

## A STUDY OF THE OCULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS AMONG PATIENTS PRESENTING TO A TERTIARY CENTRE

Dhanya Sukumaran<sup>1</sup>, Konayi Cherayath Rajini<sup>2</sup>, Jijith Krishnan<sup>3</sup>

<sup>1</sup>Junior Consultant, Department of Ophthalmology, Government Taluk Hospital, Payyanur.

<sup>2</sup>Professor and HOD, Department of Ophthalmology, Government Medical College, Thrissur.

<sup>3</sup>Associate Professor, Department of Medicine, Government Medical College, Thrissur.

### ABSTRACT

#### BACKGROUND

Rheumatoid Arthritis (RA) is a chronic inflammatory disease of unknown aetiology marked by a symmetric peripheral polyarthritis. It is the most common form of chronic inflammatory arthritis and often results in joint damage and physical disability. The name is based on the term "rheumatic fever", an illness, which includes joint pain and is derived from the Greek word ῥεῦμα-rheuma (nom.), ῥεῦματος-rheumatosis (gen.) ("flow, current"). The suffix oid ("resembling") gives the translation as joint inflammation that resembles rheumatic fever. The first recognised description of rheumatoid arthritis was made in 1800 by Dr. Augustin Jacob Landré-Beauvais (1772-1840) of Paris. Because, it is a systemic disease, RA may result in a variety of extra-articular manifestations including fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis and haematologic abnormalities.

#### MATERIALS AND METHODS

Patients who were diagnosed cases of rheumatoid arthritis attending the rheumatology clinic were referred to the Ophthalmology OPD in Government Medical College, Thrissur, for detailed eye examination.

#### RESULTS

The study was conducted in 100 patients (88 females and 12 males). Rheumatoid Factor (RF) was found to be positive in 60 patients (60%), presence of dry eye did not correlate with rheumatoid positivity (Fishers exact test- the two-tailed P value = 0.4256). Through various tests, we concluded that there was aqueous deficiency in 61% and mucin deficiency in 46% of the patients. Other ocular manifestations present were- scleritis (2%), episcleritis (2%) and keratomalacia (2%).

#### CONCLUSION

From the present study, we found out that extra-articular involvement of organs in rheumatoid arthritis is significant. The main ocular manifestations in rheumatoid arthritis found in our study were keratoconjunctivitis sicca, episcleritis, scleritis and keratomalacia. Though keratoconjunctivitis sicca was the most common, it did not show any correlation with RF factor, but showed correlation with disease activity.

#### KEYWORDS

Rheumatoid Arthritis, Episcleritis, Dry Eye.

**HOW TO CITE THIS ARTICLE:** Sukumaran D, Rajini KC, Krishnan J. A study of the ocular manifestations of rheumatoid arthritis among patients presenting to a tertiary centre. J. Evid. Based Med. Healthc. 2017; 4(64), 3836-3840. DOI: 10.18410/jebmh/2017/766

#### BACKGROUND

Rheumatoid arthritis is the most common rheumatic disorder affecting an estimated 0.8% of the general population. Classically, it is described as an additive, symmetric, deforming polyarthritis. It is a chronic debilitating autoimmune inflammatory disease affecting multiple organs. The characteristic feature causing cartilage

*Financial or Other, Competing Interest: None.*

*Submission 13-07-2017, Peer Review 20-07-2017,*

*Acceptance 02-08-2017, Published 08-08-2017.*

*Corresponding Author:*

*Dr. Konayi Cherayath Rajini,*

*Professor and HOD, Department of Ophthalmology,  
Government Medical College, Thrissur.*

*E-mail: rajinidreye@gmail.com*

*DOI: 10.18410/jebmh/2017/766*



and bone destruction leading to joint deformities and functional limitations is persistent synovial inflammation.<sup>1</sup>

Rheumatoid arthritis is a chronic inflammatory systemic disease with a variety of extra-articular manifestation, which may be present in 40% of the patients. These are more common in seropositive patients.<sup>1</sup>

Ocular manifestations include keratoconjunctivitis sicca, anterior uveitis, episcleritis, scleritis, scleromalacia perforans and massive granuloma of sclera.<sup>2</sup>

Drugs used in the systemic management of rheumatoid arthritis can also lead to serious ocular complications.<sup>3</sup>

Although, the disease primarily manifests in the joints, many other organs including eye may also be affected, which can lead to significant morbidity. Here lies the importance of knowing the ocular manifestations and treating them accordingly.

