

Assessment of the Rheumatoid Factor Titers in Extra-Articular Manifestation of Rheumatoid Arthritis

Avinash S¹, Ashwath SV²

ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a chronic multisystem disease of unknown cause. The characteristic feature of RA is persistent inflammatory synovitis usually involving the peripheral joints in a symmetric fashion. Hence; the present study was undertaken for assessing rheumatoid factor titers in extra-articular manifestation of rheumatoid arthritis.

Material and methods: A total number of 50 patients who met the inclusion criteria were included in this study. Rheumatoid arthritis diagnosed as per 2010 revised criteria for the classification of RA were enrolled. The RA patients thus selected were screened for various common clinical features, articular and extra-articular manifestations using a structured Proforma designed for this study. At the end of the study the titers of RF factor in articular and extra articular manifestations in 50 rheumatoid arthritis patients screened were calculated and expressed as percentage. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software.

Results: The clinical examination in the study revealed pallor in 34(68%) patients. Rheumatoid factor titres of 1:16 were observed in 4(13%) of patients, 1:32 in 7(24%), 1:64 in 8(28%) and 1:128 in 10(35%) of patients. Hemoglobin <8g/dl in 10 patients i.e.;(20%), 8-10g/dl in 14 patients i.e.;40%, 10-12g/dl in 10 patients i.e.; 28%. (Normal Hb 12-14g/dl in females, 14-16g/dl in males). Peripheral smear showed 24 patients i.e 70% of them had normocytic normochromic anemia. Extra-articular manifestations were seen in about 72%, Anemia in 34(68%), Lymphadenopathy in 8(16%), Purpuric rash in 4(8%), Rheumatoid nodules in 4(8%) and Splenomegaly in 2(4%).

Conclusion: Extra-articular manifestations contribute significantly to the morbidity and mortality in rheumatoid arthritis. Careful screening of all patients for extra-articular manifestations may help reduce the same, with the proper management of such patients.

Keywords: Extra-articular, Rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic multisystem disease of unknown cause. The characteristic feature of RA is persistent inflammatory synovitis usually involving the peripheral joints in a symmetric fashion. The hallmark of the disease is cartilage damage and bone destruction. Its onset could be at any age; it usually starts in the fourth decade of life. Overall, there is a 3:1 female preponderance.¹

Rheumatoid arthritis patients can present with variety of clinical features, which includes articular, sometimes

extra articular involvement, rarely various complications which can impair their physical function in. 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.^{2,3}

The highly variable and unpredictable course of the disease suggests the need for highly sensitive and specific diagnostic tests. Serological support is limited and mainly based on the presence of rheumatoid factors (RF), which can be detected in up to 70–80% of patients with rheumatoid arthritis.⁴ Rheumatoid factors (RF) are autoantibodies directed against the Fc portion of IgG. Rheumatoid factor is a well-established diagnostic and prognostic test in Rheumatoid Arthritis. RF is considered an early marker since its presence is linked with an increased risk of developing Rheumatoid Arthritis (RA) in people with mild arthritic symptoms. At present, the main clinically useful biologic markers in patients with RA are rheumatoid factors and antibodies to citrullinated peptides for both diagnosis and prediction of functional and radiographic outcomes, and erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) for aiding in ongoing assessment of disease activity and predicting functional and radiographic outcomes. Prognostic value — RF-positive patients with RA may experience more aggressive and erosive joint disease and extra-articular manifestations than those who are RF-negative. Similar findings have been observed in juvenile rheumatoid arthritis.⁵⁻⁷

Hence; the present study was undertaken for assessing rheumatoid factor titers in extra-articular manifestation of rheumatoid arthritis.

MATERIAL AND METHODS

Patients with symptoms suggestive of Rheumatoid arthritis who presented to Vydehi Institute of Medical Sciences and Research Centre to the OPD and inpatients were included in the study during a period from November 2012 to October

¹Assistant Professor, General, ²Assistant Professor, General Medicine, Vydehi Institute of Medical Science N Research Centre, Bengaluru, India

Corresponding author: Dr.Ashwath S V., Assistant Professor, General Medicine, Vydehi Institute of Medical Science N Research Centre, Bengaluru, India

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2013 were included in this study. A total number of 50 patients who met the inclusion criteria were included in this study.

Inclusion criteria

Rheumatoid arthritis diagnosed as per 2010 revised criteria for the classification of RA.

Exclusion criteria

All other cases of arthritis not fitting into the picture of rheumatoid arthritis as per 2010 revised criteria.

