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Original Article

Cardiovascular Profile of Rheumatoid Arthritis Patients and its Correlation with Disease Activity

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Abstract

Introduction: Rheumatoid arthritis (RA) is a chronic inflammatory disorder, involving joints and extra-articular manifestations. About 50% mortality in RA is due to cardiovascular disease. Cardiovascular events occur approximately a decade earlier in RA like that in diabetes mellitus.

Aim: The aim of the study was to correlate and compare the association between disease severity and various clinical and cardiovascular manifestations in RA patients.

Materials and Methods: This prospective cross-sectional study is carried out in known RA patients fulfilling the American College of Rheumatology criteria 2010 attending General Medicine and Rheumatology outpatient clinic of Tirunelveli Medical College Hospital between April 2017 and April 2018. They have been subjected to detail clinical and laboratory investigations and their cardiovascular manifestations are compared with their clinical profile and disease activity score.

Results: In this study, 50 patients were included, with a mean age of 47.76 years and 72% of female patients. The mean clinical disease activity index (CDAI) score among them is 25.16 ± 10.4. The disease severity was high among our study group with 60% of cases occupying high CDAI score with no patients under remission. The most common electrocardiogram abnormality found in the study group was left axis deviation (30%) followed by nonspecific ST-T changes (24%). Mean carotid intima-media thickness (CIMT) was found to be increased in 68% of patients. Asymptomatic carotid plaque was present in 8% of patients. The most common echocardiographic abnormality is left ventricular (LV) diastolic dysfunction, which contributes 44% in our study group.

Conclusion: Cardiovascular abnormalities such as LV diastolic and systolic dysfunction, premature atherosclerosis occur commonly in RA patients and positively correlate with CDAI score, disease duration, and treatment duration. All RA patients should be screened for chorionic villus sampling abnormalities through echocardiography and CIMT periodically.

Key words: Cardiovascular disease, Cardiovascular risk, Rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disorder characterized by both articular and extra-articular manifestations. The chronic subclinical inflammation in RA contributes to accelerated atherosclerosis and various cardiovascular events.[1] A recent study showed that 50% mortality in RA is due to cardiovascular disease-related deaths. RA is associated with disability, shortened life expectancy, and increased mortality as compared to the general population.[2] Cardiovascular events seem to occur approximately a decade earlier in RA patients like that in diabetes mellitus (DM).[3] Moreover, such as DM and dyslipidemia, there is an independent association of RA with preclinical and overt cardiovascular disease and most of the time, it is silent with unfavorable outcome leading to premature death.[4,5] In a study, if the clinical disease activity index (CDAI) score falls by 10, the risk of developing cardiovascular disease decreased by 26% has been formulated.[6] Hence, it is necessary to do screening for cardiovascular disease in all RA patients. Furthermore, the influence of disease activity on the development of cardiovascular disease should also be studied.

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Aim

The aim of the study was to correlate and compare the association between disease severity and various clinical and cardiovascular manifestations in RA patients.

MATERIALS AND METHODS

This prospective cross-sectional study is carried out in known RA patients attending the General Medicine and Rheumatology outpatient clinic or ward of Tirunelveli Medical College Hospital between April 2017 and April 2018. They have been selected after detailed investigations and found to be fulfilling the American College of Rheumatology (ACR) criteria for RA 2010 and also the inclusion and exclusion criteria of our case study.

Inclusion Criteria

The following criteria were included in the study:

1. Patients more than 16 years of age
2. Known RA patients who have been clinically examined and investigated and found to be fulfilling the ACR criteria for RA 2010.

Exclusion Criteria

The following criteria were excluded from the study:

1. RA patients with known overt cardiovascular disease such as coronary artery disease, cerebrovascular disease, and peripheral vascular disease
2. RA patients with other independent risk factors for developing cardiovascular diseases such as diabetes, hypertension, smoking, and alcoholism
3. Patients <16 years of age
4. Patients not fulfilling the ACR criteria for RA in 2010
5. RA patients not willing to participate in the study.

Written informed consent was obtained from the patients selected for the study. They have been subjected to detail clinical and laboratory investigations. Routine investigations such as complete blood count, hemoglobin, total leukocyte count, differential count, platelet count, renal function test, liver function test, serum electrolytes, fasting lipid profile, urine routine investigations, and blood sugar. In addition, investigations such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), RA factor, anti-cyclic citrullinated peptide antibody, electrocardiogram (ECG), chest X-ray posteroanterior view, echocardiogram, and carotid Doppler to detect carotid intima-media thickness (CIMT) were done for all patients.

