

**Original article****Title: Rheumatic Atrial Fibrillation. Does LA volume matters?****<sup>1</sup>Tejas Shah, <sup>2</sup>Cinosh Mathew, <sup>3</sup>Kinnari Gupta, <sup>4</sup>Chaitri Shah**<sup>1</sup>Professor, Department of Cardiology, Sumandeep Vidhyapeeth, Pipariya, Vadodara, Gujarat, India<sup>2</sup>Professor, Department of Cardiology, Sumandeep Vidhyapeeth, Pipariya, Vadodara Gujarat, India<sup>3</sup>Assistant Professor, Department of Community Medicine, Dr M K Shah Medical College, Ahmedabad, Gujarat, India<sup>4</sup>Additional Medical Superintendent, Professor, Department of Critical care Medicine, Dr M K Shah Medical College, Ahmedabad, Gujarat, India**Correspondence**

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**Abstract:**

**Background:** Atrial fibrillation (AF) is the commonest rhythm abnormality. It may occur as paroxysms of irregular tachycardia or more often it becomes established as a permanent condition. The aim of the study was to measure LA (Left Atrial) volume and f (fibrillatory) wave amplitude of ECG (Electrocardiography) in Rheumatic AF.

**Methods:** 100 cases of Rheumatic AF and 100 patients with normal sinus rhythm without any cardiovascular disease were taken as control in the present study. All the patients were evaluated clinically, by ECG findings, and echocardiographically. LA size was measured by volumetric method (LAVI) and M-mode on echocardiography.

**Results:-** Out of 100 patients with Rheumatic AF, 32% were males. Mean age of the patients was  $41 \pm 4.47$  years in the case group and  $31.2 \pm 5.0$  years in control groups. 16 patients had paroxysmal AF, 5 had persistent AF and 79 were found to have permanent AF in the case group. Mean LA size was  $4.99 \pm 1.48$  cm by M mode and  $35 \pm 8.2$  ml/m<sup>2</sup> by volumetric method in case group and  $2.69 \pm 0.29$  cm and  $30 \pm 2.4$  ml/m<sup>2</sup> in control group ( $p = 0.0001$ ). Patients with longer duration of AF (> 5 years) had larger LA size ( $P < 0.009$ ). Significantly higher number of patients (89%) had LA size >4 cm and volume > 34ml/m<sup>2</sup> as compared to the patients having LA size <4 cm and volume < 34ml/m<sup>2</sup> in the case group. ( $\chi^2=10.63$ , Df=1,  $P=0.001$ ). It was noted that chronic AF patients had significantly larger fibrillatory waves as compared to paroxysmal AF ( $\chi^2=5.99$ , D.F=1,  $P=0.014$ ). Additionally, f wave of > 1mm reported in patients with LA size >4 cm, and volume > 34 ml/m<sup>2</sup>.

**Conclusion-**

RHD patients are susceptible for development of atrial fibrillation even with normal size and volume of LA. Patients with chronic AF have larger LA volume and 'f' wave amplitude.

**Keywords-** RHD, AF, LAVI, fibrillatory wave

### **Introduction:**

In the history when William Einthoven in 1903 constructed the first electrocardiograph and James Mackenzie in 1902 published “The study of the pulse”-the first scientific treatise on irregularities of the pulse. It has been classified as the “youthful type”(sinus irregularity); “adult type(extra systole) and the “dangerous type” called at first by Mackenzie “auricular paralysis” and later “auricular fibrillation”. Atrial fibrillation is usually characterized electrocardiographically by low –amplitude baseline oscillations (fibrillatory or f waves) with rate of 300-600/minute and irregularly irregular rhythm.<sup>1</sup>

AF is one of the most common rhythm disorder, accounting 33% of arrhythmia related hospitalization. There is five times increase risk for stroke and two times increase the risk of mortality.<sup>2</sup>Incidence of AF is age and gender related as shown in Framingham Study,<sup>3</sup>life time risk of development of AF after the age of 40 years to be 26% for men and 23% for women.

