

## ORIGINAL RESEARCH

## Prevalence of atrial fibrillation in the Malaysian communities

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**ABSTRACT**

**Background and aim** Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia encountered in clinical practice. The REDISCOVER (Responding to Increasing Cardiovascular disease prevalence) study is an observational longitudinal community-based study that tracks changing lifestyles, risk factors and chronic disease in urban and rural areas of Malaysia. In this study, we aim to study the prevalence of AF and its associated risk factors.

**Methods** The study was conducted between 2007 and 2014. Participants were required to complete questionnaires on cardiovascular risk factors and medical history, and undergo physical examinations, blood tests, ECG and echocardiography examinations. Demographic variables including weight, height, blood pressure, serum glucose and serum lipid were recorded. Participants with AF were identified from their baseline ECG and at 3-year follow up.

**Results** A total of 10 805 subjects participated in the study. Mean age was 52.6(±11.6) years and 56% were female; 4.4% of subjects had a diagnosis of ischaemic heart disease, 1.3% had a previous stroke, 16.7% had diabetes mellitus and 45.6% had hypertension. There were 53 subjects diagnosed with AF at baseline, giving a prevalence of 0.49%, and 0.54% at 3 years. AF was more prevalent in males (58.5% in the AF group compared to 43.9% in sinus rhythm (SR) subjects;  $p=0.03$ ) and the older age group. Ischaemic heart disease was more prevalent in AF subjects (22.6%) compared to SR subjects (4.4%) ( $p<0.001$ ). In the AF group previous stroke had occurred in 1.9% of subjects compared to 1.3% in the SR population ( $p=0.51$ ), and 24.5% of subjects in the AF group had diabetes compared to 16.6% in the SR group ( $p=0.12$ ). There was a significant difference in the prevalence of hypertension between the AF group (59.6%) compared to the SR subjects (45.5%) ( $p=0.04$ ).

**Conclusions** The prevalence of AF in the Malaysian population was low at 0.54% compared to the global average of 1%. We found that AF was associated with older age, male sex, hypertension, and ischaemic heart disease.

improving diagnostic tools.<sup>1</sup> As AF has strong associations with cardiovascular diseases such as coronary artery disease, valvular heart disease, heart failure and hypertension, it will inevitably generate a substantial burden on the future cost of healthcare.

The prevalence and incidence of AF is well studied in the USA and Europe. Elsewhere, data on AF remains limited. Prevalence rates differ greatly between studies as well as regions. In the USA, the landmark Framingham Study found the prevalence of AF between the years 1968 and 1989 in a cohort aged 65–84 years to increase over time in men but not in women.<sup>2</sup> In the ATRIA study, the overall prevalence was 0.95%, with prevalence increasing from 0.1% among adults <55 years to 9.0% in those aged ≥80 years.<sup>3</sup>

In the UK, the overall prevalence of AF reported by the ECHOES study was 2%, with prevalence rates of 1.6% in women and 2.4% in men.<sup>4</sup> The Renfrew/Paisley study, which is one of the largest epidemiological studies with a cohort of 15 406, found an AF prevalence of 0.65% in the West of Scotland population.<sup>5</sup> In Europe, the Rotterdam Study reported an overall prevalence of 5.5%, with age adjusted prevalence rising from 0.7% in those aged 55–59 years to 17.8% in those 85 years and older.<sup>6</sup> Meanwhile, an Australian study estimated the prevalence of AF in adults aged ≥55 years at 5.35%.<sup>7</sup>

In the Asia Pacific region, most AF studies have been conducted in Japan, Taiwan and China, with little data available from South East Asia. In Japan, numerous epidemiological studies in the 1990s–2000s reported a consistent AF prevalence rate ranging from 0.6% to 1.6%.<sup>8–16</sup> In Korea, in a study with a cohort of 14 540 adults, Jeong<sup>17</sup> reported an overall AF prevalence of 0.7% in adults >40 years of age and 2.1% in those >65 years. In China, four large community based studies published from 2008 to 2010 reported an AF prevalence ranging from 0.8–2.8%.<sup>18–21</sup>

