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### RESEARCH ARTICLE

#### THE HEART IN RHEUMATOID ARTHRITIS – AN ECHOCARDIOGRAPHIC STUDY.

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#### Abstract

**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease of the joints. Joint pain, swelling and limited mobility of the joint are the most prominent features. Besides articular symptoms, RA can be associated with extra-articular features. Among those extra-articular features are cardiovascular diseases, including pericarditis, cardiomyopathy/ myocarditis, cardiac amyloidosis, coronary vasculitis, arrhythmia, valve diseases and, most importantly, congestive heart failure and ischaemic heart disease. When compared with the general population, RA is associated with an increased mortality, the majority of which is originating from cardiovascular diseases.

**Objectives:** To study cardiac manifestations in patients of rheumatoid arthritis by echocardiography with the objective of providing elements for earlier diagnosis and treatment.

**Material and Methods:** The study was conducted in the Postgraduate Department of Medicine at S.M.H.S Hospital obtaining ethical clearance from the institutional ethical committee. The study was conducted from April 2016 to September 2017. A Total of 110 patients of RA attending Rheumatology OPD in SMHS Hospital in Srinagar, were taken into this study after obtaining informed consent. All patients were either previously or newly diagnosed cases of rheumatoid arthritis. New cases were investigated in the form of ESR, CRP, RF, ANTI-CCP for the diagnosis of RA as per ACR EULAR (2010) criteria. All those who met the ACR EULAR (2010) criteria for RA were screened for cardiac manifestations. Patients were examined clinically for cardiac signs and symptoms and patients were evaluated for cardiac manifestations by echocardiography.

**Results:** Out of 110 studied patients 49% had heart involvement. Mitral regurgitation was the most common heart disease present in 20% of patients, followed by aortic regurgitation in 15.5% of patients, diastolic dysfunction in 14.5% of patients, tricuspid regurgitation in 11.8% of patients, PAH in 10.9% of patients, pericardial effusion in 9.1% of patients, systolic dysfunction in 6.3% of patients,

cardiomyopathy (DCM) in 4.5% of patients, ischemic heart disease in 4.5% of patients, mitral stenosis in 0.9% and aortic stenosis in 0.9% of patients. The mean age at detection of heart disease in RA was  $53 \pm 10.65$  years, higher than mean age of studied RA patients ( $49.8 \pm 11.5$ ). Analysing the pattern of distribution of age in RA patients with and without heart involvement, the heart involvement increased proportionately as the age advanced. Duration of illness in our study had a marked impact over the progression of heart involvement in patients of RA. Number of patients with heart disease increases with increase in duration of illness. Study showed that 9 (27.3%) patients had disease duration of  $\leq 5$  years, 23 (46.9%) patients had disease duration of 6-10 years, 16 (76.2%) patients had disease duration of 11-15 years, and 6 (85.7%) patients had disease duration of  $> 15$  years of illness, with a statistically significant P value of  $P = 0.001$ . Though females outnumbered males by a ratio of 3.6:1 as is characteristic of autoimmune disorder, once gender comparison of RA patients was done (Among these 110 patients, 24 (22%) subjects were male and 86 (78 %) subjects were female) there was no significant relation between gender and abnormal echocardiography findings in RA patients ( $p > 0.05$ ). It was also observed in our study that RA patients with positive CRP mg/L ( $p = 0.02$ ), higher levels of RF IU/ml ( $p = 0.03$ ) and higher levels of anti-CCP U/ml ( $P = 0.01$ ) were affected more than patients who had negative CRP mg/l, lower levels of RF IU/ml and anti-CCP U/ml.

**Conclusion:** An observational study conducted to see cardiac involvement in patients of rheumatoid arthritis showed that 49% had cardiac involvement. Mitral regurgitation was the most common heart disease present in 20% of patients, followed by aortic regurgitation in 15.5% of patients, diastolic dysfunction in 14.5% of patients, tricuspid regurgitation in 11.8% of patients, PAH in 10.9% of patients, pericardial effusion in 9.1% of patients, systolic dysfunction in 6.3% of patients, cardiomyopathy (DCM) in 4.5% of patients, ischemic heart disease in 4.5% of patients, mitral stenosis in 0.9% and aortic stenosis in 0.9% of patients.

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## ..... Introduction:-

Rheumatoid arthritis (RA) is a chronic inflammatory disease of the joints, and extra-articular features may also develop. Joint pain, swelling and limited mobility of the joint are the most prominent features<sup>1,2</sup>. Among those extra-articular features are cardiovascular diseases, including pericarditis, cardiomyopathy/myocarditis, cardiac amyloidosis, coronary vasculitis, arrhythmia, valve diseases and, most importantly, congestive heart failure and ischaemic heart disease. When compared with the general population, RA is associated with an increased mortality the majority of which is originating from cardiovascular diseases<sup>3</sup>.

