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PREVALENCE OF ASYMPTOMATIC DIASTOLIC CARDIAC DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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ABSTRACT **Objectives:** We conducted a study to determine the prevalence of asymptomatic left ventricular diastolic dysfunction (LVDD) in rheumatoid arthritis (RA) patients and to assess the relationship between diastolic dysfunction with RA disease duration and disease activity.

Methods: RA patients (n=100) who had completed at least 6 months of regular follow-up and treatment were included in the study. LVDD was assessed by echocardiography. Descriptive statistics and appropriate tests were used to analyze the results.

Results: Asymptomatic LVDD was present in 46(46%) participants, and there was no relation with respect to the gender of the population (*p-value*: 0.770). The group with LVDD had a significant association with longer disease duration (p-value <0.001) and high DAS28-ESR (p-value: 0.034).

Conclusion: The prevalence of asymptomatic LVDD in our cohort was significantly high. This study suggests screening all RA patients for LVDD even if they are asymptomatic.

KEYWORDS : Asymptomatic, Diastolic Dysfunction, Rheumatoid Arthritis

Introduction:

Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disorder affecting 1-3 % of the population with a female : male ratio of more than 2:1. [1] RA also results in a variety of extra-articular manifestations, particularly in patients with severe joint disease. Patients with RA have a two-fold increased incidence of congestive heart failure (CHF) as compared to the general population. [2] CHF itself is shown to be an independent risk factor for mortality in RA patients and is responsible for 1 in 8 deaths of patients with RA. [3] The left ventricular diastolic dysfunction can be due to various mechanical abnormalities that include impaired relaxation, decreased distensibility, and abnormal diastolic filling of the left ventricle.[4] The diagnosis of diastolic dysfunction is often made by echocardiography as the patients can be asymptomatic. Diastolic dysfunction could be a precursor event to the development of overt heart failure symptoms if not diagnosed at the earliest. As the previous studies suggest that there is an increased incidence of CHF in RA patients, it would be advantageous if the precursor events like diastolic dysfunction are detected early, to reduce the morbidity and mortality burden. Hence we conducted this study to see for the prevalence of asymptomatic diastolic dysfunction in RA patients and to assess the relationship between diastolic dysfunction with disease duration and severity of disease in patients with RA.

Materials and Methods:

Study Design: The present study was undertaken in the Department of Internal Medicine, Command Hospital (EC), Kolkata, WestBengal after the approval by the hospital ethics committee. This was a cross-sectional study done on 100 consecutive patients of rheumatoid arthritis who attended Rheumatology/Medicine OPD and/or admitted at Command Hospital over a period of two years(2015-2017), who were in continuous follow-up with us for at least 6 months. During this time, the disease modifying anti-rheumatic drugs (DMARDs) were adjusted according to the disease activity as per standard guidelines.

Participants: All patients, who were classified as RA based on 2010 ACR/EULAR Classification criteria, and who were in regular follow-up for at least six months, within the age group of 18 – 65 yrs were selected for the study irrespective of their disease duration or severity of the disease. The participants with the following conditions were excluded:

1. Pre-existing cardiac conditions especially CAD
2. Diabetes Mellitus
3. Hypertension
4. Known endocrine disorders like hypothyroidism, Cushing's syndrome.
5. Blood Hb < 10 g/dl
6. Patients with hepatic or renal dysfunction.

Methodology:

All the patients who met the inclusion criteria, after taking the informed consent, were subjected to routine blood investigations as a part of their routine disease assessment and DAS28-ESR was calculated for assessing disease activity. Transthoracic echocardiography was done by a senior cardiologist who was blinded to the disease parameters of the patients. The left ventricular (LV) systolic function was assessed using the modified Simpson's method of assessing the LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV). The stroke volume (SV) is the difference between LVEDV and LVESV, and LV ejection fraction (LVEF) was calculated as the ratio between the SV and LVEDV, expressed as a percentage. LV diastolic function was assessed by obtaining transmitral flow from the apical four-chamber view. The sample volume was positioned at the tip of the leaflets of the mitral valve to record transmitral flow. The following variables were examined as parameters of LV filling: peak of early (E) and late (or atrial) diastolic (A) flow velocity, E/A ratio, and deceleration time (DT).

Statistical Analysis:

Descriptive statistics were used to summarize the demographics. Quantitative and qualitative demographic characteristics were summarized, and the data were tabulated. Chi-square test was used to characterize the association of two groups with the categorical variables, and the *p*-value was derived. A *p*-value of <0.05 was used to indicate differences between groups that were statistically significant. Statistical analysis was carried out using the SPSS software version 22.

Results and analysis:

Out of 100 patients, women outnumbered men(n=71). The mean age of the participants was 39.89 ± 6.062 yrs. The mean disease duration of the study population is 6.53 ± 3.772 yrs. The mean DAS28-ESR of the study population was 4.621 ± 1.182. The prevalence of diastolic dysfunction in our study cohort was 46%. The prevalence of systolic dysfunction (i.e., EF <55%) in our study population was 15%. Participants were broadly assigned to two groups based on their disease duration as ≤ 5yrs & > 5yrs for comparison of presence or absence of left ventricular diastolic dysfunction (LVDD). In a similar manner, the study population was also divided into three groups based

on the DAS 28 ESR, i.e., < 3.2, 3.2-5.1 & > 5.1. We compared the presence or absence of left ventricular dysfunction in these two groups with respect to their disease duration and DAS28-ESR. In our study population of 100 patients, there were a total of 53 patients were having a disease duration of ≤5 years and remaining were >5 years of disease duration **(Fig 1)**. After 6 months of standard DMARD therapy, 14 were having DAS28-ESR of < 3.2, 41 patients had DAS28-ESR in the range of 3.2 - 5.1 and 45 patients were in the range of > 5.1.(**Fig 2)**

