

## Analysis of epidemiological factors and biological markers of rheumatoid arthritis

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### Abstract

**Background:** Early diagnosis is crucial in the management of rheumatoid arthritis, a prerequisite for timely intervention and to achieve better outcome. A prospective study was carried out to study epidemiological factors and biological markers of rheumatoid arthritis along with NEW ACR 2010 criteria and DAS28 aimed at early diagnosis and decreased morbidity.

**Material and Methods:** 62 patients with various complaints indicating rheumatoid arthritis were included in this study between ages of 21 to 75 years based on new ACR 2010 criteria. Age and sex distribution, duration of disease, seasonal variation, socioeconomic status, pain in various joints, presentation with deformity and its interval from onset of disease, various biological markers (RA factor, antiCCP), disability score (das28) and VAS were observed:

**Results:** Most common age group was 41-50 years with female-male ratio 4:1 and most commonly within 24 months of onset of disease and during winters. Most common pattern of joint involvement was wrist and MCP > PIP > Elbow, Shoulder and Knee > Ankle > Cervical > Lumbar spine. 28 joint involvement as DAS28 was seen in 69.35%, 19.36% presented with classic deformity. RA factor was positive in 64.52% and Anti-CCP in 72.7% of RA factor negative cases. Mean DAS28 was 7.38 and 53.23% had NEW ACR 2010 score of 9.

**Conclusion:** Anti-CCP can diagnose RA negative cases but if it is used together with DAS28 and NEW ACR 2010 score the accuracy of diagnosing rheumatoid arthritis improves and early treatment can be given improving its outcome and decreasing morbidity.

**Keyword:** Rheumatoid Arthritis, Epidemiological Factors & Biological Markers, Disability Score (Das28), New ACR 2010 Score

### Introduction

Rheumatoid arthritis is a chronic systemic inflammatory disorder that may affect many tissues and organs, but principally attack synovial joints.<sup>4</sup>

It is an inflammatory response of the synovium (synovitis) secondary to hyperplasia of synovial cells, excess synovial fluid and the development of Pannus in the synovium.<sup>10</sup>

It is usually insidious in onset and gradually adds joint over time. It has a predilection for small joints of the hand and feet<sup>3</sup>. In this condition, joints become warm and swollen but not red. Patients are often tired and don't sleep properly. It can result in significant disability very quickly.<sup>10,18</sup>

Any age can be affected but most frequent between 3<sup>rd</sup> to 5<sup>th</sup> decade and females are 3 times more commonly affected.<sup>11</sup> Its presentation is palindromic in nature. Joint involvement, although characteristically symmetrical, can range from a monoarticular pattern to a highly polyarticular pattern<sup>2,10</sup>. Joint damage can span from mild cartilage degradation to progressive erosive disease of juxtaarticular bone<sup>20,24</sup>.

There are few extra articular manifestations like Xerostomia and Xerophthalmia, Raynaud's phenomenon, Carpal tunnel syndrome, Rheumatoid nodules, Pleural effusion<sup>1</sup>, Rheumatoid vasculitis.<sup>12</sup>

### Aims and Objectives

Epidemiological factors associated with rheumatoid arthritis.

To study the pattern of joint involvement in rheumatoid arthritis.

Analysis of clinically useful biological markers in rheumatoid arthritis.

Analysis of clinical score depicting severity in rheumatoid arthritis.

### Material and Methods

Patients with joint pain attending the out patient department and those admitted in LLRH were included detailed history, relevant clinical, radiological and hematological investigations were done.

New classification criteria, jointly published by American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) 2010 was used which has a point value between 0 to 10.

Every patient with a point total of 6 or higher is unequivocally classified as a RA patient, provided he has synovitis in atleast one joint and given that there is no other diagnosis better explaining synovitis.

Four areas are covered in the diagnosis:

- Joint involvement
- Serological parameter
- Acute phase reactant
- Duration of symptoms

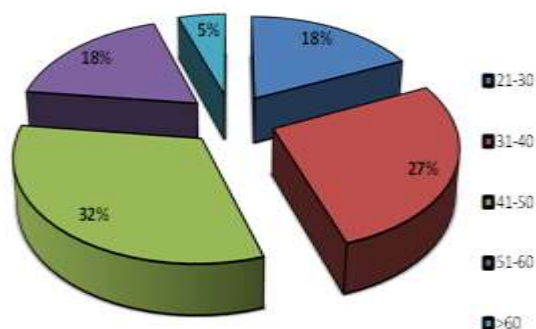
### Observation & Results

A total of 62 patients were classified as rheumatoid arthritis from January 2011 to September 2012. These studies were conducted in orthopedic surgery

department GSVM Medical College, and associated LLR Hospital, Kanpur.