To date, there have been only four published studies on AF prevalence in the community in South East Asia. The Thai community based studies reported differing prevalence from 0.4–2.2%<sup>22–23</sup> while Yap *et al*<sup>24</sup> in Singapore reported a prevalence of 1.5% in the Chinese community aged ≥55 years. There have been two AF studies in Malaysia: one community based study by Wong *et al*<sup>25</sup> reported an AF prevalence of 0.75% in the



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hypertensive Sarawak population with no prevalence difference between gender; another study reported an AF prevalence of 2.8% in acute medical admissions to a single centre.<sup>26</sup>

A large scale community-based study on the prevalence of AF has never been carried out in a multiracial country such as Malaysia. Being a growing nation with a current population of 30 million, it is important to determine the prevalence of AF and its associated risk factors in the Malaysian cohort in order to project and estimate future healthcare cost implications from the rising prevalence of AF.

## METHODS

The REDISCOVER (*Responding to Increasing Cardiovascular disease prevalence*) study is a longitudinal epidemiological study that was initiated by Universiti Teknologi MARA (UiTM) in the year 2007 with funding from the Ministry of Higher Education and Ministry of Science, Technology and Innovation Malaysia. It is an ongoing prospective community-based study which spans a period of 15 years, with a 3-yearly follow-up. Subjects recruited into the study included adults aged  $\geq 30$  years from 18 urban and 22 rural communities across Malaysia. Figure 1 shows the map of the REDISCOVER study sites. The methodology of the sampling process and recruitment has been previously described.<sup>27</sup> The institutional ethics committee approved the study protocol.

## Study population

Participants recruited into this study were from five states in Malaysia to ensure adequate representation of the major ethnic groups. A standardised method of recruitment was adopted, in which announcements and invitations were made through local community leaders. All household members above 30 years of age residing in each locality were invited via written invitation to attend a screening session at their local community centres. Participants were requested to fast before screening. Overall, a response rate of 60–70% was recorded. All interviewers and investigators were trained regarding the study procedures before conducting the study. Standardised, interviewer-based questionnaires were used to collect information regarding age, gender, ethnicity and educational attainment.<sup>27</sup> Questions asked in the questionnaires (which were in English and Malay) included cardiovascular risk factors, past medical history, drug history, social history, physical activities and dietary history.

Anthropometric measurements included height, weight, waist circumference and blood pressure. Blood pressure was measured twice after a 5 min rest using an automatic digital blood pressure monitor (Omron HEM 757) with a standard adult size cuff. ECG was recorded on a standard 12-lead format and calibrated

with GE Marquette MAC 5000, while echocardiography examinations were performed using GE model Vivid I and Philips CX 5000.

Fasting venous blood samples were collected for plasma glucose, plasma lipid and haemoglobin A1c and analysed with an automated enzymatic method. The participants were re-examined in two follow-up rounds. The first examination round was performed between July 2007 and December 2011. Follow-up data are currently being collected every 3 years for a period of 15 years. Hypercholesterolaemia was defined as fasting total plasma cholesterol  $\geq 5.2$  mmol/L and diabetes was diagnosed when fasting glucose was  $\geq 7.0$  mmol/L. Hypertension was defined as mean blood pressure  $\geq 140/90$  mm Hg or if the subjects were on antihypertensive medications or were aware of being hypertensive.

## Evaluation of AF

Initial screenings of all ECGs were done by clinicians who attended the recruitments and follow-ups. The diagnosis of AF was made retrospectively based on baseline screening 12-lead surface ECG. To verify the diagnosis of AF, all ECGs with a diagnosis of AF or atrial flutter or any other rhythm disorder were analysed independently by two cardiologists. Other ECG abnormalities indicative of prior myocardial infarction, ischaemia and left ventricular hypertrophy were also identified.