AF that terminates within 7 days is paroxysmal, and lasting more than 7 days is called persistent. AF lasting for more than 1 year is longstanding whereas longstanding AF refractory to cardioversion is termed permanent. Lone AF defined as patients younger than 60 years without hypertension or structural heart disease.<sup>4</sup>AF can be valvular or non valvular (Hypertension, Hyperthyroidism, Alcohol intake, Coronary Artery Disease, Congestive Cardiac Failure, Chronic Obstructive Pulmonary Disease, Obesity etc.). In Asian country Rheumatic Heart Disease (RHD) is one of the most common valvular cause for AF.<sup>5</sup>

Left atrium dimension as determined by echocardiography, is strong predictor of occurrence of AF<sup>6</sup>. LA volume provides a more accurate measure of LA size than conventional M-mode LA dimension <sup>7,8</sup>. There are very limited study of LA volume in rheumatic AF. Herein, we present an overview of LA Volume and its clinical implications in duration of rheumatic AF in Indian subset of patients.

### **Materials and Method**

This is single centre, case-control study conducted at tertiary care hospital. As illustrated in figure 1, 100 consecutive cases of rheumatic atrial fibrillation and 100 patients with normal sinus rhythm without any cardiovascular disease were studied after meeting inclusion and exclusion criteria over a period of 6 months. Informed verbal consent was taken from each participant. In each case, a detailed history and thorough clinical examination was carried out in addition to ECG and echocardiographic examination.

### **Inclusion Criteria**

All patients aged between 15-65 years with recently diagnosed or on treatment (Penicillin prophylaxis, beta blockers, calcium channel blockers, amiodarone, diuretics, anticoagulants, etc) for rheumatic AF were selected as cases.

## Exclusion Criteria

Patients with hemodynamic instability which required electrical cardioversion. ECG evidence of acute myocardial infarction. Patients with congenital heart disease, prosthetic valve and with pacemaker in situ were excluded.

All the cases were divided into two groups. One group included patients with AF lasting from 24 hours to 7 days before restoration to sinus rhythm (paroxysmal AF), another group of chronic AF where AF lasting for more than 7 days categorized into persistent AF and AF consistent for more than 12 months defined as permanent AF.

For each patient, height, body weight, 12 lead ECG (including lead II and V1 rhythm strips) was obtained. Echocardiography was performed with GE vivid S6 machine. Left atrial size was obtained. (M mode and LA Volume by area length method)<sup>9</sup>. LA size was measured by leading edge to leading edge at the level of the aortic sinuses in M-mode. Figure-2 shows the method by which area length method was used to calculate LA volume.<sup>10</sup> Reference range for M-mode LA dimension 2.5-4 cm and volume <34 ml/m<sup>2</sup> was taken as normal. Average of five cycle's dimension/volume of LA was taken in AF. RHD was diagnosed by echocardiographic criteria.<sup>11</sup> In acute rheumatic valvulitis changes were annular dilation, chordal elongation, chordal rupture resulting in flail leaflet, anterior leaflet tip prolapsed and beading nodularity of leaflet tip. Chronic rheumatic valvulitis were associated with thickened and doming of AML, PML fixed and paradoxical, chordal thickening and fusion, restricted leaflet motion and calcification.

## Statistical analysis

Statistical analysis was performed using SPSS 21. Data were summarized using descriptive statistics, presented as proportions (%), count/sample size) or mean  $\pm$  SD. Continuous variables were compared with the use of the student t test; differences in discrete variables were assessed by means of the chi-square test or Fisher exact test as appropriate. P value of < 0.05 was taken as significant.

## Results:

Age and gender wise distribution of the study population is seen in Table 1. Almost half of the patients into case group was in their 3<sup>rd</sup> and 4<sup>th</sup> decade while the mean age of males and females in the control group was  $33.5 \pm 5.40$  and  $28.8 \pm 4.61$  years respectively. As per table 2, all patients had palpitation as predominant symptoms. Half of the patients had NYHA class III dyspnea followed by NYHA IV(38%), NYHA II(10%) and NYHA I(2%) dyspnea without any significant gender difference(p=0.896). Symptoms like pedal edema and cough were significantly higher in females (p value= 0.01 and 0.027 respectively), however, chest pain was prominent symptom in males (p value =0.009). On echocardiography, multi-valvular involvement (MS+MR+TR, 24%) was the most common followed by two valve affection (MS+MR+AR, 22%) were noted in rheumatic AF patients.

