

## FREQUENCY OF LEFT ATRIAL THROMBUS IN PATIENTS OF MITRAL STENOSIS WITH ATRIAL FIBRILLATION

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### Contribution

SDS & SAB conceived the idea, planned the study and drafted the manuscript. HA & MZK collected data, did statistical analysis, drafted the manuscript and critically reviewed manuscript. All authors contributed significantly to the submitted manuscript.

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### ABSTRACT

**Objective:** To determine the frequency of left atrial thrombus in patients with mitral stenosis having atrial fibrillation.

**Methodology:** This cross sectional study was conducted at Bolan Medical College and Sandeman Teaching Hospital, Quetta. from 17 February 2015 to 2016. Both male and female patients between 25 to 70 years with moderate to severe mitral stenosis and atrial fibrillation were included while patients with mitral stenosis and normal sinus rhythm, mitral regurgitation, congestive heart failure, significant aortic valve or coronary artery disease were excluded.

**Results:** In this study a total of 110 patients with mean age of  $45 \pm 2.16$  years were included with 35% patients were males. About 22% patients were hypertensive and 80% patients were non hypertensive, 27% were diabetics. About 70% patients had BMI  $<30$  while 30% patients had BMI  $> 30$ , 28% patients had moderate mitral stenosis and 72% patients had severe mitral stenosis with left atrial thrombus in 27% patients.

**Conclusion:** Our study shows that patients with AF have raised risk of atrial thrombus. Therefore proper screening for thrombus is needed in patients with AF so that in time anti coagulation can be done.

**Key Words:** Atrial fibrillation, Mitral stenosis, Left Atrial Thrombus.

## INTRODUCTION

Rheumatic heart valve disease is one of the most serious complications of rheumatic fever, and rheumatic mitral valve stenosis (RMVS) is the most frequently seen part of this disease. Rheumatic heart disease is a major burden in developing countries and is the leading cause of the cardiovascular morbidity and mortality in young people, in this way causes about 25,000 deaths per year worldwide. The most common symptoms in Mitral stenosis reduced exercise capacity and fatigue. Development of clinical symptoms such as exercise capacity and prognosis, and survival in MS largely depends on right ventricular function.<sup>1,2</sup> Left atrium (LA) thrombus is a common source of thromboemboli and it is usually seen in atrial fibrillation (AF), valve disease, and serves left ventricular systolic and diastolic dysfunction. In patients with mitral stenosis (MS) and AF, the risk of thrombus formation in the left atrium is very high. In 90% cases of atrial fibrillation, blood clots forms in the left atrial appendage and they may lead to emboli, which in turn results in ischemic damage to the brain, kidneys or various other organs that are supplied by the systemic circulation.<sup>3,4</sup>

Left atrial thrombus can be detected by various modalities like transthoracic echocardiography (TTE), transesophageal echocardiography (TEE). Transesophageal echocardiography (TEE) is most commonly used because due to its ability to visualize the LAA structure and to identify a thrombus with high spatial and temporal resolution. In a study done in South Korea prevalence of left atrial thrombus in patients of mitral stenosis with atrial fibrillation was 24%.<sup>5</sup> In another study done in Peshawar, Pakistan, the prevalence of atrial fibrillation in severe mitral stenosis was 18.7% and frequency of clot in such patients was 14.5%.<sup>6</sup>

Early detection of left atrial thrombus and treating it in time may prevent complication such as stroke and damage to various organs. The aim of this study is to find out the frequency left atrial thrombus in patients of mitral stenosis with atrial fibrillation in our population.

## METHODOLOGY

This cross sectional study was conducted at Bolan Medical College and Sandeman Teaching Hospital, Quetta. The duration of the study was one year from 17<sup>th</sup> February, 2015 to 17<sup>th</sup> February, 2016. Total sample size was calculated by using WHO sample size formula using prevalence of left atrial thrombus in patients of mitral stenosis with atrial fibrillation to be 24% with confidence interval 95% and absolute precision 7%. Consecutive non probability sampling was used for sample collection. Both male and female patients age between 25 to 70 years with moderate to severe mitral stenosis and atrial fibrillation were included