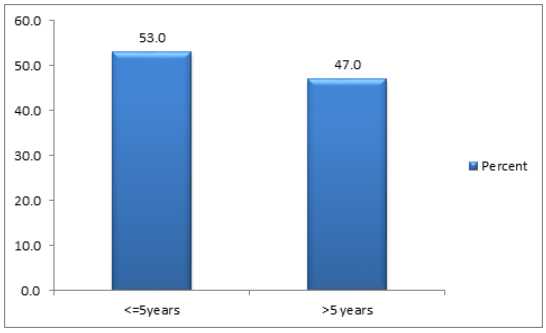

Fig 1: Bar diagram showing the Distribution of study population based on disease duration

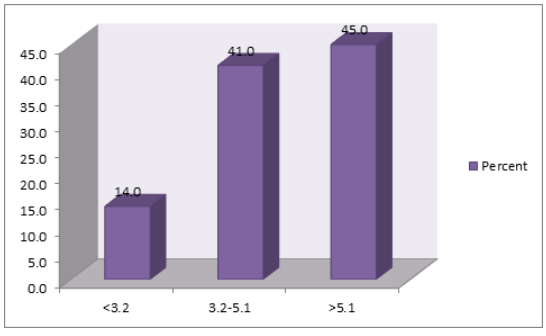

Fig 2: Bar diagram showing the distribution of the study population according to DAS28

The data were analyzed using the Chi-square test, and there was no statistical significance related to gender among patients with LVDD and without LVDD. Comparison of presence or absence of LVDD with respect to disease duration (i.e. ≤5 or > 5 yrs) and disease activity scores (DAS28 ESR) showed significant association with a p-value of <001 and 0.034 respectively. **(Table 1)**

Table 1: Statistical analysis of the study population

	LVDD		p-value
	Present	Absent	
Gender			
Female (71)	32(45.1)	39(54.9)	0.770
Male (29)	14(48.3)	15(51.7)	
Disease Duration			
≤5years(53)	10(18.5)	43(81.1)	<0.001
>5 years(47)	36(76.6)	11(23.4)	
DAS-28 ESR			
<3.2(14)	2(14.3)	12(85.7)	0.034
3.2-5.1(41)	20(48.8)	21(51.2)	
>5.1(45)	24(53.3)	21(46.7)	

DISCUSSION:

The cardiac involvement in the patients of RA can be endocardial (Libman–Sacks endocarditis and valvular regurgitant lesions), myocardial (Heart failure, left ventricular dysfunction, fibrosis, and amyloidosis), pericardial (pericarditis and effusion), electrical (arrhythmias, sudden cardiac deaths, & atrioventricular blocks), and vascular (coronary artery disease, vasculitis, and thrombosis). Diastolic dysfunction is recognized as a significant cause of cardiac morbidity.[5] The association of RA with LVDD has been conflicting, as found in earlier studies and there are also very few studies from India[6].

In our study, the prevalence of LVDD among RA patients was 46%, which is relatively high compared to the existing literature, which could be explained due to the dietary habits, socio-economic status, poor health screening facilities in India. In one study, conducted in the same population of eastern India but not in the RA population, the prevalence of isolated LVDD was 41%. However, they included patients with symptoms of heart failure and risk factors like diabetes mellitus and systemic hypertension. [7]

Our study did not show any significant association between gender and LVDD in RA patients, even though 71% of the study population constituted females.

In this study, we found that there is a significant association between patients with LVDD and without LVDD with respect to disease duration, which suggests longer disease duration is associated with LVDD. The similar observation noted in a study conducted by Kimberly P Liang et al., comparing RA patients with the general population, diastolic dysfunction was more common in subjects with RA at 31% compared with 26% (age and sex adjusted) in non-RA subjects.[8] They also found that RA duration and interleukin 6 (IL-6) level were independently associated with diastolic dysfunction in RA even after adjustment for cardiovascular risk factors.

We also found that 15% of our study population has LV systolic dysfunction(EF<55%), who were asymptomatic. The reason for asymptomatic nature could be due to their inactivity because of their deformities and joint pain. In a similar study conducted in Northern part of India, the systolic dysfunction was 9%, and the LVDD was seen in 55% of the RA patients, higher than our study. [9] However, they included symptomatic patients of heart failure in their study, whereas we had only asymptomatic LVDD patients.

Our study has also concluded a significant association of DAS28-ESR between the RA patients with LVDD and without LVDD, suggesting high DAS28 scores are associated with LVDD. The similar finding was seen in a study by Renjith AS et al.[9] Other study performed in Poland also opined that higher disease duration and severity might predispose to LVDD.[10]

Conclusion:

In our study, we have observed that the longer disease duration and high disease activity scores are associated with increased LVDD. However, this was a cross-sectional study, done in a small group of the population, and hence extrapolating its results to a large population is difficult. But the significant results in our study suggests the need for the further studies to confirm the association, and also suggests that all the patients of rheumatoid arthritis are to be screened for LVDD especially if they have high disease activity and the duration of disease is more than 5 years.

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