

# Correlation of ocular manifestations with the duration and activity of disease in patients with rheumatoid arthritis

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## Abstract

**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory arthritis which can affect extra-articular tissues including eyes.

**Objective:** This study was aimed to evaluate the ocular manifestations, their correlation with the duration and activity of disease in patients with RA.

**Materials and Methods:** Patients diagnosed with RA of disease onset age >20 years, irrespective of sex were selected for the study. The eye manifestations were done clinically and also with the help of slit lamp, ophthalmoscope and Schirmer's test. The findings were statistically analysed.

**Result:** One hundred cases of RA were selected (mean age 52.54 years). Keratoconjunctivitis sicca was the commonest finding (40%) along with few cases of keratitis (3%), scleritis (1%) and episcleritis (1%). A statistically significant negative correlation was found between the duration of disease and the Schirmer score ( $r = -0.785$ ;  $p = 0.001$ ). Further, no statistically significant correlation between ocular manifestation and the disease severity were found. Higher ophthalmic involvement was found in seropositive patients.

**Conclusion:** The commonest ocular manifestation found was keratoconjunctivitis sicca. The frequency and severity of involvement of eyes were found to be significantly associated with the duration of the disease. This emphasizes the need for the routine ophthalmic evaluation of RA patients on a periodic basis for the early detection as well as the prevention of ophthalmic complications and thereby modifying treatment.

**KEYWORDS:** Rheumatoid arthritis, keratoconjunctivitis sicca, episcleritis, keratitis, scleritis

## Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease. It has a worldwide prevalence of 1% of the population (0.3–2.1%) and 0.75% in Indian

population with an average age of onset in the 4th to 5th decade of life. The synovial membrane of the joints is the main target of damage, but patients can also have involvement of extra-articular tissues such as eyes, skin, lungs, heart, and peripheral nerves.<sup>[1]</sup> Extra-articular manifestation in RA are present in 10–20% of patients which are more frequently observed in seropositive patients.<sup>[2]</sup> Three times greater predilection was found in women than in men.<sup>[3]</sup>

Systemic manifestations of RA can be accounted by the release of the pro-inflammatory molecules like interleukin-1, interleukin-6 and tumor necrosis factor-alpha from the synovium.<sup>[1,4]</sup> Keratoconjunctivitis sicca (dry eye syndrome) is one of the most common ocular manifestations described in RA.<sup>[5]</sup> Further, RA is by far the most common systemic condition associated with scleritis. Scleral inflammation in RA may

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extend to adjacent structures and may cause keratitis, anterior uveitis, glaucoma, cataract, retinal vasculitis, choroidal and optic nerve changes, and motility disturbances. Patients with rheumatoid scleritis have more advanced joint disease and more extra-articular manifestations than do rheumatoid patients without scleritis. The onset of scleritis may even be a harbinger of occult systemic vasculitis.<sup>[6]</sup> Understanding the correlation between the duration of disease or disease activity in RA with the ocular complications may contribute to an early diagnose in order to preserve the visual function. Therefore, this study was aimed to find out the various ocular manifestations and their correlation with the duration and activity of disease in patients presented with RA.

## Materials and Methods

In this retrospective study, patients either inpatients or out patients of both genders (age 20–80 years) during the 5 year period (from 2010 to 2015) who were diagnosed to have onset of RA by American College of Rheumatology criteria were selected. A detailed history and clinical examination were taken. Patients were examined by an experienced Ophthalmologist. Tests for visual acuity and other ocular examination using slit lamp, Ophthalmoscope, and Schirmer's test were done in all the selected patients. Disease activity was assessed in patients with positive findings pertaining to RA by means of disease activity score 28 (DAS28). The correlation between the Schirmer's test and duration or diseases activity was statistically analysed.

### Statistical analysis

Statistical analysis was done using SPSS (version 16, IBM, US). The correlation between variables was found with the Spearman's correlation coefficient.  $P < 0.05$  was considered as significant.

## Result

Total of 100 patients were included in the study. Among them, 87 were females and 13 were males (Table 1) making a ratio of 6.7:1. The common age of presentation in the study group was noted in the 6th decade followed by 5th decade in both sexes (Table 1). Ocular manifestations (Table 2) were noted in 46 out of 100 patients (46%) and keratoconjunctivitis sicca was the common disease, being present in 40 patients (40%). Among those with keratoconjunctivitis sicca, 32 patients were found to have moderate to severe dry eyes by the Schirmer's test (32%). Keratitis was observed in 3 patients (3%), scleritis in 1 patient (1%), and episcleritis in 1 patient (1%). Lenticular opacity related to RA was seen in 1 patient in the form of posterior subcapsular cataract in a steroid abuser. There were no cases with retinal involvement detected in the study group.