The significant difference in LA size and volume noted between cases and control as demonstrated in Table 3 (P vale 0.0001). Surprisingly, 11% of the patients in the case group whose LA size was

< 4 cm and LA volume was <34ml/m<sup>2</sup> even had AF as observed in Table

4. On applying Chi-square test for associated between LA size and LA volume with type of AF,

chronic AF patients had higher LA size and volume ( $\chi^2=10.63$ , P value 0.001). Furthermore, Table 5 depicts that patient with AF duration of more than 5 year had larger LA size as compare to the patients with shorter duration (p=0.0001). On analyzing fibrillatory wave (f wave) amplitude in ECG in the case group (Table 6) larger f wave (>1 mm) was consistently higher in chronic AF patients (p value 0.009) and in patients with LA size more than > 4 cm, LA volume>34ml/m<sup>2</sup> (p value 0.037).

### Discussion:

According to Global Burden of Disease Study, the worldwide age-adjusted prevalence of AF is 5.96/1000 in men and 3.73/1000 in female but in our study shows female preponderance with ratio of 1:2.12.<sup>11</sup> Randomized Evaluation of Long-term anticoagulant therapY (RE-LY) Atrial fibrillation Registry showed that patients with AF in India, Middle east and Africa are on average 10-12 years younger than other countries which was ranging from 57.2 to 58.6 years in these countries while in our study the average age of rheumatic AF patients was 41± 4.47 years.<sup>12</sup> This discrepancy could be explained by the fact that former registry included all causes of AF in the study.

In a patient with AF, atria showed altered structural and electrical remodeling (descriptive term “AF begets AF”) which has cause interstitial fibrosis. Fibrosis is thought to increase AF vulnerability by causing local conduction slowing and predisposing to re-entry.<sup>13</sup> Study conducted by Dittrich et al<sup>14</sup> showed that AF per se causes diffuse atrophy of atrial muscle and enlargement, increase inhomogeneity, refractoriness and conduction. All lead to irreversible atrial fibrillation. The evidence of LA enlargement indicates clinically significant risk of adverse cardiovascular outcomes for the patient with AF.<sup>15,16</sup> LA size measurement is therefore requisite for any complete transthoracic echocardiographic evaluation. Conventionally, M-mode echocardiography is use for LA measurements. This measurement does not represent the true LA size.<sup>17</sup> Thus, volume- based methods of chamber quantification have evolved.<sup>9</sup> There are very limited numbers of Indian data on volumetric methods of LA measurements in patients with RHD and atrial fibrillation. The results of the present study support previous suggestions given by Henry et al<sup>18</sup> that atrial fibrillation is closely related to the degree of left atrial dilatation. Left atrial size by echocardiography provides a relatively sharp numerical cut off in left atrial dimension that separates patients in normal sinus rhythm from those with chronic or paroxysmal atrial fibrillation.

While study published in Mayo clinic showed when LA volume was >34 ml/m<sup>2</sup>, it was independent predictor for development of atrial fibrillation, stroke, congestive cardiac failure and death without valvular heart disease.<sup>7,19</sup> So LA volume definitely predicts development of AF. Atrial fibrillation was rare in patients with a left atrial dimension below 40 mm however common when this dimension exceeded 40 mm. Interestingly in our study, even though, 11(11%) patients had left atrial dimension of <4 cm and volume <34 ml/m<sup>2</sup> had atrial fibrillation with RHD. Out of these 11 patients, 7 (63%) had ‘f’ wave amplitude < 1mm, while 4 (27%) had

