

A Study of the Cardiac Manifestations in Rheumatoid Arthritis Patients with Special Reference to Echocardiography

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Abstract

Introduction: Cardiac abnormalities have been documented in several studies using echocardiography and Doppler analysis in various European and western countries. Studies have shown pericardial effusion, valvular abnormalities, pulmonary hypertension and cardiac conduction defects, and ventricular dysfunctions. The present study is therefore undertaken to evaluate the various cardiac manifestations including echo-Doppler evaluation of left ventricular function in Indian patients suffering from rheumatoid arthritis.

Material and methods: The study was performed on patients attending the out-patient and in-patients departments of medicine at JLN MC and Hospital, Ajmer. A total of 60 rheumatoid arthritis patients were enrolled. Patients satisfying the revised ACR-EULAR classification criteria (2010) for RA were included in the study. Any type of heart diseases or any other disease affecting heart directly or indirectly were excluded from the study. Total duration of the study was 2 years.

Results: The most common cardiac abnormality seen in this study was left ventricular diastolic dysfunction in 21.6%. Other abnormalities included pericardial disease in 10%, pulmonary hypertension in 6.66%, mitral regurgitation in 5%, and tricuspid regurgitation in 1.66%.

Conclusion: Cardiac abnormalities are largely sub-clinical, hence the early detection of cardiac abnormalities especially by echocardiography can be very important in the correct assessment and management of the RA patients.

Key word: Rheumatoid arthritis, left ventricular diastolic dysfunction, pericardial disease.

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown aetiology marked by a symmetric peripheral polyarthritis. It is the most common form of chronic inflammatory arthritis and often results in joint damage and physical disability. Because it is a systemic disease, RA may result in a variety of extra-articular manifestations including fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis and haematologic abnormalities¹.

It has a progressive course with exacerbations and remissions being part of its natural history. Its onset could be at any age, although it usually starts in the fourth decade of life. Overall, there is a 3:1 female preponderance, but this excess is greater in young people and the age-related incidence is approximately equal in elderly people².

The incidence of RA increases between 25 and 55 years of age, after which it plateaus until the age of 75 and then decreases³. The presenting symptoms of RA typically result from inflammation of the joints, tendons, and bursae. Patients often complain of early morning joint stiffness

lasting more than 1 h that eases with physical activity. The earliest involved joints are typically the small joints of the hands and feet. The initial pattern of joint involvement may be monoarticular, oligoarticular (< 5 joints), or polyarticular (> 5 joints), usually in a symmetric distribution³.

Though being principally a disease of joints, several extra-articular manifestations are also noted. The systemic manifestations include involvement of cardiac, pulmonary, haematological, ocular, and neurological systems. The prevalence of rheumatoid arthritis is between 0.7% to 1.5%.

Many cardiac lesions have been described since then including pericardial effusion, constrictive pericarditis, mitral regurgitation, mitral stenosis, aortic root dilatation and aortic regurgitation, left ventricular systolic and diastolic dysfunction, pulmonary arterial hypertension in many Western and European studies.

Pericardial disease is a common autopsy finding in patients with rheumatoid arthritis, but is frequently asymptomatic during life.

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Material and methods

The study was performed on patients attending the out-patient and in-patient departments of Medicine, JLN Medical College and Hospital, Ajmer. A total of 60 rheumatoid arthritis patients were enrolled. All cases of rheumatoid arthritis of both sexes from eighteen years, who fulfill inclusion and exclusion criteria were studied for a period of two years – from August, 2015 to July, 2017.

Inclusion criteria

- Patients aged above 18 years.
- Patients who were already diagnosed to have RA, come to OPD for non specific complaints (who were satisfying New ACR-EULAR Criteria).
- Patients who were satisfying New ACR-EULAR (American College of Rheumatology and the European League Against Rheumatism 2010) classification criteria.

