assessment

Echocardiography was done in 13 participants. Eleven had non-valvular AF. All had good left ventricular function. The left atrium was enlarged in five and left ventricular hypertrophy was seen in three participants. One had moderate mitral stenosis (RHD). Severe mitral regurgitation was seen in one participant.

3.3. Stroke risk and prophylaxis

Ten of the thirteen participants with non-valvular AF (NVAF) had a CHA$_2$DS$_2$-VASc score of $\geq$2. Of the fourteen participants with AF, two were on vitamin K antagonists (VKA) (one valvular and one non-valvular) and one on regular monitoring of prothrombin time/INR. The risk factors for stroke, stroke risk and stroke prophylaxis of each participant are given in Table 4.

4. Discussion

In this systematic, cross-sectional survey of a general population in rural South India, we studied the prevalence of AF, risk factors of AF, stroke risk and prophylaxis against stroke. Important findings of this study are: 1) Using a smart phone-based ECG device, we found the prevalence of AF to be 0.3%. 2) Thirteen (92.85%) out of 14 patients with AF were non-valvular AF. 3) Ten out of 13 patients with NVAF had a CHA$_2$DS$_2$-VASc score of $\geq$2. Among the high stroke risk category (10 NVAF and 1 Valvular AF), only 2 (18%) out of 11 patients who required stroke prophylaxis were on OAC. Both these

Table 3
Age and sex stratified prevalence of atrial fibrillation.

Age category (In years)	Prevalence percentage of atrial fibrillation (95% Confidence Interval)		
	Overall	Men	Women
50–60	0.11 (0.002–0.64)	0.27 (0.006–1.5)	0
61–70	0.9 (0.36–1.85)	1.9 (0.6–5.3)	0.4 (0.01–2.25)
71–75	1.8 (0.21–6.35)	3.5 (0.42–12.1)	0
>75	3.5 (0.97–8.81)	3.9 (0.47–13.4)	3.2 (0.39–11.1)

Table 4
Risk factors for stroke, $CHA_2D_2S_2Vasc$ score and antithrombotic therapy in participants with atrial fibrillation.

Age (Years)	Sex	HTN	DM	PVD	H/O stroke	Repeat ECG	VAF	$CHA_2D_2S_2Vasc$ score	Antithrombotic therapy
67	M	+	−	−	−	Sinus	−	2	−
70	M	−	−	−	−	Sinus	−	1	−
80	M	−	+	−	−	Sinus	−	3	−
66	M	+	−	−	−	Sinus	−	2	−
55	M	+	−	+	−	AF	−	2	−
74	M	−	−	−	−	Sinus	−	1	−
85	F	−	−	+	−	AF	−	4	−
80	F	+	−	−	−	AF	−	4	−
77	M	−	−	−	−	AF	−	2	−
75	M	−	−	−	−	AF	+	1*	−
64	F	+	−	−	+	AF	+	4**	Coumadin
66	M	+	−	−	+	AF	−	4	Coumadin
70	M	−	−	−	+	AF	−	3	−
70	F	−	−	−	−	AF	−	2	Aspirin

+ and − sign indicates the presence or absence of a condition respectively. * Degenerative mitral valve with severe regurgitation, **Rheumatic heart disease with moderate mitral stenosis.

HTN: Hypertension; DM: Diabetes Mellitus; ECG − Electrocardiogram PVD: Peripheral Vascular Disease; VAF: Valvular Atrial Fibrillation; M: Male; F: Female; AF: Atrial Fibrillation.

patients were on VKA, and only one was monitoring INR. None of the patient was on direct oral anticoagulation (DOAC).

4.1. Comparisons on AF prevalence

The estimates of AF prevalence of the general population (through systematic screening) range from 0.54% to 4.4%.[1–4,15–17] These studies included participants above the age of 30 years. In all the studies, the mean age of the participants was above fifty years, an age group where the prevalence of AF is likely to be high. The prevalence of hypertension, an independent risk factor for AF was also substantially high ranging from 22% to 51%. As age and hypertension are independent risk factors for AF, they were likely contributors for the higher prevalence of AF in these studies. In comparison, the mean age of the participants in AP-AF study was 44 years with 63% under 50 years of age. The prevalence of hypertension was also comparatively lower (19.5%). Consistent with findings from other studies,[18–21] the prevalence of AF in the elderly was high (1.5%) in our study as well. The mean age of the participants with AF was 71 years. This further supports our assumption that the overall low prevalence of AF is because of the younger age group studied.

