Epidemiology of Atrial Fibrillation - An Indian Perspective

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice and accounts for 1/3 of hospital admissions for cardiac rhythm disturbances. Recent worldwide epidemiological data have reaffirmed the fact that AF is a global epidemic and has adverse effects on long term morbidity and mortality. Although the effect of AF on the quality of life and survival has been well documented in the western population, similar data on incidence, prevalence, etiology, mortality and morbidity in the Indian population are limited. Most of the published epidemiologic studies have focused on predominantly Caucasian populations in North America or Europe, and information pertaining to AF in the Asian population is lacking. There have been only sporadic observational studies on the epidemiology of AF reported from India. However with the knowledge about the Indian cohort from the REALIZE-AF and RELY-AF studies and the IHRS-AF registry, more insight is now available on contemporary AF data amongst Indian patients. This review analyses the current epidemiological evidence of AF in the Indian population and highlights how the Indian subset differs from the Western counterparts.

Incidence and Prevalence

The overall prevalence of AF in the general population in North America and Europe is reported to be 1-2%.

Recent worldwide epidemiological data have given important insights into the changing trends in the incidence, prevalence and gender relation of AF. In 1990 the estimated prevalence rates for men and women for every 1,00,000 population was 569.5 and 359.9 respectively while the estimated incidence rates were 60.7 and 43.8. Over a span of two decades, there was a steady but modest increase in the prevalence rates- 596.2 in men and 373.1 in women per 1,00,000 population, while the incidence rates significantly increased to 77.5 and 59.5 in men and women respectively. For both men and women, prevalence and incidence of AF were disproportionately higher in developed nations compared with developing nations. This was explained by the increasing frequency of diagnosis and reporting of the AF by the physicians as well as due to the rising age and cardiovascular co-morbidities in the subject population.

There is a significant difference in the incidence of AF in various populations with studies having reported a lower incidence of AF in Indo-Asians and African Americans as compared with white populations.

Lip et al performed a systematic review of the epidemiology of AF in regions outside North America and Europe in an attempt to obtain information on AF in nonwhite populations. The majority of the included studies were from Japan and China, while other representatives were from Australia, Kuwait, India, Malaysia, New Zealand, Qatar, Singapore, South Korea, Thailand, Brazil and Taiwan. The reported prevalence of AF varied markedly among countries, primarily due to differences in prevalence data derived from community- and hospital-based cohorts. The prevalence of AF ranged from 0.1%-4% in community-based and 2.8%-14%, respectively in hospital-based studies. Lip et al further commented that the paucity of data was particularly striking for India with only one relatively small-scale study qualifying for inclusion in the review.

In this population based study of 984 healthy subjects residing in a Himalayan village who underwent a 12 lead ECG, a prevalence of AF of 0.1% was reported which was quite low as compared to the western population. However this study included young, healthy participants (only 6% > 65 years of age) from only one village in the Himalayas who were subjected to only a one time ECG. Although based on a single small study, this low prevalence of AF among Indo-Asians is consistent with data from the West Birmingham AF Project and the E-Echocardiographic Heart of England Screening Study, where the prevalence of AF was lower among Indo-Asians (0.6%) as compared to the general population (2.4%).

Age and Gender

Age is an important risk factor for development of new onset AF. With population trends worldwide showing an increase in the mean survival age due to improved health care, the ageing population...
is more prone to develop AF. The reported annual incidence of AF in men and women in the age group of 55–64 years has been reported to be 0.003% and 0.001% respectively, which increases to 0.038 in men and 0.031 in women in the 85–94 age group. In general, the incidence of AF is 0.1% per year in the population below forty years and increases to 2% in those older than 80 years.11 The adjusted incidence and prevalence of AF roughly doubles for each advancing decade of life and at any given age, men have an ≈50% higher incidence of AF than women. The reported prevalence of AF ranges from 0.1% among adults less than 55 years of age to 9% in those >80 years of age.12

However, studies from India have consistently shown that the mean age of patients with AF is nearly a decade younger than the Western cohort. Hospital data records of patients with chronic AF from Andhra Pradesh, revealed a mean age of 45.4 years, with most (51%) aged <50 years and only 16.3% older than 60 years.13 In an observational hospital based study carried amongst indoor patients of AF in Bihar, Vidya et al reported that the mean age of the patients was 47 years and majority of patients were aged between 51-60 years (48%).14 Amongst 137 patients with AF from a rural back ground in North India, Bhardwaj reported that the mean age of patients was 51.2 years, while analysis of patients with AF presenting at a tertiary care hospital in Gujarat, revealed that most (46%) patients with AF were between the age of 31-40 years, 31% were between 41-50 years and 15% were between the age of 15-30 years.15,16 Recent analysis of a sample of 2231 US and 1053 Indian patients using the NUVANT Mobile Cardiac Telemetry System revealed mean age of 61.3 for the US and 57.8 for Indian patients with AF.17

