

## CLINICAL AND EPIDEMIOLOGICAL STUDY ON ATRIAL FIBRILLATION: ORIGINAL REPORT

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**ABSTRACT: CONTEXT:** Atrial fibrillation is the most common cardiac arrhythmia in clinical practice. In developing countries like India, the high morbidity and mortality associated with this condition, warrants detailed assessment. **AIMS:** To find the epidemiological and etiological factors associated with atrial fibrillation. **SETTINGS & DESIGN:** The study was conducted in Shyam Shah Medical College and associated Sanjay Gandhi Medical Hospital in Rewa (MP), during 2010 and 2011 on 125 patients. **METHODS & MATERIAL:** A complete general and systemic examination to be carried out on subjects presenting with Atrial Fibrillation on Electrocardiography followed by Echocardiographic analysis. **RESULTS:** Out of 125 patients, who presented with Atrial Fibrillation (AF), 56.8% were females and 43.2% were males. While 102(81.6%) patients were above 40 years, 23(18.4%) were below 40 years of age. 84% of cases were reported from rural area whereas 16% were from urban area. Most common aetiology associated with AF was rheumatic heart disease (RHD) (45.6%) followed by coronary artery disease (CAD) (18.4%) and hypertension (12%). Most common etiologic factor found among rural population was RHD (51.4%). Among the urban population 30% had CAD while 15% had RHD aetiology. Above 50 years of age, most common etiologic factor associated was CAD (30%), followed by RHD (24%). Echocardiographic Left Atrium (LA) size was more than 4cm in 79.2% of patients. Maximum LA enlargement was found in RHD patients (57.07±10.8mm). Among valvular lesions, maximum LA size was seen with mitral regurgitation (68.7±9.1mm). Coarse AF was present in 48% of patients studied. Of these majority were associated with RHD (63.3%) and 86.6% of these patients had LA size more than 4 cm. LA thrombus was seen in 4.8% patients. **CONCLUSION:** Most common aetiology associated with atrial fibrillation in our set up is RHD. In our population the disease is more common in rural area having a female predominance and younger age of onset. Risk of atrial fibrillation increases with age, and it is more frequently associated with CAD than RHD. Patients with Echocardiographic LA size more than 4 cm had an increased risk of atrial fibrillation.

**KEYWORDS:** Atrial Fibrillation, MeSH Heading, Atrial Fibrillation.

**INTRODUCTION:** Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical practice. It is associated with increase in cardiac morbidity and mortality. The overall prevalence in general population is estimated to be 0.4%. Western studies show that the incidence and prevalence of AF steadily increases with age such that this arrhythmia occurs in 0.5% of population less than 50yrs of age and increases to approximately 9% in patients 80 years or older.<sup>1</sup>

It is associated with various modifiable and non-modifiable risk factors. Most important non-modifiable risk factors are age and sex. Modifiable risk factors include systemic hypertension, diabetes mellitus, heart failure, myocardial infarction and valvular heart disease.

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The epidemiological importance of AF as an important precursor of cardiac and cerebrovascular death was investigated in detail in the Framingham study by William Kannell and colleagues in 1982.<sup>2</sup>

Based on 38 year follow up data from Framingham study, men had a 1.5 fold greater risk of developing AF compared to women, while diabetes and hypertension conferred a higher risk.<sup>3</sup>

Atrial fibrillation is principally an acquired disease but rare familial forms have been described, associated with abnormalities of chromosome 10 which may segregate in an autosomal dominant pattern.<sup>4</sup> Recent studies by Patrick Ellinor et al show mutation in chromosome 6 associated with long QT syndrome and early onset AF.<sup>5</sup>

In the Indian subcontinent, even though the exact data regarding incidence and prevalence of AF is not available, the prevalence is likely to be high due to morbidity due to RHD. Rheumatic heart disease continues to remain the most frequent cause of AF in a recent survey in public and private institutes in India. However, hypertension and ischemic heart disease also contributes to its high incidence in India.<sup>6</sup>

Thus, the present study aims at identifying the epidemiological and co-morbid factors involved, so that we may understand, and treat, this arrhythmia in a better manner.

### **MATERIALS AND METHODS:**

#### **AIMS & OBJECTIVES:**

- To find the epidemiological and etiological factors associated with atrial fibrillation.