The RA patients thus selected were screened for various common clinical features, articular and extra-articular manifestations using a structured Proforma designed for this study. These patients were clinically examined for evidence of articular and extra-articular manifestations like skin, skeletal, eye, serosal, vascular, nervous and respiratory system involvement. At the end of the study the titers of RF factor in articular and extra articular manifestations in 50 rheumatoid arthritis patients screened were calculated and expressed as percentage. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software.

RESULTS

In the current study, 10 patients were between the ages 21-30 i.e.; 20%, 28 patients were between the ages 31-40 i.e.; 56%, 24% patients were between the age group of 41-50 (Table 1). In the study, of 50 patients 12 were males i.e. 24% and 38 are female patient's i. e. 76%. Among the patients included in the study, all the patients had the symptom of pain i.e.; 100%. 46 of them i.e.; 92% had stiffness, 40 patients i.e.; 80% had swelling. 10 of them i.e.; 20% of them had malaise. 2 of them i.e.; 4% had dryness of eyes. 2 of them i.e.; 4% had dryness of mouth. 1 of the patient i.e.; 2% had subcutaneous nodules respectively as shown in Graph 1. The clinical examination in the study revealed pallor in 34(68%) patients as shown in Table 2. Rheumatoid factor titres of 1:16 were observed in 4(13%) of patients, 1:32 in 7(24%), 1:64 in 8(28%) and 1;128 in 10(35%) of patients as shown in Table 3. Hemoglobin <8g/dl in 10 patients i.e.;(20%), 8-10g/dl in 14 patients i.e.;40%, 10-12g/dl in 10 patients i.e.; 28%. (Normal Hb 12-14g/dl in females, 14-16g/

dl in males). Extra-articular manifestations were present in 72 percent of the patients while it was absent in 28 percent of the patients (Table 4). Graph 2 shows the extra-articular manifestations. Episcleritis and scleritis was seen in 2.4 percent of the patients each. Keratitis was seen I 3.6 percent of the patients. Glomerulonephritis was seen in 2.4 percent of the patients. Pulmonary hypertension was seen in 2.4 percent of the patients. Anemia was seen in 34.68 percent of the patients. Lymphadenopathy was seen in 8.16 percent of the patients. Purpuric –rash in 4(8%), Rheumatoid nodules in 4(8%), Splenomegaly in 2(4%), Peripheral neuropathy in 2(4%), Pericardial effusion in 2(4%), Left ventricle diastolic

Age distribution	No. of patients	Percentage (%)
21-30	10	20%
31-40	28	56%
41-50	12	24%

Table-1: Age-wise distribution

Clinical examination	No. of patients	Percentage (%)
Pallor	34	68%
Lymphadenopathy	10	20%
Edema	10	20%
Corneal opacity	7	14%
Scleritis	4	8%

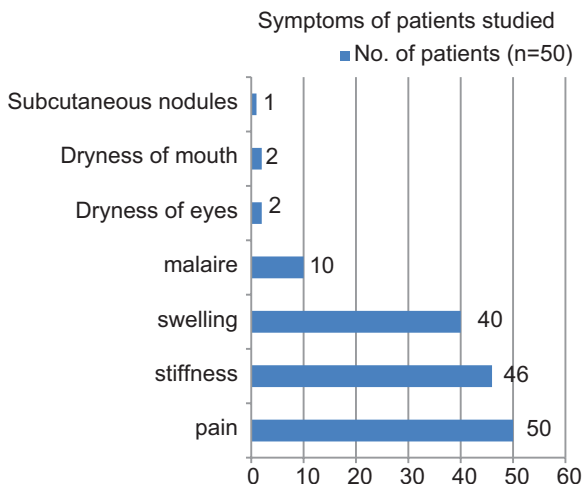
Table-2: General physical examination

Rheumatoid factor titres	No of patients (n=29)	Percentage
1:16	4	13%
1:32	7	24%
1:64	8	28%
1:128	10	35%