## Statistical analysis

All data were analysed using SPSS (V22; SPSS, IBM, Chicago, Illinois, USA). All parametric or normally distributed data were reported as mean (SD) and comparison of the means were performed using t-test. Categorical variables were described with frequency and percentage. Age-adjusted prevalence was computed using direct standardisation method. Significance level was set at  $p < 0.05$ .

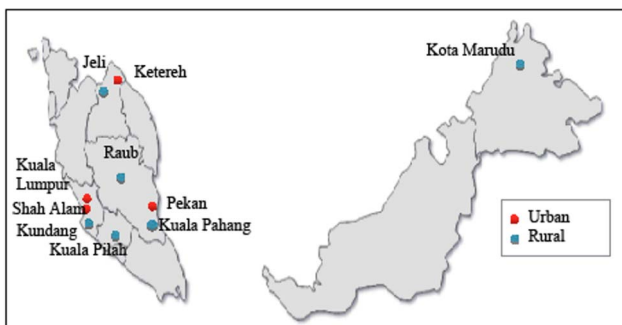
## RESULTS

A total of 12 701 subjects were recruited. The population for analysis consisted of 10 805 participants for whom a baseline ECG was available. In this population, which had a female predominance of 56% (6048), prevalence at baseline and at first follow-up was measured.

The baseline characteristics of our study cohort are presented in table 1. There was a Malay ethnic predominance of 71.9%, Chinese ethnicity of 10.7%, Indian ethnicity of 2.9% and other ethnicities of 14.5%; 5565 subjects lived in the urban areas while 5240 came from rural parts of Malaysia. Of this population cohort, 16.7% were diagnosed with diabetes mellitus, 45.6% with hypertension and 68.1% with hypercholesterolaemia. Only a small percentage reported as having ischaemic heart disease and stroke in the interview-based questionnaires (4.4% and 1.3%, respectively).

## Prevalence of AF

Analysis of ECG data from our cohort of 10 805 found 53 documented cases of AF at baseline, giving an overall prevalence of 0.49%. At the third year follow-up, there were eight new cases of AF; however, three deaths were recorded in the AF cohort. The overall prevalence of AF at the third year was 0.54%. There is an increasing trend of AF prevalence with age, which concurs with worldwide data on the prevalence of AF. The prevalence for those  $< 45$  years old was 0.14%, those between 45–54 was 0.09%, rising to 0.64% in the age group 55–64, and increasing steeply to 2.03% in those between 65