#### **METHODOLOGY:**

**INCLUSION CRITERIA:** The present study was conducted on patients who presented with Atrial Fibrillation, admitted in medicine wards of Sanjay Gandhi Memorial Hospital, Rewa during 2010-11.

**METHODS:** All patients with clinical history and examination suggestive of atrial fibrillation were included in study. Twelve lead electrocardiogram and transthoracic echocardiogram were analyzed in each patient.

#### **ANALYSIS:**

1. On Electrocardiogram, absence of a definite P wave with varying R-R interval and presence of f wave, was diagnostic of AF. Based on the morphology of 'f' waves, patients were broadly classified as 'fine AF' (f wave amplitude <0.5mm) and 'coarse AF' (f wave amplitude >0.5mm).<sup>7</sup> ECG's were further analysed for evidence of conduction disturbances, Ashman phenomenon,<sup>8</sup> chamber enlargement and variation in electrical axis of QRS complexes depending on different aetiology.
2. Trans-thoracic 2D echocardiography study was conducted to find out structural heart lesions, to measure the left atrial size, estimate of left ventricular function and to detect left atrial thrombus in LA cavity and appendage.
  - a) Left atrial size was assessed by M mode on the parasternal long axis in accordance with American Society of Echocardiography recommendations. The measurement was made between the leading edge of posterior aortic wall to the leading edge of posterior left atrial wall at the end of systole.

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- b) Regardless of body surface area or aortic diameter any absolute measurement of LAD more than 3.8cm is indicative of left atrial enlargement.<sup>9</sup>
3. Other investigations including serum electrolytes, thyroid function tests were done in indicated patients.

### OBSERVATIONS:

Age Distribution		
< 40 years		18.4%
> 40 years		81.6%
Mean age:		
Males	57.3	57.35±16.9
Females		51.46±15.5
Male: Female ratio (M/F) (P=0.0601)		1: 1.3
Rural / urban ratio: (R/U) (p=0.8014)		5.25:1

**Table 1: Epidemiological Features**

In the present study it was observed that prevalence of AF increases as the age advances. Out of 125 patients studied 102 (81.6%) patients were above 40 years and 23 (18.4%) patients were below 40 years.

The mean age of study population was 54 years. Of these, mean age of males were 57.35 years and females were 51.46 years. This shows an early age onset of this cardiac condition in females.

On analyzing the etiologic factors, the most common aetiology i.e. RHD, was associated with higher prevalence in younger age (mean age of 44.3±14) whereas CAD was associated with an older age (mean age 65.3±9.8).

In the present series, a female preponderance was seen, with a greater number of females (56.8%) than males (43.2%).

It was also observed that 105 (84%) patients were from the rural area whereas only 20 (16%) were from urban areas. There is also a difference in the distribution of etiologic factors associated with atrial fibrillation in rural and urban areas.

Most common etiological factor in the rural area was RHD (51.5%) followed by CAD (16%) and hypertension (9.5%) whereas in urban areas the most common etiological factor was CAD (30%) and hypertension (20%) followed by RHD (15%).

Etiology	N	Mean age	M/F (p=0.009)	R/U (p=0.0803)
RHD	57(45.6%)	44.3±14	1: 3.1	54/3
Non-rheumatic valvular heart disease	9(7.2%)	71.3±8.2	1.25:1	6/3
CAD	23(18.4%)	65.3±9.8	2.3:1	17/6
Hypertension	14(12.0%)	63.14±15.6	1.3: 1	10/4
Cardiomyopathy	9(7.2%)	47.6±13.6	1:1.25	8/1
Lone AF	7(5.6%)	54.4±10.3	1.3:1	5/2
Other causes	6(4.8%)	64.3±15.2	1:1	5/1
Thyrotoxicosis	1	-	-	-

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COPD	4	-	-	-
Ebsteins Anomaly	1	-	-	-
<b>TOTAL</b>	<b>125</b>	<b>54.0±16.3</b>	<b>1:1.3</b>	<b>105/20</b>

**Table 2: Etiologic Factors among study population**

Most common etiology associated with atrial fibrillation in the total study group was Rheumatic heart disease (45.6%). It was followed by coronary artery disease (18.4%) and hypertension (12%).