Table-3: Rheumatoid factor titres

EAM	No. of patients (n=50)	Percentage%
Yes	36	72%
Nil	14	28%

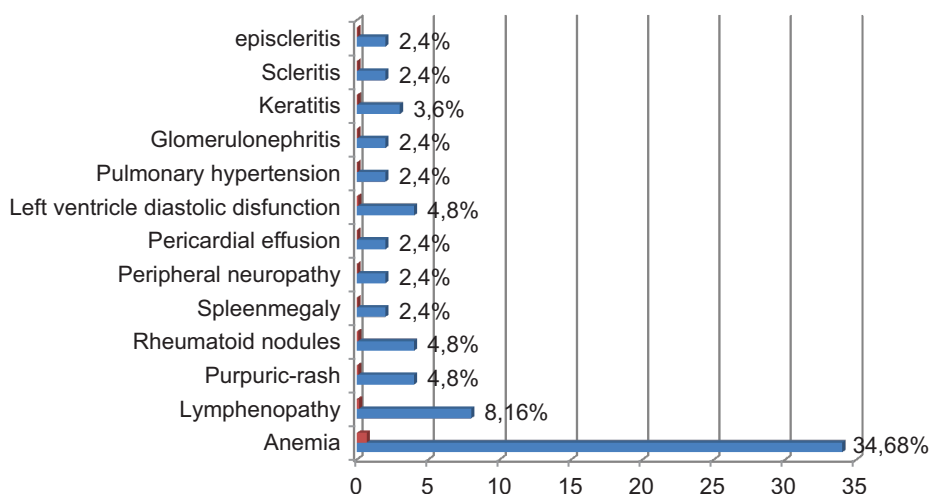
Table 4: Extra-articular Manifestation



Graph-1: Symptoms of the patients studied

Parameters	No. of patients (n=50)	Percentage (%)
Hemoglobin -Less than 8	10	23%
8 to 10	14	45%
10 to 12	10	32%
Peripheral smear- NCNC	24	70%
Peripheral smear- MCHC	10	30%
ESR- Normal	12	24%
Increased	38	76%
RBS-Normal	24	48%
Increased	26	52%
RFT- Normal	20	40%
Increased	30	60%
RF- Negative	11	32%
Positive	39	78%

Table-5: Investigations



Graph-2: Extra-articular manifestation

dysfunctions in 4(8%), Pulmonary hypertension in 2(4%), Glomeronephritis in 2(4%), Keratitis in 3(6%), Scleritis in 2(4%) and Episcleritis 2(4%) of the patients respectively (Graph 2). Peripheral smear showed 24 patients i.e 70% of them had normocytic normochromic anemia (Table 5).

DISCUSSION

Rheumatoid arthritis (RA) is a systemic inflammatory disease, which is associated with a number of extra-articular organ manifestations. Arthritis is only one manifestation of rheumatoid disease.¹

The study was done for a period of 1 year from November 2012 to October 2013 and included patient aged between 18-50 years. Among the 50 patients included in our study, the incidence of RA varied between the age groups of 18 -50 years with maximum incidence of 82%, observed between the ages of 30 -50 yrs. The incidence of RA increases between 25 and 55 years of age, after which it plateaus until the age of 75 and then decreases. 80% of all patients developing the disease are between the ages of 35 and 50.² Alamosky, Yougari, Drosos et al in his study the risk of developing disease is greatest between 40 and 50 years. In our study the risk also is between 40 to 49 years around 36.4%.¹⁰

In the present study, Extra articular manifestations were seen in 36 patients, 32 being females. 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 hour and easing with physical activity. The earliest involved joints are typically the small joints of the hands and feet.¹ The initial pattern of joint involvement may be monoarticular, or polyarticular (>5 joints), usually in a symmetric distribution. The onset is monoarticular in 20-25% and polyarticular in 30-35%. The onset is usually insidious but may be acute or systemic. Symmetrical joint involvement is common. The affected joints are painful to start with, then become swollen, warm, tender with restriction of movement.⁴ In the present study, anemia is predominant extra-articular manifestation. 68% of the cases had anemia. The anemia is predominantly normocytic normochromic type, the other being microcytic

hypochromic type. In the study done by Bowman et al. also, anemia was the predominant manifestation.¹¹

In the present study, among the 50 cases, who clinically suspected to have RA (i.e., those satisfying the ACR criteria).¹ 12% of cases were seronegative, 78% showed seropositivity values of RA factor >20 IU/ml were taken to be positive. Among 78% of seropositivity, 74% were with extra-articular manifestations and increase in rheumatoid factor titres were seen in more severe patients. It has been shown that the increased titres of RF are associated with severity of the disease.⁸⁻¹⁰

Chest X-ray of 8% cases showed abnormality in the form of reticulonodular pattern suggestive of interstitial lung disease. X-ray of the involved joint was done in all of which revealed abnormal picture in the form of juxtaarticular osteopenia & deformities. A study involving¹² anti-CCP2 assays were done on sera from 242 RA patients who were followed for 3 years. Anti-CCP antibodies were positively correlated with higher erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), swollen joint count. Rheumatoid factor sensitivity ranged from 59% to 79% and specificity from 80% to 84% in the same groups.¹²⁻¹⁴

In the present study, rheumatoid nodules are seen in cases with high titres of rheumatoid factor. This is comparable to the study by both Sahatciu-Meka et al and Turesson et al.^{15,16}

CONCLUSION

Extra-articular manifestations contribute significantly to the morbidity and mortality in rheumatoid arthritis. Careful screening of all patients for extra-articular manifestations may help reduce the same, with the proper management of such patients.

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