while patients with mitral stenosis and normal sinus rhythm, Mitral regurgitation, congestive heart failure, significant aortic valve or coronary artery disease were excluded. The study was approved by the hospital ethical committee. Patients admitted to Cardiology unit Bolan Medical College, Quetta through OPD or casualty department were included. An informed consent was obtained. Patients of mitral stenosis were diagnosed on transthoracic echocardiographic assessment using Acuson CV 70 Siemens using planimetry and Doppler method. Mitral valve was graded as moderate with valve area of 1-1.5cm<sup>2</sup> and a transmitral valve pressure gradient of 5-10mmHg and severe when valve area was  $\leq$  1cm<sup>2</sup> and transmitral valve pressure gradient of  $\geq$  10mmHg. An electrocardiogram was done on these patients and atrial fibrillation was diagnosed as absent P waves and irregularly irregular QRS complexes. If left atrial thrombus not detected on transthoracic echocardiography, then these patients were then subjected to transesophageal echocardiography for assessment of left atrial thrombi (including both left atrial cavity and appendage thrombus). Frequency of left atrial thrombus was recorded. Confounding variables like severe mitral regurgitation and congestive heart failure was excluded following exclusion criteria. Echocardiography was done on same machine by two operators to avoid operator bias, by the findings upon which both operators agree. The statistical analysis was performed using the statistical software for social sciences (SPSS Ver. 10.0). Categorical variables like gender, hypertension, diabetes, BMI, severity of stenosis and left atrial thrombus were presented in the form of frequencies and percentages. Numerical variables like age and BMI presented as Means  $\pm$  SD. Left atrial thrombus stratified among the age, gender, hypertension, diabetes, BMI and severity of stenosis to see the effect modifiers.

## RESULTS

In this study age distribution among 110 patients was analyzed. About 10(9%) patients were in age range 25-35 years, 21(21%) patients were in age range 36-45 years, 29(26%) patients were in age range 46-55 years, 28(25%) patients were in age range 56-65 years and 20(19%) patients were above 65 years. Mean age was  $45 \pm 2.16$  years (Table 1). Male patients were 38(35%). About 22(20%) patients were hypertensive, 30(27%) patients were diabetic, 77(70%) patients had BMI  $<$ 30 while 33(30%) patients had BMI  $>$  30.

In patients, 31(28%) patients had moderate mitral stenosis and 79(72%) patients had severe mitral stenosis. Left atrial thrombus was present in 30(27%) patients (Table 2). Stratification of left atrial thrombus with age, gender, hypertension, diabetes, BMI and severity of mitral stenosis is given in table 3 and 4. Mean BMI was  $23 \pm 7.83$ .

**Table 1: Age Distribution in Study Population (n=110)**

| Age            | Frequency (n) | Percentage (%) |
|----------------|---------------|----------------|
| 25-35 years    | 10            | 9%             |
| 36-45 years    | 23            | 21%            |
| 46-55 years    | 29            | 26%            |
| 56-65 years    | 28            | 25%            |
| Above 65 years | 20            | 19%            |
| <b>Total</b>   | <b>110</b>    | <b>100%</b>    |

**Table 2: Distribution of Gender, Hypertension, Diabetes Mellitus, BMI, Mitral Stenosis and Left Atrial Thrombus in Study Population (n=110)**

| Gender                      | Frequency (n) | Percentage (%) |
|-----------------------------|---------------|----------------|
| Male                        | 38            | 35%            |
| Female                      | 72            | 65%            |
| Total                       | 110           | 100%           |
| <b>Hypertension</b>         |               |                |
| Hypertensive                | 22            | 20%            |
| Non Hypertensive            | 88            | 80%            |
| Total                       | <b>110</b>    | <b>100%</b>    |
| <b>DIABETES</b>             |               |                |
| Diabetic                    | 30            | 27%            |
| Non diabetic                | 80            | 73%            |
| Total                       | <b>110</b>    | <b>100%</b>    |
| <b>BMI</b>                  |               |                |
| = 30                        | 77            | 70%            |
| > 30                        | 33            | 30%            |
| Total                       | <b>110</b>    | <b>100%</b>    |
| <b>Mitral Stenosis</b>      |               |                |
| MODERATE                    | 31            | 28%            |
| SEVERE                      | 79            | 72%            |
| Total                       | 110           | 100%           |
| <b>Left Atrial Thrombus</b> |               |                |
| Yes                         | 30            | 27%            |
| No                          | 80            | 73%            |
| Total                       | 110           | 100%           |

