

# Extra-articular Manifestation of Rheumatoid Arthritis

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## Abstract

**Introduction:** Rheumatoid arthritis is an autoimmune disorder of unknown etiology characterized by symmetric, erosive synovitis, and in some cases, extra-articular involvement. Most patients experience a chronic fluctuating course despite therapy, may result in progressive joint destruction, deformity, disability, and even premature death.

**Materials and Methods:** It is a study conducted on patients admitted to K R Hospital, Mysore, from January 2013 to January 2015, a total of 50 patients were admitted during this period. As per inclusion criteria and exclusion criteria cases are included and excluded, and a pre-structured proforma was used and data were entered. The study is approved by the Institutional Ethical Committee.

**Results:** In the present study, the most common extra-articular manifestation was noted in the cardiovascular system (12%). Next, in the order of involvement were respiratory manifestations (8%) and lymphadenopathy (8%), followed by vasculitis (6%) and rheumatoid nodule (2%).

**Conclusion:** Our study showed male gender, older age group, longer duration of illness, severe degree of anemia, very high erythrocyte sedimentation rate, positive RA factor with higher titer values, all are suggestive of a higher incidence of extra-articular manifestation.

**Key words:** Anti-cyclic citrullinated peptides, Extra-articular manifestations, Rheumatoid arthritis, Rheumatoid arthritis factor

## INTRODUCTION

Diseases of musculoskeletal system are among the most common human afflictions. Their prevalence is highest among the elderly, but these conditions affect all age groups and are associated with disability, impairment, handicaps, and job loss.<sup>1</sup>

The impact of rheumatic diseases is enormous. They account for more impairment and functional limitation among middle age and older adults than any other disease category.

Rheumatoid arthritis (RA) is a chronic inflammatory arthropathy of unknown cause that can affect most joints,

and hence an important cause of potentially preventable disability.<sup>2</sup>

RA is an autoimmune disorder of unknown etiology characterized by symmetric, erosive synovitis, and in some cases, extra-articular involvement. Most patients experience a chronic fluctuating course despite therapy, may result in progressive joint destruction, deformity, disability, and even premature death.

### Epidemiology

RA has been identified in all parts of the world in every ethnic, racial group. Climate, geography, and altitude do not appear to affect the prevalence of the disease. However, climate does appear to influence the symptoms. Those with the disease reported increased discomfort in a wet or humid climate.<sup>3</sup>

The prevalence ranges from 0.1% to 5.3% in all population. The lowest is seen in South African population, and highest prevalence is noted in Chippewa Indians, USA and Pima-Indians, USA.

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**Month of Submission :** 02-2016  
**Month of Peer Review :** 03-2016  
**Month of Acceptance :** 03-2016  
**Month of Publishing :** 04-2016

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The low prevalence in certain developing countries is probably because of mortality associated with infections in RA.<sup>4</sup>

RA is two to three times more frequent in women compared to men. This has been noted in all population and all age groups studied. The prevalence of RA appears to increase in both males and females with age.<sup>5,6</sup>

**Clinical Manifestation**

Articular manifestation:

1. Hands
  - a. Joint involvement
  - b. Tendon involvement.

Hasting’s classification of rheumatoid hand:<sup>7</sup>

Joint involved	MCP	Synovitis, passively correctable ulnar drift, fixed volar subluxation, ulnar drift
	PIP	Synovitis, boutonniere deformity, flail IP joint
	Thumb	Flail IP joint, boutonniere deformity, duckbill thumb, dislocation
	Wrist	Synovitis, carpal supination, subluxation, radiocarpal dislocation
Tendon involvement	Flexor tendon disease	Loss of active flexion, triggering, tendon rupture, median nerve involvement
	Extensor tendon disease	Synovitis, dorsal mass, extensor tendon rupture, extensor tendon dislocation

MCP: Metacarpophalangeal, PIP: Proximal interphalangeal, IP: Interphalangeal

2. Other joints are an elbow, shoulder, temporomandibular, cricoarytenoid, sternoclavicular and manubriosternal, cervical spine, hip, knee, and ankle joint.

Extra-articular manifestations:

- a. Cardiac involvement
- b. Pulmonary involvement
- c. Ocular involvement
- d. Vasculitis
- e. Skin involvement
- f. Hematological involvement.

**MATERIALS AND METHODS**

In this study, 50 cases of RA attending either the outpatient department or admitted to the wards of Krishnarajendra Hospital, and Princess Krishnajammanni Tuberculosis and Chest Diseases Hospital attached to Mysore Medical College were selected.

About 50 cases were selected on the basis of the simple random sampling, during the study period January 2013 to June 2015. The cases were diagnosed as RA using the “ACR and European league against rheumatism (EULAR) criteria 2010.”

The data were collected in a pretested questionnaire meeting the objective of the study. Analysis was made using the various statistical parameters such as the mean, standard deviation, standard error, *t*-test (unpaired), Chi-square test, and percentages.