Cardiomyopathy and lone AF were responsible for 7.2% and 5.6% of cases respectively. Other less common causes were found in 4.8% (Chronic obstructive Pulmonary Disease, thyrotoxicosis and Ebsteins anomaly).

Among females most common etiology for atrial fibrillation was rheumatic heart disease (34.4%) followed by hypertension (5.6%) and CAD (5.6%) whereas in males the most common etiologic factor was CAD (12.8%) followed by RHD (11.2%) and hypertension (6.4%). The difference was found to be statistically significant ( $p=0.009$ ).

Rheumatic heart disease had maximum prevalence (61.4%) in the 26-50 years age group whereas the second most common etiology of CAD had maximum prevalence (86.9%) in the >50 years age group.

In the above 50 years age group, most common etiologic factors are coronary artery disease 30%, followed by RHD (24%), hypertension (16.4%), lone atrial fibrillation (5.9%) and non-rheumatic valvular heart disease (13.4%). The difference was statistically highly significant ( $p=0.0001$ ).

In the 26-50 year age group most common etiologic factors were RHD (60.0%), cardiomyopathy (12.0%), CAD (6.0%), hypertension (2.0%) and lone AF (6.0%)

The mean age of atrial fibrillation in RHD was 44.36 years while mean age was 71.1 years for non-rheumatic valvular heart disease.

For CAD and hypertension, the mean age was 65.3 and 63.14 years respectively. This may be related to the increased incidence of risk factors like diabetes and hyperlipidemia associated with this etiology in old age.

For cardiomyopathy the mean age was 47.6 years. In this study out of 9 patients, 6 were had dilated cardiomyopathy while two had hypertrophic cardiomyopathy with one had WPW syndrome associated with HOCM.

Lone atrial fibrillation showed maximum prevalence towards middle age (54.4 years) whereas atrial fibrillation with thyrotoxicosis was present in younger age (36 years).

<b>Echocardiography findings</b>	<b>N</b>	<b>%</b>
<b>Valvular lesion:</b>	89	71.2%
Mitral valve	63	70.3%
Aortic valve	5	5.6%
Mitral + Aortic	21	23.5%
LV dysfunction	39	31.2%
LA clot	6	4.8%

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Hypertrophic Cardiomyopathy	2	1.6%
Ebsteins Anomaly	1	0.8%

**Table 3: Echocardiography findings**

In this study LA clot was present in 6 (4.8%) patients of which 66.66% had associated LA size >5cm. However, the correlation of increased risk between cases of AF with LA clot versus left atrial size was not statistically significant. This may be because of a small sample size or due to lower sensitivity of trans-thoracic echo in finding LA clots.

Etiology	N	Mean LA size	ECG type of AF(p=0.001)		LA >4cm (p=0.0001)
			Coarse	Fine	
Valvular Heart Disease	66	56.37±10.8	45	21	63
CAD	23	43.4±9.3	4	19	15
HTN	14	43.8±8.5	6	8	9
Cardiomyopathy	9	51.1±8.19	2	7	9
Lone AF	7	32.1±8.08	1	6	1
Other causes	6	35.5±8.9	2	4	2
	<b>125</b>		<b>60(48%)</b>	<b>65(52%)</b>	

**Table 4: ECG and Echocardiographic Findings**

In this study 79% of patients with AF had a left atrial size more than 4cm. Comparing this across various etiologic factors, 95.45% valvular heart disease (RHD and Non-RHD) patients, 65.2% of CAD patients, 64.2% of hypertension patients and 54.5% patients with rest of the etiology were associated with a large LA size (more than 4cm). This difference was statistically significant (p=0.0001).

Predominant Mitral Stenosis(MS) with Mitral Regurgitation (MR)	56.19±9.8
Predominant Mitral Regurgitation (MR) with Mitral Stenosis (MS)	68.7±9.1
Aortic Stenosis	48.0
Aortic Regurgitation	32.75±9.8

**Table 5: Mean LA size in different valve lesions**

Patients of RHD etiology had the largest LA size (mean 57.07±10.8mm). Among these, LA size for MR predominant lesion was 68.79 mm followed by MS predominant lesions (56.19mm).