**Table 1: Age Distribution**

| Age Group(Years) | No. of Patients | Percentage |
|------------------|-----------------|------------|
| 21-30            | 11              | 17.74      |
| 31-40            | 17              | 27.42      |
| 41-50            | 20              | 32.26      |
| 51-60            | 11              | 17.74      |
| 61-70            | 3               | 4.84       |
| <b>Total</b>     | <b>62</b>       | <b>100</b> |

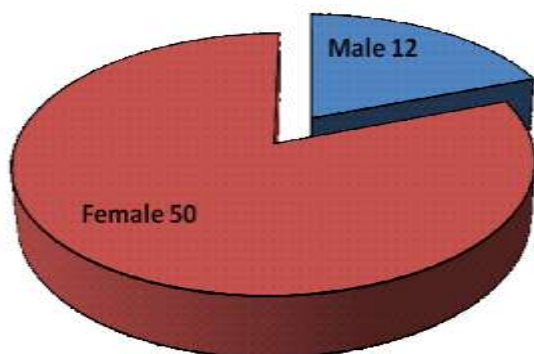


- Mean age for presentation was 42.06 years  $\pm$ 9.48 yrs. Most common age group of presentation was 41-50 years (32.26%).

**Table 2: Sex Distribution**

| Sex          | Numbers   | Percentage |
|--------------|-----------|------------|
| Male         | 12        | 19.35      |
| Female       | 50        | 80.65      |
| <b>Total</b> | <b>62</b> | <b>100</b> |

In males mean age for presentation was 47 Yrs  $\pm$ 9.33 yrs. Most common age group was 41-50 years (41.67%) followed by 51-60 Years (16.67%).



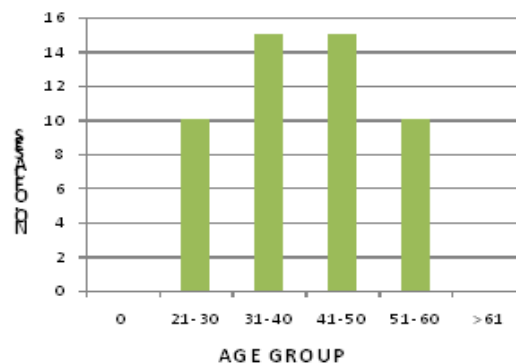
- The female: male ratio was 4:1 with total number of female patients 50 (80.65%) and male patient 12 (19.35%).

In females the mean age for presentation of rheumatoid arthritis was 37.5 years  $\pm$ 9.17 years. Most

common age group in female for presentation was 31-40 years (30%) and 41-50 years (30%).

**Table 3: Distribution of age in Gender**

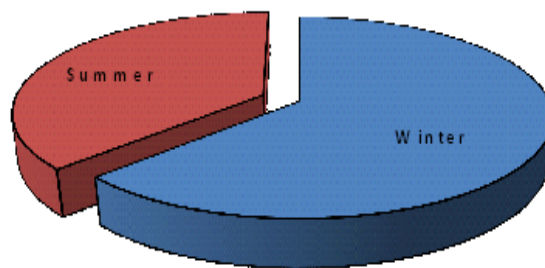
| Age Group    | Males           |            | Females         |            |
|--------------|-----------------|------------|-----------------|------------|
|              | No. of Patients | Percentage | No. of Patients | Percentage |
| 21-30        | 1               | 8.33       | 10              | 20         |
| 31-40        | 1               | 8.33       | 15              | 30         |
| 41-50        | 5               | 41.67      | 15              | 30         |
| 51-60        | 2               | 16.67      | 10              | 20         |
| >60          | 3               | 25         | 0               | 0          |
| <b>Total</b> | <b>12</b>       |            | <b>50</b>       |            |



- Most patients of rheumatoid arthritis presented during winter season 39 patients (62.91%) and 23 (37.09%) were seen in summer.

**Table 4: Seasonal Variation**

| Season       | Numbers   | Percentage |
|--------------|-----------|------------|
| Winter       | 39        | 62.91      |
| Summer       | 23        | 37.09      |
| <b>Total</b> | <b>62</b> | <b>100</b> |



- Most of the patients came with the disease within 24 months of onset (69.36%).
- Mean duration of disease presentation from onset of disease was 26.67 months  $\pm$ 18.29 months.