**Aims and Objectives**

To find the prevalence of various ophthalmological manifestations in diagnosed cases of rheumatoid arthritis attending the Rheumatology Clinic in Government Medical College, Thrissur.

**MATERIALS AND METHODS**

Diagnosed cases of rheumatoid arthritis attending the rheumatology clinic were asked to attend Ophthalmology OPD at Government Medical College, Trissur.

These patients were examined for any ocular associations by torch light, slit lamp, ophthalmoscope and 90D lens.

Design of the Study- Observational study.

Period of Study- April 2011-December 2012.

Place of Study- Department of Ophthalmology, Government Medical College, Trissur.

Sample Size- 100.

Selection of Cases- Old and new-diagnosed cases of rheumatoid arthritis attending the Rheumatology Clinic in Government Medical College, Trissur.

**Inclusion Criteria**

Diagnosed cases of rheumatoid arthritis attending Rheumatology Clinic at Government Medical College, Trissur.

**Exclusion Criteria**

1. Diagnosed cases of juvenile rheumatoid arthritis.
2. Those who are unable to sit for slit-lamp examination.
3. Those who are not willing for the study.
4. History of recent trauma.
5. Diabetes mellitus.
6. Diagnosed cases of other collagen vascular diseases.

**Data Collection-** History- A detailed history of duration of RA, history of any systemic illness pertaining to the ocular manifestations were sought.

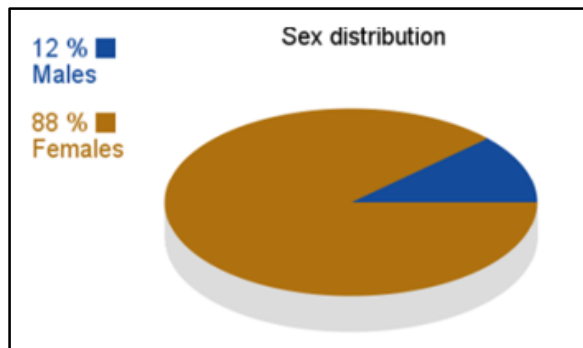
**Examination-** General physical and systemic examination for any systemic involvement.

**Ocular Examination-** To evaluate for the various ocular manifestations like dry eye, episcleritis, scleritis, anterior uveitis, keratitis and also for any complications of systemic treatment. It included best corrected visual acuity, colour vision, Amsler’s grid, detailed slit-lamp examination of anterior segment, refraction, intraocular pressure, detailed fundus examination and tests for detecting dry eyes.

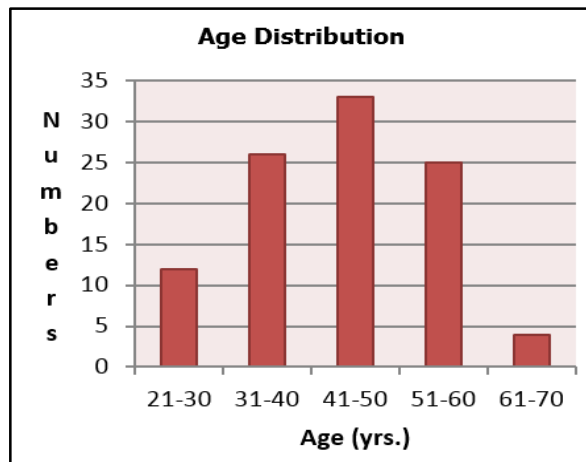
**Dry Eye Tests/Tear Function Tests-** This included Tear Film Breakup Time (TBUT), Schirmer’s test and lissamine green staining. Patients with dry eyes were treated with topical and systemic drugs.