**Table 3: Stratification of Left Atrial Thrombus with Age (n=110)**

| Left Atrial Thrombus | 25-35 years | 36-45 years | 46-55 years | 56-65 years | >65 years | Total |
|----------------------|-------------|-------------|-------------|-------------|-----------|-------|
| Yes                  | 3           | 6           | 8           | 7           | 6         | 30    |
| No                   | 7           | 17          | 21          | 21          | 14        | 80    |
| Total                | 10          | 23          | 29          | 28          | 20        | 110   |

Chi square test was applied in which P value was 0.993

**Table 4: Stratification of Left Atrial Thrombus with Gender, Hypertension, Diabetes Mellitus, BMI and Mitral Stenosis (n=110)**

| Left Atrial Thrombus | Male         | Female           | Total | p-value |
|----------------------|--------------|------------------|-------|---------|
| Yes                  | 11           | 19               | 30    | 0.872   |
| No                   | 27           | 53               | 80    |         |
| Total                | 38           | 72               | 110   |         |
| Left atrial thrombus | Hypertensive | Non Hypertensive |       |         |
| Yes                  | 6            | 24               | 30    | 0.731   |
| No                   | 16           | 64               | 80    |         |
| Total                | 22           | 88               | 110   |         |
| Left atrial thrombus | Diabetic     | Non Diabetic     |       |         |
| Yes                  | 8            | 22               | 30    | 0.675   |
| No                   | 22           | 58               | 80    |         |
| Total                | 30           | 80               | 110   |         |
| Left Atrial Thrombus | = 30         | > 30             |       |         |
| Yes                  | 21           | 9                | 30    | 0.738   |
| No                   | 56           | 24               | 80    |         |
| Total                | 77           | 33               | 110   |         |
| Left atrial thrombus | Moderate     | Severe           |       |         |
| Yes                  | 8            | 22               | 30    | 0.675   |
| No                   | 23           | 57               | 80    |         |
| Total                | 31           | 79               | 110   |         |

## DISCUSSION

Rheumatic mitral stenosis with atrial fibrillation is a common clinical problem in Pakistan.<sup>7-9</sup> It is a potential source of thrombus formation and associated with a very high risk of embolic cerebro-vascular accidents, which is reported to be as much as seventeen times greater than in unaffected controls.<sup>10</sup>

TEE is well established as the gold standard for detecting thrombi in the left atrium and the LA appendage. The sensitivity and the specificity of TEE are reported to be 100% and 99%, respectively.<sup>11</sup> Through it is known that thrombi are common in patients with MS and AF, until recently only small studies have documented the exact frequency of occurrence of these thrombi. In a small group of 50 patients with MS and AF, Hwang et al.<sup>12</sup> Observed an LA thrombus in 28 patients (56%) by TEE. In another small study of 22 patients with MS and AF karatasakis et al.<sup>13</sup> Observed an LA thrombus in 12 patients (54%). A study performed in NICVD Karachi found 38% with severe mitral stenosis and atrial fibrillation.<sup>14</sup>

In our study we found LA thrombus in 27% of patients, the results of our study is in contrary with study performed in NICVD which shows higher prevalence of left atrial thrombus 38%,<sup>14</sup> But the reason for discrepancy is that we have included both moderate and severe mitral stenosis while in

their study they have included only severe mitral stenosis patients.

However, recently Srimannarayana J et al. studied 490 patients with severe MS and AF and observed LA thrombi in 163 (33.5%) patients.<sup>15</sup> We found LA thrombus in 27% patients in a group of 152 consecutive patients. Considering the size of the study group though the number of patients in our study group is little less for the prevalence of LA thrombi in patients with moderate and severe MS and AF, but our results were comparable. Thus, it can be stated that 1 out of every 4 patients with MS and AF will have an LA thrombus.

Another important finding emerged in our study is male to female ratio of disease (male : female = 1:1.6). whereas it is a known fact that the mitral stenosis affected women more than the men but majorities of these studies are western. In our study the same ratio has been maintained by gender distribution as Rehman S in his study.<sup>16</sup>

There is another study Movahed et al which also show high prevalence of mitral stenosis in females 53%, while in males the prevalence of mitral stenosis was 47%.<sup>17</sup> This is in comparison with our study in which the frequency of female patients with mitral stenosis is 57.24% while male patients with mitral stenosis are 42.76%. Although there is little difference in the percentage of the patients but the overall predominance of female gender of mitral stenosis is

determined.

