



## Tricuspid valve involvement in chronic rheumatic mitral stenosis: An observational study.

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**ABSTRACT... Objective:** The aim of this study was to assess the incidence of tricuspid valve involvement in rheumatic mitral stenosis among Pakistani patients that helps in the medical decisions and special consideration for the management of disease. **Study Design:** Prospective Study. **Setting:** National Institute of Cardiovascular Disease (NICVD), Karachi. **Period:** February 2018 to November 2019. **Material & Methods:** As per the study inclusion criteria, Three fifty eight (358) Pakistani patients' diagnosed with Rheumatic Mitral stenosis. The study was compiled as per international standards (ICH-GCP-E6), prior to initiation, the ethics review committee approved the study and informed consent was taken from all recruited subjects. **Results:** The study prospectively assessed the echocardiographic profile of rheumatic heart disease patients and recruited 358 patients with chronic Rheumatic Mitral Stenosis. Out of these patients, 93.9% (336) had tricuspid regurgitation and 7% (25) had tricuspid stenosis. Their ages ranged from 14 to 85 years (mean 40.3 years). Of these, 73.6% (263) were females and 26.5% (95) were males. On the basis of severity, in case of tricuspid stenosis, 3.9% (14) were mild, 1.1% (4) were moderate and 2% (7) were progress from mild to moderate. In case of Tricuspid regurgitation, 42.5% (143) were mild, 31.2% (105) moderate and 26.1% (88) were severe. **Conclusion:** The study concluded that in the local population, the patients with chronic Rheumatic Mitral Stenosis had common involvement of Tricuspid valvular disease, more come in female and affected all age groups. Hence, before management of Rheumatic Mitral Stenosis with other lesions, especially the Tricuspid valve involvement, detailed assessment is required in order to achieve the best outcome in patients with the Mitral valve disease.

**Key words:** Pakistani Population, Rheumatic Mitral Stenosis, Tricuspid Valve Disease.

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## INTRODUCTION

Rheumatic Heart Disease (RHD) continues to impose a significant health burden across the globe.<sup>1</sup> As per disease global prevalence, at least 33.4 million individuals were affected with RHD, around 10.5 million were lifetime disabled and 319,400 deaths attributed to RHD.<sup>1</sup> In developing countries, the RHD contributed to the significant morbidity and mortality and the incidence is highest in Oceania, central sub-Saharan Africa, and South Asia.<sup>2</sup> In Pakistan, the prevalence of RHD in the rural community affected between 12 per 1000 people and prominent cause of premature death and disability.<sup>3</sup> The RHD may affect any cardiac valve, however, left sided heart is the most affected region and frequently

involved the mitral valve.<sup>4</sup> The mitral stenosis (MS) is most prevalent isolated valvular heart disease in developing countries.<sup>5</sup> The Mitral stenosis can lead to many cardiovascular complications, including the involvement of tricuspid valve disease.<sup>6</sup> The Tricuspid valve stenosis is relatively a rare condition and is usually accompanied by mitral stenosis.<sup>7,8</sup> The condition is almost always related to rheumatic disease, may also associated with other rare conditions like endocarditis, Lupus erythematosus, right atrial myoma, endomyocardial fibrosis and congenital tricuspid atresia.<sup>9</sup> Tricuspid stenosis can exist as a congenital lesion or present later in the life with other conditions.<sup>10</sup> Although, the contribution of the tricuspid valve is well recognized in Rheumatic

patients, still the disorders of right-sided cardiac valves attract less attention than left-sided valves.<sup>7,10,11</sup> Generally, the rheumatic tricuspid valve disease is commonly missed during routine clinical examination exception being advanced cases with a high degree of clinical suspicion.<sup>7,11,12</sup> The several studies reported that during autopsies, the tricuspid disease was present in 22–44% of the cases of RHD.<sup>11,13</sup> Even during routine cardiac catheterization, tricuspid stenosis can easily be missed so less is studied and more rarely described.<sup>14</sup> Different studies have analysed the results that unobserved and uncorrected lesions increase perioperative mortality and of morbidity and, following surgical correction of Mitral valvular lesions, may lead to worsen the prognosis that altering the treatment options followed by long term outcomes and complications even after surgical treatment of rheumatic mitral stenosis.<sup>6</sup> Therefore, as the tricuspid valve pathogenesis is remain complex, and challenge to manage, however the early recognition and appropriate treatment of Tricuspid disease may improve the long-term functional outcome.

In Pakistan, multiple studies were conducted on Rheumatic heart disease,<sup>3,9,11,15-21</sup> however, very few studies<sup>22,23</sup> were described and studied the association of Tricuspid Mitral stenosis with tricuspid valvular disease among Pakistani patients. The aim of the current study was to assess the presence of tricuspid valve disease, its severity and associated clinical factors in patient with chronic rheumatic mitral stenosis with local Pakistani population.