**Statistics-** Analysis of data was done by GraphPad InStat 3 Biostatistics Software.

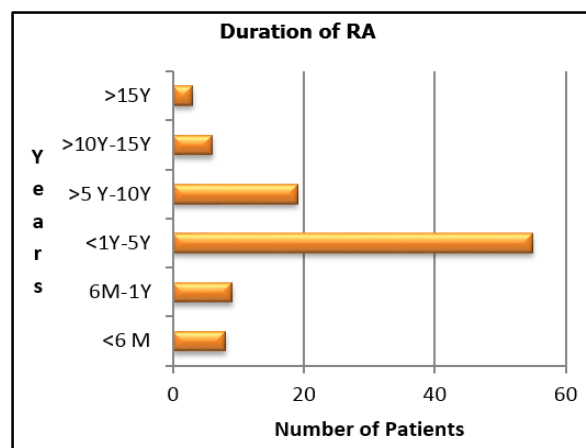
**RESULTS**



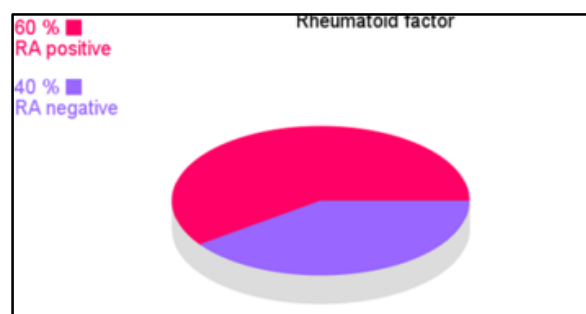
**Figure 1. Sex Ratio**



**Figure 2. Age Distribution**



**Figure 3. Duration of Rheumatoid Arthritis**



**Figure 4. Rheumatoid Factor**

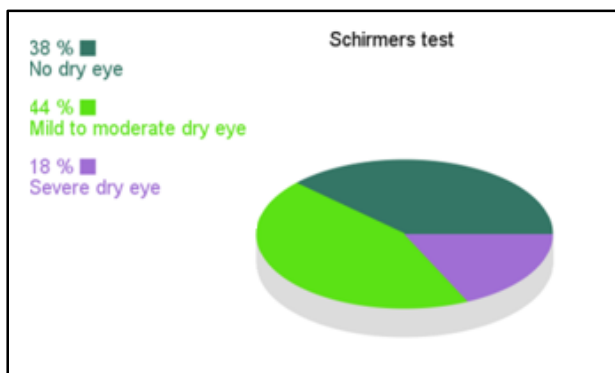


Figure 5. Schirmer's Test

Abnormal tear-film breakup time was found in 46 patients (46%). Abnormal staining with lissamine green was found in 20 patients (20%). Hence, aqueous deficiency in 61% and mucin deficiency in 46% can be inferred.

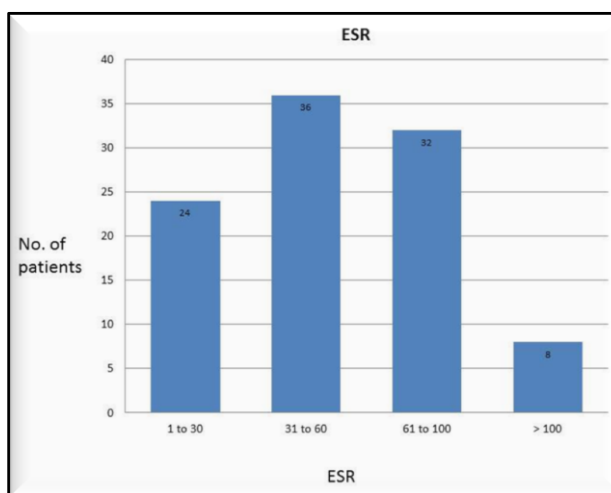


Figure 6. ESR

Mean ESR- 57 mm/first hr.