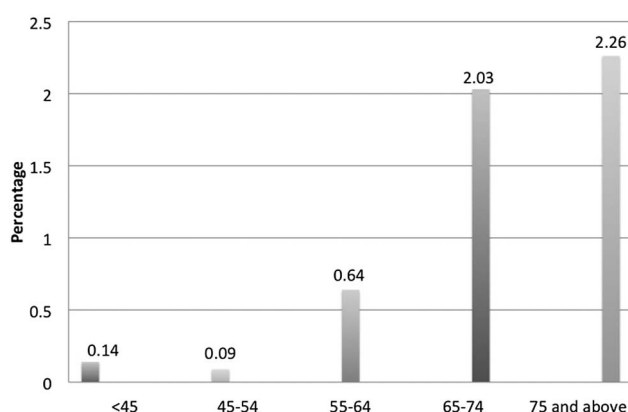


**Figure 1** REDISCOVER (*Responding to Increasing Cardiovascular disease prevalence*) site map.

**Table 1** Baseline characteristics of subjects participating in the REDISCOVER study

Baseline characteristics	Total cohort Mean	AF cohort n=53	Sinus rhythm cohort n=10 752	p Value
Age (years)	52.6 (±11.6)	64.5 (±10.4)	52.5 (±11.6)	<0.001
Weight (kg)	64.12 (±13.8)	62.08 (±15.84)	64.14 (±13.8)	0.32
Height (m)	1.57 (±0.08)	1.56 (±0.10)	1.57 (±0.09)	0.79
Body mass index (kg/m <sup>2</sup> )	25.98 (±4.88)	25.30 (±5.65)	25.99 (±4.88)	0.21
Systolic BP (mm Hg)	136.1 (±22.8)	139.0 (±25.8)	136.1 (±22.7)	0.59
Diastolic BP (mm Hg)	80.4 (±12.1)	83.0 (±15.77)	80.4 (±12.1)	0.20
Serum glucose (mmol/L)	5.7 (±2.37)	5.68 (±2.09)	5.70 (±2.37)	0.85
Total cholesterol (mmol/L)	5.7 (±1.2)	5.38 (±1.06)	5.70 (±1.2)	0.029
Triglycerides (mmol/L)	1.75 (±1.04)	1.70 (±0.92)	1.75 (±1.04)	0.41
LDL cholesterol (mmol/L)	3.67 (±1.06)	3.29 (±1.03)	3.67 (±1.07)	0.025
HDL cholesterol (mmol/L)	1.25 (±0.35)	1.30 (±0.44)	1.25 (±0.35)	0.66

AF, atrial fibrillation; BP, blood pressure; HDL, high density lipoprotein; LDL, low density lipoprotein; REDISCOVER, Responding to Increasing Cardiovascular disease prevalence.

**Figure 2** Prevalence of atrial fibrillation according to age group (years).

and 74 years old. There were a total of eight AF cases screened in the  $\geq 75$  age group, giving a prevalence of 2.26% (figure 2).

In our cohort, AF prevalence was higher among males ( $p=0.03$ ) as shown in table 2. However, there was no significant difference between ethnicity or urbanisation. Ischaemic heart disease was more prevalent in the AF cohort (22.6%) compared to the subjects in sinus rhythm (SR) (4.4%) ( $p<0.001$ ). There was also a significant difference in hypertension in the AF group (59.6%) compared to the SR subjects (45.5%) ( $p=0.04$ ). In the AF group, the prevalence for previous stroke was 1.9% compared to 1.3% in the SR population ( $p=0.51$ ). There was no significant difference in the prevalence of diabetes between the two cohorts. In our population, smoking prevalence did not differ between the AF and normal cohort ( $p=0.84$ ). However, smoking prevalence was significantly higher in the rural communities ( $p<0.001$ ).

**Table 2** Comparison between sinus rhythm and AF subjects at baseline in the REDISCOVER cohort

	Sinus rhythm N=10 752	AF N=53	p Value
Gender	Male 4726 (43.9%) Female 6026 (56.1%)	Male 31 (58.5%) Female 22 (41.5%)	0.03
Urban	5544	21	0.08
Rural	5208	32	
Ethnicity			0.73
Malay	7724	41	
Chinese	1155	5	
Indian	313	0	
Others	1560	7	
Hypertension	4891/10 752 (45.5%)	31/53 (59.6%)	0.04
Ischaemic heart disease	469/10 752 (4.4%)	12/53 (22.6%)	<0.001
Stroke	138/10 752 (1.3%)	1/53 (1.9%)	0.51
Diabetes mellitus	1788/10 752 (16.6%)	13/53 (24.5%)	0.12
Smoking			0.84
Current	1385/10 752 (12.9%)	6/53 (11.3%)	
Ceased	1163/10 752 (10.8%)	5/53 (9.4%)	
Non	8204/10 752 (76.3%)	42/53 (79.3%)	
Death at 3 years	140/10 752 (1.3%)	3/53 (5.7%)	0.05

AF, atrial fibrillation; REDISCOVER, Responding to Increasing Cardiovascular disease prevalence.

There was a total of three reported deaths (5.7%) in the third year follow-up in the AF cohort, compared to 140 deaths (1.3%) in the SR cohort, as shown in table 2. All three deaths were attributed to cardiovascular causes, with one death from stroke.