Data from the IHRS-AF registry and the Indian subset of REALISE AF and RELY-AF study also reaffirmed these findings.16,21 The IHRS-AF registry is a national atrial fibrillation (AF) registry conducted under the aegis of the Indian Heart Rhythm Society (IHRS) to study the epidemiological characteristics of AF in India and understand the current treatment practices and its impact on a one year follow-up. The Randomized Evaluation of Long-Term Anticoagulation Therapy (RELY-AF) registry enrolled patients presenting to an emergency department with AF at 164 sites in 46 countries and included a significant number of subjects from middle- and low-income countries while the Real-life global survey evaluating patients with atrial fibrillation (REALISE-AF) was an international registry which investigated the management of AF and its control in nonhospitalized subjects who had ≥1 episode in the past 12 months.

The mean age of Indian patients with AF in the REALIZE-AF study was 60 years while that in the IHRS-AF registry was 54.2 years (range 15-96).18,20 Analysis of the IHRS-AF data (comprising of 1532 patients with AF from 24 participating centres) further revealed that 36% patients were older than 60 years while 18% patients were <40 years. The average age of the registry patients in RELY-AF was 65.9 years, with a significantly higher average age reported in patients enrolled in North and South America and Western and Eastern Europe.21 In contrast, patients in India, the Middle East, and Africa were on average ≈10 to 12 years younger. This can be attributed to the fact that rheumatic valvular heart disease (RVHD) which is an important cause of AF amongst Indian patients, is more frequent in the younger population. The CRRAFT study which exclusively included AF patients with RHVD reported a mean age of only 38 years.22

Data from the West reveals that the incidence and prevalence of AF are higher in men as compared to females with reported male: female rates of appx 1.1% vs 0.8%.1,12,23 In both Framingham Heart Study and Atherosclerosis Risk in Communities Study, men had a 1.5-fold greater risk of developing AF than women and the lifetime risk of developing AF after age of 40 in the Framingham cohort was reported to be 26% for men and 23% for women.23,24 However studies from India have revealed a slightly higher female preponderance with reported male: female ratio in the range of 1:1.38,1:1.2. and 1:1.24,13,15,16

While the REALIZE-AF and RELY-AF studies reported an almost equal gender distribution in the Indian subset, the IHRS-AF registry observed that 51% patients were females, again confirming the higher prevalence of AF amongst females in the Indian cohort. The female preponderance is explained by the fact that RHVD is more frequent in females and RHVD is the commonest cause of AF amongst Indian patients.

**Types of AF**

Region-specific variations in the type of AF are common, and in America and Western Europe there is an almost equal distribution between paroxysmal, persistent, and permanent AF. In contrast, the RELY-AF registry reported that in Africa and the Middle East, 81.4% and 71.7%, respectively, of the patients had permanent AF.21 Permanent AF is also expected to be more frequent in the Indian population due to the irreversible structural remodelling of the atria seen especially in RHVD and also due to the fact that patients often present late in the course of the disease.

The reported rates of paroxysmal AF were 38%, 43% and 19.5% in the REALIZE-AF, RELY-AF and the IHRS-AF studies while permanent AF was present in 34.3%, 18.6% and 35% respectively. This discrepancy is likely due to the fact that IHRS-AF registry had a greater representation of government hospitals, with a higher proportion of patients with RHVD and established AF.
Analysis of the IHRS-AF data also provides interesting insight into the evolving patterns of AF amongst Indian patients. At baseline visit, paroxysmal, persistent and permanent AF was seen in 20%, 33% and 35% patients respectively. Amongst patients with paroxysmal AF at baseline, on a one year follow-up, permanent AF developed in 22% and persistent AF in 10%. In the persistent AF group at baseline, 22% progressed to permanent AF at one year. Most patients with permanent AF (90%) remained in permanent AF. Of the 11% who presented with first episode of AF at baseline, one-third did not develop any further AF episodes, however 50% developed persistent AF by one year.25,26

Valvular AF

Valvular heart disease has been associated with a 1.8- and 3.4-fold increased risk for AF in men and women, respectively.25 Rheumatic heart disease is an important cause of AF in Africa, China, the Middle East, and particularly in India, where it is reported in nearly one-third of patients with AF. Although Afro-Asian countries may have an even higher prevalence of RHVD leading to AF, the exact burden is difficult to estimate given the lack of quality scientific epidemiological and detailed echocardiographic community based data. Initial observational studies from India reported that RHD was present in nearly 75% (Andhra Pradesh) and 61% (rural North India) of AF patients.13,15 The study by Rao et al further observed that while RHD was seen more commonly in people below the age of 50 years, hypertension and ischemic heart disease was more frequent after 50 years.13 Amongst patients with AF presenting at a tertiary care hospital in Gujarat, Patel et al reported that 78% had RHD while Vidya et al reported that amongst patients with AF, structural heart disease was found in 86.36% of cases; among those with structural heart disease, VHD was the most frequent cause and was seen in 51.51% cases as a cause of AF.14,16