Exclusion criteria

- Congenital heart disease.
- Ischemic heart disease.
- Valvular heart disease with rheumatic history (Rheumatic heart disease).
- Diabetes mellitus.
- Chronic obstructive pulmonary disease.
- Essential hypertension of more than one year duration.
- Severe anaemia (Hb < 6 gm%).
- Thyroid dysfunction.
- Drug-induced cardiac abnormalities, i.e., beta-blockers, lithium, oral contraceptives, anti-arrhythmic agents, etc.
- Any other disease affecting heart directly or indirectly.

A detailed history – age, sex, duration of RA, presence and duration of morning stiffness, chest symptoms, list of painful joints, presence of other systemic disease, and history of extra-articular manifestations of RA were documented. Treatment history was also documented. Functional status of the patients was recorded on the Steinbrocker's scale. A systemic examination of all joints was done for features of activity, tender joint count and swollen joint count estimation was done. A simplified 28 joint articular index as described by Fuch's *et al* was used to assess disease activity. Twenty-eight joints included 10 proximal interphalangeal joints of the fingers, 10 metacarpophalangeal joints, and the wrist, elbow, shoulder and the knee joints bilaterally⁴.

Cardiovascular examination was done in detail. Abdominal, respiratory and neurological examination was also done. Extra-articular manifestations were carefully looked for and documented.

This study highlights the cardiac manifestations in RA as they are some of the most profound and reproducible clinical findings. It assesses the CVS parameters in RA patients without other underlying disorder by echocardiography and ECG. Hence, this study aims at studying the cardiac manifestations of RA thereby reassessing the need for early recognition and aggressive management in the form of anti RA drugs therapy aiming at preventing the before-mentioned complications.

To see significant differences between the groups for continuous variables students "t" test (unpaired two tailed) was performed and to see the difference between the means in skewed distribution, Mann Whitney U test was used. For comparing categorical variables Chi square and Fisher's exact test were used, $p \leq 0.05$ has been considered as statistically significant.

Results

The study was done in Department of Medicine, JLN Medical College, Groups of Hospitals, Ajmer between August 2015 to July 2017. Sixty patients of rheumatoid arthritis diagnosed by revised ACR-EULAR criteria (in 2010, a collaborative effort between The American College of Rheumatology (ACR) and The European League Against Rheumatism (EULAR) had fulfilled the inclusion and exclusion criteria. The study group included 42 females (70%) and 18 males (30%).

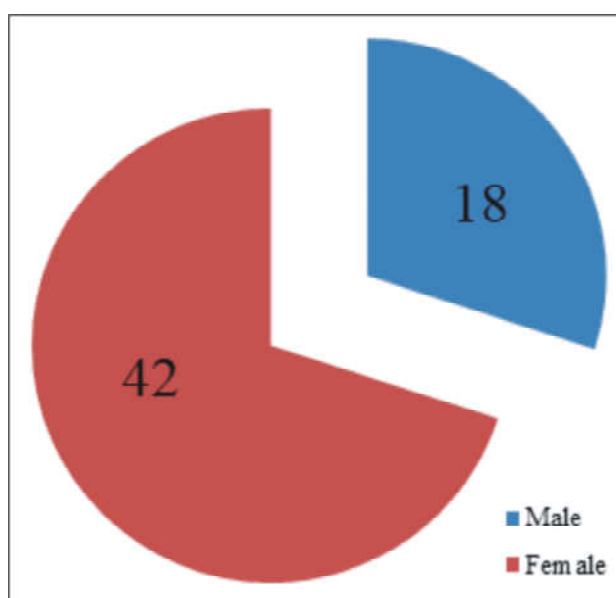


Fig. 1: Gender distribution.

The age and sex distribution of patients with RA is shown in Fig. 2.

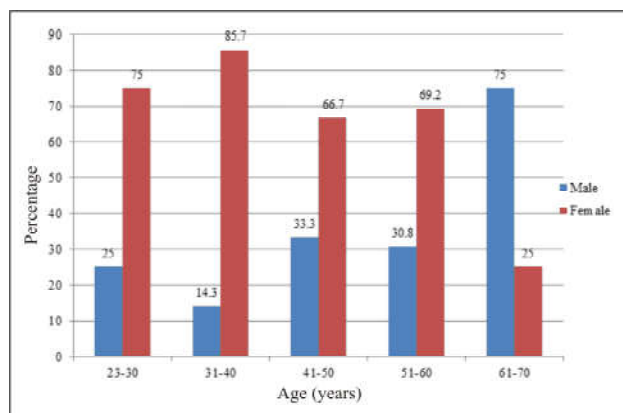


Fig. 2: Age distribution with sex.