Clinical disease severity index (CDAI) score was calculated for all selected patients in the study, which denotes the disease severity and activity in the patient. It was calculated using the formula,

$$CDAI = SJC(28) + TJC(28) + PGA + EGA.$$

Whereas

- SJC denotes swollen joint count (28)
- TJC denoted tender joint count (28)
- PGA denotes patient global disease activity scale and
- EGA denotes evaluator's global disease activity scale, latter two ranging from 1 to 10.

RESULTS

Our study group consists of 50 RA patients who fell in the age group of 21–74 years with a mean age of 47.76 years. Males among the study group occupy 28% and females 72%, respectively. The mean duration of RA among the study population is 8.63 ± 5.85 years. The disease severity among patients was assessed with clinical disease severity score and the mean CDAI score among them is 25.16 ± 10.4. The disease severity was high among our study group with 60% of cases occupying a high CDAI score with no patients under remission. Metacarpophalangeal, proximal interphalangeal joint, and wrist joints are the most commonly involved joints among the study population [Figures 1 and 2]. Anemia seems to occur more commonly in RA patients, being in 72% of our study population. Lymphocytosis was found in 20% of our study group. Thrombocytopenia

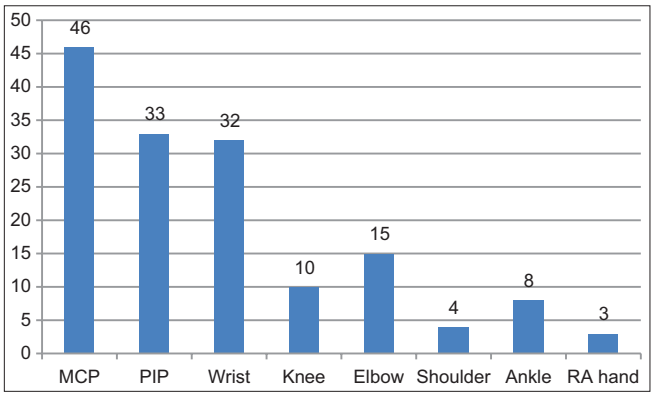

Figure 1: Distribution of joint involvement

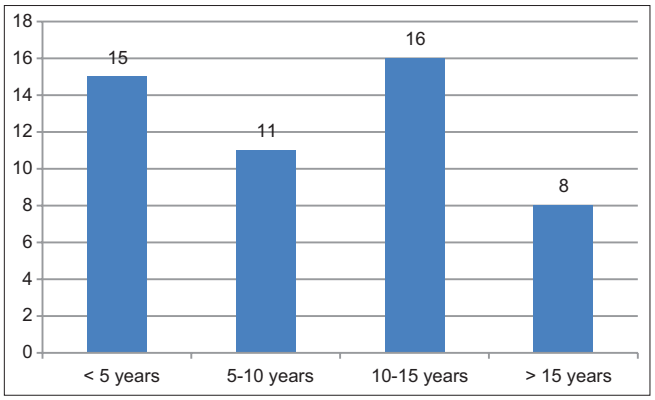

Figure 2: Distribution of disease duration

and thrombocytosis occur in minority groups of patients (14% and 4%, respectively). Dyslipidemia in the form of hypercholesterolemia and hypertriglyceridemia was found in 10% and 4% of our study population, respectively. Markers of inflammation such as ESR and CRP are raised more commonly among RA patients, ESR being more commonly raised in 96% of patients, and CRP raised in 46% of patients in the study group [Figures 3 and 4].

The disease severity was high among our study group with 60% of cases occupying a high CDAI score with no patients under remission.

Mean CIMT of the study population was correlated with various parameters such as age of patient, duration of disease, duration of treatment, ESR, and CDAI score.

There is a significant relationship between the mean CIMT and the CDAI score ($P = 0.043$).

There is a significant relationship between the mean CIMT and duration of RA, duration of treatment ($P = 0.015$ and 0.010, respectively). There is no significant relationship between mean CIMT and age of the patient and ESR values ($P = 0.347$ and 0.732, respectively).

There is no significant relationship between mean CIMT and CRP levels.

