

## Pericardial Effusion in Patients of Rheumatoid Arthritis

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### ABSTRACT

**Objectives:** Pericardial effusion a cardiovascular manifestation of Rheumatoid arthritis has never been studied before therefore this study was designed to evaluate it in patients suffering from rheumatoid arthritis.

**Materials and methods:** Sixty patients of Rheumatoid Arthritis presenting in Out Patient, Emergency and Rheumatology Clinic of Mayo Hospital Lahore and Emergency Department of the Punjab Institute of Cardiology Lahore from March 1998 till January 2001 were studied. All of them full filled the criteria for the diagnosis of Rheumatoid Arthritis as described by the American Rheumatism Association. After history and physical examination, a clinical assessment of the patient was made of whether he / she had Cardiac Manifestations of Rheumatoid Arthritis or not.

**Results:** Out of 60 patients seen 42(70%) were female, and 18(30%) were male. Giving a female to male ratio of 2.3 to 1. Maximum number of patients seen were between 26 – 45 years i.e 38(63.3%) In which 22 (36.6%) were between 26 to 35 years and 16 (26.6%) were between 36-45 years. Next most frequent group was of 10(16.6%) patients, between 15-25 years of age. Short systolic murmurs were heard in four patients. Three patients showed pulsus paradoxus while in the rest no rhythm irregularity was felt. Myocarditis or Coronary Rheumatoid disease was not noticed in any patient. No heart block of any degree was seen. In 6 patients low voltage Electrocardiogram (ECG) was demonstrated in the limb leads. Out of 60 Patients only 5(8.3%) had pericardial effusion. In one patient it was only a thin rim more prominent posteriorly than anteriorly.

**Conclusion:** Pericardial effusion is rare occurrence in patients of Rheumatoid Arthritis in Pakistani Population, although not with the same frequency as in the Western world.

**Key words:** Rheumatoid arthritis, Cardiovascular disease, ischemic heart disease, Pericardial effusion

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### INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammatory polyarthritis and systemic features, with a prevalence of 1% in Western populations<sup>1</sup>.

Clinically, pericardial heart disease is one of the more infrequent types of cardiac diseases, but morphologically, it is common<sup>2</sup>. Pericardial heart disease has been found clinically in <1% of patients admitted to one large general hospital and in about 5% of consecutive necropsies at another large general hospital<sup>2</sup>.

At necropsy, nearly 50% of patients with rheumatoid arthritis have fibrous obliterative pericardial heart disease and, rarely, calcific or cholesterol pericardial disease.<sup>3</sup> Usually, no functional consequence results from the obliterative pericardial heart disease<sup>2</sup>.

Pericardial disease is a well recognised extraarticular manifestation of RA occurring in up to

50% of patients in both postmortem<sup>1</sup> and antemortem echocardiography studies<sup>4</sup>. As pericarditis in RA is often asymptomatic, severe or prolonged pericardial pain, should perhaps suggest an infective aetiology requiring appropriate investigation<sup>5</sup>.

Rheumatoid arthritis associated factors In general, myocardial nodules, restrictive pericarditis, and coronary vasculitis are exceedingly rare causes of CHF;<sup>6</sup> however, older necropsy studies of RA hearts<sup>7-9</sup> have indicated a higher prevalence of each of these complications compared to the hearts of autopsied non-RA patients. More recent series using transthoracic echocardiography<sup>10,11</sup> have identified a much lower prevalence of pericarditis than that reported in the autopsy studies (2% versus 29% to 40%). In a series using transesophageal echocardiography<sup>12</sup>, however, thirteen percent of RA patients were found to have clinically silent pericarditis versus zero percent of non-RA controls. Case reports of rheumatoid nodules<sup>13,14</sup>, restrictive pericarditis<sup>15,16</sup>, and coronary vasculitis<sup>17</sup> in RA patients resulting in CHF are not uncommon in the literature, although it is likely that these entities account for only a small portion of the excess cases of CHF in RA. So far in Pakistan pericardial effusion

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in patients of Rheumatoid arthritis has never been studied before therefore this study was designed to evaluate the incidence and consequences of pericardial disease in patients suffering from rheumatoid arthritis.

