

## ORIGINAL ARTICLE

## SUBCLINICAL LEFT VENTRICULAR DYSFUNCTION IN PATIENTS WITH ISOLATED SEVERE RHEUMATIC MITRAL STENOSIS HAVING NORMAL LEFT VENTRICULAR EJECTION FRACTION

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**Background:** Mitral stenosis (MS) is a prevalent disease in the developing world. It is a preventable disease associated with considerably high morbidity and mortality rates. Myocarditis secondary to rheumatic MS can cause left ventricular (LV) dysfunction. In majority of the case this LV dysfunction is subclinical. Recent development in imaging techniques like tissue Doppler imaging (TDI) and strain imaging enabled us to detect subclinical LV dysfunction. One such example is Global Longitudinal Strain (GLS), which is a reliable mean of assessing LV dysfunction in patients diagnosed with mitral stenosis. This study is design to determine the frequency of subclinical LV dysfunction in patients presenting with severe MS of rheumatic etiology in our institute. Objective of the study was to determine frequency of subclinical LV dysfunction by mean GLS in patients with isolated severe Rheumatic MS having normal LV Ejection fraction measured by 2D/M-mode echocardiography. It was an observational cross-sectional study, conducted at Department of Cardiology, Rawalpindi Institute of Cardiology, Rawalpindi, during the period of six months from 1<sup>st</sup> January to 30<sup>th</sup> June 2016. **Methods:** Fifty-five patients with isolated severe mitral stenosis of underlying rheumatic aetiology with preserve LV function (EF>50%) were selected as per other inclusion and exclusion criteria. All patients were evaluated with detailed history, physical examination and echocardiographic examination. GLS was also noted and all other information was recorded on data collection form. **Results:** The average age and mean GLS was 48.20±11.62 years and -19.24±1.15% respectively. Left ventricular systolic impairment in patients under study using the Global Longitudinal Strain was seen in 16.36% (9/55) cases. **Conclusion:** Our results suggest that GLS helps in detecting impairment of LV systolic function at an early stage in patients with mitral stenosis which helps in their risk stratification thus warranting their early management

**Keywords:** Mitral stenosis; Subclinical LV dysfunction; GLS; Severe Rheumatic MS

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### INTRODUCTION

Mitral stenosis (MS) of underlying rheumatic aetiology has a high degree of prevalence in the developing world.<sup>1</sup> This disease is not only preventable but can also be diagnosed early; which is important to reduce morbidity and mortality associated with it. Pakistan being a developing country has a high prevalence rate of MS accounting to up to 22/1000 population in one study.<sup>2</sup> MS can have different underlying aetiologies and the most common aetiology of MS worldwide is rheumatic fever.<sup>3</sup>

Myocarditis secondary to rheumatic MS can cause left ventricular (LV) dysfunction. This decrease in LV myocardial contractility is most likely secondary to inflammatory rheumatic process. Lee *et al*<sup>4</sup> in a study found that tissue and cellular segments of left ventricle exhibited ultra-structural changes in patients diagnosed with mitral stenosis. In patients with valvular heart disease there are different

predictors of poor outcome and LV dysfunction is one of the common ones.<sup>5</sup> In majority of cases of MS this LV dysfunction is subclinical.<sup>6</sup> Identification of such LV dysfunction is pivotal in the diagnosis and treatment of such patients but at times even the conventional methods of imaging including echocardiographic 2 D and M mode modalities fail to detect LV dysfunction in such patients. The advent of tissue Doppler imaging (TDI) and strain imaging have however enabled us to detect subclinical LV dysfunction.<sup>7,8</sup> One such domain is Global Longitudinal Strain (GLS). This domain has become a reliable mean of detection of sub clinical LV dysfunction in patients with MS which has been validated in different studies as well.<sup>9</sup> Using this domain; Global Longitudinal Strain (GLS) a comparison was made to assess the LV function of patients with isolated Rheumatic MS with those without MS (control) by Younan *et al*<sup>10</sup> This study showed that the mean GLS was significantly higher in patients with isolated MS {mean GLS -18.6±2.82

(controls) vs  $-12.77 \pm 1.44$  (MS):  $p=0.001$  as compare to controls. The normal values of GLS ranges from  $-15.9\%$  to  $-22.1\%$  (mean,  $-19.7\%$ ).<sup>7</sup> Another study showed that in patients with isolated rheumatic mitral stenosis, approximately 17% of the patients had LV systolic dysfunction; ejection fraction (EF)  $< 50\%$ .<sup>11</sup>

In epidemic areas like Pakistan recurrence of rheumatic fever as well as the associated myocarditis can lead to LV dysfunction. Early detection of LV dysfunction and subsequent prompt management can reduce the morbidity and mortality associated with isolated MS. To date no study has been conducted in Pakistan regarding assessment of impairment of LV systolic function in MS patients. So, we planned to conduct this study to determine the frequency of subclinical LV dysfunction in patients presenting with severe rheumatic MS in our institute.