S. N.	ECG Findings	No. of Cases	%
1.	Chamber Hypertrophy	41	32.8%
2.	Conduction Disturbances	21	16.8%

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	RBBB	16	
	LBBB	2	
	CHB	2	
	LAHB	2	
3.	Ashman Phenomenon	10	8%
4.	Pre Excitation (WPW)	01	0.8%
5.	ST/T changes	35	28%

**Table 6: ECG findings**

The most common associated ECG abnormalities were chamber hypertrophy (32.8%) and conduction disturbances (16.8%).

S. N.	LA size	Coarse	Fine	Total
1.	Less than 4 cm	8	18	26(20.8%)
2.	≥ 4cm	52	47	99(79.2%)
<b>Total</b>		<b>60</b>	<b>65</b>	<b>125(100%)</b>

**Table 7: Distribution of cases according to Type of Atrial Fibrillation and Left Atrial Size**

$p = 0.04$

Coarse AF was present in 48% of patients studied. Of these; majority had associated valvular heart disease (63.3%). LA size was more than 4 cm in 86.6% of coarse AF patients while 72.3% of fine AF was associated with a large LA size (more than 40mm). 13.3% (8/60) of coarse AF and 27.8% (18/65) of fine AF were associated with normal LA size. The difference was statistically significant ( $p=0.0481$ ).

**DISCUSSION:** The present study analyzed that prevalence of AF increases as the age advances. Similarly, William B. Kannel et al, based on 38 years follow up data from Framingham study, found that prevalence of atrial fibrillation doubles with each decade of age from 0.5% at ages 50-59 to 9% at age 80-89 years.<sup>3</sup> The Rotterdam study<sup>10</sup> also found a similar increase in the prevalence of AF with advancing age (0.5% in 50 years to 9.2% at 80 years).

The patients presenting with atrial fibrillation were predominantly females (56.8%) in this study. On the contrary, the Framingham study<sup>2</sup> and the ATRIA study<sup>11</sup> reports atrial fibrillation to be more common in males. However, Stefansdottir et al, found that the incidence of AF increased significantly in women (by 0.9% per year) but not in men (by 0.12% per year)<sup>12</sup> in the study period as compared to older studies. Increased prevalence among females in the present study may be due to high prevalence of rheumatic etiology in the study population.

In this study, a higher number of patients were from rural population (84%) as compared to the urban population (16%). The distribution of etiology of atrial fibrillation also differed between the two areas. While RHD was the most common etiology (51.5%) in rural area, CAD (30%), hypertension (20%) followed by RHD (15%) were the most common aetiologies in urban area. But the difference was not statistically significant. It may be because of the large proportion of rural population in the study group.

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The most common cardiac morbidities of AF were heart failure and myocardial infarction followed by valvular heart disease, according to the Framingham Study<sup>2</sup>. These cardiac conditions accounted for 20% of AF in men and 31% of AF in females. Valvular heart disease has a 1.8 and 3.4 fold higher risk for AF in men and women respectively.<sup>3</sup>

Rheumatic heart disease was the most frequent cause of AF in a recent survey in public and private institutes in India. Hypertension and ischemic heart disease contributed to the second most common cause<sup>6</sup>. Similarly, among our patients the most common aetiology among the study group was Rheumatic heart disease (45.6%), followed by CAD (18.4%) and hypertension (12%).

Among our female patients, the most common etiology for atrial fibrillation was rheumatic heart disease (34.4%) followed by hypertension (5.6%) and CAD (5.6%). In males the most common etiologic factor was CAD (12.8%) followed by RHD (11.2%) and hypertension (6.4%). The difference was found to be statistically significant ( $p=0.009$ ). The Framingham study also found 10% of males and 26% of females had RHD whereas CAD was present in 16% of males and 4% of female cases.<sup>3</sup>

The study shows a significant difference in the aetiology associated with atrial fibrillation in different age groups. Among those above 50 years of age, the most common aetiologies were coronary artery disease (30%), followed by RHD (24%), hypertension (16.4%), lone atrial fibrillation (5.9%) and non-rheumatic valvular heart disease (13.4%). In younger age (26-50 years age group) most common etiologic factors were RHD (60.0%), cardiomyopathy (12.0%), CAD (6.0%), hypertension (2.0%) and lone AF (6.0%). The difference was statistically significant ( $p=0.0001$ ).