The SMART-AF study which began around the same period as the AP-AF study also engaged smart phone-based ECG recordings for the survey. SMART-AF study investigators relied upon Alive cor device algorithm for the diagnosis of AF. It used repeated screenings over five days to identify AF in participants aged 40 years and above. In the 2074 participants screened, the prevalence was 1% on a single screening and 1.6% with repeated screenings. In AP-AF study, device-generated diagnosis was verified by cardiologists and ECGs with artifacts were repeated. In our study, nearly half of the population was in the age group ≤40 years. In addition, the study employed a cross-sectional design for ECG screening and hence the comparatively lower prevalence.

4.2. Rheumatic heart disease

A surprising finding from our study is that RHD was the causative factor for AF only in one participant (7%), despite of mean age of study population is low (44.5 years ±16.5) and predominant female participants (56%). This contrasts with our findings in Nagpur-AF study, and hospital-based registries from India, where RHD was seen in 40 %–70% of the AF patients.[5,22] The reason for the low prevalence of AF in our study despite the inclusion of younger

population and female predominance (RHD is more common in females) could be consequent to the low prevalence of RHD. This theory needs exploration as in India, though there is an overall decrease in prevalence of RHD the global burden of disease estimates that India has the highest incidence of RHD compared to the rest of the world.[23]

4.3. Stroke risk and prophylaxis

The other important finding from our study is eleven of the fourteen participants (79%) with AF had a $CHA_2D_2S_2Vasc$ score of ≥2 but only 18% were on OAC without monitoring of INR.

4.4. Strengths and limitations

This is the largest systematic population-based study on AF prevalence done for the first time in India. It is also for the first time that a detailed clinical and echocardiographic assessments of participants with AF was done.

Our study has two major limitations. Firstly, it is the underestimation of AF prevalence due to cross-sectional design. As we recorded ECG only once, we could have missed capturing all the paroxysmal AFs. Paroxysmal AF comprises anywhere between 25% and 62% of AF[24]. The second limitation is that our study findings are not representative of the entire Indian population. By its very nature of geographical and socio-economic diversity, the prevalence of a condition studied in one region in India may not be representative of the entire population. Besides this general limitation, our study suffers from sampling bias. Though our intent was to study the prevalence of AF in the rural areas of AP, we used convenience sampling in the first stage; we selected the districts (East and West Godavari) and the villages where CRHM was operational for our administrative convenience. Also, due to logistic reasons, we aborted the study after screening only 40% of the sample that was exclusively within West Godavari district.

4.5. Implications for research and public health interventions

Though the prevalence of AF in our study is low compared to others, when extrapolated to the population of India, a minimum of 415 million may have the arrhythmia.[25] As the population of the country is expected to reach 1.6 billion in another 30 years, it is hard to imagine the burden of AF in India and consequently stroke and other complications. The need of the hour is to plan and initiate

large scale public health interventions to identify AF, initiate treatment, and simultaneously reduce the incidence of risk factors. The National Programme for control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke programme rolled out by the government of India can be exploited for this purpose as it conducts periodic, opportunistic screenings for diabetes and hypertension for people above 30 years. Screening for AF by ECG can also be introduced in this intervention. The availability of validated ECG monitors using smart phone makes this possible.

India is a country diverse in many ways: geographically, racially, and ethnically. A wide inter-state as well as urban-rural variability exists in socio-economic factors. These factors necessitate a decentralized public health planning backed by research-based evidence derived from local communities.

5. Conclusions

In this single time point study, the prevalence of AF is lower (0.3%) compared to studies from the developed countries. As compared to the major studies from India, number of AFs related to RHD is far less in the present study. Non-rheumatic cardiovascular risk factors were the main reasons for AF. Non-adherence to stroke prophylaxis is a major threat that needs to be addressed.

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