**Inclusion Criteria**

Subjects fulfilling the following criteria, the “American College of Rheumatism (ACR)” and the EULAR criteria 2010 for RA are as follows:

Joint involvement	1 large joint (knee, ankle, shoulder, elbow)	0
	2-10 large joints	1
	1-3 small joint (PIP, MCP, thumb IP, MTP, wrists)	2
	4-10 small joints	3
	>10 joints (at least one small joint)	5
Serology	Negative RF or negative ACPA	0
	Low positive RF or low positive anti-CCP antibodies (<3 times ULN)	2
	High positive RF or high positive anti-CCP antibodies (>3 times ULN)	3
Acute phase reactants	Normal CRP and normal ESR	0
	Abnormal CRP or abnormal ESR	1
Duration of symptoms (weeks)	<6	0
	>6	1

PIP: Proximal interphalangeal joint, MCP: Metacarpophalangeal joint, IP: Interphalangeal joint, MTP: Metatarsophalangeal joint, RF: Rheumatoid factor, ACPA: Anti-citrullinated peptide antibodies, CCP: Cyclic citrullinated peptides, ULN: Upper limit of normal, CRP: C-reactive protein, ESR: Erythrocyte sediment rate

A score of >6 fulfills requirements for definitive of RA.

**Exclusion Criteria**

Patients presenting with polyarthritis but not satisfying the ACR and EULAR criteria 2010.

**OBSERVATION AND RESULTS**

Present study shows majority of patient shows 20 to 39 years (58%) as shown in Table 1, and in the extra-articular manifestation majority of patient are older (51.2 years) compared to articular manifestation (33 years) as shown in Table 2. This study also shows that majority are females as shown in Table 1.

In the present study, the most common extra-articular manifestation was noted in the cardiovascular system (12%). Next, in the order of involvement were respiratory manifestations (8%) and lymphadenopathy (8%), followed by vasculitis (6%) and rheumatoid nodule (2%) (Table 3).

The mean Hb was 10.24 ± 2.365 g/dl. The difference in the mean Hb between two groups was statistically significant (*P* < 0.05) (Table 4).

RA factor was positive in 33 (66%) cases. RA titer ranged from 1:16 to 1:64. All the patients in EAG (100%) were rheumatoid factor positive (Table 5).

**Table 1: The age and sex distribution of the cases**

Age group (in years)	NEAG			EAG			Total (%)
	Male	Female	Total	Male	Female	Total	
20-29	3	10	13	1	0	1	14 (28)
30-39	3	9	12	1	2	3	15 (30)
40-49	1	4	5	1	2	3	8 (16)
50-59	0	1	1	3	2	5	6 (12)
>60	0	1	1	4	2	6	7 (14)

NEAG: Non-extra-articular group, EAG: Extra-articular group

**Table 2: The mean age and SD (years) of non-extra-articular group and extra-articular group**

Group	Mean±SD
NEAG	33.6±9.8
EAG	51.2±12.5
Total	42.4±11.15

NEAG: Non-extra-articular group, EAG: Extra-articular group, SD: Standard deviation

**Table 3: Extra-articular manifestations**

Extra-articular manifestation	Male	Female	Total (%)
Cardiac involvement	4	2	6 (12)
Pulmonary involvement	3	1	4 (8)
Lymphadenopathy	1	3	4 (8)
Vasculitis	1	2	3 (6)
Rheumatoid nodule	1	0	1 (2)
Total	10	8	18 (36)

**Table 4: The mean Hb and SD (g/dl) of NEAG and EAG**

Group	Mean±SD
NEAG	11.38±2.59
EAG	9.11±2.14
Total	10.24±2.365

NEAG: Non-extra-articular group, EAG: Extra-articular group, SD: Standard deviation, Hb: Hemoglobin

**Table 5: Rheumatoid factor**

RA titers	NEAG	EAG	Total (%)
1:16	5	3	8 (16)
1:32	7	4	11 (22)
1:64	3	11	14 (28)

NEAG: Non-extra-articular group, EAG: Extra-articular group, RA: Rheumatoid arthritis

## DISCUSSION

The maximum incidence (58%) was observed in the age group of 20-39 years in the present study and is similar to the study of Banerjea (78% in 16-45 year).<sup>5</sup>

In the present study, the most common extra-articular manifestation observed was cardiac involvement (12%)

followed by pulmonary involvement and lymphadenopathy (8% each), vasculitis (6%) and subcutaneous nodule (2%).

In the present study, the incidence of extra-articular manifestations in 50 consecutive RA patients was studied.

In the EAG, all the 18 patients (100%) were RA factor positive, and majority had a higher titer as compared to the NEAG wherein 46.87% were RA factor positive.<sup>8-10</sup>

## CONCLUSION

About 50 cases of RA fulfilling the ARA and EULAR criteria of 2010 were evaluated clinically, bio-chemically, radiographically, echocardiographically and with pulmonary function tests for evidence of extra-articular manifestations.

The mean age was significantly higher in the extra-articular group (EAG) as compared to the non-extra-articular group (NEAG).

The extra-articular manifestations were more common in males as compared to females.

The mean duration of illness was more in the EAG as compared to the NEAG.

There was not much difference in the mode of onset, clinical presentation, type of joint involvement, or the type of deformities between the two groups.

Male gender, older age group, longer duration of illness, severe degree of anemia, very high erythrocyte sedimentation rate, positive RA factor with higher titer values, all are suggestive of a higher incidence of extra-articular manifestations.

## ACKNOWLEDGMENT

The authors would like to thank HOD of Medicine Department, MMC & RI, Mysore, Scientific and Ethical Committee for permitting us to conduct this study and the medical record section in KR Hospital, for giving all poisoning case sheets for collecting data. Moreover, we also thank all our patients without whom study would have not been possible.

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**How to cite this article:** Inbanathan J, Suneetha DK, Harsha G, George M, Shashank MS. Extra-articular Manifestation of Rheumatoid Arthritis. *Int J Sci Stud* 2016;4(1):81-84.

**Source of Support:** Nil, **Conflict of Interest:** None declared.