In the study group, total echocardiographic abnormalities were found in 21 patients out of 60 cases and the maximum incidence was between 24 - 60 years (90.47%) age group. The oldest patient was 62 years and the youngest was 24 years. The mean age group was 43.83 with standard deviation of 11.01 years. The disease was found to be more common in females with the female: male ratio being 2.3: 1 (7 : 3). Cardiac abnormalities were seen maximum in 41 - 50 years age group (Table I).

Table I: Age and sex distribution in Rheumatoid arthritis patients with echocardiography abnormality.

Age groups	No. of cases (%)	Male (%)	Female (%)	Echocardiography abnormality (%)	ECG
20 - 30	8 (13.3)	2 (25)	6 (75)	1	LAHB, Non sp ST-T
31 - 40	14 (23.3)	2 (14.3)	12 (85.7)	3	—
41 - 50	21 (35)	7 (33.3)	14 (66.7)	10	Incomp RBBB, Non sp ST-T
51 - 60	13 (21.7)	4 (30.8)	9 (69.2)	5	LVH, Non sp ST-T, RBBB
61 - 70	4 (6.7)	3 (75)	1 (25)	2	LVH
Total	60 (100)	18 (30)	42 (70)	21	—

The duration of the disease ranged from 1 year to 20 years and the mean duration being 4.55 years with a standard deviation of 3.52. In general, cardiac abnormalities were more common in patients with longer duration of illness (Table II).

Discussion

Cardiac involvement is a well-documented extra-articular manifestation in autopsy studies. These abnormalities have

also been documented in several studies using echocardiography and Doppler analysis. In this study cardiac structural and functional abnormalities were seen in 21 patients. Left ventricular filling abnormalities were the most common and were seen in 13 (21.6%) patients. Pericardial involvement was seen in 6 (10%) patients of whom 4 (6.66%) patients had pericardial effusion and 2 (3.33%) patients had pericardial thickening. One patient with pericardial thickening was also found to have aortic root dilatation. Pulmonary hypertension was seen in 4 patients (6.66%), and tricuspid regurgitation were present in one patient. Mitral regurgitation was seen in 3 patients (5%) of total RA cases.

Table II: Duration of disease among RA patients with echocardiographic abnormalities.

Duration of disease (years)	No. of RA patients	No. with Echocardiographic abnormalities	Specifics
1 - 2	11	4	LV dysfunction, PAH, pericardial effusion
>2 - 3	14	2	LV dysfunction, pericardial thickening + aortic root dilatation
> 3 - 4	16	7	LV dysfunction, MR, PAH, pericardial effusion, pulmonary hypertension (PAH), TR
> 4 - 5	7	2	LV dysfunction
> 5 - 10	8	5	LV dysfunction, pericardial effusion
> 10	4	2	LV dysfunction, MR, PAH

Maione *et al* found the incidence of cardiac involvement to be 43% in their study and the most common abnormality was LV diastolic dysfunction (26%)⁵.

Corrao *et al* in 1996 evaluated 40 patients for ventricular function in patients of RA and found that ventricular filling abnormalities were significantly higher in RA patients⁶.

Levendoglu *et al* in 2002 evaluated forty patients with rheumatoid arthritis for ventricular function using Doppler echocardiography. They found a significantly increased incidence of left ventricular diastolic dysfunction⁷.

The mean age of patients with RA in this study was 43.83 ± 11.011 years with a range of 24 to 62 years. Maximum patients were found with cardiac abnormalities¹⁰ in 41 - 50 years age group. The maximum incidence of cardiac abnormalities (50%) was found in the 61 - 70 years age group. The female to male ratio in this study was 2.3: 1.0.