## MATERIAL & METHODS

It was a single-centre, prospective, hospital based study conducted at the National Institute of Cardiovascular Disease (NICVD), Karachi. As per the study inclusion criteria, three fifty three (358) Pakistani patients' diagnosed with chronic Rheumatic Mitral were recruited from the period of February 2018 to November 2019. The study was compiled as per international standards (ICH-GCP-E6), prior to initiation, the ethics review committee approved the study (ERC-10/2019) and informed consent was taken from all recruited subjects.

## Data Collection Procedure

Inclusion criteria for the study were either gender, age between 18 to 80 years, underwent transthoracic echocardiography, and diagnosed with Chronic Rheumatic Mitral Stenosis. Patients' demographic characteristics, clinical history, indications for the procedure, and echocardiographic diagnoses such as, severity of MS, tricuspid valve involvement and type, tricuspid stenosis and severity, tricuspid regurgitation and severity, and pulmonary hypertension and severity, will be obtained using a structured questionnaire. Patient related information will be kept secured and no personal level information will be disclosed during all the stages of dissemination of the study finding.

## Operational Definitions<sup>24</sup>

### Mitral Stenosis (MS)

MS will be defined based on Transthoracic Echocardiogram (TTE), the mitral leaflet tips become calcified and thickened. A characteristic "hockey stick" appearance of the anterior mitral leaflet is seen. Mitral stenosis is categorized as mild, moderate or severe. The parameters associated with the severity is summarized below.

### Pressure Gradient (mmHg) Mitral Valve Area (cm<sup>2</sup>)

Normal	0	> 4.0
Mild	1-5	2.5-4.0
Moderate	6-10	1.0-1.5
Severe	> 10	< 2.0

### Tricuspid Valve Involvement

Severe tricuspid stenosis will be defined by a Doppler mean pressure gradient >5 mm Hg, pressure half-time ≥190 ms, or valve area ≤1.0 cm<sup>2</sup>. And will be classified as mild, moderate, and severe

### Tricuspid Regurgitation

will be measured based on echocardiography and severity will be measured according to the regurgitant jet area with;

- Mild = < 5 cm<sup>2</sup>
- Moderate = 5-10 cm<sup>2</sup>
- Severe = >10 cm<sup>2</sup>

Statistical package for social sciences (SPSS 21) will be used for the analysis of baseline characteristics. Shapiro-Wilk test will be applied to check the hypothesis of normality for quantitative (continuous) variables. Descriptive statistics such as mean  $\pm$  SD, median (IQR), skewness, maximum and minimum will be calculated for quantitative (continuous) variables. Frequency and percentages will be calculated for categorical variables. For between the group comparison of quantitative (continuous) variables, t-test will be employed and in case quantitative (continuous) variables fail to comply with the normality assumption Mann-Whitney U test will be used. Chi-square test or Fisher exact test will be performed to evaluate the effect of effect modifiers (confounding variables) on study outcome. A two-sided p-value  $\leq$  0.05 will be taken as criteria for significance.

## RESULTS

As per study results on based of echocardiographic profile, 358 patients with Rheumatic Mitral Stenosis were recruited. Out of these patients, 93.9% (336) had tricuspid regurgitation and 7% (25) had tricuspid stenosis. The ages ranged from 14 to 85 years (mean 40.3 years). Of these, 73.6% (263) were females and 26.5% (95) were males. The details for involvement of Mitral valvular lesion and associated lesions in Table-I.

As per study results and compare the involvement and its severity of Mitral stenosis and other lesions. The females (6.8%) were more affected than male (4.2%). For MS, the severity is higher with TR (100) followed by MR (96.4%) whereas for TS the severity is associated with MS (6.1%). The details of rest of the lesions in Table-II.

To compare the differences between age, PA pressure and lesions with Mitral stenosis, the details mentioned in Table-III.

If we specifically compare the TS with MS and the differences in terms of Age and PA pressure, the details mentioned in Table-IV.

