

A Study of Ophthalmological Manifestations of Rheumatoid Arthritis in Eastern India

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Abstract

Introduction: Patients with rheumatoid arthritis (RA) who are positive for anti-cyclic citrullinated peptide (CCP)/rheumatoid factor (RF) have more extra-articular manifestations.

Purpose: We tried to evaluate the magnitude of ocular manifestations in RA patients and to find out whether there is any correlation of anti-CCP or RF or disease duration to ocular involvement.

Materials and Methods: A total of 288 patients diagnosed as RA with ocular symptoms were evaluated. Drug-induced effects and cataract were excluded from the study.

Results: About 18.1% were male and 81.9% were female. The minimum age was 21 and the maximum was 80 years. The average age was 45.66 years. About 36.8% of patients had ocular manifestations. They were bilateral in 66% of patients. Multiple ocular manifestations were shown in 60.4% of patients. Dry eye was observed in 30.5%, anterior uveitis in 6.25%, and episcleritis and scleritis in 7.6% each. Anti-CCP was present in 86.8% and RF in 78.5% of patients. The duration of disease was found to be statistically significant with respect to the presentation of ocular manifestations. Anti-CCP was found to be statistically significant with respect to ocular manifestations but statistically insignificant in case of RF. No statistical significance was found between gender and ocular manifestations.

Conclusion: So far, no published Indian study with such large number of patients looked at ocular manifestations of RA correlating with disease duration and impact of both anti-CCP and RF at the same time. Our study indicates that patients suffering from RA with anti-CCP positivity and long duration of disease should be evaluated ophthalmologically.

Key words: Anti-cyclic citrullinated peptide, Disease duration, Ocular, Rheumatoid arthritis, Rheumatoid factor

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic disease; therefore, many patients exhibit extra-articular manifestations.^[1] Patients with RA who have high titers of rheumatoid factor (RF) or antibodies to anti-cyclic citrullinated peptide (anti-CCP) are most likely to have extra-articular manifestations of their disease, including rheumatoid vasculitis, pleuropulmonary, neurologic, digestive,

cardiovascular, cutaneous, hematologic, and ocular complications.^[2]

Common ocular manifestations of RA include keratoconjunctivitis sicca (dry eye syndrome), episcleritis, scleritis, peripheral ulcerative keratitis (PUK), retinal vasculitis, uveitis, and cataract.^[3] Inflammatory ocular diseases are associated with excess mortality.^[4]

So far, no published Indian study looked at ocular manifestations of RA correlating with disease duration and impact of both anti-CCP and RF at the same time.

Aims and Objectives

The objectives of this study were as follows:

- To evaluate the magnitude of ocular manifestations in patients suffering from RA.

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- To establish a relation between the duration of RA and frequency of ocular manifestations.
- To find out the statistical significance of anti-CCP/RF if any, to the presentation of ocular manifestations.

MATERIALS AND METHODS

Study Design

This was a cross-sectional observational study.

Selection of cases

Patients diagnosed with RA were evaluated after a thorough ophthalmological evaluation. These patients fulfilled the ACR/EULAR criteria for RA.^[5]

These patients were studied in the department of ophthalmology and rheumatology clinic of a tertiary care center of Eastern India between January and December 2018.

Sample size

The sample size was 288.

Inclusion Criteria

All patients diagnosed as having RA were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

- Patients with other autoimmune connective tissue disorders.
- Patients with malignancy/history of chemotherapy/history of exposure to radiation.
- Probable drug-induced ocular manifestations.
- Patients with 7.5 mg or more prednisolone equivalents per day for the past 3 months.
- Patients with a history of any ocular infection, ocular surgery, and trauma.
- Cataract, as they have multifactorial cause and itself make examination difficult.

Ophthalmological Examination

Visual acuity was tested using Snellen's chart. Color vision was recording with Ishihara's pseudoisochromatic charts. Corneal staining was done with fluorescein stain.

Schirmer's test was used to find out cases of dry eye. Normal is ≥ 15 mm wetting of the paper after 5 min. Severe dry eye is < 5 mm wetting of the paper after 5 min.

Standard ophthalmological tools such as slit-lamp biomicroscopy for anterior segment examination, applanation tonometer for IOP measurement, Goldmann two mirror gonioscope, indirect ophthalmoscopy for retina examination, and automated perimetry were used.

Table 1: Percentage of various ocular manifestations

Ocular manifestation	Number of individuals
Dry eye	88
Episcleritis	22
Scleritis	22
Anterior uveitis	18

Table 2: Prevalence of anti-CCP and rheumatoid factor in the study population

Status	Rheumatoid factor (%)	Anti-CCP (%)
Absent	21.5 (62)	13.2 (38)
Present	78.5 (226)	86.8 (250)
Total	100.0	100.0

CCP: Cyclic citrullinated peptide

Table 3: Mean duration of disease with and without ocular manifestations

Ocular manifestations	Duration of disease in years		
	Mean	Median	Std. deviation
No	3.82	3.00	2.46
Yes	6.40	6.00	2.46
P value	<0.001		
Significance	Significant		

Blood tests included complete blood count, random blood sugar, creatinine, liver function test, RF, and anti-CCP.

RESULTS AND ANALYSIS

In the present study, 288 patients were studied. Of these, 52 (18.1%) were male and 236 (81.9%) were female. A total of 576 eyes were examined.

One hundred and sixteen (40.3%) patients were in the 21–40 age group, 118 (41%) patients in the 41–60 age group, and 54 (18.8%) patients above 60 years. The minimum age was 21 and the maximum was 80 years.