Manifestation	Percentage of Patients
Dry eye	44
Scleritis	2
Episcleritis	2
Keratitis	2
Uveitis	1
HCQS retinopathy	1

**Table 1. Ocular Manifestations of RA**

Correlation between RA factor and dry eye was investigated by the Fisher's exact test.

Results are shown below.

No correlation was found between RA factor and dry eye.

	Dry Eye +	Dry Eye -	Total
RA +	25	27	52
RA -	19	29	48
<b>Total</b>	<b>44</b>	<b>56</b>	<b>100</b>

**Table 2. Dry Eye Vs. RA Factor**

Fishers exact test- the two-tailed P value = 0.4256.

Thus, presence of dry eye did not correlate with rheumatoid positivity.

**Correlation of Dry Eye Severity with Rheumatoid Arthritis Duration-**

By Pearson correlation, the two-tailed P value = 0.0094, which showed that there was statistically significant increase in the severity of dry eye with the increase in the duration of rheumatoid arthritis.

**DISCUSSION**

This study on 100 rheumatoid arthritis patients was conducted to find out the various ocular manifestations of rheumatoid arthritis among patients presenting to a tertiary care centre.

Rheumatoid arthritis is considered to be an autoimmune disease, principally producing a progressively crippling polyarthritis. Ocular involvement is an important non-articular manifestation. Parts of the eye can become inflamed causing pain and even some loss of vision.

The association of ocular lesions with rheumatoid arthritis has long been recognised.

The well-documented ocular complications of this disease are keratoconjunctivitis sicca, anterior uveitis, episcleritis, scleritis, scleromalacia perforans and massive granuloma of sclera.<sup>1</sup>

SC Reddy et al reported the incidence of ocular lesions (39%) is much higher than the earlier reports, i.e. 6.2% by Smith and 20.8% Williamson et al. Keratoconjunctivitis Sicca (KCS) was the commonest ocular manifestation of rheumatoid arthritis. The incidence of keratoconjunctivitis sicca in the study was 29%.<sup>2</sup>

Sl. No.	Parameter	Current Study	Study by Al Temini F. <sup>4</sup>
1.	Mean age	41-50	44.5-14.5
2.	Mean duration of RA (yrs.)	4.05 ± 3.8	2.5
3.	Female:male	7.33:1	3.125:1
4.	Scleritis (%)	2	1.5
5.	Rheumatoid factor (%)	52	57.57
6.	Dry eye (%)	44	24.42

**Table 3. Comparison with Study by Al-Temini F**

According to Zlatanovic G et al, the most common manifestation of ocular involvement was keratoconjunctivitis sicca. Episcleritis was diagnosed in 5.06% patients with RA, while scleritis was present in 2.06% of patients. Ocular manifestation was present in 27.2% of patients. Women were more affected.<sup>3</sup>

**Ocular Manifestations-** The incidence of ocular lesions in the present study (50%) is much higher than the earlier studies, i.e. 6.2% by Smith<sup>5</sup> and 20.8% Williamson et al.<sup>6</sup> The former of the two studies is not comparable to the current study since it was a retrospective study of case histories of rheumatoid arthritis patients and the tests for keratoconjunctivitis sicca were not done in those patients.

**KCS-** In the present study, the incidence of ocular manifestations was 50% and the most common manifestation was dry eye (44%). In a study conducted by Fujita M et al, the incidence of dry eye was 47%. In a study by Al-Temini F, the dry eye incidence was 24.42%.<sup>4</sup> Dry eye has been reported in 10%-40% of RA patients by various authors (Table no. 4). Rheumatoid process has been considered to be aetiologically related to keratoconjunctivitis sicca by Stenstam,<sup>7</sup> Holm<sup>8</sup> and Thompson and Eadie.<sup>9</sup>

Author	Year	Percentage of KCS in RA
T Stenstam <sup>7</sup>	1947	10%
Holm <sup>8</sup>	1949	30%
Lackington et al	1951	35%
Thompson and Eadie <sup>9</sup>	1956	15%
Williamson et al	1969	14.7%
Ericson and Sundmark	1970	21%
Sheran	1971	40%
SC Reddy et al <sup>10</sup>	1977	29%
Current study	2012	44%

**Table 4. Comparative Incidence of KCS in RA**

In the current study, 64% of patients were asymptomatic and dry eye was detected by tests.