The rationale of the study is to assess the frequency of subclinical LV dysfunction by means of the GLS method in patients with isolated mitral stenosis of underlying rheumatic aetiology having preserved LV systolic fraction measured by 2 dimensional/M-mode echocardiography; so that such patients can be identified and managed early to reduce adverse outcomes.

Any of the following features: Thickening, calcification, reduced mobility, commissural fusion and/or diastolic doming of mitral leaflets as observed by 2D-Echocardiography.

Mitral valve area  $< 1.5 \text{ cm}^2$  (Planimetry) and diastolic pressure half time  $\geq 220$  msec & Mean pressure gradient of (mPG)  $> 10$  mmHg measured by 2D-Echocardiography.

Normal LV Ejection fraction ( $> 50\%$ ) by 2D and/or M-mode using Simpson's method of disks with mean GLS value of  $> -19.7\%$ .<sup>6</sup>

A novel method in assessing global left ventricular function using tissue Doppler in 2D echocardiography mode.

## MATERIAL AND METHODS

This observational cross-sectional study was conducted at Cardiac imaging department, Rawalpindi Institute of Cardiology, Rawalpindi in six months from 1<sup>st</sup> January 2016 to 30<sup>th</sup> June 2016.

Sample size of 55 cases; calculated by using sample sized calculator introduced by World Health Organization (WHO), with 95% confidence level, population proportion = 17.02%, Precision 10%.

**Sampling Technique:** Non probability consecutive sampling

### Inclusion Criteria:

- Age 30–70 years of either gender

- Individuals with rheumatic mitral stenosis (as per operational definition) with preserved LV (EF  $> 50\%$ ).

### Exclusion Criteria:

- CAD (on medical record), DM (BSR  $> 186$ mg/dl), HTN (BP  $\geq 140/90$ mmHg)
- Other mitral and aortic valve abnormalities.
- Patients with tachyarrhythmias.
- Hyperthyroidism (TSH  $< 5$ IU), COPD (medical record).
- ECG showing abnormal rhythm.
- Patients with any degree of systolic dysfunction (LVEF  $\leq 50\%$ ).

Prior approval by the local ethical committee was taken. Patients presenting in the outpatient department (OPD) of our institute and fulfilling the inclusion criteria and willing to participate by giving informed consent. The patients were evaluated with detailed history, physical examination and echocardiographic examination. Demographic features of all patients (name, age, gender) were noted. 2D and M-mode echocardiography (Toshiba Apilo Japan 400) was used to measure mitral valve area by using planimetry and pressure half time methods. Peak and mean trans-valvular gradients were measured using similar technique. LV systolic function was assessed using Simpson's method. The left ventricular strain was then assessed using Doppler echocardiography by principal investigator and supervised by single consultant cardiologist. 2D echocardiographic images were obtained from LV apical views with frame rates of 20–59 frames/s. Manual tracing of left ventricular endocardium was performed in Left ventricular (LV) apical four chamber view. Similarly, modified speckle tracking width was obtained. In this way the left ventricular wall thickness in totality was studied to obtain curves. GLS was noted (as per operational definition) and using the above-mentioned parameters. All this information was recorded on data collection form.

SPSS 19.0 was used for data entry and analysis. Quantitative data like age and GLS was described by Mean  $\pm$  S.D. Qualitative data like gender an LV systolic dysfunction was described using frequency and percentage. Stratification of effect modifiers likes age and gender. Post stratified chi-square test was applied. The  $p$ -value of  $< 0.05$  was considered significant.