Although any valvular pathology can be related to AF, stenotic left-sided rheumatic valvular lesions are most frequently associated with AF. The prevalence of AF varies with the complexity of rheumatic heart disease: from 16% with isolated mitral regurgitation to 29% with isolated mitral stenosis, to 52% with coexisting mitral regurgitation and stenosis, and to 70% with mixed mitral and tricuspid valve disease.26 Bhardwaj et al also reported that amongst 84 patients with AF due to RHD, all patients had involvement of mitral valve, with mixed MS and MR being most common (26.61%) while isolated MS was observed in 15.47% and isolated MR in 9.5%.15

The commonest underlying etiology in Indian patients with AF in the IHRS-AF registry was also reported to be RHD (47.8%).18,19 The RELY-AF registry reported that amongst the AF patients, VHD was most common in India (46.7%) and Africa (32.6%) and much less common in Eastern Europe (10.7%) and Western Europe (8.8%).21 While the overall prevalence of RHD was 11.6%, it was noted in only 1.5-2.2% of patients in Western Europe and North America respectively. In contrast, underlying RHD was seen in >15% of the patients in Africa, Middle East and China and in up to 31.5% patients in India.21 The prevalence of VHD in patients with AF was 26.7% in the REALIZE-AF global study as compared to 40.7% amongst the Indian cohort.27

Nonvalvular AF

Hypertension (HTN) is an important predisposing factor for AF due to associated left ventricular hypertrophy and its effect on left atrial remodelling. Although the increase in risk is relatively modest (relative risk, 1.2–1.5), the high prevalence of HTN in the general population makes it a significant risk factor for non valvular AF in the general population. Apart from overt systolic hypertension, blood pressure in the prehypertensive range (130–139 mm Hg) and widened pulse pressure are also associated with increased risk of AF (adjusted hazard ratios [HRs], 1.28 versus systolic blood pressure <120 and 1.26 per 20 mm Hg increment, respectively).25,28

In the REALISE-AF registry around 72% of AF patient worldwide and 51% of AF patients from India had HTN. The RELY-AF study also reported that HTN was the most prevalent AF risk factor, being present in ~62% patients. Patients from Eastern Europe had the highest prevalence of (80.7%), while a lower prevalence of HTN was observed in Western Europe, India, China, Southeast Asia, the Middle East and Africa. The lowest prevalence of HTN was reported from India (41.6%). Hypertension was reported to be present in 31% patients in the IHRS-AF registry.

Other risk factors: Although the prevalence of AF in patients with stable CAD does not seem to be substantially higher than in populations without CAD, both conditions often co-exist with some studies having reported that patients with AF may have an increased prevalence of both non-obstructive and obstructive CAD compared with those without AF. The prevalence of AF in heart failure (HF) increases with the severity of HF and appx 30-50% patients with severe HF develop atrial fibrillation.29 Other risk factors like diabetes, obesity, sleep apnoea, hyperthyroidism, chronic obstructive lung diseases, hypertrophic cardiomyopathy, alcohol consumption, chronic kidney diseases account for few of the causative factors of nonvalvular AF, although their exact prevalence amongst Indian patients with AF is not well documented.

In the Indian substudy from the REALISE-AF registry, CAD was noted in 32%, HF in 26%, diabetes in 20% and dyslipidemia in 16% patients. In the RELY-AF study,
while HF was present in 1/3rd of patients with AF, the prevalence of HF ranged from 17.7% (in India) to 63.8% (in Africa). The percentage of patients with CAD and HF in the IHRS-AF registry was 27% and 18% respectively. The RELY-AF study reported that diabetes mellitus was present in 21.8% of patients with AF, with rates ranging from 15.5% in India to 36.2% in the Middle East; chronic obstructive pulmonary disease was present in 11.5% of the patients, ranging from <5% in India and Africa to 23.4% in Eastern Europe. While the worldwide prevalence rate of lone AF was 10.7%, the proportion of patients with lone AF was much less in South America, Africa, and India 6.3%.

**Conclusion**

The incidence, prevalence, risk factors and economic burden of AF has been addressed in various studies and registries in the western population. Current available data indicates that Indian patients with AF are different from their Western counterparts; not only are they about a decade younger but RHVD is the underlying etiology in ~ 30-40% cases. Hence more proportion of Indian patients have persistent/permanent AF thus representing a high stroke risk. From the Indian perspective, more registries like the IHRS-AF registry are warranted to document the epidemiologic data on AF and assess the impact of RHVD as well as the proportion of nonvalvular AF due to existing cardiovascular co-morbidities. This is likely to help in better understanding the changing trends in patients of AF in the Indian population and provide opportunities to improve care, with better prevention and management strategies.

**References**