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ADULT CARDIOLOGY

Association of Left Atrial Size with Atrial Fibrillation in Rheumatic Mitral Stenosis

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ABSTRACT

Objective: To determine the association of Left Atrial (LA) size with atrial fibrillation (AF) in patients with Rheumatic Mitral Stenosis.
Study Design: Analytical Cross-sectional study.
Place and Duration of Study: Adult Cardiology Department, Armed Force Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi Pakistan, from Aug 2023 to Mar 2024.
Methodology: One hundred and twenty-eight patients with an age range of 20-60 years who were diagnosed with rheumatic mitral stenosis based on echo findings were included via consecutive sampling technique. Left atrium size, mitral valve area, and left ventricular ejection fraction were measured with a transthoracic echocardiogram (TTE) to assess the severity of stenosis and the risk of atrial fibrillation.
Results: Out of 128 study participants, 73(57.0%) were females, whereas 55(42.3%) were males and mean age was 44.52±11.88 years. The median size of the left atrium and mitral valve area was 47.00(42.00-51.00) mm and 1.04(0.83-1.30) cm^2 respectively. Atrial Fibrillation was reported in 86(67.2%) patients, and majority of them 85(98.8%) had LA size >40mm, while 26(61.9%) out of 42 patients with no AF had LA size >40mm (p<0.001). Patients with AF also showed lower median ejection fraction (55.00% vs 60.00%) and higher mean values of age and median LA size (47.25±10.22 vs 38.92±13.17 years; 49.00mm vs 42.00mm respectively) compared to those who had no AF (p<0.01).
Conclusion: Left atrial enlargement is significantly associated with development of atrial fibrillation in patients with rheumatic mitral stenosis.

Keywords: Atrial Fibrillation, Left Atrial Size, Rheumatic Mitral Stenosis.

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INTRODUCTION

Acute rheumatic fever (ARF) results from an autoimmune reaction to group A streptococci, leading to the development of rheumatic heart disease (RHD) and chronic heart failure.[1] RHD is global health issue, about 33 million people are suffering from RHD and accounts for 2,75,000 death annually, 95% of which is contributed by low-income countries.[2]

Mitral stenosis, a progressive condition following rheumatic fever, reduces mitral valve area, causing symptoms like exercise intolerance, palpitations, thromboembolism and pulmonary congestion.[3] As it advances, left atrial pressure rises, leading to left atrial enlargement and ultimately resulting in atrial fibrillation.[4]

The occurrence of atrial fibrillation in mitral stenosis exacerbates the patient hemodynamically, primarily due to rapid ventricular response causing shortened diastole and increased left atrial (LA) pressure. Patients with mitral stenosis and atrial fibrillation (AF) have escalating risk for systemic embolization.[5] Cardiac output is influenced by the atrial kick, and its absence due to atrial fibrillation can lead to pulmonary congestion. Irregular rhythms can cause blood stasis and clot formation, heightening the risk of thromboembolism, particularly as mitral stenosis progresses.[6] Anticoagulation in mitral stenosis is indicated for history of systemic embolization, atrial fibrillation, left atrial or appendage clots, and enlarged left atrium. Early initiation helps prevent systemic thromboembolism.[7]

Rheumatic fever is prevalent in our region, with mitral stenosis as its most severe complication. Although, the link between LA size and AF is well-known in other cardiac conditions, it remains underexplored in local cases of rheumatic mitral stenosis, highlighting a significant knowledge gap compared to studies from Western countries.[8-10]

Understanding the link between LA size and AF in rheumatic mitral stenosis is crucial for effective management by timely anticoagulation, rhythm

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control, and interventional strategies. It also aids in tailoring follow-up and monitoring to prevent complications. Insights gained could enhance patient outcomes, inform effective screening tools, and lead to better interventions, ultimately reducing stroke and other atrial fibrillation-related complications. Thus the study aimed to evaluate the association between LA size and AF in patients with rheumatic mitral stenosis.

METHODOLOGY

This analytical cross-sectional study was conducted at the Armed Forces Institute of Cardiology, National Institute of Heart Diseases, Rawalpindi Pakistan from August 2023 to March 2024 after obtaining approval from the Institutional Ethical Review Board (IERB Ltr#9/2/R&D/2023/281; Dated:18th Aug, 2023). Consecutive sampling was employed for data collection.

Sample size of 63 was calculated as per the calculation by WHO sample size calculator, using 4.3% population proportion for atrial fibrillation in RHD,[11] 95% confidence level and 5% margin of error. However, data was gathered from 128 patients.