We also reported higher frequency of presence of LA thrombus in female patients (29.9%) as compared to male. This may represent female predominant study population.

Our study showed that LA size is relevant with the presence of LA thrombus ( $63.53 \pm 15.79$  mm versus  $55.55 \pm 10.94$  mm). This means that larger the atrial size greater the chances of presence of LA thrombus in patients with severity of MS and AF. While describing clinical risk factors for thrombus formation among patients with severe MS Goswami et al documented the same finding. Apart from LA diameter he found that longer duration of symptoms and more frequent atrial fibrillation with spontaneous echo contrast were independent risk factors for LA thrombus formation.<sup>18</sup>

Surprisingly we did not find the LASEC to be relevant with the presence of LA thrombus. We found it in 54% of patients, out of them 28 had LA thrombi while 26 were free of any thrombus. Goswami et al observed LASEC in 53.5% of cases in their study but they enrolled all the patients with severe MS irrespective of having AF.<sup>19</sup> This may be the reason of difference in our finding.

However, at least it can be said that larger LA diameter is an alarming sign and one has to carefully look for LA thrombus in these patients. In our study moderate Ms patients was found to have thrombus in 5(17.9%) and severe Ms patients was found to have thrombus in 36(29%). In our study we performed TEE in 149 patients in whom LA thrombus was not detected by TTE. In remaining 3 patients LA thrombus was detected by TTE.

Goswami addressed the issue of sensitivity of transthoracic echocardiography for detecting LA/LAA thrombus in a study and concluded that sensitivity of TTE in visualizing the clot in LA appendage in south East Asian patients is not so bad as reported in west.<sup>19</sup>

In our part of the world patients are generally younger, have lesser body weight and thinner chest walls resulting in better transthoracic echogenicity. Due to these factors we did not perform TEE in those patients in whom LA thrombi were already detected with TTE. It would be unethical if TEE was performed unnecessarily, as it is comparatively an invasive procedure.

In the subgroup analysis we found the majority of our patients were in their 3<sup>rd</sup> and fourth decade of their lives i.e 23.7% and 42.6% patients, respectively. This is in consistent with previous studies as Islam et al has shown 34% frequency in 3<sup>rd</sup> decade of patients with rheumatic mitral value disease.<sup>20</sup>

In our study the majority of our patients presented in 4<sup>th</sup> decade (42.6%), where as in the study of Islam et al, their majority of patients presented in their 3<sup>rd</sup> decade. The late

presentation of patients in our study may be because of lack of awareness and delaying of the patients to seek medical attention until severe symptoms develop. We found that left atrial thrombus was more frequently present in the fourth decade of their life (n=20).

We also reported that frequency of left atrial thrombus is directly proportional to the severity of mitral stenosis. Moderate mitral stenosis were having left atrial thrombus in only 5 patients while in case of severe mitral stenosis left atrial thrombus was present in 36 patients. This has been proven in multiple randomized trial that left atrial enlargement is directly correlated with severity of MS and a nidus for formation of thrombus as well.<sup>21</sup>

## CONCLUSION

The proportion of patients with LA thrombi in patients suffering from severe and moderate MS and AF observed in this study was 27%. Therefore it can be stated that more than one fourth of the patients with severe and moderate rheumatic MS and AF may have LA thrombi. Larger LA diameter was observed associated with presence of LA thrombus.

Therefore, larger the LA size in patients with severe MS and AF greater the frequency of having LA thrombus is expected. Hence, it is prudent to anticoagulate this high-risk group of patients to prevent them from serious implications of systemic thromboembolism.