The most common cardiac involvement in RA is pericarditis. Varying the method of assessment (echographic or postmortem studies), pericarditis occurs in 30–50% of the patients<sup>4</sup>. The majority of patients develop pericarditis after the onset of arthritis; however, pericarditis may precede the diagnosis of RA in some patients.

The RA-associated cardiomyopathy may be the result of focal non-specific, diffuse necrotizing or granulomatous myocarditis. These entities are histological diagnoses, which may be found in 3–30% of RA patients in postmortem studies<sup>4</sup>.

Cardiac amyloidosis is one of the causes of restrictive cardio- myopathy, and the infiltration with fibrillar proteins can cause a loss of compliance and impairs diastolic function as well as systolic function. Although a definite diagnosis of cardiac amyloidosis is made histologically, a ‘sparkling’ pattern on echography of the heart may suggest its presence<sup>5</sup>.

Rheumatoid nodules (also called rheumatoid granuloma) may occur in all organs and also in the epicardial fat, epicardium, myocardium, interventricular septum, chordae tendinae, aorta and valves. These nodules may cause functional impairment such as arrhythmias and valve disease.

Arrhythmia is an important cause of mortality in RA and may be secondary to ischaemia, conduction abnormalities due to rheumatoid nodules, amyloidosis or congestive heart failure. Valve disease.

The most prevalent valve disease in RA is mitral valve insufficiency, varying from 30 to 80% in small case series followed by aortic valve insufficiency varying from 9 to 33%<sup>6,7</sup>. The risk of developing CHF in RA is twice the risk of developing CHF in persons without RA, and this excess is not explained by traditional cardiovascular risk factors and/or clinical ischaemic heart disease<sup>8,9</sup>. Recurrence of cardiac events appears to be higher among RA patients compared with matched controls<sup>10</sup>.

Cardiovascular death seems to be associated with markers of systemic inflammation in RA, i.e. increased sedimentation rate, RA vasculitis and RA lung disease<sup>11</sup>.

Finally, it has been shown that untreated comorbidity in patients with RA is an important problem and joint efforts of rheumatologists and cardiologists may help to improve the cardiovascular morbidity and mortality in RA<sup>12,13</sup>.

### **Aims And Objectives**

To study cardiac manifestations in patients of rheumatoid arthritis by echocardiography with the objective of providing elements for earlier diagnosis and treatment.

### **Materials And Methods:-**

This cross-sectional study was conducted in the Postgraduate Department of Medicine at S.M.H.S Hospital, an associated hospital of Government Medical College, Srinagar; after obtaining ethical clearance from the institutional ethical committee. The study was conducted from April 2016 to September 2017, on 110 patients of rheumatoid arthritis attending Rheumatology OPD.

#### **Inclusion criteria**

1. All patients of either sex having age >21 years.
2. All those who met the ACR EULAR (2010) criteria for RA.

#### **Exclusion Criteria**

1. Patients not meeting ACR and EULAR 2010 criteria.
2. Patients not willing to participate in the study.
3. Patient with congenital heart disease.
4. Patients with known progressive heart disease including ischemic heart disease, valvular heart disease, rheumatic heart disease, dilated cardiomyopathy.
5. Patients with hypertension, diabetes mellitus.
6. Pregnant patients
7. Patients with Other collagen vascular disease (SLE, scleroderma, polymyositis, MCTD etc).
8. Patients with poor follow up.
9. Patients with other chronic systemic illnesses COPD, CKD, CLD.

All patients were either previously or newly diagnosed cases of rheumatoid arthritis. New cases were investigated in the form of ESR, CRP, RF, ANTI-CCP for the diagnosis of RA as per ACR EULAR (2010) criteria. All those who met the ACR EULAR (2010) criteria for RA were screened for cardiac manifestations. Patients were examined clinically for cardiac signs and symptoms and Patients were evaluated for cardiac manifestations by echocardiography.

CRP was done by CRP-Latex Slide agglutination method with reference value upto 6 mg/L was taken as negative.

ESR was done by Westergren's method and levels upto 0-15 mm and 0-20mm in first hour in males and females respectively was taken as normal.

RF was done by RF-Latex Slide agglutination method with reference value upto 8 IU/ml was taken as negative.

Anti CCP was done by ELISA method and values of less than 6.25 IU/ml was taken as negative.

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables.