**Table 5: Duration of Disease Presentation**

| Months   | Numbers |        | Total | Percentage |
|----------|---------|--------|-------|------------|
|          | Males   | Female |       |            |
| <24      | 5       | 38     | 43    | 69.36      |
| 24months | 8       | 4      | 8     | 12.91      |

|                |    |    |    |       |
|----------------|----|----|----|-------|
| 1Day-48 months |    |    |    |       |
| >48 Months     | 3  | 8  | 11 | 17.73 |
| Total          | 12 | 50 | 62 | 100   |

- Mean duration of disease in female was 23.96±16.59 months and in males it was 38±19 months.
- Most of the patients were of middle (80.65%) and low (17.74%) class socio economics status.
- Out of 62 patients 58 (93.55%) presented with involvement of bilateral MCP and wrist joint, 57 (91.94%) presented with involvement of PIP joint 49 (79.03%) with involvement of elbow, shoulder and knee joint. Bilateral ankle joint was involved in 11(17.74%) patients. Cervical spine was involved in 11(17.74%) patients followed by lumbar spine involvement in 04 (6.45%) patients.

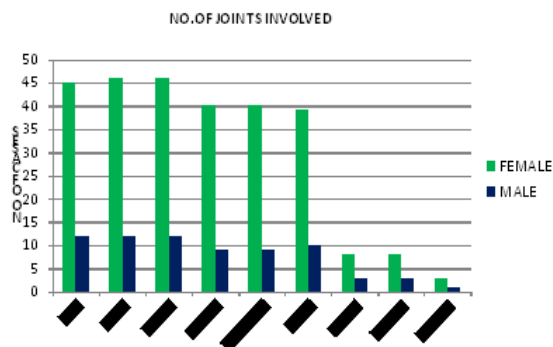
In males most common pattern of involvement was MCP, PIP, Wrist > Knee > Elbow and Shoulder> Ankle > Cervical Spine > Lumbar Spine.

**Table 6: Pattern of Joint Involment**

| Joints         | Numbers |         | Total | Percentage |
|----------------|---------|---------|-------|------------|
|                | Males   | Females |       |            |
| PIP            | 12      | 45      | 57    | 91.94      |
| MCP            | 12      | 46      | 58    | 93.55      |
| Wrist          | 12      | 46      | 58    | 93.55      |
| Elbow          | 09      | 40      | 49    | 79.03      |
| Shoulder       | 09      | 40      | 49    | 79.03      |
| Knee           | 10      | 39      | 49    | 79.03      |
| Ankle          | 03      | 08      | 11    | 17.74      |
| Cervical spine | 03      | 08      | 11    | 17.74      |
| Lumber spine   | 01      | 03      | 04    | 6.45       |

In females pattern of joint involvement was MCP, Wrist> PIP> Elbow and Shoulder > Knee > Ankle > Cervical Spine > Lumbar Spine

- Out of 62 patients in 43 patients 28 joints were involved, of which 31 solely presented with 28 joints involvement, 5 with bilateral ankle joint and cervical spine, 2 with bilateral ankle joint, 2 with cervical spine, 1 with bilateral ankle joint and lumbar spine, 1 with lumbar spine and cervical spine and 1 with bilateral Ankle joint, Cervical spine and Lumbar spine.



11 patients had 22 joints involvement, of which 7 solely presented with 22 joints involvement, 2 with bilateral elbow and shoulder joints, 1 with bilateral ankle joint and 1 with bilateral knee, ankle and cervical.

- Out of 62 patients 12 presented with classic deformity seen in rheumatoid arthritis. Mean age for presentation of patients along with deformity was 39.5 years ±7.25 years. 9 of them were females and 3 males. Most common age group presenting with deformity was 31-40 years (41.66%) followed by age group of 41- 50 years (25%). Earliest presentation of deformity was by 29 years of age.
- Out of 12 patients with deformity interval of more than 60 months which was in six (50%), followed by interval of 48 months 1 day to 60 months in five(41.67%), followed by 36 months 1 day to 48 months which was in one (8.33%) patient.

Mean interval from onset of disease for presentation along with deformity was 69 months ± 13 months.

Least interval from onset of disease for presentation along with deformity was 42 months.