There is a significant relationship between variation in ejection fraction and CDAI score ($P = 0.030$). There is a strong correlation between left ventricular systolic dysfunction (LVSD) and clinical disease severity index score ($P < 0.0001$). There is no significant relationship between left ventricular (LV) diastolic dysfunction and CDAI score ($P = 0.196$). There is a significant relationship between the occurrence of pericardial effusion and clinical disease severity index score ($P = 0.007$). There is no significant relationship between the occurrence of pulmonary hypertension and the clinical disease severity index score ($P = 0.975$). There is no significant relationship between the occurrence of mitral regurgitation and the clinical disease severity index score ($P = 0.080$). There is no significant relationship between the occurrence of aortic sclerosis and clinical disease severity index score

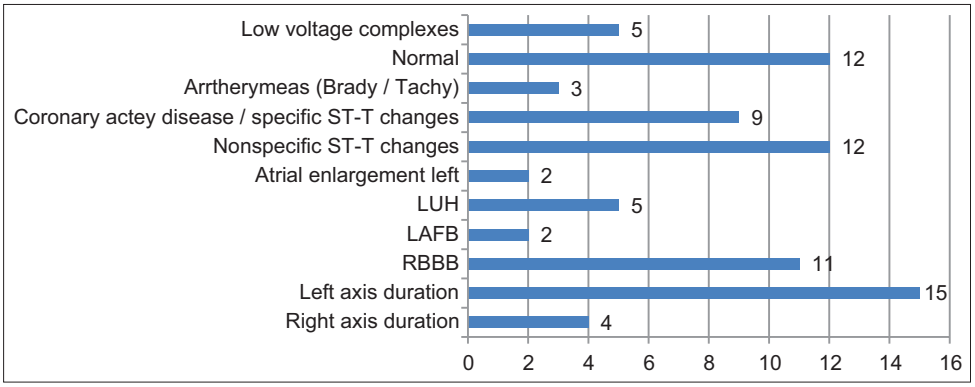

Figure 3: Electrocardiogram changes in the study group

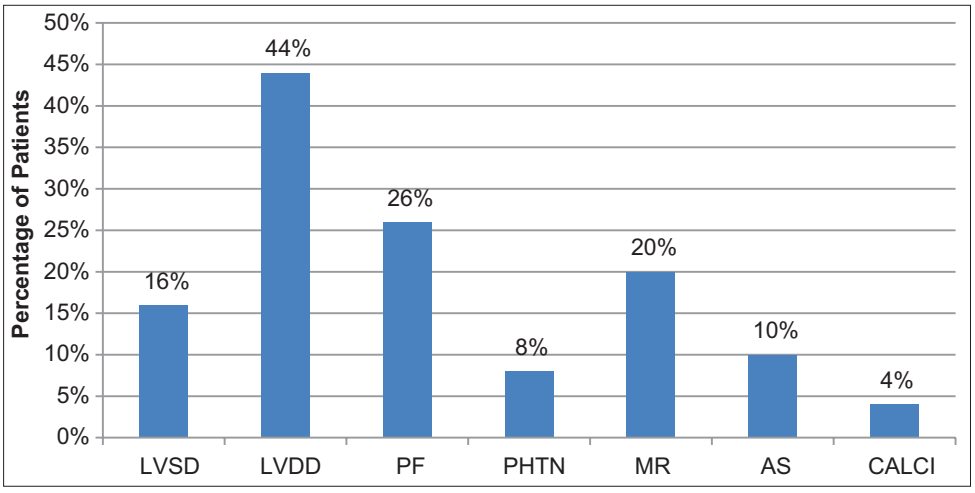

Figure 4: Distribution of echo cardiographic

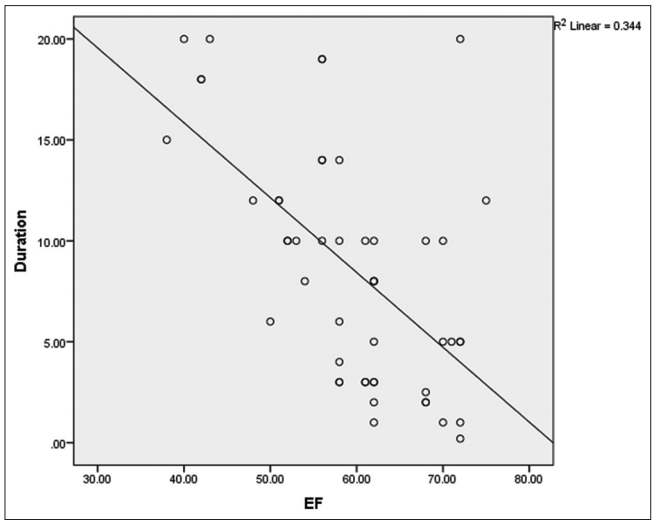

Figure 5: Correlation of duration of disease with ejection fraction

($P = 0.165$). There is no significant relationship between the occurrence of coronary calcifications and clinical disease severity index score ($P = 0.507$).