## REFERENCES

1. Gandapur AJ, Rahim F, Asghar AH, Shafique M, Hameed A, Khawar N. Changing clinical pattern of rheumatic fever at Peshawar (Pakistan). *J Postgrad Med Inst* 2004;18(2):250-4.
2. Jan H, Hassan M, Hafizullah M. Long term echocardiographic follow up of percutaneous transvenous mitral commissurotomy. *J Postgrad Med Inst* 2004;18(3):529-34.
3. Kronzon I, Tunick PA, Charney LH. Echocardiography as a tool in the evaluation of conditions with a high likelihood of cardiogenic embolism. *Isr Med Assoc J* 2006;8(11):768-72.
4. Otto CM, Bonow OR. Valvular heart disease. *Braunwald's Heart Disease: text book of cardiovascular medicine*. 8th ed. New Delhi: Saunderson Elsevier; 2008. p. 1625-712.
5. Saidi SJ, Motamedi MH. Incidence and factors influencing left atrial clot in patients with mitral stenosis and normal sinus rhythm. *Heart* 2004;90(11):1342-3.
6. Ali M, Abid AR, Mallick NH, Sheikh SS, Ahmad S. Clinical and echocardiographic predictors of left atrial



- thrombus in rheumatic mitral stenosis. *Ann King Edwa Med Coll* 2009;15(2):75-9.
7. Ullah K, Ahmed SA, Badsha S, Khan A, Kiani MR. Rheumatic Heart disease: a study of surgically excised cardiac valves and biopsies. *J Coll Physicians Surg Pak* 2002;12(9):542-5.
  8. Chagani H, Aziz KU. Clinical profile of acute rheumatic fever in Pakistan: a prospective study. *Pak Paed Cardiol J* 2001;3(1-2):9-10.
  9. Khan RF, Imtiaz Y, Ali H, Khan MU, Ali M, Riaz N, et al. Natural history and relative distribution of different valvular heart diseases in Mayo Hospital, Lahore. *Ann King Edward Med Coll* 2002;8(2):90-1.
  10. Greenblatt DJ, Sellers EM, Shader RI. Drug therapy: drug disposition in old age. *N Engl J Med* 1982;306(18):1081-8.
  11. Manning WJ, Weintraub RM, Waksmonski CA, Haering JM, Rooney PS, Maslow AD, et al. Accuracy of transesophageal echocardiography for identifying left atrial thrombi. A prospective, intra-operative study. *Ann Intern Med* 1995;123(11):817-22.
  12. Hwang JJ, Chen JJ, Lin SC, Tseng YZ, Kuan P, Lien WP, et al. Diagnostic accuracy of transesophageal echocardiography for detecting left atrial thrombi in patients with rheumatic heart disease having undergone mitral valve operations. *Am J Cardiol* 1993;72(9):677-81.
  13. Karatasakis GT, Gotsis AC, Cokkinos DV. Influence of mitral regurgitation on left atrial thrombus and spontaneous echocardiographic contrast in patients with rheumatic mitral valve disease. *Am J Cardiol* 1995;76(4):279-81.
  14. Farman MT, Sial JA, Khan N, Rahu QA, Tasneem H, Ishaq M. Severe mitral stenosis with atrial fibrillation--a harbinger of thromboembolism. *J Pak Med Assoc* 2010;(60):439-43.
  15. Srimannarayana J, Varma RS, Satheesh S, Anilkumar R, Balachander J. Prevalence of left atrial thrombus in rheumatic mitral stenosis with atrial fibrillation and its response to anticoagulation: a transesophageal echocardiographic study. *Indian Heart J* 2003;55(4):358-61.
  16. Rehman S, Shabbier G, Shahid M. Clinical presentation of infective endocarditis. *J Postgrad Med Inst* 2002;16(1):55-63.
  17. Movahed MR, Ahmadi-Kashani M, Kasravi B, Saito Y. Increased prevalence of mitral stenosis in women. *J Am Soc Echocardiogr* 2006;19(7):911-3.
  18. Sim EK, Lim YT, Ng WL, Goh JJ, Reebye S. Co-existing left atrial thrombus and myxoma in mitral stenosis--a diagnostic challenge. *Singapore Med J* 1999;40(1):46-7.
  19. Goswami KC, Narang R, Bahl VK, Talwar KK, Manchanda SC. Comparative evaluation of transthoracic and transesophageal echocardiography in detection of left atrial thrombus before percutaneous transvenous mitral commissurotomy. Do all patients need transesophageal examination? *Int J Cardiol* 1997;62(3):237-49.
  20. Islam MM, Haque ZM, Haque AM, Mahmood I, Islam FM, Azhar AM. Clinical profile of patients with mitral stenosis: a study of 100 cases in Rajshahi Medical College Hospital. *J Teach Assoc* 2009;22(1):101-5.
  21. Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, et al. 2011 ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College Of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2011;123(10):e269-367.