Further multiple regression analysis as shown in table 3 shows that AF itself did not significantly increase the risk of death; however, factors such as increasing age, female gender as well as rural locality carry significantly higher death rates. Associated co-morbidities such as diabetes and ischaemic heart disease are also associated with significantly higher death rates.

Subanalysis of the rural population in REDISCOVER shows significant differences between the prevalence of co-morbidities between these communities compared to the urban population. The prevalence of hypertension, diabetes, ischaemic heart disease and stroke are found to be significantly higher in the rural communities, as shown in table 4.

## DISCUSSION

As evident by multiple community and hospital studies across the world, AF prevalence differs greatly between regions. AF has been found to be more prevalent in Western countries compared to Asian countries. North America has the highest burden of AF, whereas the Asia Pacific region, specifically Japan, Korea and China, has the lowest AF prevalence. A survey of acute medical admissions for AF at a city centre hospital in Birmingham, UK, which serves a multi-ethnic population of 300 000, also indicated that there was a lower prevalence of AF in Indo-Asians compared to Caucasians.<sup>28</sup> Our community-based study findings concur with those of other studies in the Asia Pacific regions, with an even lower prevalence of AF.

Factors driving the differences between regions are not clear but could be explained by the following. First, higher detection rates of AF in Western countries can be due to greater awareness, better diagnostic tools and a more structured healthcare system. Second, diversity in the prevalence of risk factors for

**Table 3** Risk factors associated with death in the REDISCOVER cohort

	Unadjusted OR (95% CI)	p Value	Adjusted OR (95% CI)	p Value
Age	1.06 (1.05 to 1.08)	<0.001	1.04 (1.02 to 1.06)	<0.001
Gender				
Male	Ref		Ref	
Female	0.41 (0.29 to 0.57)	<0.001	0.53 (0.36 to 0.78)	0.001
AF	4.55 (1.40 to 14.76)	0.012	2.39 (0.72 to 7.97)	0.155
Geographical area				
Urban	Ref		Ref	
Rural	3.08 (2.12 to 4.49)	<0.001	2.71 (1.85 to 3.97)	<0.001
Hypertension	1.82 (1.30 to 2.55)	0.001	0.99 (0.69 to 1.42)	0.944
Ischaemic heart disease	3.38 (2.07 to 5.53)	<0.001	2.03 (1.21 to 3.41)	0.007
Stroke	1.09 (0.27 to 4.44)	0.905	0.49 (0.12 to 2.06)	0.336
Diabetes mellitus	2.57 (1.81 to 3.65)	<0.001	2.27 (1.58 to 3.27)	<0.001
Smoking				
Never	Ref		Ref	
Current	1.81 (1.16 to 2.81)	0.009	1.18 (0.73 to 1.91)	0.495
Previous	2.58 (1.71 to 3.91)	<0.001	1.48 (0.94 to 2.33)	0.088

AF, atrial fibrillation; REDISCOVER, *Responding to Increasing Cardiovascular disease prevalence*.

**Table 4** Comparison of characteristics and co-morbidities between urban and rural population

	Urban N=5565	Rural N=5240	p Value
Gender			
Male	2484 (44.6%)	2273 (43.4%)	0.188
Female	3081 (55.4%)	2967 (56.6%)	
Hypertension	2354 (42.3%)	2568 (49.0%)	<0.001
Ischaemic heart disease	211 (3.8%)	269 (5.1%)	0.001
Stroke	59 (1.1%)	81 (1.5%)	0.027
Diabetes mellitus	991 (17.8%)	810 (15.5%)	0.001
Smoking			
Never	4112 (78.3%)	3680 (72.2%)	<0.001
Current	564 (10.7%)	827 (16.2%)	
Previous	579 (11.0%)	590 (11.6%)	

AF, such as ischaemic heart disease, obesity or hypertension, could be responsible for inter-region variability. Cardiovascular diseases such as ischaemic heart disease are now the most prevalent diseases in developed nations, as compared to communicable illnesses in the developing countries. Higher survival rates from myocardial infarction also contribute to the rising trend of AF prevalence and incidence in Western countries, as AF is strongly associated with ischaemic heart disease and cardiomyopathy. Finally, differences in the underlying risks resulting from genetic factors might justify this regional heterogeneity.

