

# Prevalence and Predictors of Atrial Fibrillation and its Embolic Complications in Patients with Rheumatic Heart Disease at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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## Abstract

**Background:** Atrial fibrillation is one of the complications of rheumatic heart disease, with substantial morbidity and mortality. The prevalence and predictors of atrial fibrillation and its thrombo-embolic complications in Ethiopian patients with rheumatic heart disease are unknown. The objective of this study was to determine the prevalence and predictors of atrial fibrillation and its thromboembolic complications.

**Methods:** A retrospective chart review of 500 patients with rheumatic heart disease at the adult cardiology clinic of Tikur Anbessa Specialized Hospital was carried out from 01 January to 31 June 2016. Data were entered into a pre-tested questionnaire and were analyzed using SPSS version 23.

**Results:** Records of 500 patients (72% female) with electrocardiographic recordings and echocardiographic reports were available for analysis. Atrial fibrillation was found in 234 (46.8%) of the patients. Predictors of atrial fibrillation were found to be: age  $\geq 50$  years ( $p=0.01$ ), left atrial size  $\geq 45$ mm ( $p=0.01$ ), the presence of mitral stenosis ( $p<0.01$ ) and the presence of tricuspid regurgitation ( $p=0.01$ ). Cardioembolic events were reported in 67 (9.2%) patients, and the presence of atrial fibrillation ( $p=0.02$ ) and sub-therapeutic anticoagulation status ( $p<0.01$ ) were significant predictors of cardioembolic events.

**Conclusions and recommendations:** The study reveals a high prevalence of atrial fibrillation and cardioembolic events in Ethiopian patients with rheumatic heart disease. Hence, active screening of atrial fibrillation and optimal anticoagulation are recommended. [*Ethiop. J. Health Dev.* 2019;33(1):12-16]

**Key words:** Rheumatic Heart Disease, Atrial Fibrillation, Cardioembolic Complications, Stroke, Ethiopia

## Background

Atrial fibrillation (AF) is a cardiac rhythm disorder where the normal sinus rhythm is replaced by a chaotic, ineffective atrial rhythm. AF is relatively common arrhythmia and may cause significant mortality and impair both functional status and the quality of life (1-3). In developed countries, coronary artery disease and hypertensive heart disease are the two most common causes, while rheumatic heart disease (RHD) is the major cause in developing countries such as Ethiopia (4). RHD causes considerable morbidity and mortality as a result of cardioembolic stroke, congestive heart failure and infective endocarditis. Carapetis and colleagues estimate that up to 7.5% of all strokes that occur in less developed countries could be a direct result of RHD (5).

In Ethiopia, RHD is a significant cause of cardiovascular morbidity and mortality (6-9). According to previous studies, up to two-thirds of cases of AF in Ethiopian patients could be attributed to RHD (6-10, 11). AF is one of the main contributors of stroke in the young, worsening heart failure and mortality (12,13) (12,13). A retrospective study of stroke patients at Tikur Anbessa Hospital showed that 28.8% of strokes in the young (aged 15-44 years) were attributed to RHD (14). RHD patients with or without coexistent overt AF are predisposed to the development of

cardioembolic stroke (15). For high-risk patients with AF, anticoagulation with rate and rhythm control is the main treatment modality. These high-risk patients include those with left atrial thrombus, previous systemic embolism, and rheumatic mitral stenosis (MS) (16). Several observational studies have documented lower rates of recurrent cerebral embolic events among RHD patients who receive warfarin (17,18).

We are unaware of any study which has examined the prevalence and determinants of AF and its cardioembolic complications in Ethiopian RHD patients. Hence, this study aims to investigate the prevalence, determinants, anticoagulation status and complications of AF in Ethiopian patients with RHD at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. The findings of the study will be valuable for planning preventive measures to reduce the complications of AF caused by RHD by showing the prevalence and determinants of the disease.

## Methods

This was a retrospective review of medical records of 500 RHD patients who had clinical follow-up at the adult cardiac clinic of Tikur Anbessa Specialized Hospital between January 2011 and January 2016. The hospital is the largest referral hospital in the country and provides cardiovascular care for patients older than 13 years of age at adult cardiac clinic. All new

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cardiovascular patients referred to the clinic are evaluated by cardiologists for diagnosis, initiation and optimization of treatment.