- Out of 62 patients, RA factor was positive in 40 cases (64.52%) and negative in 22 (35.48%) cases. In 32 patients Anti-CCP was done and it was positive in 26 cases (81.25%) and negative in 6 (18.75%) cases, in 22 cases in which RA factor was negative, 16 (72.73%) were Anti-CCP positive and 6 (27.27%) were negative.
- Mean DAS28-ESR score was 7.38±0.74 and in females mean DAS28-ESR score was calculated to be 7.31±0.83 in males average DAS28-ESR was calculated to be 7.69±0.29.
- With increasing duration of disease at the time of presentation DAS score increased. In less than 24 months of duration of disease it was calculated 7.08±0.82, in 24 months one day to 48 months. It was 7.86±0.16 and in more than 48 months duration it was 8.18±0.21.
- Mean disability score based on visual analogue scale of general health (GH in mm) was calculated to be 57.74±19.06, in female it was 57.5+ 19.8 and in males it was 62.08±17.92.

- Mean ESR was calculated to be  $37.77 \pm 7.59$ , in female it was  $37.76 \pm 8.14$  and in males it was  $37.83 \pm 5.33$ . There was not significant difference between male and female and presentation.
- Out of 62 patients, thirty three patients (53.23%) had NEW RA score of 9, seventeen (27.42%) had score of 10, nine (14.51%) had score of 7 and three (4.84%) patients had score of 6.

## Discussion

Early diagnosis is crucial in the management of rheumatoid arthritis, a prerequisite for timely intervention and to achieve better outcome. The disease progression and outcomes in rheumatoid arthritis can be assessed in different ways and important aspects from patients and physician's perspective are clinical, radiological and functional.

This thesis aimed to study epidemiological factors and biological markers of rheumatoid arthritis over 20 months and to examine the correlation of them with severity of rheumatoid arthritis.

Temimi Faisal Al et al. (2010)<sup>1</sup> found that out of the 66 patients studied, 16 were males and 50 were females. The mean age of patients at onset was  $44.5 \pm 14.5$  years, and the females younger than males at presentation.

In a study by da Mota LM et al (2011)<sup>6,8</sup>, 40 early rheumatoid arthritis were evaluated and followed up for 3 years. They reported that the patient mean age for presentation of rheumatoid was 45 years and 90% of them were females at the time of diagnosis.

In a study by Ton E et al (2012)<sup>24</sup>, 196 patients of rheumatoid arthritis were seen in which 70% were females, mean age was 59 years.

In a study by Benbouazza K et al (2011)<sup>3</sup>, 51 patients were examined of which 88% were women and mean age of presentation was  $46.9 \pm 10.8$  years.

In our study, 62 patients were evaluated with a mean age of  $42.06 \pm 9.48$  years. 80.65% were females and the most common age group of presentation was 41 to 50 years.

Among the females most of the patients were in the age group of 31 to 40 and 41 to 50 years and there mean age of presentation was  $37.5 \text{ years} \pm 9.17 \text{ years}$ .

Among males the scenario was different as compared to females Here most of the patients were of 41 to 50 years age group, mean age being  $47 \text{ years} \pm 9.33 \text{ years}$ .

In our patients, seasonal variation was found with regards to the time of presentation which was 62.91% during winters and 37.09% during summers.

In a study by Benbouazza K et al (2011)<sup>3</sup>, 51 patients were evaluated in which mean disease duration was  $24 \pm 13.9$  weeks.

In a study of ours of 62 patients, mean duration was  $26.67 \text{ months} \pm 18.29 \text{ months}$ . In cases of female

patients mean duration was  $23.96 \text{ months} \pm 16.59 \text{ months}$  and in males it was  $38 \text{ month} \pm 19 \text{ months}$ .

In our study 3/5th of the patients had disease duration at the time of presentation less than a year and rest having more than that.

Massardo L et al (2012)<sup>17</sup>, 1093 patients were evaluated with influence of age, sex and socioeconomic status, they found that 58% were low/ low middle socioeconomic status.

In our study 80.65% patients were of middle class and 17.74% patients were of low class socioeconomic status.

Temimi Faisal Al et al (2010)<sup>1</sup> found that Of the 66 patients studied, the upper limb joints were affected more than the lower limbs and the most commonly involved joint was the wrist (81%) followed by the metacarpophalangeal (MCP) (66.66%) joints, the knee (57.57%), ankle (45.45%), elbow (42.42%), shoulder (42.42%), and the proximal interphalangeal (PIP) (36.36%) joints.

Pattern of joint involvement in our study, most common joint involved were MCP and wrist joint (93.55%) followed by PIP (91.94%), elbow (79.03%), shoulder (79.03%), knee (79.03%), ankle (17.74%), cervical spine (17.74%) and lumbar spine (6.45%).

In females it was MCP, Wrist > PIP > Elbow > Shoulder > Knee > Ankle > Cervical spine > Lumbar spine.

In males it was MCP, Wrist, PIP > Knee > Elbow, Shoulder, Ankle, Cervical Spine, Lumbar Spine.