AF burden in Asia and in Malaysia is expected to increase if the prevalence of predisposing factors such as prior myocardial infarction, heart failure, hypertension, diabetes, valvular disease and obesity increases, as in Western countries. The reason for the discrepancy in the prevalence of AF between Asian and Western countries could then be explained by a time lag in the trends of predisposing factors between Asian and Western countries. In the Prospective Urban Rural Epidemiology (PURE) survey which recruited 160 000 adults in 17 countries,<sup>29</sup> the pooled prevalence of hypertension among the three high-income countries included in the study was 41%.<sup>30</sup> In the lower

to upper middle income countries, the prevalence of hypertension varied from of 27% in Iran to 67% in Poland.<sup>30</sup> Compared to other cohorts, the prevalence of hypertension in the REDISCOVER population is above the global prevalence and that of high income countries. This inevitably will lead to increases in cardiovascular related morbidity and mortality, including a rising trend in AF in years to come.

In our study, there was a trend towards a significant difference in AF prevalence between rural and urban populations, with AF being more prevalent in the rural populations. This can be explained by the significantly higher prevalence of its associated risk factors such as hypertension, stroke, smoking and ischaemic heart disease observed in the rural communities. The possible explanation for our finding is that the rural population in Malaysia has limited access to healthcare, and thus poorer awareness, control and optimisation of their cardiovascular risk factors. Hence this population group is at a higher risk of cardiovascular-related illnesses. However, in terms of racial differences, we found that there was no difference in AF prevalence between different ethnic groups in the Malaysia population.

The prevalence of AF in our cohort is lower than that found in a previous local study in a group of hypertensive patients in Sarawak (0.75% vs 0.54%).<sup>25</sup> This can be explained by the higher prevalence of hypertension in that group. In a large community study from Korea, a higher prevalence of 0.7% is seen across the cohort.<sup>17</sup> This is mainly driven by a higher rate of AF in the older age group (4% in those subjects >80 years old).<sup>17</sup>

Despite being an epidemiological study, our follow-up rate is satisfactory at 90% with a low fallout rate. The limitation of our study is under-reporting of chronic illnesses in the interview-based questionnaires and inter-observer variability in questionnaire completion. This will undoubtedly result in underestimation of the prevalence of chronic illnesses.

## CONCLUSION

Our study found an overall prevalence of AF of 0.54%, which is lower than the global average of 1%. The most likely explanation for our finding is the lower burden of cardiovascular disease as well as a population cohort that is younger on



average, with a mean age of 53 years. In our study, AF was found to be more prevalent in males, and its prevalence increased with age. It was also associated with ischaemic heart disease and hypertension. Global burden of AF is predicted to rise in years to come and with the urbanisation in the Asian countries, we may soon see a trend similar to that in developed nations. Physicians in Singapore and Malaysia report that AF patient numbers have increased by approximately 10% over the last 3 years and will continue to rise.<sup>31</sup> AF will continue to pose a major burden to the public health cost in years to come with its associated morbidity and mortality.

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**Contributors** CWL and SK wrote the manuscript and were involved in the data collection of the REDISCOVER Study. JRI performed the statistical analysis and contributed to the critical discussion of the results. NCYC, RNK, EAR, MKMA, HAZA and ZIO contributed to the critical revision of the manuscript and were involved in the data collection. KY is the Principal Investigator of this study. He played a major role in the conception and design of the study, contributed to the critical revision of the manuscript and intellectual content, and provided expertise and oversight throughout the process. All authors read and approved the final version.

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**Competing interests** None declared.

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