#### **Correlation of Dry Eye with CRP (Disease Activity)-**

There was statistically significant correlation between the CRP levels and dry eye (P value- 0.0002). CRP, also known as C-reactive protein is a test, which measures the concentration in blood serum of a special type of protein produced in the liver that is present during episodes of acute inflammation or infection.

In the body, CRP plays the important role of interacting with the complement system, an immunologic defense mechanism. A high result serves as a general indication of acute inflammation. In cases of inflammatory rheumatic diseases such as rheumatoid arthritis, we can use CRP test to assess the effectiveness of a specific arthritis treatment and monitor periods of disease flare-up. Its value is as a general indicator, not specific.

**Duration of Disease-** In the current study, the mean duration of RA was 4.05 yrs. (SD- 3.8 yrs.) We have found out a strong correlation between severity of dry eye and the duration of the disease (P value-0.0094). Polanska et al proved statistical connection between the presence of dry eye syndrome and the duration of rheumatoid arthritis longer than 10 years. Keratoconjunctivitis sicca was the most common ocular complication in RA patients in their study. They did not find the dependence among the RF presence and stage of the rheumatoid arthritis and the appearance of the dry eye syndrome.<sup>11</sup>

**RF Titre-** In the current study, we did not find statistically significant correlation between the RF positive rheumatoid arthritis and dry eye syndrome (P value-0.4256). Polanska et al not find statistically significant correlation between the RF positive rheumatoid arthritis appearance and dry eye

syndrome, nor between the stage of the rheumatoid arthritis and presence of the dry eye syndrome.<sup>10</sup>

**ESR-** The mean ESR in the study population was 57 mm/1st hr. (SD-31). Statistically significant association was found between the dry eye severity and ESR (P value-0.0001).

**Scleritis and Episcleritis-** The scleral lesions seem to be rare in RA. The prevalence of scleritis in rheumatoid arthritis is reported to be 0.67%-6.3% in other various studies. In a study conducted by Jayson and Jones,<sup>12</sup> 6.3% incidence of scleritis in rheumatoid arthritis was found and concluded that scleritis was significantly associated with rheumatoid nodules and other systemic complications of rheumatoid arthritis. They did not find any case of episcleritis in their study of 142 patients.

In the current study, the prevalence of scleritis was found to be 2%. Two cases of episcleritis was seen in the current study.

**Keratitis-** Sterile corneal ulceration can occur in either the central or peripheral cornea with a paucity of ocular symptoms and may lead to corneal perforation. Systemic immune-mediated inflammation, keratoconjunctivitis sicca and ocular surface infections trigger the process of corneal ulceration. In the present study, 2 patients presented with corneal melt. They were started on systemic methotrexate (with folic acid), topical steroids, lubricants and autologous serum.

**Anterior Uveitis-** Foresteir et al did not find any case of iritis in their study of 100 cases of rheumatoid arthritis. In the current study, one patient showed evidence of chronic uveitis. Even though anterior uveitis occurs in other rheumatic diseases, it is not more common in RA patients than in general population.<sup>2</sup>

**Posterior Uveitis-** Choroiditis is<sup>13</sup> seen rarely in rheumatoid arthritis. Kimura et al<sup>14</sup> found one case of choroiditis among 16 adults with rheumatoid arthritis. Hogan et al<sup>14</sup> pointed out that choroiditis practically never occurs in rheumatoid arthritis and the selective involvement of iris or iris and ciliary body is remarkable.

**Retinal Lesions-** Primary involvement of retina in rheumatoid arthritis is very rare. In the current study on 100 patients, no retinal lesions were found. It might be due to the small study group.