'f' wave amplitude > 1mm. 89 patients whose left atrial size > 4cm and volume >34 ml/m<sup>2</sup>, 26 (29.22%) had 'f' wave amplitude < 1mm while 63 (70.79%) had 'f' wave amplitude > 1 mm (p=0.05). Study conducted by Ayesha and Hassan out of 40 patients who had

left atrium size < 4cm, 34 patients (85%) had 'f' wave amplitude <1 mm while 6 patients (15%) had 'f' wave amplitude >1mm, while 49 patients who had left atrium size > 4cm, 36 patients (73%) had 'f' wave amplitude >1mm and 13 patients (27%) had 'f' wave amplitude < 1mm.<sup>20</sup>

In a study conducted by Jayprakash et al, negative fibrillary waves were associated with large left atrium and bidirectional fibrillary waves were present only in rheumatic atrial fibrillation.<sup>21</sup> In our study coarse or high 'f' wave amplitude was accompanied by large volume of atria in the rheumatic atrial fibrillation patients. In contrast, fine or low 'f' wave amplitude was found in nearly normal left atrial size in paroxysmal atrial fibrillation patients. While recent study published by Leili Pourafkari et al showed that though coarse AF is common in rheumatic MS.<sup>22</sup>

In conclusion, Rheumatic heart disease being the most common valvular heart disease with early age for occurrence of atrial fibrillation is noted in our study. Even with normal size and volume of LA, they are susceptible for development of atrial fibrillation therefore close echo follow up of such patients is necessary. Patients with chronic rheumatic AF have larger left atrium and larger 'f' wave amplitude was significantly higher in chronic AF patients and patients with larger LA size and volume.

### Limitations:

This is single center study with small sample size. Single operator performed the echocardiography so inter-observer variability was not considered.

**Conflict of interest** None.

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**Figure 1: Flowchart of patients' selection**

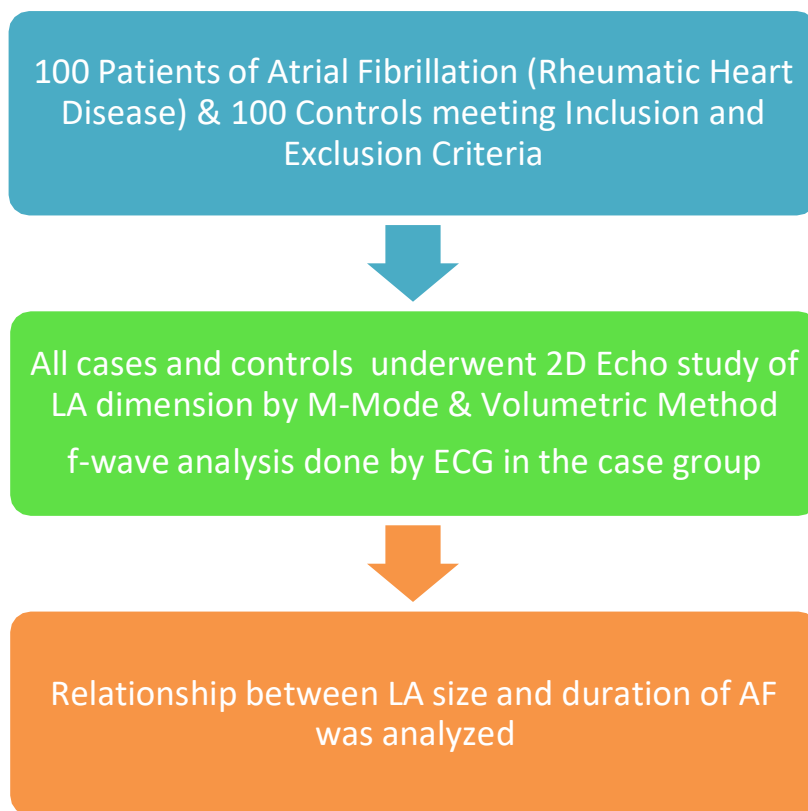




Figure-2 Measurement of LA in conventional M mode in systole (AP dimension)