Inclusion Criteria: Patients with an age range from 20-60 years of age who were diagnosed with rheumatic mitral stenosis based on echo findings were included in this study.

Exclusion Criteria: Patients having a history of percutaneous transmitral commissurotomy (PTMC), mechanical valve replacement and non-valvular atrial fibrillation due to other causes were excluded.

Patients who met the specified inclusion and exclusion criteria were chosen from the Outpatient Department (OPD), wards, and emergency department following their provision of written consent. Demographics and a comprehensive medical history regarding the patient's symptoms, occurrences of systemic embolization, and any prior interventions such as valve replacement or percutaneous mitral valve commissurotomy were gathered. Additionally, a detailed physical and cardiac examination, including auscultation for diastolic murmur, was done. Patient particulars including age, gender, and medical record number (MR#) were documented from the patient's profile, progress notes, or chart. Base line Electrocardiogram (ECG), X-RAY Chest and echocardiogram was done. Left atrium size, mitral valve area, and left ventricular ejection fraction were measured with a transthoracic echocardiogram (TTE) to assess the severity of stenosis and the frequency of atrial fibrillation. LA size was measured by TTE, measuring anteroposterior dimensions by M-mode directed by two-dimensional (2-D) (real-time) echo in parasternal long axis view measured from LA posterior wall to leading edge at the level of aortic sinuses. AF was defined on ECG as absent or fibrillatory P-waves with narrow QRS complexes and variable R-R interval. Mitral stenosis was defined on echo as progressive MS having Mitral valve area (MVA) >1.5 cm^2, sever MS with MVA 1-1.5cm^2 and very severe having MVA <1cm^2.

A statistical software, Statistical Package for Social Sciences (SPSS) version 23:00 was used for data entry and analysis. Frequencies/percentages and Mean±SD were calculated for qualitative and quantitative variables respectively. Chi-square test was applied to find the association of LA size with atrial fibrillation. Normality of data was checked by Kolmogorov Smirnov test that revealed that only the age was normality distributed. Student t-test/Man Whitney U test was employed to find the mean difference of quantitative variables in patients with and without atrial fibrillation. The *p*-value of ≤0.05 was considered statistically significant.

RESULTS

One hundred and twenty eight patients were recruited for the given study, who were comprised of 73 (57.0%) females and 55 (42.3%) males with mean age of 44.52 ± 11.88 years. Meanwhile, majority of the participants were struggling with Atrial Fibrillation 86 (67.2%). The median (IQR) of left atrium size, mitral valve area and LVEF have also been reported in Table-I.

Table-I: Baseline and Clinical Characteristics of Study Participants (n=128)

Variables			Frequency (%)
Demographics	Gender	Male	55(42.3%)
		Female	73(57.0%)
	Age (years) (Mean±SD)		44.52±11.88
Clinical Characteristics	Systemic Embolization		11(8.6%)
	Atrial Fibrillation		86(67.2%)
	Mitral Regurgitation		25(19.5%)
	Left Atrial Clot		7(5.5%)
			Median(IQR)
	Left Atrial Size (mm)		47.00(42.0051.00)
	Mitral Valve Area (cm^2)		1.04(0.83-1.30)
	Left Ventricular Ejection Fraction (%)		55.00(55.00-60.00)

Atrial fibrillation was more common in females 51(59.3%), compared to males 35(40.7%) (*p*=0.56).

Majority of the patients having LA clot, mitral regurgitation, systemic embolization and LA size >40mm, exhibited atrial fibrillation. A significant association was noted between LA size and atrial fibrillation, with 85(98.8%) patients having left atrial size greater than 40 mm in the atrial fibrillation group (p<0.001). These results emphasize the crucial role of left atrial size in identifying AF risk (Table-II).

Table-II: Comparison of Demographics and Clinical Characteristics Between Patients With and Without Atrial Fibrillation (n=128)

Variables		Atrial Fibrillation		*p*-value
		Yes Frequency (%) (n=86)	No Frequency (%) (n=42)	
Gender	Male	35(40.7%)	20(47.6%)	0.56
	Female	51(59.3%)	22(52.4%)	
Left Atrial Clot	Yes	7(8.1%)	-	0.09
	No	79(91.9)	42(100)	
Mitral Regurgitation	Yes	20(23.3%)	5(11.9%)	0.15
	No	66(76.7)	37(88.1)	
Systemic Embolization	Yes	10(11.6%)	1(2.4%)	0.10
	No	76(88.4%)	41(97.6%)	
Left AtrialSize	≤40mm	1(1.2%)	16(38.1%)	<0.001
	>40mm	85(98.8%)	26(61.9%)	

Patients with atrial fibrillation were significantly older, with a mean age of 47.25±10.22 years (p=0.001), and had a larger left atrial size (49.00mm vs. 42.00mm; p<0.001). There was no significant difference in mitral valve area (p>0.05). However, left ventricular ejection fraction was significantly lower in patients with atrial fibrillation in comparison to those having normal sinus rhythm (55.00% vs 60.00%; p<0.001). (Table-III).