**Retinopathy-** In a study conducted by Carr R et al, 50% of patients had CQ retinopathy after 7 years of treatment with CQ. In another study conducted by Shinjo S K et al, there was 4.5% incidence of CQ retinopathy.

#### **CONCLUSION**

1. The most common ocular manifestation was dry eye (44%).

2. The presence of dry eye was independent of rheumatoid factor.
3. Inflammatory markers like ESR and CRP, which indicate disease activity showed significant correlation with dry eye.

Thus, regular ophthalmic evaluation of RA patients is needed on a long-term basis, as-

- a. Most of the RA patients with dry eye are asymptomatic.
- b. The drugs used to control disease activity like corticosteroids, chloroquine and hydroxychloroquine are known to cause ocular side effects leading to decreased visual acuity. Early recognition and management can save the eye.

Extra-articular involvement of organs in rheumatoid arthritis is significant. In the present study, ocular manifestations in rheumatoid arthritis found were keratoconjunctivitis sicca, episcleritis, scleritis and keratomalacia. Most common manifestation was keratoconjunctivitis sicca, which did not show correlation with RF factor, but showed correlation with disease activity.

#### REFERENCES

- [1] Lipsky PE. Rheumatoid arthritis. Chapter 314. Section 2. Part 14. In: Fauci AS, Kasper DL, Longo DL, eds. Harrison's principles of internal medicine. 17<sup>th</sup> edn. New York: McGraw-Hill 2008:p. 2958.
- [2] Dana R, Chong E, Foster CS. Adult rheumatoid arthritis. In: Albert DM, Miller JW, eds. Albert & Jakobiec's principles & practice of ophthalmology. 3<sup>rd</sup> edn. Philadelphia: Saunders Elsevier 2008:p. 1427.
- [3] Lowe TA. Rheumatoid arthritis. In: Thomann KH, Marks ES, Adamczyk DT, eds. Primary eye care in systemic diseases. 2<sup>nd</sup> edn. New York: McGraw-Hill 2001:p. 793.
- [4] Al-Temini F. The spectrum of rheumatoid arthritis in patients attending rheumatology clinic in Nizwa hospital-Oman. *Oman Med J* 2010;25(3):184-189.
- [5] Smith JL. Ocular complications of rheumatic fever and rheumatoid arthritis. *Amer J Ophth* 1957;43:575.
- [6] Williamson J, Paterson RW, McGavin DD, et al. Posterior subcapsular cataracts and glaucoma associated with long-term oral corticosteroid therapy. In patients with rheumatoid arthritis and related conditions. *Br J Ophthalmol* 1969;53(6):361-363.
- [7] Stenstam T. On the occurrence of Keratoconjunctivitis sicca in cases of rheumatoid arthritis. *J Int Med* 1947;127(1-2):130-148.
- [8] Holm SJ. Keratoconjunctivitis sicca and the sicca syndrome. *Acta Ophthalmol* 1949;(Suppl 33):217-230.
- [9] Thompson M, Eadie S. Kerato-conjunctivitis sicca and rheumatoid arthritis. *Ann Rheum Dis* 1956;15(1):21-25.
- [10] Reddy SC, Gupta SD, Jain IS, et al. Ocular manifestations of rheumatoid arthritis. *Indian Journal of Ophthalmology* 1977;25(3):20-26.
- [11] Polanska V, Hlinomazova Z, Fojtik Z, et al. Dry eye syndrome in rheumatoid arthritis patients. *Cesk Slov Oftalmol* 2007;63(6):422-430.
- [12] Jayson MIV, Jones DEP. Scleritis and rheumatoid arthritis. *Ann Rheum Dis* 1971;30:343.
- [13] Hogan MJ, Kimura SJ, Thygeson P. Uveitis in association with rheumatism. *Arch Ophthalmol* 1957;57(3):400-413.
- [14] Kimura SJ, Hogan MJ, Connor GR, et al. Uveitis and joint disease: a review of 191 cases. *Trans Amer Ophth Soc* 1966;64:291.