Patients with a diagnosis of RHD who had both electrocardiographic (ECG) recordings and standard echocardiographic reports were included in the study. Echocardiography is currently the gold standard diagnostic test for RHD. Data on patient socio-demographics, clinical characteristics – including the presence or absence of hypertension, diabetes mellitus, dyslipidemia, heart failure, current drug treatment, and history of cardioembolic events, average International Normalized Ratio (INR) test results done in the past six months and echocardiographic findings, were collected using a standardized pre-tested questionnaire. A presumed cardioembolic event was considered when imaging evidence of ischemic stroke and/or peripheral acute ischemic events were found in known RHD patients.

Preliminary ECG readings were performed by senior medical residents and confirmed by a senior cardiologist (the investigator). Medical residents at Tikur Anbessa Hospital who were trained on the study protocol participated in the review of patients' charts and collection of the research data. The investigators were also involved in the training of data collectors and supervision of data collection. Quality assurance of the data was made in a two-tier fashion. First, the supervisor checked for the completeness of the data on a daily basis. Incomplete and poor-quality questionnaires were filled in the next day. The second tier was a rejection of the incomplete data for which corrections could not be made.

#### Ethical considerations

Ethical approval from the Institutional Review Board (IRB) of Addis Ababa University – College of Health Sciences was obtained. Permission was obtained from

the registrar office of the hospital after approval by the IRB. To ensure the confidentiality of participants' medical records, patient information (such as name and telephone number) was not collected.

#### Methods

Data were entered into SPSS version 23 for analysis. Prevalence was calculated as the percentage of patients with ECG-confirmed AF and cardioembolic events among the total number of study participants. Continuous variables such as age and INR values were displayed as medians (interquartile range). Chi-squared tests were used to test for the association of independent variables with the dependent variables (prevalence of AF and embolism). All factors with a p-value <0.05 in the bivariate analysis were further analyzed with a logistic regression model to control for confounding effects.

#### Results

**Socio-demographic characteristics and type of valve lesions** Of the 833 patient records initially screened for the study, a total of 500 (72% female) patients older than 13 years of age (median age 29, Interquartile Range (IQR) 13.8) fulfilled the inclusion criteria. The lack of an electrocardiogram was the primary reason for exclusion. Mitral stenosis (MS), defined by mitral valve area <2cm<sup>2</sup>, was the most common valve lesion found in 391 (78.2%) of the patients, followed by mitral regurgitation (MR) in 348 (69.6%), tricuspid regurgitation (TR) in 297 (59.4%) and aortic regurgitation (AR) in 240 (48.0%). Close to half (49.8%) of these valve lesions were mixed lesions (regurgitation and stenosis) of the mitral valve or combined aortic and mitral valve lesions. All tricuspid lesions were associated with mitral and/or aortic lesions. Table 1 shows the socio-demographic characteristics of the patients and types of valve lesions.

Table 1: Socio-demographic characteristics of the study participants and types of valve lesion, 2017

Variables	Number	Percent	
Gender	Female	360	72.0
	Male	140	28.0
	Total	500	100.0
Age range	<20	70	14.0
	20-29	199	39.8
	30-39	143	28.6
	40-49	50	10.0
	Above 50	38	7.6
	Total	500	100.0
Type of valve lesion	Mitral stenosis	391	78.2
	Mitral regurgitation	348	69.6
	Tricuspid regurgitation	297	59.4
	Aortic regurgitation	240	48.0

**Prevalence and determinants of AF:** Of the 500 patients included in the study, 234 (46.8%) had ECG evidence of AF. Rates of AF were similar between females (47.5%) and males (44.6%), (p=0.6). The prevalence of AF was most common in the ≥50 age

group, and least common in the ≤20 age group (p=0.01). Table 2 shows the prevalence of AF across different age groups.

Nearly a quarter of the study participants were not taking benzathine penicillin for secondary prevention of RHD. Patients with AF were less likely to take prophylaxis than those with no AF (69.7% versus 83.5%). Other prescribed drugs used were furesmide (77.5%), spironolactone (63.4%), digoxin (42.3%), warfarin (35.6%), atenolol (36%), metoprolol (12.4%) and aspirin (5.4%). Aspirin was prescribed for those patients who could not afford INR monitoring with warfarin treatment. The presence or absence of non-valvular risk factors for AF – such as hypertension, smoking, diabetes and dyslipidemia – was not recorded as primary diagnoses of these patients, but we found the number of cases with these risk factors was only 9 (1.8%) from indirect observation of recorded BP values and prescribed medication for these risk factors.