## PATIENTS AND METHODS

Sixty patients of Rheumatoid Arthritis presenting in Out Patient, Emergency and Rheumatology Clinic of Mayo Hospital Lahore and Emergency Department of the Punjab Institute of Cardiology Lahore from March 1998 till January 2001 were studied. All of them full filled the criteria for the diagnosis of Rheumatoid Arthritis as described by the American Rheumatism Association. A detailed history was taken with special attention towards complaints suggestive of cardiac involvement. A thorough physical examination was done with extra attention towards Rheumatoid nodules and Cardiovascular signs. After this a clinical assessment was made of whether the patient had cardiac manifestation of rheumatoid arthritis or not. Following investigations were carried out to determine patient's condition, his Rheumatoid score, and if there was any cardiac involvement:

1. Rheumatoid Arthritis factor. If found positive when possible titers were also done.
2. Radiograph of the involved joints.
3. Hb, T.L.C., D.L.C.
4. E.S.R
5. Platelet count.
6. Blood urea.
7. Serum Creatinine.
8. Fasting Blood Sugar.
9. Liver function tests. (Bilirubin, direct and indirect, S.G.O.T., SG.P.T Alkaline phosphatase).
10. Serum Uric Acid (if required)
11. Complete examination of urine.

## RESULTS

A total of 60 patients were seen, in all of them the diagnosis of Rheumatoid Arthritis was established after this Cardiac status was examined. Out of 60 patients seen 42(70%) were female, and 18(30%) were male. Giving a female to male ratio of 2.3 to 1. Maximum number of patients seen were between 26–45 years i.e., 38(63.3%) In which 22 (36.6%) were between 26 to 35 years and 16 (26.6%) were between 36-45 years. Next most frequent group was of 10(16.6%) patients, between 15-25 years of age. Of the 18 Male patients seen the youngest was 25 while the oldest was only 41. While in case of female patients the youngest was only 18 years of age and the eldest was 77 years old. Out of the 22 patients examined, between the age group 26-35, 13 were

female and 9 male giving a ratio of 1.4 to 1 While in the age group of 36-45 , 8 were female and 8 were male thus a ratio of 1:1. In the age group of 15-25, 8 were females and 2 male. In rest of the age groups only female patients were seen. RA factor was positive in 51(85%) patients and negative in 9(15%). Of the 51 positive patients 35 were female, and 16 male. Thus a ratio of 2.3 to 1, similarly of the 9 RA factor negative patients, 6 were female and 3 male, so a ratio of 2.0: 1. All the 60 patients were diagnosed and scored according to the criteria described by the American Rheumatism association -1988 revision. In all of these patients the first four criteria were present for a duration of more than six weeks i.e., morning stiffness of more than one hour duration, arthritis of 3 or more joint areas, arthritis of hand joints, symmetrical arthritis.

Variation of score resulted because of the 3 R' s i.e., rheumatoid factor, radiological changes, rheumatoid nodule. A score of 4 was seen in only 3 patients. 5 was scored by 16 patients. Out of these 16, 6 were R.A factor negative with radiological changes while 10 had R.A. factor positive but no radiological change. In 41 patients the score was 6. Rheumatoid nodule was not seen in any patient thus no one had the score of 7.

Of the 60 patient seen, 15 did not have any radiological change. Forty five patients who showed radiological changes the least common was periarticular Osteoporosis noted only in 8 patients, while the most common was Periarticular Osteoporosis along with loss of articular cartilage – reduction in joint space-observed in 22 patients. The stage of erosion was seen in 12 patients and the end stage i.e. of subluxation and ankylosis was noted in 14 patients.

Of the 60 patients seen 26(43.3%) had symptoms for 1-5 years. The next most common groups was of 6 months to 1 year of 14 patients and of 10 patients between 5 year to 10 years. The average duration of the symptoms was 4 years 7 months. Out of the 60 patients seen, there were only 10 (16.6%) patients who definitely had not used steroids. It is worth noting that the symptoms of arthritis in all these 10 patients had not been for more than one year.