In the study by Kaushal *et al*, the median age was 29 years with a range of 14 - 56 years, and the male to female ratio was 1:5. The age group in this study was similar to that of the present study⁸.

In this study there was significantly higher incidence of cardiac involvement in patients with increased disease duration. The mean duration of disease in patients was 4.55 ± 3.52 years and the mean duration of disease in patients presenting with cardiac abnormalities was 5.07 ± 3.23 years. The mean age of patients with LV diastolic dysfunction was found to be 4.61 ± 2.85 years.

Franco *et al* evaluated 32 patients of RA to assess LV diastolic abnormalities by Doppler echocardiography. They found a direct relationship with a linear increase in incidence of left ventricular diastolic dysfunction with increasing duration of disease⁹. The present study also had similar findings with an increasing duration of disease in patients with left ventricular filling abnormalities.

The extra-articular manifestations noted apart from cardiac abnormalities were rheumatoid nodules in 5 patients, pleural effusion in 1 patient. In the present study there was significantly increased incidence of cardiac manifestations in patients with rheumatoid nodules (Odds ratio - 4.08, $p < 0.001$ S).

Wisłowska *et al* evaluated echocardiographic findings in RA patients with subcutaneous nodules and compared them with RA patients without subcutaneous nodules. Their study revealed a significantly increased incidence of cardiac abnormalities in RA patients with subcutaneous nodules (odds ratio - 15, $p < 0.0002$)¹⁰.

None of our 6 patients with LV filling defects had symptoms or signs of cardiovascular disease. One female patient presented with chest pain on the right side which was dull aching, diffuse and a constant type of pain. On further evaluation this patient was found to have right-sided moderate pleural effusion which on investigation was found to be of rheumatoid aetiology. Pulmonary component of second heart sound was loud in one patient. This patient was found to have pulmonary hypertension with tricuspid regurgitation on echocardiography. Raised jugular venous pressure was found in one patient. This patient was found to have biventricular diastolic dysfunction.

The mean tender joint count in the present study in RA patients was 17.53 ± 5.39 in the entire group, in those without cardiac abnormalities 16.25 ± 5.52 , and in those with cardiac abnormalities 19.9 ± 4.31 . The mean swollen joint count was 7.96 ± 5.54 in the entire group of RA patients and 8.205 ± 6.03 in RA patients without cardiac abnormalities. The mean swollen joint count in RA patients with cardiac abnormalities was 7.52 ± 4.6 .

There was significant correlation ($p = 0.01$ S) between the tender joints count and occurrence of cardiac abnormalities; however, there was no correlation between swollen joints count and incidence of cardiac lesions ($p = 0.65$ NS).

The mean ESR in the study group was 52.25 ± 24.17 mm/hr and ranged from 12 mm to 100 mm/hour. The mean ESR in RA patients without cardiac abnormalities was 50.71 ± 25.32 mm/hr, and in those with cardiac abnormalities 55.09 ± 22.205 mm/hr. Patients with cardiac abnormalities were found to have higher ESR values; however, the association was not found to be statistically significant ($p = 0.5$ NS).

The rheumatoid factor was positive in 85.7% of patients with cardiac abnormalities as compared to 69.23% in RA patients without cardiac abnormalities. This study shows mean RA factor 81.57 ± 31.02 mm/hr in patients with cardiac abnormalities and mean RA factor 75.15 ± 24.48 mm/hr in patients without cardiac abnormalities ($p = 0.38$). Hence, patients with cardiac abnormalities were found to be more likely to be seropositive; however, this correlation was not found to be statistically significant ($p = 0.38$).

The CRP was positive in 51.66% in RA patients. This study shows mean CRP 3.95 ± 2.63 mg/dl in patients with cardiac abnormalities and mean CRP factor 2.407 ± 1.11 mg/dl in patients without cardiac abnormalities ($p = 0.002$ S).

The ACPA was positive in 70% in RA patients. This study shows mean ACPA 237.39 ± 76.04 unit/ml in patients with cardiac abnormalities and mean ACPA 247.85 ± 39.33 unit/ml in patients without cardiac abnormalities ($p = 0.89$ NS)¹¹.