Table-III: Association of Age, Left Atrial Size, Mitral Valve Area, and Ejection Fraction with Atrial Fibrillation (n=128)

Variables (Mean±SD)	Atrial fibrillation		*p*-value
	Yes (n=86)	No (n=42)	
Age (years)	47.25±10.22	38.92±13.17	0.001
Left atrial size (mm)	49.00(46.0-52.00)	42.00(40.00-45.00)	<0.001
Mitral valve area (cm²)	1.04(0.90-1.30)	1.05(0.80-1.30)	0.80
Left ventricular ejection fraction (%)	55.00(55.00-58.00)	60.00(55.00-60.00)	<0.001

Figure-1 illustrated a large proportion of patients with atrial fibrillation 86(67.2%) in the study sample and 42(32.8%) patients with no atrial fibrillation.

The majority of participants with smaller LA sizes (≤40 mm) as well as larger LA sizes (>40 mm) fall in the MVA category of 1.0–1.5 cm² (64.7% and 50.5% respectively, but participants with larger LA size have a higher proportion (38.7%) in MVA <1.0 cm² compared to those with smaller LA sizes. The proportion of participants with MVA >1.5 cm² decreases in both LA size groups but is slightly higher in participants with smaller LA sizes (17.6% vs. 10.8%). However, the association was not significant (p>0.05).

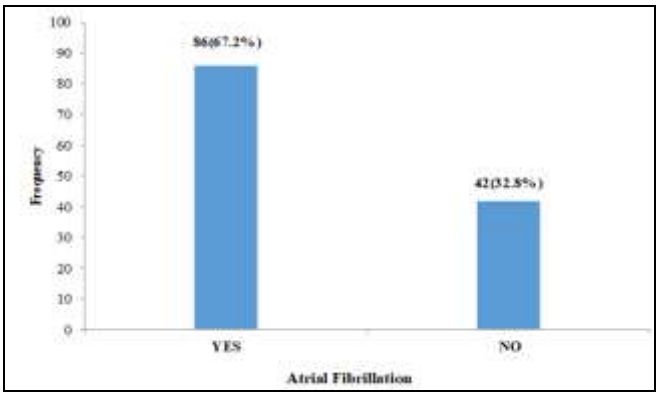

Figure: Frequency of Atrial Fibrillation in study Participants (n=128)

Table-IV: Association between Mitral Valve Area and Left Atrial Size of Study Participants (n=128)

Variables Frequency (%)		Left Atrial Size		*p*-value
		≤40mm (Total=17)	>40mm (Total=111)	
Mitral Valve Area	<1.0 cm²	3(17.6%)	43(38.7%)	0.21
	1.0-1.5 cm²	11(64.7%)	56(50.5%)	
	>1.5 cm²	3(17.6%)	12(10.8%)	

DISCUSSION

Current study, revealed that atrial fibrillation was prevalent in more than half of the patients having Rheumatic Mitral Stenosis, and affected individuals showed notable structural differences such as; LA size and mitral valve area. Specifically, patients with atrial fibrillation had larger left atrial sizes, and reduced left ventricular ejection fractions (p<0.001) compared to those without the condition. These findings suggested a clear association between atrial fibrillation and both increased atrial size and reduced cardiac function, reinforcing the need for close monitoring of patients with this arrhythmia.

AF is a common complication of RHD and is associated with significant morbidity and mortality.[12] Understanding the burden of AF and its associated factors is essential for prevention and management. Various studies have reported AF prevalence in RHD patients, ranging from 13.9% to 79.9%.[8,9,10] In our

study, 67.2% of patients with rheumatic mitral stenosis presented with AF, highlighting the importance of early detection and targeted treatment to mitigate AF-related complications in RHD patients.