Variables	Frequency (%)
Age (Mean and Range)	(40.3 $\pm$ 12.2yrs) 14 to 85
<b>Gender</b>	
Male	95(26.5)
Female	263(73.5)
<b>Mitral Stenosis (MS)</b>	
No	0
Yes	358(100%)
<b>Mitral Regurgitation</b>	
No	92(25.7)
Yes	266(74.3)
<b>Tricuspid Stenosis</b>	
No	333(93)
Yes	25(7)
<b>Tricuspid Regurgitation</b>	
No	22(6.1)
Yes	336(93.9)
<b>Aortic Stenosis</b>	
No	259(71)
Yes	104(29)
<b>Aortic Regurgitation</b>	
No	236(66)
Yes	123(34)
<b>Pulmonary Arterial Hypertension</b>	
No	50(14)
Yes	308(86)

**Table-I. Frequency of valvular lesions associated with Mitral valve stenosis.**

Valvular Disease	Mitral Stenosis	Tricuspid Stenosis	P-Value
<b>Variables</b>			
<b>Gender</b>	n(%)	n(%)	
Male	4(4.2)	91(95.8)	0.36
Female	18(6.8)	245(93.2)	
<b>MS Severity</b>			
Mild	0(0)	18(100)	
Moderate	4(10.3)	35(89.7)	0.321
Severe	18(6.1)	276(73.9)	
<b>MR Severity</b>			
Mild	8(8.1)	91(91.9)	
Moderate	1(2)	48(98)	0.532
Severe	2(3.6)	53(96.4)	
Mild	2(7.1)	26(92.9)	
Moderate	1(3.6)	27(96.4)	
<b>TR Severity</b>			
Mild	0(0)	143(42.5%)	<.001
Moderate	0(0)	105(31.2%)	
Severe	0(0)	88(26.1%)	
<b>AS Severity</b>			
Mild	3(6.4)	44(93.6)	0.53
Moderate	1(4.3)	22(95.7)	
Severe	4(11.8)	30(88.2)	
<b>AR Severity</b>			
Mild	7(10)	63(90)	
Moderate	1(3.3)	29(96.7)	0.641
Severe	1(14.3)	6(85.7)	
Mild To Moderate	1(6.3)	15(93.8)	

**Table-II. Comparing MS with other valvular lesions on the basis of severity.**

Variables	N	Mean	Std. Deviation	Minimum	Maximum	Median
Age	358	40.3492	12.19558	14	85	40.00
PA_Pressure	325	57.2892	19.65731	25	120	55.00
Mitral Stenosis	358	0.0698	0.25522	0	1	.000

**Table-III. Mann-Whitney Test, Descriptive details for Mitral Stenosis.**

	Tricuspid Stenosis	N	Mean Rank	Sum of Ranks	P-Value
Age	No	333	181.63	60482.5	0.155
	Yes	25	151.14	3778.5	
	Total	358			
Pulmonary arterial Pressure	No	308	160.98	49582	0.097

**Table-IV. Mann-Whitney Test, Descriptive details for Mitral Stenosis and involvement of TS.  
P value  $\leq 0.05$  Significant**

## DISCUSSION

Rheumatic heart disease with an association of valvular disease endures to be a significant disease entity in developing countries including Pakistan.<sup>1,2</sup> The local population data of 2004 from the National Institute of Cardiovascular Disease, NICVD), the country leading tertiary care hospital, managing the cardiovascular cases reported, 8%-29% admissions and 62% of the surgical procedure is attributable to RHD.<sup>25</sup> The present study was undertaken at the same study site (NICVD) with an aim to systematically analyse the incidence of Rheumatic Mitral stenosis Pakistani patients with the involvement of Tricuspid valvular disease in the light of Echocardiographic examinations. Globally, the Rheumatic mitral stenosis with the involvement of tricuspid valvular disease is well recognized.<sup>5,6</sup> In Pakistan, previously multiple local studies and surveys addressed the overall patterns of RHD and association of different valvular disease, based on the examination of local communities or frequency and incidence in the hospital settings.<sup>3,9,11,15-23</sup> The Fahim et al (2007) study results on 3060 RHD patients showed that 70% patients affected by MS followed by MR in 58.59% cases.<sup>23</sup> Similarly, the screening study by MA Shaikh et al on valvular lesions on 100 RHD patients, reported mitral stenosis (MS, 48%), followed by mitral regurgitation (MR, 42%).<sup>17</sup> Another small sample of study on 34 MS patients by Rehan et al (2016) revealed that 22 (62.85%) MS patients were accompanied with TR.<sup>8</sup> The retrospective study by Aurakzai et al (2009) screened 13,414 patients with RHD patients, the mixed mitral valve disease was seen in 3,185

(23.7%).<sup>22</sup>

Overall, our current study results endorsed the past studies both local and international studies, as in 358 Pakistani patients with Rheumatic Mitral Stenosis, the association the Tricuspid valvular disease was not uncommon and the combined MS with TR was 93.3% (336) with moderate to severe in 41.1% patients followed by TS of 7% (25) with severe in 20% of patients on echocardiographic examination. The TR is commonly exist in MV disease and shared one-third of the patients with mitral stenosis<sup>5,6</sup>. Clinically severe TR has been reported in 23% to 37% RHD patients.<sup>7,8</sup> In our study, the patients Rheumatic Mitral Stenosis with moderate to severe TR were 41.1% patients. In past study reported the incidence of moderate or severe TR in RHD patients is even higher (68%).<sup>8</sup> In case of combined MS with TS, globally, only 3% of TS exists, more commonly in women and usually with the Rheumatic mitral stenosis.<sup>7,8,10</sup> The congenital form is the rare lesion of TS, only contributed the 0.3% of all valvular lesions occurring primarily in association with mitral stenosis.<sup>10</sup> In our study, 72%<sup>18</sup> female observed TS in combination with rheumatic mitral stenosis (7%) and Tricuspid regurgitation.