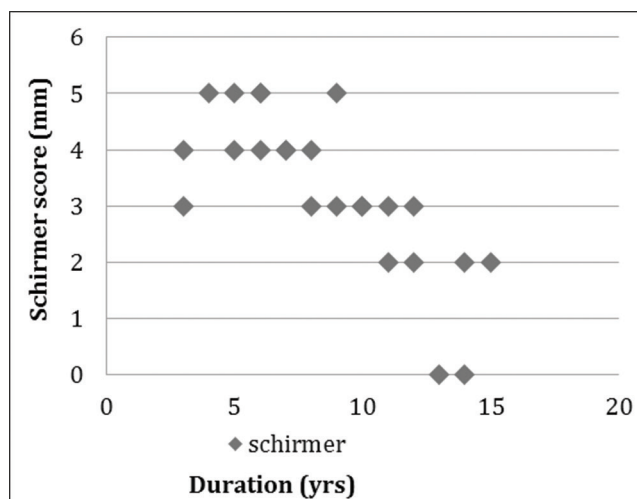
There was negative correlation between duration (in years) and the Schirmer's test (in mm) and this correlation was

**Table 1:** Age and sex distribution of subjects

Age group	Sex	
	Male	Female
21–30		12
31–40		15
41–50	4	21
51–60	5	27
61–70	4	9
71–80		3

**Table 2:** Frequency of ocular manifestations

Ocular manifestations	Frequency
Keratoconjunctivitis sicca	40
Keratitis	3
Scleritis	1
Episcleritis	1
Lenticular opacity (related to RA)	1



**Figure 1:** Correlation between duration of rheumatoid arthritis and the Schirmer score.

statistically significant ( $r = -0.785$ ,  $p < 0.001$ ) (Figure 1). Among all the patients with dry eyes, 24 (60%) were found to have positive rheumatoid factor and all the keratitis, scleritis, and episcleritis patients were seropositive. There was no statistically significant correlation between ocular manifestation and the disease severity as even the patient with necrotising scleritis had a low DAS28 score (2.3) and only few of the patients with severe schirmer's had a significantly high DAS28 score ( $> 5.1$ ).

## Discussion

RA like other systemic inflammatory diseases is known to affect the extra-articular tissues in variable frequencies.

The mean age of the study group was 52.5 years which does not reflect the age of onset of the disease as patients were selected at the point of time of their presentation at hospital. However, the female to male ratio was found to be (6.7:1) higher than the usual ratios in similar studies.<sup>[9]</sup> The female dominance may be probably ascribed to the increased prevalence of RA in female of above 50 years age.<sup>[10]</sup>

Among the ocular manifestations, scleritis and peripheral keratitis were found to be the most severe condition. Other ocular manifestations in RA include episcleritis, corneal involvement which includes filamentary keratitis, sterile central ulceration, microbial keratitis, peripheral ulcerative keratitis, sclerosing keratitis, stromal keratitis, and keratolysis.<sup>[6,7]</sup> Episcleritis may be simple or nodular. Scleral manifestations of the disease include an anterior scleritis which may be diffuse, nodular, necrotizing or can present as scleromalacia perforans or posterior scleritis which is uncommon. The common ocular manifestation found was keratoconjunctivitis sicca which was found to vary from 6 to 50% in literature.<sup>[5]</sup> Among the various causes for dry-eye syndrome, in diseases with systemic inflammation, the cause is ascribed to the decreased tear production.

While the avascular cornea is protected from the inflammatory cells, the peripheral cornea because of its close proximity to the limbal conjunctiva can subject to inflammatory response. In this study, keratitis in 3% of cases was found (which was peripheral ulcerative keratitis in one patient and filamentary keratitis in 2 others), whereas only 1.6% was reported in a Bosnian study group.<sup>[11]</sup> Scleritis and episcleritis were seen in 1% each of our subjects, when compared to 0.67% and 0.17%, respectively as found in a study by Mc Gavin *et al.*<sup>[12]</sup> The Schirmer score was inversely correlated with the duration of the disease which indicated that severity of dry eyes increasing with the duration of the disease. But it was not associated with disease activity which was similar to the observation of Fujita *et al.*<sup>[13]</sup> Among the patients who had eye findings, 57% of the dry eye subjects and all the patients with keratitis, scleritis, and episcleritis were RA factor positive. Though the RA factor was found to be non-specific, a higher ophthalmic involvement can be suggested in seropositive patients.

Frequent application of artificial tear formulations which contain minimum preservative and punctual plugs to prevent tear drainage.<sup>[14]</sup> Topical application of cyclosporine A ophthalmic emulsion drops was also suggested for the moderate to severe dry-eye patients.<sup>[15]</sup> Simple diffuse scleritis is treated with oral non steroidal anti-inflammatory drugs. Further, immunosuppressive therapy is suggested for patients with necrotizing scleritis. Episcleritis is a self-limiting condition. There were no cases in which eye movements or retina was affected either as a part of disease or treatment which could have been because of the relatively lesser sample size of the study. Though the less number of patients was the main limitation of this study, the exhibited positive correlation of dry eye with the disease duration remains the strength of the study. This observation emphasizes the need for routine ophthalmic evaluation of RA patients on a periodic basis for early

detection and prevention of ophthalmic complications and thereby modifying treatment.

## Conclusion

The results of the study concluded that the ocular manifestations were found in a significant proportion of patients with RA of which keratoconjunctivitis sicca was the common disease. Keratitis, scleritis, and episcleritis were also seen in a few seropositive patients with long standing RA.

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