Only 14 patients needed admission due to severity of arthritis or some other medical reason. After history and physical examination, a clinical assessment of the patient was made of whether he / she had Cardiac Manifestations of Rheumatoid Arthritis or not. Out of 60 patients there was a strong suspicion of pericardial effusion in 6 patients. Short systolic murmurs were heard in four patients. Three patients showed pulsus paradoxus while in the rest no rhythm irregularity was felt. Myocarditis or

Coronary Rheumatoid disease was not suspected in any patient. No heart block of any degree was seen.

In 6 patients low voltage Electrocardiogram (ECG) was demonstrated in the limb leads. Out of these 6, 4 had low voltage i.e. less than 0.5 mV in all the six limb leads. One patient had low voltage in 5 limb leads. One patient had low voltage in 4 limb leads and 0.6 mV in 2 limb leads. Later it was observed that pericardial Effusion was responsible for low voltage in all the six limb leads in three patients, and also in another patient who had low voltage in 4 of the 6 limb leads. Low voltage in all the limb leads in the other patient was attributed to the thick chest wall. While in the sixth patient no definite reason for low voltage in 5 of the 6 limb could be determined. Out of 60 patients examined cardiothoracic ratio on X-Ray Chest P-A view was found more than 1:2 in only 8 patients. Out of these, the heart's shape was globular in only 4. Later it was seen that all 4 had pericardial Effusion. Out of 60 Patients only 5(8.3%) had pericardial effusion. In one patient it was only a thin rim more prominent posteriorly than anteriorly. Pericardial tap was not done due to small amount of fluid. The pericardial effusion in the other three was of sufficient quantity that they could be safely tapped.

One patient refused and was managed conservatively. Second echocardiography on this patient after one month showed that the fluid had slightly decreased. Pericardial effusion tapped in the three patients was a transudate with low sugar and R.A factor positive. After one month of treatment and tap a thin rim of effusion was seen only posteriorly on echocardiography. No valve abnormality was seen on echocardiography.

All chambers and L.V. function were within normal limits. However in 3 patients 1 or 2 small segments of pericardial thickening were noted. These thickenings were not considered to be of any significance.

Out of the 60 patients seen, Pericardial Effusion was noted in 5 patients. It was proven to be secondary to Rheumatoid Arthritis in only 3 patients. In the other 2 it was strongly suspected to be secondary to Rheumatoid Arthritis, other reasons especially tuberculosis was ruled out. No valve lesion or heart block was seen. No diagnosis of Myocarditis or Coronary Arteritis secondary to Rheumatoid Arthritis was made.

## DISCUSSION

Rheumatoid arthritis is a chronic inflammatory disease that leads to progressive joint deformity, disability, and to premature death. Rheumatoid Arthritis – a chronic systemic, inflammatory, connective tissue disease is mainly known as

disease affecting the diarthroidal joints which usually has a symmetrical involvement. However this disease has serious extra-articular complications too.

This study of 60 Rheumatoid Arthritis patients revealed 5(8.3%) patients having pericardial effusion apart from other manifestations of Rheumatoid arthritis. Our findings are consistent with previous studies<sup>18-20</sup>.

Sugiura et al<sup>18</sup> performed echocardiography and electrocardiography in 87 consecutive patients with RA. Asymptomatic PE was correlated with electrocardiographic changes and laboratory findings. Among 87 patients with RA, 20 patients (23%) had PE and 28 patients (32%) had hypoalbuminemia. The patients with PE had significantly lower serum albumin level, higher rheumatoid factor titer and higher incidence of impaired left ventricular relaxation and tended to have a higher incidence of PR-segment depression than those without PE. In our study none of the patients had impaired left ventricular relaxation and the cause of pericardial effusion was confirmed to be rheumatoid arthritis in 3 patients.

Trustochowicz et al<sup>19</sup> reported 26 out of 100 patients with rheumatoid arthritis had pericardial effusion, 10 revealed the signs of chronic pericarditis, in the control group 4 had pericardial effusion while none had chronic pericarditis. No difference was shown in the wall contractions disturbances, size of the cardiac cavity, or thicknesses of the interventricular septum or posterior wall. In 3 rheumatoid arthritis patients, a valvular heart disease was diagnosed, this number was not significantly different from that in the control group<sup>19</sup>.