Our findings also demonstrated a strong association between LA enlargement and AF. All patients with AF had a median LA size of 49.00(46.00-52.00)mm. This is consistent with a study that found patients with an anterior-posterior diameter of the LA (LAAPd) greater than 38.5 mm had a significantly higher rate of postoperative AF (30.3%) compared to those with an LAAPd ≤38.5 mm (22.4%) (OR 1.5, p=0.015).[13]

Similarly, a study conducted by Suryabanshi et al. revealed that LA size in patients with AF was larger than in those with normal sinus rhythm. In their study, the mean LA size in AF patients was 54 mm (range, 38–96 mm), compared to 46 mm (range, 28–75 mm) in normal sinus rhythm patients, which parallels with our findings where the median LA size in AF patients was 49.00mm, and 42.00mm in those with normal sinus rhythm.[14] Dorasanamma *et al*., further supported this link, showed that LA enlargement (LA size >4 cm) is a key factor in AF development.[15] In our study, 98.8% of patients with LA size >4 cm had AF, reinforcing the critical role of LA size in AF risk assessment. Ashmawy *et al*., similarly found that persistent AF was associated with a significantly larger mean LA diameter (5.16±0.45 cm) and reduced left ventricular ejection fraction (LVEF) (56.33±8.41%) compared to those in normal sinus rhythm.[16]

Saddeh *et al*., also investigated the relationship between AF and LA size in patients with essential hypertension, showing a 3.2% increase in AF risk with large LA size, and a 16% rise in AF risk for every 1 cm increase in LA size.[17] These findings, consistent with our study, indicate that while LA enlargement is a critical predictor of AF, other factors such as atrial remodeling and fibrosis may also play a role. Further research is needed to establish standardized LA size thresholds for predicting AF risk across different populations.

A Pakistani study conducted at Mayo Hospital, came up with 43.3% AF cases with larger mean area of the mitral valve and marked difference in mean LA column of AF patient than that of non-AF patients.[18] The high frequency of AF in patients with RHD, particularly those with rheumatic mitral stenosis, underscores the need for clinical guidelines on AF screening in this population. Early detection of AF is crucial, as the duration of AF is inversely related to the success of cardioversion. Developing predictive tools for identifying high-risk patients could facilitate early intervention and improve outcomes.[19,20] Additionally, the likelihood of AF may influence decisions regarding the timing of valvular interventions in RHD patients.

In our study, the mean age of patients with AF was 47.25±10.22 years, and 98.8% had an LA size >40 mm. By comparison, a recent study found an AF prevalence of 23.5% in individuals aged 65 and older, and 12.7% in those younger than 65. This suggests that while LA enlargement is an important risk factor, age also plays a significant role in AF development across different populations.[21] A meta-analysis by Noubiap *et al*., on the frequency and correlates of AF in RHD also found that AF prevalence increases with age, with older RHD patients more likely to develop AF than younger patients.[11] In our study, the mean age of AF patients was 47.25±10.22 years, higher than the 38.92±13.17 years observed in patients with normal sinus rhythm (p<0.01). This aligned with the findings that AF risk is heightened with LA enlargement and advancing age.

We also observed that patients with AF had lower LVEF compared to those without AF (55.00% vs. 60.00%). Another study reported that 17% of AF patients had decreased LVEF, though the prevalence of reduced LVEF was lower than in our study. This suggested that AF can significantly impair left ventricular function, contributing to the clinical severity of the condition.[22]

Our study also reported systemic embolization in 11.6% of AF patients. Dakay *et al*., emphasized the importance of LA size in stratifying embolic risk and managing embolic events, showing that LA enlargement increases the risk of systemic embolization and may indicate failure of anticoagulation therapy in AF patients.[23] This highlights the need for close monitoring of LA size to prevent and manage embolic complications effectively.

Therefore, if the patient is in sinus rhythm and high-risk features like Left Atrial enlargement then the prophylactic initiation of antiarrhythmic, anti-coagulants or rate limiting agents may help minimize the risk of systemic embolization and symptomatic deterioration. So, there is a need to evaluate left atrium size regularly. Early diagnosis and treatment are very

important to address all these risk factors that are associated with long-term outcomes.

LIMITATIONS OF STUDY

The study's cross-sectional design limits the ability to establish causal relationships. Moreover, patients with atrial fibrillation were not assessed for additional outcomes through follow-up.

CONCLUSION

The study demonstrated a significant association between left atrial enlargement and the occurrence of atrial fibrillation in patients with rheumatic mitral stenosis. Specifically, the data indicate that patients exhibiting a left atrial size greater than 40 mm are at a markedly increased risk for developing atrial fibrillation.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AGA & NA: Data acquisition, data analysis, critical review, approval of the final version to be published.

ZI & MN: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SS & SKK: Study concept, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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