69.35% of patients presented with 28 joint involvement and 17.74% presented with 22 joint involvement.

Out of 62 patients 12 patients presented with classic deformity. 9 of them were females and 3 were males with a mean age of  $39.5 \text{ years} \pm 7.25 \text{ years}$  and most common age group presenting with deformity was 31-40 years (41.66%) followed by 41-50 years (16.67%).

The duration between onset of disease and there first presentation along with deformity in our OPD in 50% cases was more than 60 months with a mean duration of  $69 \text{ months} \pm 13 \text{ months}$ .

Temimi Faisal Al et al (2010)<sup>1</sup> found that in the 66 patients studied, 38 (57.57%) were positive for rheumatoid factor.

Ida Mota LM et al (2011)<sup>6,8</sup> reported Forty ERA patients of the Brasilia cohort. At the time of diagnosis, RF was identified in 50% of the patients and anti-CCP in 52.5%.

In our study of 62 patients, Rheumatoid factor was found positive in 64.52% cases. Anti CCP was done in 32 cases and was found to be positive in 81.25% of them.

In our study of 62 patients, erythrocyte sedimentation rate and c- reactive protein was raised in all cases with a mean for erythrocyte sedimentation rate calculated to be  $37.77 \pm 7.59$ .

In a study Hamdi w et al (2011)<sup>13,16</sup>, a total of 100 patients were evaluated and calculated to have DAS28-(ESR) mean score as 5.53±1.46.

As per our study DAS28 (ESR) mean score was ±0.73 and in females it was calculated to be 7.31±0.83. In males DAS28 (ESR) mean score was calculated to be 7.69±0.29.

Mean DAS28 (ESR) SCORE was 7.67 ± 0.34 in smokers.

DAS28 (ESR) score was elevated with increasing duration of disease at the time of presentation. In patients presenting at 24 months or earlier DAS28(ESR) mean score was 7.08 ±0.82, in patients presenting at more than 24 months to upto 48 months it was 7.86 ±0.16 and in patients presenting at more than 48 months it was calculated to be 8.18±0.208.

Disability score based on visual analogue scale was most common in range of 26-50 that was 38.71% followed by 32.26% with visual analogue scale 51-75. Mean for disability score based on visual analogue scale was 57.74 ±19.06, in females it was 57.50 ±19.80 and in males it was 62.08 ±17.92. In our study new ACR 2010 criteria was used and in 62 patients classified as rheumatoid arthritis 33 patients (53.23%) were found to be having score of 9 followed by 17 patients (27.42) having score of 10.

Most common pattern of joints involvement was Wrist and MCP Joint> PiP Joint> Elbow Shoulder and Knee Joint> Ankle Joint > Cervical Spine> Lumber Spine; in females MCP, Wrist> PIP> Elbow and Shoulder > Knee > Ankle > Cervical Spine > Lumber Spine and in males MCP, PIP, Wrist> Knee > Elbow and Shoulder > Ankle > Cervical Spine > Lumber Spine.

- Involvement of 28 joints as mentioned in DAS28 was seen in 69.35% patients.
- 19.36% presented with classic deformity seen in rheumatoid arthritis.
- Mean age for presentation with deformity was 39.5 years. Most common age group presenting with deformity was 31-40 years. Most common interval from onset of disease for presentation with deformity was of more than 60 months and interval was 69 months.
- RA factor was positive in 64.52%. Anti-CCP was positive in 81.25% and in 72.73% of RA factor negative cases.
- Mean DAS28 ESR score was 7.38. With increasing duration of disease at the time of presentation DAS score increased.
- 53.23% had new RA score (2010) of nine, 27.42% of ten, 14.51% of seven and 4.84% of six.

### Conclusion

The study entitled "Analysis of epidemiological factors and biological markers of Rheumatoid arthritis" represents the study of 62 cases with various complaints

indicating rheumatoid arthritis were included in this study and following conclusion were made:

- Mean age for presentation was 42.06 years, in females 37.5 years and in males 47 yrs. The female: male ratio was 4:1.
- Most common age group of presentation was 41-50 years; in females 31-50 years and in males 41-50 years.
- Most of the patients presented during winter.
- Most of the patients presented within 24 months from onset. Mean duration of presentation was 2667 months; in females 23.96 months and in males 38 months.
- Most of the patients were of middle (80.65%) and lower (17.74%) socio economics status.

To conclude, though our study shows better biological marker for diagnosing rheumatoid arthritis but if it is used together with DAS28 and NEW ACR 2010 score the accuracy will definitely improve so that early treatment can be started.

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