## Results:-

In our study, 10% of patients were in age group of 25-34 years, 20.9% in age group of 35-44 years, 35.5% in age group of 45-54 years, 20.9% in age group of 55-64 years, 10% in age group of 65-74 years and 2.7% in age group of  $\geq 75$  years. There were 22% males and 78% females in our study with a female to male ratio of 3.6:1. Duration of illness was  $\leq 5$  years in 30% patients, 6-10 years in 44.5% patients, 11-15 years in 19.1% patients and  $>15$  years in 6.4% patients in our study.

In our patients, ESR mm/h was elevated in 80 (72.7%) while as it was normal in 30 (27.3%) patients. CRP mg/L was positive in 70 (63.6%) patients while as it was negative in 40 (36.4%) patients. RF IU/ML was more than 3 times elevated in 75 (68.2%) patients,  $\leq 3$  times raised in 35 (31.8%) patients. Anti CCP U/ml was more than 3 times elevated in 85 (77.3%) patients,  $\leq 3$  times raised in 8 (7.3%) patients and negative in 17 (15.4%) patients. Palpitation was present in 6.4% of our patients, orthopnea was present in 2.7%, chest pain was present in 5.4% and breathlessness on exertion was present in 11.8% patient in our study. Systolic murmur at apex (MR) was present in 7.2% of patients, systolic [murmur](#) at [lower left sternal border](#) (TR) was present in 3.6% of patients, pericardial rub was present in 4.5% of patients and Diastolic murmur in 3<sup>rd</sup> intercostals space left sternal border (AR) was present in 3.6% of patients.

In our study, echocardiography was normal in 50.9% of patients. mitral regurgitation was present in 20% of patients, aortic regurgitation was present in 15.5% of patients, tricuspid regurgitation was present in 11.8%, pericardial effusion in 9.1%, pulmonary artery hypertension in 10.9%, mitral stenosis in 0.9%, aortic stenosis in 0.9%, Systolic dysfunction in 6.3%, Cardiomyopathy (DCM) in 4.5 %, Ischemic heart disease in 4.5% and diastolic dysfunction in 14.5% of patients.

Number of patients with heart disease increases with increase in duration of illness. 9 (27.3%) patients had  $\leq 5$  years, 23 (46.9%) patients had 6-10 years, 16 (76.2%) patients had 11-15 years, and 6 (85.7%) patients had  $> 15$  years of illness with a statistically significant P value of  $P = 0.001$ .

ESR (mm) in 1<sup>st</sup> hour was elevated in 80 (72.7%) patients and out of these 80 patients, heart disease was absent in 37 (46.2%) patients and present in 43 (53.8 %) patients. While as ESR mm in 1<sup>st</sup> hour was normal in 30 (27.3%) patients and out of these 30 patients, heart disease was absent in 19 (63.3%) and present in 11 (36.7%). CRP mg/L was positive in 70 (63.6%) patients and out of these 70 patients, heart disease was absent in 30 (42.8%) patients and present in 40 (57.2%) patients. While as CRP mg/L was negative in 40 (36.4%) patients and out of these 40 patients, heart disease was absent in 26 (65%) and present in 14 (35%) patients. RF IU/ML was more than 3 times elevated in 75 (68.2%) patients and out of these 75 patients, heart disease was absent in 33 (44 %) patients and present in 42 (56 %) patients. While as RF IU/ML was  $\leq 3$  times raised in 35 (31.8%) patients and out of these 35 patients, heart disease was absent in 23 (65.7%) and present in 12 (34.3%) patients. Anti CCP U/ml was more than 3 times elevated in 85 (77.3%) patients, and out of these 85 patients, heart disease was absent in 37 (43.5 %) patients and present in 48 (56.5%) patients. Anti CCP U/ml was  $\leq 3$  times raised in 8 (7.3%) patients and out of these 8 patients, heart disease was absent in 6 (75%) and present in 2 (25%) patients. Anti CCP U/ml was negative in 17 (15.4%) patients and out of these 17 patients, heart disease was absent in 13 (76.5%) and present in 4 (23.5%) patients.