X-ray of the hands were taken for all RA patients and were staged under Steinbrocker's radiological classification. There was significant association of cardiac abnormalities with higher stages of Steinbrocker's radiological classification.

Dawson *et al* found that cardiac abnormalities were found to occur more commonly in patients with erosive arthritis¹².

Two patients were found to have left ventricular hypertrophy as per the Romhilt Estes criteria. This patient was found to be having hypertension and was on regular treatment since last 1 year. Echocardiography revealed left ventricular diastolic dysfunction with increase in the LV muscle mass. Other ECG changes were nonspecific ST-T changes and minor conduction abnormalities which were comparable to the ECG findings in the control group¹³.

Echocardiography was done in all the 60 RA patients. Structural and functional abnormalities were found in 21 RA patients. Left ventricular diastolic dysfunction was found to be the most common abnormality (21.6%). One patient was found to have biventricular diastolic filling abnormality. Decreased E/A ratio and increased S/D ratio were suggestive of decreased ventricular filling which was evident in Doppler echocardiography especially in the early part of diastole. However, there was no change in the left atrial indices or gross reversals in pulmonary flow suggesting that the LV dysfunctions were of mild-to-moderate grade.

Among all the ventricular dysfunction patients, only one had increase in LV mass and comparable to that of the controls. This patient was found to be hypertensive and had been on regular anti-hypertensive treatment since 1 year. In the remaining patients with LV dysfunction in the absence of change in the LV mass, the diastolic filling abnormalities were suggestive of a reduction in ventricular elasticity and an intrinsic myocardial abnormality. Autopsy studies have shown non-specific myocarditis, granulomatous lesions, coronary in 1% of patients only. This is comparable with the low incidence vasculitis, secondary amyloidosis and diffuse fibrosis are histopathological features in patients with RA¹⁴.

None of our patients were found to have any evidence of ischemic heart disease as a possible cause for the diastolic dysfunctions. Pericardial involvement was seen in 6 patients. Four patients were found to have pericardial effusion. The effusion in both cases was small (< 300 ml) and hence not associated with any ventricular dysfunctions, or significant clinical manifestations. Two patients were found to have pericardial thickening, and aortic root dilation was seen in 1 patient.

Four patients were found to have pulmonary hypertension, and three patients had mitral regurgitation out of 60 RA patients. Pulmonary hypertension with tricuspid regurgitation was seen in 1 female patient.

Conclusion

Cardiac manifestations were seen in 21 patients (35%) out of 60 cases studied the maximum incidence of the disease was seen in the 41 - 50 years age group and the female to male ratio was 2.3: 1.0. The mean duration of the disease was found to be 4.55 ± 3.52 years in the entire study group and 5.07 ± 3.23 years in patients presenting with cardiac abnormalities. There was positive correlation of patients with cardiac abnormalities to tender joints count, subcutaneous nodules, erosive arthritis and mean duration of disease, C-reactive protein. However, there was no significant correlation between cardiac abnormalities and swollen joints count, ESR, seropositivity, functional class and anti-CCP antibody. Most patients with cardiac abnormalities had normal chest X-ray. The electrocardiogram revealed minor conduction abnormalities in patients.

The most common cardiac abnormality seen in this study was left ventricular diastolic dysfunction in 21.6%. Other abnormalities included pericardial disease in 10%, pulmonary hypertension in 6.66%, mitral regurgitation in 5%, and tricuspid regurgitation in 1.66%.

None of the patients had clinical manifestations of cardiac

involvement, suggesting that cardiac involvement in rheumatoid arthritis is a sub-clinical disease.

Summary

Cardiac abnormalities are an important extra-articular manifestation of rheumatoid arthritis. These abnormalities are largely sub-clinical. The early detection of cardiac abnormalities can be very important in the correct assessment and management of the RA patients, especially in light of the fact that the most common cause of mortality in RA patients is cardiovascular disease. Therefore, every patient should be submitted to a cardiological assessment (in particular echocardiography) in order that cardiac involvement can be detected early and treated, and the incidence of morbidity and mortality reduced.

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