For the gender distribution of RHD, in majority of the past study data from local and international studies, RHD tends to be more likely and predominance among females, however its cause is unclear.<sup>26,27</sup> The multiple factors leading to difference in the gender RHD prevalence including social factors (such as child caring might

exposed repeatedly to group A streptococcus), genetically-mediated immunological factors that predispose an autoimmune responses or often during pregnancy due to the high cardiac burden.<sup>4</sup> The majority of the local studies in past also reported the high rates of RHD among females with Abrar A et al (66.6%)<sup>21</sup>, Faheem et al. (58.2%)<sup>23</sup>, Rizvi S et al (53%)<sup>3</sup>, Ahmed R et al (77%)<sup>8</sup> among females predominance with RHD. Contrary, the study by Aurakzai et al had male (46%) predominance for reported RHD.<sup>22</sup> In our study the female prevalence were very high as female patients with Rheumatic Mitral Stenosis and involvement of Tricuspid valvular disease were 73.5% as compared to males (26.5%).

In RHD patients, the multiple valvular disease is a common condition, occurs in 51% of Rheumatic patients and often associated with graver prognosis and requires specialized therapeutic challenges.<sup>28</sup> The severity of the multiple valve disease based on the specific combination of valve lesions.<sup>28</sup> In our study, the patients with rheumatic mitral stenosis presented with at least one severe valvular lesion (24%, n=89) and TR was the most prevalent of these (n=336, 93.9%). Overall, the patients with Rheumatic mitral stenosis, 3% (n=9) were presented with the involvement of five valvular lesions and all were found to be severe in nature. The database of American Society of Thoracic Surgeons (n=290000 patients) from period from 2003 and 2007, 11% had double valve disease, mainly aortic and mitral, and only 1% had triple valve disease.<sup>29</sup> Another Swedish study reported 11% patients with multiple Valvular disease mainly associated with aortic stenosis (AS) plus aortic regurgitation (AR), AS plus mitral regurgitation (MR) and AR plus MR.<sup>30</sup>

In Beaton et al study (n=301), in RHD patients at least one valvular lesion with MR as the most prevalent of valvular disease (275 out of 301).<sup>31</sup> Majority of the patient with MS and 22 RHD patients with severe MS and only 4 had severe MR.<sup>31</sup> It was reported earlier that cases with severe MS were unlikely to have severe MR and were small in number.<sup>32</sup> However, the previously reported study data showed that the cases with

severe TR may also associated with other severe valvular lesions (either MR, MS or AR) and with pulmonary hypertension.<sup>33</sup> The Rashid et al study also described the pattern and extent of tricuspid valve involvement in chronic rheumatic heart disease.<sup>7</sup> The total of 173 patients with rheumatic heart disease patients, 21% (n=36) patients had rheumatic tricuspid regurgitation and 41.6% (n=15) were associated with tricuspid stenosis.<sup>7</sup> In our study, 91% of cases of Tricuspid regurgitation with Rheumatic Mitral Stenosis and 26% of cases were severe in nature and 82% were pulmonary hypertension (Secondary, 82% & Primary, 9%). The severe Tricuspid regurgitation with MS was associated with other lesion (MR, 69%, TS, 13%, AS, 20%, AR, 32%). Overall, in our study results, the TR is the most common associated (n=336, 93.9%) valvular disease and exclusively seen in association with Rheumatic MS whereas, 7% (n=25) of patients were presence of tricuspid stenosis in chronic rheumatic mitral stenosis.

The data presented are derived from a single center of the leading tertiary care hospital of largest city of Pakistan managing RHD, however, the data may not reflect the circumstances of other institutes specializing in the management of patients with RHD. Furthermore, the data was acquired in the setting of an observational prospective setup in the routine practice from clinical data and echocardiographic reports, which in some cases may not be as detailed as would be desirable. However, the data collected reflect the actual profiles of patients with RHD in routine practice in the tertiary hospital.

## CONCLUSION

The study concluded that in the local population, the patients with chronic Rheumatic Mitral Stenosis had common involvement of Tricuspid valvular disease mainly TR, more come in female and affected all age groups. Therefore, before management (surgery), the detailed assessment is required especially Tricuspid valve involvement in order achieved the better outcome in RHD patient with Mitral valve disease.






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