The mean age of atrial fibrillation in RHD was 44.36 years and 71.1 years for non-rheumatic valvular heart disease. This may be because of the sclerodegenerative etiology of valve lesion in old age.

For CAD and hypertension the mean age was 65.3 and 63.14 years respectively. This may be related to the increased incidence of risk factors like diabetes and hyperlipidemia associated with this aetiology in old age.

In this study, atrial fibrillation shows significant association with left atrial size ( $>4\text{cm}$ ). Large LA size is associated with increased risk of AF. 79% of patients with AF had a left atrial size more than 4cm. Comparing this across various etiologic factors, 95.45% of the valvular heart disease (RHD and Non RHD) patients, 65.2% of CAD patients, 64.2% of hypertension patients and 100% patients with cardiomyopathy were associated with a large LA size. This difference was statistically significant. ( $p=0.001$ )

According to the Framingham study, the main echocardiographic predictors of atrial fibrillation were large left atrial size, left ventricular end diastolic dimensions, left ventricular wall thickness and mitral annular calcification. Of these most important was left atrial size. Each 5mm increment in left atrial size increased AF risk of 39.0%.<sup>3</sup>

Henry et al studied 85 patients with isolated mitral valve disease, 50 patients of aortic valve disease and 130 patients with asymptomatic septal hypertrophy. They found out that in all three groups of patients, atrial fibrillation was rare when left atrial dimension was below 40mm but common when it exceeded 40mm (54%). They also found that when LA size was more than 45 mm the chance of recurrence of AF after successful cardio version was high.<sup>13</sup>

Teresa S. et al studied left atrial volume as risk marker of incident atrial fibrillation in 1655 men and women found that a 30.0% increase in left atrial volume was associated with 43.0% increased risk of atrial fibrillation.<sup>14</sup>

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As results in this study were consistent with other Indian and Western studies, it can be concluded that left atrial size of more than 4cm is associated with increased prevalence of atrial fibrillation irrespective of the etiology for atrial fibrillation

On Echocardiography, LA clot was seen in 6 (4.8%) patients of whom 66.66% had associated LA size of more than 5cm. However, the correlation of increased risk between cases of AF with LA clot versus left atrial size was statistically not significant. This may be because of a small sample size or due to low sensitivity of trans-thoracic echo in finding the LA clots.

According to James W. McCready et al, hypertension, age >75, and cardiomyopathy were independent risk factors for LA thrombus. Type of AF and LA size >50 mm were not associated risk factors for LA thrombus.<sup>15</sup>

This study showed a significant relation between coarse AF and large LA size. 68.18% of valvular heart disease patients with AF had coarse AF whereas only 25.4% of patients with non-valvular heart disease had coarse AF. 86.6% of patients with coarse AF were associated with a large LA size. But among patients with large LA size only 52% had coarse AF on ECG. The difference was statistically significant (p=0.0481).

Mareo H Aysha et al mentioned in their study that fibrillary 'f' wave amplitude correlates strongly with echocardiographic left atrial size especially in rheumatic atrial fibrillation.<sup>16</sup>

Haim Bartal measured the size of 'f' waves using vector cardiogram, and predicted LA enlargement in 66.0% patients with atrial fibrillation and large LA size.

**RECOMMENDATIONS:** Most common etiologic factor associated with atrial fibrillation in Indian scenario is rheumatic heart disease. As compared to western studies, this cardiac condition is more common in rural area and had female predominance with younger age of onset. As risk of atrial fibrillation increases with age, its aetiology with coronary artery disease is more significant than with RHD. On Echocardiography left atrial size more than 4 cm is associated with increased risk of atrial fibrillation. Coarse AF in ECG is mainly associated with underlying RHD etiology and large left atrial size.

Thus, our study delineates conditions and risk factors which may help us predict the propensity of a patient to develop atrial fibrillation. Based on this, we may conduct echocardiographic analysis on patients who have cardiovascular morbidities like rheumatic heart disease, coronary artery disease and hypertension. Undoubtedly, this will make us more vigilant towards identifying the condition and initiating an effective treatment plan at an appropriate time.

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