Corrao et al<sup>20</sup> used echocardiography to determine the prevalence of pericardial effusion in rheumatoid arthritis (RA) patients without cardiac systems and compared our results to those obtained in a control group of age-matched subjects. Thirty-six patients with RA were selected from a patient population in treatment at our outpatient Rheumatology Clinic. None of the patients had any symptoms of cardiac disease, In the RA patients, a high prevalence of pericardial involvement, especially minimal pericardial effusion was observed. There was no statistically significant difference among subgroups of RA patients based on stage and duration of disease respectively. There was no correlation between pericardial involvement and inflammatory indexes or drug therapy. The minimal pericardial effusion found in their patients was attributed to the extra-articular inflammatory process<sup>20</sup>.

Pericarditis is the most common cardiac manifestation of Rheumatoid Arthritis.<sup>21</sup> This is supported by various reports e.g. by Esclante et al<sup>22</sup>,

and Stollerman et al<sup>23</sup>. In this study of 60 patients, Pericardial Effusion was seen in 5 patients. This was the most common Cardiac Manifestation of Rheumatoid Arthritis. In all these patients this disease had produced grade 4 radiological changes of the joints affected. Other Extra-articular manifestations, besides the heart, were also seen. Out of these 5, 2 had Scleritis, all had G.I symptoms (these could even be due to NSAID.). One patient who had the illness for more than 12 years also complained of distal neuropathy. At the time of presentation in these five patients markers of disease activity were elevated E.S.R., C.R.P., Platelet Count, etc. It has been pointed out by Cosh et al<sup>24</sup>, that there was no specific relationship between disease activity and pericarditis, but broadly speaking it is more common in advanced active disease.

The diagnosis of pericardial Effusion after clinical examination was only in three cases. While after investigations especially Echocardiography – where one can “See” the Effusion – was in five.

One reason for the low incidence documented in the Pakistani Population could be that in none of these patients Rheumatoid Nodule was seen. Incidence of pericardial Effusion with Rheumatoid Nodule is higher.<sup>23,24</sup> Secondly the average duration of illness in our cases was only 4 year and 7 month where as Cardiac complications manifest in many patients of longer duration<sup>25</sup>.

Pericardial Effusion could only be tapped in three patients (One patient refused and the other had a very thin rim mainly posteriorly which could not be tapped). Results of the tap showed RA Factor positive with low sugar level – findings consistent with Rheumatoid Effusion.

Pericardial Effusion was tapped by the Sub-Xiphisternal approach. This was a diagnostic-therapeutic procedure. There were no complications during or after the paracentesis. Echocardiography after one month showed only a thin rim of fluid with no further re-accumulation.

Non-specific E.C.G changes were seen in 6 these 60 patients None of these E.C.G showed any evidence of Heart Block or Myocardial Infarction. E.C.G done after one month in the patients whose pericardial tap was done, showed increased voltage. Arthritis of these patients limited us from performing an exercise test to elicit Heart Block<sup>24</sup>.

On Doppler Echocardiography a mild Aortic Regurgitation was seen in only two patients. Also Doppler Echocardiography showed in one patient mild Mitral regurgitation. None of these patients had any other Cardiac finding (Valves were normal in patients who had Pericardial Effusion). Final diagnosis for these regurgitations could not be established, as this could only be done on Biopsy of

the valve. In our patients the valve functions were sufficiently good and did not require replacement or repair.

The diagnosis of Myocarditis which was seen in nearly 19% of autopsies<sup>23</sup> was not suggested in any of my patients. In all of these patients both the Ventricles was normal, and did not suggest Myocarditis.<sup>26,27</sup> Also since there was no Heart Block Myocarditis was further ruled out as a possibility<sup>23</sup>.

Coronary Arteritis is a feature of sero-positive, nodular, erosive Rheumatoid Arthritis. None of my sixty patients had Rheumatoid Nodule and neither did any one's E.C.G show any evidence of Myocardial Infarction or Heart Block. Thus no patient of Coronary Arteritis was either seen.

## CONCLUSION

Pericardial effusion is rare occurrence in patients of Rheumatoid Arthritis in Pakistan and, not with the same frequency as in the Western world. Rheumatoid arthritis warrants earlier cardiac evaluation in view of increased morbidity and mortality due to associated cardiovascular disease.

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