On bivariate analysis using a chi-square test, AF was found more in those with TR than without TR (54.4% versus 35.8%;  $p < 0.01$ ); more in those with MS than with no MS (51.9% versus 28.4%;  $p < 0.01$ ); more in those with MR than in those with no MR (49.9% versus 39.9%;  $p = 0.31$ ); and where the left atrial size was greater than 40mm ( $p < 0.01$ ). AF was found more in those with heart failure of at least functional class II than in those with no heart failure (47.4% versus 43.5%;  $p = 0.06$ ).

On multivariable analysis, age  $\geq 50$  years ( $p = 0.01$ ), left atrial size greater than 45mm ( $p = 0.01$ ), the presence of MS ( $p < 0.01$ ) and the presence of TR ( $p = 0.01$ ) were found to be predictors of AF. Table 2 shows the association of different variables with the prevalence of AF.

**Table 2: Multivariable analysis of prevalence of atrial fibrillation with different covariates, 2017**

Variables	Atrial fibrillation		Multivariable analysis AOR (95% CI)	
	Absent N (%)	Present N (%)		
Age range	<20	43 (61.4)	27 (38.6)	1.0
	20-29	127 (63.8)	72 (36.2)	0.803 (0.406,1.590)
	30-39	62 (43.4)	81 (56.6)	2.093 (1.014-4.316)
	40-49	21 (42.0)	29 (58.0)	1.395 (0.575,3.385)
	Above 50	13 (34.2)	25 (65.8)	3.985 (1.332,11.390)
Mitral stenosis	Absent	78 (71.6)	31 (28.4)	1.0
	Present	188 (48.1)	203 (51.9)	4.664 (1.996,10.900)
Mitral regurgitation	Absent	92 (60.1)	61 (39.9)	1.0
	Present	174 (50.1)	173 (49.9)	1.592 (0.967,2.620)
Tricuspid regurgitation	Absent	131 (64.2)	73 (35.8)	1.0
	Present	135 (45.6)	161 (54.4)	1.913 (1.213,3.017)
Left atrial size (minor dimensions)	<40	51 (86.4)	8 (13.6)	1.0
	40-45	70 (83.3)	14 (16.7)	0.843 (0.299,2.372)
	45-50	57 (57.0)	43 (43.0)	3.559 (1.361,9.327)
	>50	88 (34.2)	169 (65.8)	8.064 (3.317,19.603)

**Anticoagulation and prevalence of cardioembolic events:** Among 234 patients with AF, 178 (76.1%) were taking warfarin as an anticoagulant and 10.5% of those with no AF were also taking warfarin for a presumed cardioembolic event. At least one INR determination in the past six months was found for 82% of those on warfarin. Half of the patients on warfarin had average INR values between 2.0 and 4.0, and a substantial proportion of patients on warfarin 74 (40%) had a sub-therapeutic INR (INR values below 2) with a median INR of 2.2 and IQR of 1.29; the remaining 9.7% had values above 4.

Out of the 500 patients, 67 (9.2%) had presumed cardioembolic events. Patients with AF were twice as likely to have these events than those with no AF (12.4% versus 6.4%;  $p < 0.01$ ). Of the 67 patients with cardioembolic events, 41 (61%) had INR values less than 2.0. The presence of MS, the absence of MR, left atrial size greater than 40mm and INR values less than 2.0 were found to be predictors of a cardioembolic event on bivariate analysis using a chi-square test. However, on multivariable analysis, only the presence of AF ( $p = 0.02$ ) and an INR value less than 2.0 ( $p < 0.01$ ) were related to the occurrence of an acute vascular event. Table 3 depicts the relationship between different variables and embolic manifestations.