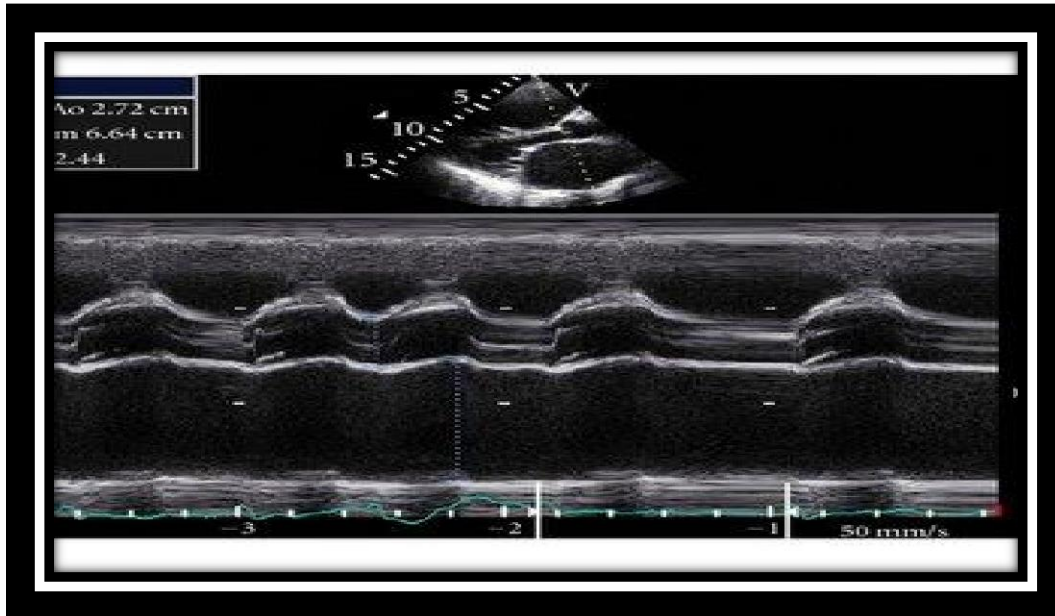
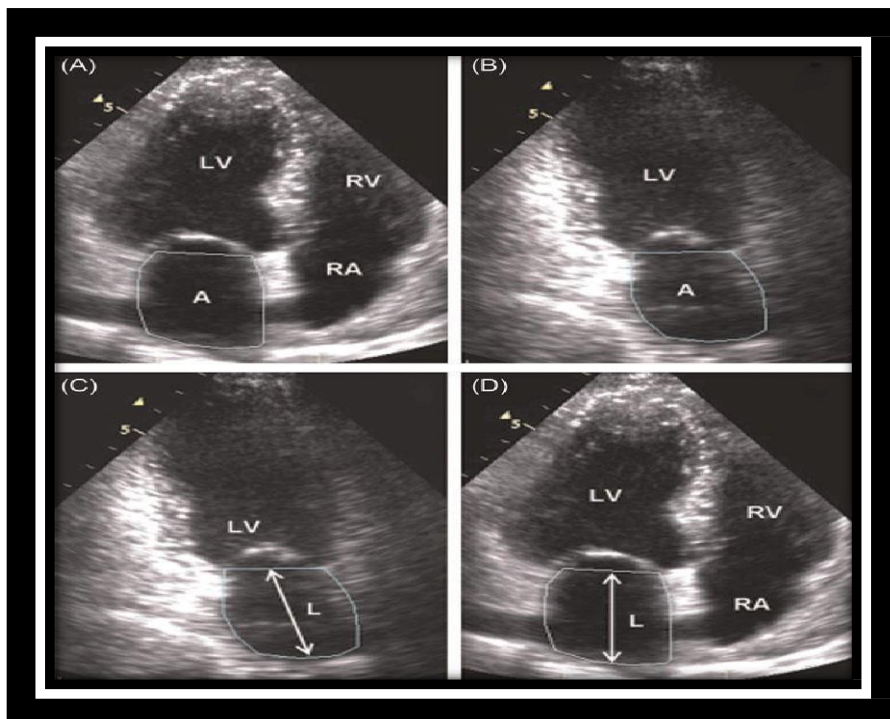