## RESULTS

Fifty-five patients diagnosed with severe mitral stenosis of underlying rheumatic aetiology with preserve LV function (EF  $> 50\%$ ) were selected as per inclusion and exclusion criteria. The average age was

48.20±11.62 years with almost equal gender distribution; 27 (49.09%) male and 28 (50.91%) female patients. Age, gender and were similar in control group and patients with MS. The mean global longitudinal strain (LGS) was -15.24±5.08%. Frequency of subclinical left ventricular systolic dysfunction as calculated by the mean GLS in patients with isolated severe rheumatic mitral stenosis was found in 16.36% (9/55) cases. Demographical characteristics of patients is shown in table-1

**Table-1: Demographic characteristics of patients**

Baseline characteristics	Case n = 55	p-value
Sex	Male: 27 (49.1%) Female: 28 (50.9%)	
Age	48.20±11.62 years	
Mean GLS	-15.24±5.08%	
Subclinical systolic dysfunction	9 (16.4%)	<0.001*

**Table-2: The frequency of subclinical systolic dysfunction in regards to age**

Age Groups (Years)	Subclinical left ventricular systolic dysfunction		Total	p-Value
	Yes	No		
≤40	4 (25%)	12 (75%)	16	0.61
41-50	2 (11.8%)	15 (88.2%)	17	
51-60	1 (8.3%)	11 (91.7%)	12	
61-70	2 (20%)	8 (80%)	10	

**Table-3: Frequency of subclinical systolic dysfunction in regards to gender**

Gender	Subclinical Left Ventricular Systolic Dysfunction		Total	p-value
	Yes	No		
Male	5 (18.5%)	22 (81.5%)	27	0.67
Female	4 (14.3%)	24 (85.7%)	28	

## DISCUSSION

Despite the improvement in public health care systems mitral stenosis of underlying rheumatic aetiology is still prevalent in the developing countries.<sup>12</sup> Quite a few clinical studies have been conducted in the recent past on the incidence and disease progression of rheumatic carditis leading to various valvular pathology including MS<sup>13,14</sup> however, studies to assess the left ventricular dysfunction and its impact on disease progression have been lacking. The indicators of MS progression and any subsequent subclinical LV dysfunction have been investigated in such subset of patients.<sup>15,16</sup> Assessment of LV global longitudinal strain (GLS) can detect LV dysfunction in isolated MS even if the left ventricular contractility as assessed by ejection fraction (EF) measured by other parameters is found to be in the normal range.<sup>17</sup> In fact, certain studies have shown subclinical LV dysfunction detected by GLS to have prognostic importance in patients with

isolated MS and this was found to be independent of LVEF.<sup>18</sup>

Mitral stenosis secondary to rheumatic carditis is more commonly seen in females. The exact cause of this is not known. In their classical study, Roberts and Virmani<sup>19</sup> found Aschoff bodies mitral stenosis patients which is pathognomic of rheumatic carditis and 70% of such patients were females. In our study we found 49.09% were males and 50.91% females showing similar incidence in both sexes which is however similar to a study conducted by Devereux *et al.*<sup>20</sup> This could be because of the cultural norms of our country with women being less likely to show up in tertiary hospitals and are mostly treated locally.

In our study 55 patients with mitral stenosis (MS) of underlying rheumatic aetiology and with preserve LV function (EF>50%) were selected. The frequency of subclinical impairment of left ventricular systolic function by mean GLS in patients with isolated severe mitral stenosis of rheumatic aetiology was found in 16.36% (9/55) cases. So approximately one sixth of isolated rheumatic MS patients with normal LVEF had subclinical LV systolic dysfunction. Similar pattern of LV dysfunction as assessed by the GLS method was seen in a study conducted by Sengupta *et al.*<sup>21</sup> Now this 16.36% is a staggering proportion of MS patients who can be managed early so as to reduce their subsequent morbidity. We also found out that this subclinical LV systolic dysfunction as detected by the GLS was independent of age and gender. Similar pattern was observed in a study conducted by Dogan *et al.*<sup>22</sup> who ascertained that the degree of subclinical LV systolic dysfunction was equally distributed across different age groups and different sexes.

## CONCLUSION

Recurrent rheumatic fever is a known risk factor for not only the progression and extension of rheumatic valvular disease but is also known to cause rheumatic myocarditis leading to LV dysfunction especially in epidemic areas like Pakistan. Our results suggest that Left ventricular function assessment by GLS may improve cardiovascular risk stratification in subjects which suggest that earlier intervention in these patients may be beneficial in reducing morbidity and mortality.

The limitations of the study are that it is a single centre study and non-randomized.

## AUTHORS' CONTRIBUTION

WAA: Data collection, result. HSK: Data analysis, Discussion, methodology. AN: References. MS: Introduction, methodology.

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