Table 3: Multivariable analysis of cardioembolic event with other covariates, 2017

Variables		Cardioembolic event		Multivariable analysis
		Absent N (%)	Present N (%)	AOR (95% CI)
Mitral stenosis	Absent	106 (97.2)	3 (2.8)	1.0
	Present	330 (84.4)	61 (15.6)	2.224 (0.473,10.635)
Mitral regurgitation	Absent	126 (82.4)	27 (17.6)	0.575 (0.299,0.891)
	Present	310 (89.3)	37 (10.7)	1.0
Mitral valve area	>2cmsq	141 (94.0)	9 (6.0)	1.0
	1.5-2.cm <sup>2</sup>	40 (85.1)	7 (14.9)	0.675 (0.240,1.903)
	1-1.49cm <sup>2</sup>	109 (90.1)	12 (9.9)	0.893 (0.337,2.391)
	<1cm <sup>2</sup>	146 (80.2)	36 (19.8)	0.575 (0.266,1.245)
Left atrial size (minor dimensions)	<40mm	56 (94.9)	3 (5.1)	1.0
	40-45mm	79 (94.0)	5 (6.0)	0.550 (0.105,2.876)
	45-50mm	83 (83.0)	17 (17.0)	0.789 (0.176,3.538)
Atrial fibrillation	>50mm	218 (84.8)	39 (15.2)	0.588 (0.137,2.529)
	Absent	245 (92.1)	21 (7.9)	1.0
INR values	Present	191 (81.6)	43 (18.4)	2.624 (1.172,5.877)
	INR<2.0	51 (85.6)	9 (14.4)	23.286 (8.289,65.423)
	INR>2.0	85 (94.1)	5 (5.9)	1.0

### Discussion

Our study shows that RHD patients have a high prevalence of AF (46.8%), a high prevalence of cardioembolic event (9.2%) and a high proportion (40%) of sub-therapeutic anticoagulation levels (INR values less than 2). The prevalence of AF in our study is close to the prevalence of 50% reported in another prospective study by Shimada (19), but much higher than the 21.8% reported in the REMEDY study (20). This could be related to the higher proportion of MS in our study (78%) compared to the REMEDY study (45%). Approximately 40% of patients initially screened for the study had no ECG examination, which may underestimate the true prevalence of AF in our study.

Age was one of the significant predictors of AF in our study, with a marked increase at age  $\geq 50$  years. Other predictors included the type of valve lesion and left atrial size. The highest prevalence was found in those patients with TR. The high prevalence of AF in patients with TR may be explained by the fact that such patients have a larger right atrial size and elevated right atrial pressure, both of which can increase the risk of developing AF (21,22). Left atrial size was another independent predictor of AF, as shown in several other studies. The mean left atrial size in our study was significantly larger in patients with AF than patients without AF ( $p= 0.001$ ). Several studies have also shown a strong correlation between left atrial size and new-onset AF (23,24).

The prevalence of cardioembolic events in our study was higher (9.2% versus 5.2%) than that reported in the REMEDY study (18). The prevalence of cardioembolic events was lower in those with MR than those with no MR. This has been shown in transesophageal echocardiographic studies, where the presence of significant MR is associated with a lower incidence of spontaneous echo contrast in the left atrium and thus with a lower risk of thrombi and embolization compared to rheumatic MS (25,26). In our study, the use of oral anticoagulant was slightly better than that of

the REMEDY study (76.1% versus 69.5%), and of the global use of oral anticoagulant (OAC) for non-valvular AF study (76.1% versus 58%) (20,27). However, as in the REMEDY study, a significant proportion of patients (40%) on warfarin had a sub-therapeutic level (INR values less than 2). Lack of proper titration of warfarin dose to recommended therapeutic INR range and inter-individual variability of anticoagulant effects of warfarin could be possible explanations for the sub-therapeutic INR values (28). The presence of AF and a sub-therapeutic INR level were significantly associated with the presumed cardioembolic event.

**Limitations of the study:** Our study is a retrospective review of medical records and may not show the true prevalence of AF. A lack of proper documentation for other risk factors, such as hypertension, diabetes and dyslipidemia, might underestimate the contribution of these risk factors to AF. Finally, all patients were from a major referral center of the country, which would likely attract more severe cases.

### Conclusions and recommendations:

Our study shows a high prevalence of AF and cardioembolic events in patients with RHD. Nearly half of the patients on oral anticoagulants had suboptimal anticoagulation. ECG evaluation of RHD patients for detection of AF, and maintenance of optimal anticoagulation status for high-risk patients with AF, are recommended.

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