There were 53.7% asymptomatic patients in our study, 12.9% of patients had palpitations, 5.5% of patients had Orthopnea, 11.1% of patients had chest pain, and 16.8% of patients had breathlessness. Systolic murmur at apex (MR) was present in 14.8% of patients, systolic murmur at lower left sternal border (TR) was present in 7.4% of patients, pericardial rub was present in 9.3% of patients and Diastolic murmur in 3<sup>rd</sup> intercostals space left sternal border (AR) was present in 7.4% of patients. Mitral regurgitation was present in 40.7% of patients, aortic regurgitation was present in 31.5% of patients, tricuspid regurgitation was present in 24.1%, pericardial effusion in

18.5%, pulmonary artery hypertension in 22.2%, mitral stenosis in 1.8%, aortic stenosis in 1.8%, Systolic dysfunction in 12.9%, Cardiomyopathy (DCM) in 9.3%, Ischemic heart disease in 9.3% and diastolic dysfunction in 29.6% of patients. 45.8% of males and 50% of females had heart involvement, male to female ratio 0.91 with a P value of  $P = 0.719$  statistically not significant.

### Discussion:-

Out of 110 studied patients 49% had heart involvement. Mitral regurgitation was the most common heart disease present in 20% of patients, followed by aortic regurgitation in 15.5% of patients, diastolic dysfunction in 14.5% of patients, tricuspid regurgitation in 11.8% of patients, PAH in 10.9% of patients, pericardial effusion in 9.1% of patients, systolic dysfunction in 6.3% of patients, cardiomyopathy (DCM) in 4.5% of patients, ischemic heart disease in 4.5% of patients, mitral stenosis in 0.9% and aortic stenosis in 0.9% of patients. In a study done by Amer K et al (2012)<sup>14</sup> heart involvement was present in 53% of patients in echocardiography. Similar results were demonstrated by Dodo-Siddo MN, et al (2015)<sup>15</sup>, [Nomeir AM](#) et al (1979)<sup>16</sup>, Mohyidin BS et al (1998)<sup>17</sup> and Merza RR et al (2008)<sup>18</sup>.

The mean age at detection of heart disease in RA was  $53 \pm 10.65$  years, higher than mean age of studied RA patients ( $49.8 \pm 11.5$ ). Analysing the pattern of distribution of age in RA patients with and without heart involvement, the heart involvement increased proportionately as the age advanced. Similar results were demonstrated in a study conducted by Masooleh IS et al (2015)<sup>19</sup> and Merza RR et al (2008)<sup>18</sup>.

Duration of illness in our study had a marked impact over the progression of heart involvement in patients of RA. Number of patients with heart disease increases with increase in duration of illness. Study showed that 9 (27.3%) patients had disease duration of  $\leq 5$  years, 23 (46.9%) patients had disease duration of 6-10 years, 16 (76.2%) patients had disease duration of 11-15 years, and 6 (85.7%) patients had disease duration of  $> 15$  years of illness, with a statistically significant P value of  $P = 0.001$ . Longer duration of illness had significant impact in heart involvement in study conducted by Masooleh IS et al (2015)<sup>19</sup>.

Though females outnumbered males by a ratio of 3.6:1 as is characteristic of autoimmune disorder, once gender comparison of RA patients was done. Among these 110 patients, 24 (22%) subjects were male and 86 (78%) subjects were female) there was no significant relation between gender and abnormal echocardiography findings in RA patients ( $p > 0.05$ ). The results of our studies were similar to the study conducted by Masooleh IS et al (2015)<sup>19</sup> where in his study, there was no significant relation between gender and abnormal echocardiography findings in RA patients ( $p > 0.05$ ).

It was also observed in our study that RA patients with positive CRPmg/L ( $p = 0.02$ ), higher levels of RF IU/ml ( $p = 0.03$ ) i.e. elevated more than 3 times and higher levels of anti-CCP U/ml ( $P = 0.01$ ) i.e. elevated more than 3 times, were affected more than patients who had negative CRP mg/l, lower levels of RF IU/ml and anti-CCP U/ml i.e. levels elevated less than 3 times. Results similar to this were observed by Maradit-Kremers H et al (2007)<sup>20</sup> and Roman MJ et al (2005)<sup>21</sup>.

### Conclusion:-

Analysing the pattern of distribution of age in RA patients with and without heart involvement, the heart involvement increased proportionately as the age advanced.

Duration of illness in our study had a marked impact over the progression of heart involvement in patients of RA. Number of patients with heart disease increases with increase in duration of illness P value of  $P = 0.001$ .

Though females outnumbered males by a ratio of 3.6:1 as is characteristic of autoimmune disorder, once gender comparison of RA patients was done there was no significant relation between gender and abnormal echocardiography findings in RA patients ( $p > 0.05$ ).

It was also observed in our study that RA patients with positive CRPmg/L ( $p = 0.02$ ), higher levels of RF IU/ml ( $p = 0.03$ ) and higher levels of anti-CCP U/ml ( $P = 0.01$ ) were affected more than patients who had negative CRP mg/l, lower levels of RF IU/ml and anti-CCP U/ml

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