The average age was 45.66 years; males 40.23 and females 46.86 years.

Ocular manifestations [Table 1] were seen in 106 (36.8%) of the study population. These manifestations were bilateral in 70 (66%) patients and unilateral in 36 (34%) patients. Multiple ocular manifestations were shown in 64 (60.4%) patients.

Dry eye was the most common ocular manifestation, observed in 88 patients (30.5%). Anterior uveitis was noticed in 18 patients (6.25%). Episcleritis and scleritis were observed in 22 patients each (7.6%).

No cases of retinal vasculitis or PUK were found.

Table 4: Significance of anti-CCP in relation to ocular manifestations

Anti-CCP	Ocular manifestations		Total	P value	Significance
	No	Yes			
Absent	32 (17.58)	6 (5.66)	38 (13.19)	0.041	Significant
Present	150 (82.42)	100 (94.34)	250 (86.81)		
Total	182 (100)	106 (100)	288 (100)		

CCP: Cyclic citrullinated peptide

Table 5: Significance of rheumatoid factor in relation to ocular manifestations

Rheumatoid factor	Ocular manifestations		Total	P value	Significance
	No	Yes			
Absent	34 (18.68)	28 (26.42)	62 (21.53)	0.276	Not significant
Present	148 (81.32)	78 (73.58)	226 (78.47)		
Total	182 (100)	106 (100)	288 (100)		

Anti-CCP [Table 2] was present in 250 patients (86.8%). RF was positive in 226 patients (78.5%). One hundred and eighty-eight (65.2%) patients had both anti-CCP and RF. Hundred patients with anti-CCP positivity and 78 patients with RF had ocular manifestations.

The duration of [Table 3] disease was found to be statistically significant ($P = 0.001$) with respect to the presentation of ocular manifestations.

Anti-CCP [Table 4] was found to be statistically significant ($P = 0.04$, odds ratio 3.55) with respect to ocular manifestations but statistically insignificant ($P = 0.276$, odds ratio 0.64) in case of RF [Table 5].

No statistical significance was found between gender and ocular manifestations ($P = 0.481$).

The statistical software SPSS version 20 has been used for the analysis.

DISCUSSION

Our study was based on a study population of 288 diagnosed with RA, having ocular complaints visiting the ophthalmology department and rheumatology clinic of our tertiary care center of Eastern India from January to December 2018. Suspected drug-induced ocular changes such as hydroxychloroquine or steroid-induced retinopathy were excluded from the study. Cases of cataract were not enumerated as it has multifactorial causes. A total of 576 eyes were examined, highest in comparison of all previous published Indian studies evaluating eyes of rheumatoid patients.

In our study, 52 patients (18.1%) were male and 236 (81.9%) were female. This is comparable to the study by Vignesh

and Srinivasan^[6] who had 77% of females and 23% of males.

Ocular manifestations were seen in 106 (36.8%) of the study population. These manifestations were bilateral in 70 (66%) patients and unilateral in 36 (34%) patients. Multiple ocular manifestations were shown in 64 (60.4%) patients. These findings are compatible with a study by Vignesh and Srinivasan^[6] who had 39% of patients with ocular manifestations. However, in his study, 85% of patients had bilateral findings and 80% of patients had multiple findings. Reddy *et al.*^[7] also had 39% of patients with ocular findings. About 65% of patients had bilateral findings. The prevalence of ocular lesions was 27.2% reported by Zlatanović *et al.*^[8]. It seems that Indian rheumatoid patients have more ocular involvement, probably due to less than adequate treatment of this autoimmune disease.

Dry eye was the most common ocular manifestation observed in 88 patients (30.5%). Episcleritis and scleritis were observed in 22 patients each (7.6%). Anterior uveitis was noticed in 18 patients (6.25%). Zlatanović *et al.*^[8] carried out a study, in which dry eye was appreciated in 17.65% of patients and episcleritis and scleritis in 5.06% and 2.06% of patients, respectively.

Anti-CCP was present in 250 patients (86.8%). RF was present in 226 patients (78.5%). Kaur *et al.*^[9] had ocular signs in 38% of rheumatoid patients with 83% anti-CCP positivity and 77% RF positivity. We found positive correlation of anti-CCP with ocular manifestations, compatible with Vignesh *et al.* On the other hand, there was no significant relation between ocular involvement and RF. Same result was reported by Markovitz *et al.*^[10]

The mean duration of disease was found to be 6.40 ± 2.46 years in patients with ocular manifestations

and 3.82 ± 2.46 years in patients without ocular manifestations. The duration of disease was found to be statistically significant ($P = 0.001$) with respect to the presentation of ocular manifestations. This is comparable to the study by Vignesh and Srinivasan^[6] who found it to be 5.4 ± 2.7 years and 2.1 ± 1.6 years, respectively. In our study, we also found that the duration of disease was found to be statistically significant ($P = 0.016$) with respect to unilateral/bilateral presentation of ocular manifestations.

Although Zlatanović *et al.*^[8] reported more female susceptibility, we did not find any correlation between gender and ocular involvement.

CONCLUSION

We emphasize the need to ask the patients suffering from RA whether they have any eye symptoms and if affirmative then examination of both eyes in detail. Particular attention is to be given to those rheumatoid patients who have long disease duration and anti-CCP positivity. Please note that inflammatory ocular diseases are associated with excess mortality.^[4]

Limitations

- Only those patients who have ocular symptoms were evaluated. If all patients with RA were examined irrespective of symptoms, data would have been more robust.

- The study group was conducted purely on Indian (mostly Bengali) ethnic background.
- This was a single-center study.

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