Figure-3 Measurement of left atrial (LA) volume from the biplane area-length method using the apical 4-chamber and apical 2-chamber views at ventricular end systole (maximum LA size). LA inner border, excluding the area under the MV annulus, pulmonary veins, and LA appendage should be taken. A, area; L, length measured from the mitral annular plane to the back wall; LV, left ventricle; RA, right atrium; RV, right ventricle. LA volume  $(0.85 \times A1 \times A2)/L$ . (Courtesy Panupong Jiamsripong et al.)<sup>10</sup>



**Table 1: Baseline characteristics of the study population**

		Cases	Control
Age (in years)		41± 4.47	31 ± 2.0
Sex	Male	32	50
	Female	68	50

**Table 2 Distribution of clinical characteristics as per sex in the case group**

Age	Total Cases	Male (%) (N=32)	Female (%) (N=68)	p value
Mean Age	100	42.56±5.57	40±3.37	NA*
<b>Symptomatology</b>				
Palpitation	100	32(100.00%)	68(100.00%)	
Dyspnea(NYHA Class) †				
I	2	0 (0.00%)	2 (2.94%)	0.896
II	10	4 (12.50%)	6 (8.82%)	
III	50	14 (43.75%)	36 (52.94%)	
IV	38	12 (37.50%)	26 (38.24%)	
Pedal Edema	50	16(32.00%)	34(68.00%)	<b>0.010</b>
Chest Pain	25	19(76.00%)	6(24.00%)	<b>0.009</b>
Cough	25	7(28.00%)	18(72.00%)	<b>0.027</b>
<b>Valve Involvement</b>				
MS†	17	7(22%)	10(15%)	
MR	7	1(3%)	6(9%)	
MS+MR§	16	7(22%)	9(13%)	
MS+MR+TR	24	6(19%)	18(26%)	
MS+MR+AR ¶	22	7(22%)	15(22%)	
MS+AR	14	4(12%)	10(15%)	

\*Not Applied, †New York Heart Association, ‡Mitral stenosis, §Mitral regurgitation, || Tricuspid regurgitation,

¶Aortic regurgitation

**Table 3 Measurement of LA size and volume in the study population by echocardiography**

Group	Cases (n=100)	Controls (n=100)	p value
LA size (in cm)	4.99 ± 1.48	2.69 ± 0.29	0.0001
LA Volume (ml/m <sup>2</sup> )	34.0 ± 6.20	19.0 ± 2.40	0.0001

**Table 4: LA size and volume assessment Vs type of AF in the case group**

Variable	LA Size (≤4 cm) & LA Volume (≤34 ml/m <sup>2</sup> )	LA Size (>4 cm) & LA Volume (>34 ml/m <sup>2</sup> )	Total	P value
Paroxysmal	6	10	16	<0.0001
Chronic (Persistent & Permanent)	5	79	84	
Total	11	89	100	

**Table 5: LA size and volume assessment Vs duration of AF in years in the case group**

Duration of AF (in years)	LA Size (≤4 cm) & LA Volume (≤34 ml/m <sup>2</sup> )	LA Size (>4 cm) & LA Volume (>34 ml/m <sup>2</sup> )	Total	p value
≤1 year	7	15	22	<b>0.009</b>
1-2 Yrs	2	8	10	
3-5 Yrs	1	13	14	
>5 Yrs	1	53	54	
<b>Total</b>	<b>11</b>	<b>89</b>	<b>100</b>	

**Table-6 Amplitude of fibrillatory wave in ECG Vs type of AF and LA size**

<b>Type of AF</b>	<b>' f ' wave amplitude</b>		<b>p value</b>
	<b>&lt; 1 mm</b>	<b>&gt; 1 mm</b>	
Paroxysmal	10	6	<b>0.009</b>
Chronic (Persistent & Permanent)	23	61	
<b>Total</b>	<b>33</b>	<b>67</b>	
<b>LA size</b>			
< 4 cm, Volume≤34 ml/m <sup>2</sup>	7	4	<b>0.037</b>
> 4 cm, volume>34ml/m <sup>2</sup>	26	63	
<b>Total</b>	<b>33</b>	<b>67</b>	