There is a strong significant relationship between variation in ejection fraction and duration of RA ($P < 0.0001$) [Figure 5].

There is a strong significant relationship between LVSD and the duration of RA ($P = 0.003$). There is a strong significant relationship between LVSD and the duration of RA ($P = 0.003$). There is no significant relationship between the occurrence of pericardial effusion and the duration of RA ($P = 0.707$). There is no significant relationship between the occurrence of pulmonary hypertension and the duration of RA ($P = 0.246$). There is a significant relationship between the occurrence of mitral regurgitation and the duration of RA ($P = 0.016$). There is a significant relationship between the occurrence of aortic sclerosis and the duration of RA ($P = 0.038$). There is no significant relationship between the occurrence of coronary calcifications and the duration of RA ($P = 0.890$).

DISCUSSION

Most common ECG abnormality found in the study group was left axis deviation (30%) followed by nonspecific ST-T changes (24%). ST-T changes suggestive of coronary artery disease in asymptomatic patients of our study group was found in 18% of individuals, which was comparable to Shenavar Masooleh *et al.*,[7] in which 15% cases had ST-T changes. In chest X-ray screening, cardiomegaly was found in 40% of patients and other abnormalities such as fibrotic changes in lungs, prosthetic heart valve shadows, and bronchiectasis changes in lungs were present in a minority of patients. Mean CIMT (cutoff among normal individuals is 0.57 mm) is increased in RA patients when matched with age-related controls, which signifies the presence of premature atherosclerosis. In our case series, mean CIMT was found to be increased in 68% of patients. Asymptomatic carotid plaque was present in 8% of patients. The presence of carotid plaque suggests that the patients are in the stage of preclinical atherosclerosis and emphasize the need for more aggressive risk reduction strategies in these patients. The most common echocardiographic abnormality is LV diastolic dysfunction, which contributes 44% of the study group, comparable to 14.54% in study conducted by Raof[8] followed by pericardial effusion contributing to 26%, which was comparable to the study conducted by Coskun *et al.*,[9] in which it was 15%. A high prevalence of this complication (47%) was found in the study done by Shenavar Masooleh *et al.*[7] Other abnormalities such as mitral regurgitation, LVSD was present in 20% and 16% of the study population, respectively, whereas it was as high as 31% (LVSD) in the study by Dawson *et al.*[10] Coronary calcifications were found in two patients. ESR correlates positively with CDAI score, duration of RA, and mean CIMT. This proves that increased CIMT was associated with an inflammatory burden due to more severe disease, and also the chronic inflammation, which reflects the duration of the disease. Dyslipidemia and CRP show no significant correlation with CIMT or other chorionic villus sampling (CVS) abnormalities, as compared to the results by Mahajan *et al.*[11] who did not find significantly correlated dyslipidemia with accelerated atherosclerosis in RA patients. According to Homma *et al.*[12] CIMT increases linearly from 0.48 mm at 40 years of age to 1.02 mm at 100 years of age. Mean age group in our study was 47.76 years and mean CIMT was 0.72 mm; hence, in our study group, CIMT was higher than age-related controls and correlates positively with the severity of disease as evidenced by high CDAI score ($P = 0.043$) and duration of disease ($P = 0.015$), similar observation made by Gonzalez *et al.* and Alkaabi *et al.*[1] in their respective studies. In an Indian study, Mahajan *et al.*[11] also showed similar observations that showed higher CIMT values in RA patients when compared to a control group matched age and related parameters. Among echocardiographic findings, LVSD, variation in ejection fraction, and pericardial effusion positively correlate with clinical disease severity index (CDAI) score in our study group. Left ventricular systolic function, left ventricular diastolic dysfunction, and valvular abnormalities such as mitral regurgitation and aortic sclerosis correlate positively with the duration of RA. Coronary calcification was found in 4% of patients in our study, was an indirect marker of subclinical atherosclerosis, and serves as a marker of cardiovascular events. In our case series, coronary calcification has no significant association with disease severity and duration of disease, in contrast to the study by Giles *et al.*, which shows increasing disease

severity in RA, is associated with increased prevalence and extent of coronary calcification, irrespective of gender and age.

CONCLUSION

Cardiovascular abnormalities such as non-atherosclerotic features such as LV diastolic and systolic dysfunction, valvular abnormalities, pericardial effusion, and mainly premature atherosclerosis occur commonly in RA patients and their occurrence positively correlates with CDAI score, disease duration, and treatment duration. All RA patients should be screened for CVS abnormalities through modalities such as electrocardiography, echocardiography, and CIMT periodically.

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