

Ocular Manifestations in Rheumatoid Arthritis and their Co-Relation with Anti Cyclic Citrullinated Peptide Antibodies

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Abstract: Aims & Objective: To study ocular manifestations in RA & co- relate with Anti CCP Ab. Materials& Method: 114 patients attending Rheumatology & Ophthalmology OPD of a tertiary care hospital were screened. Examination and tests: Detailed slit lamp examination, BCVA by Snellen's chart, IOP taken by Goldman's tonometry. Schirmer's & ocular staining score done. Dilated fundus examined by IDO. Chi square test used to co - relate their significance & P value calculated. Results: 42.10 % (48) of 114 cases had ocular manifestation. Dry eye being commonest 31.57 % (36) followed by cataract in 6 (5.26%) of cases. 1 case each of Sjogren's syndrome & scleritis. 1.75% (2) cases had peripheral keratitis, anterior uveitis & episcleritis each. Strong association seen between presence of Anti CCP Ab & ocular manifestation by significant P value. Conclusion: Ocular manifestations are significant extra articular manifestation. Flaring up of ocular manifestation may signal impending deterioration or relapse of RA.

1. Introduction

- Rheumatoid arthritis (RA) is a chronic progressive, antibody mediated autoimmune disease with articular and extra-articular manifestations.^[1]
- Women more affected than men.^[2]
- Primarily affects small joints characterized by symmetrical inflammation of the synovium
- Results in tenderness, destruction of bone and cartilage results in functional disability.
- Involves many organs. Ophthalmic involvement is often significant, causing varying degrees of ocular morbidity.
- Ocular manifestations of RA include dry eye, cataract, episcleritis, scleritis and peripheral ulcerative keratitis (PUK) etc.^[3]

2. Aims and Objectives

- To study the ocular manifestations in rheumatoid arthritis
- To correlate the role of anti-cyclic citrullinated peptide antibody (anti-CCP antibody) with the ocular manifestations.

3. Materials and Method

A cross sectional clinical study.

A) Inclusion criteria

All patients with RA attending Rheumatology and Ophthalmology OPD, AMCH, Dibrugarh undergoing routine ophthalmologic screening.

B) Exclusion criteria

- Presence of other autoimmune systemic disorders like systemic lupus erythematosus, graft versus host disease, and any immunosuppressive disorders.
- Age less than 18 years.

3.1 Method of Data Collection

- Medical history and Ocular History** taken and recorded.
- Systemic examination** : A thorough systemic examination was done specially of the skeletal system giving extra importance to *number of swollen and*

painful joints and any structural deformity caused by the disease

- Ocular examination** – A thorough ocular examination is done for each eye under slit lamp along with fundoscopy done
 - Vital Staining Of The Cornea without anesthesia
 - Schirmers test I
 - Tear film break up time (TBUT)

4. Results and Observations

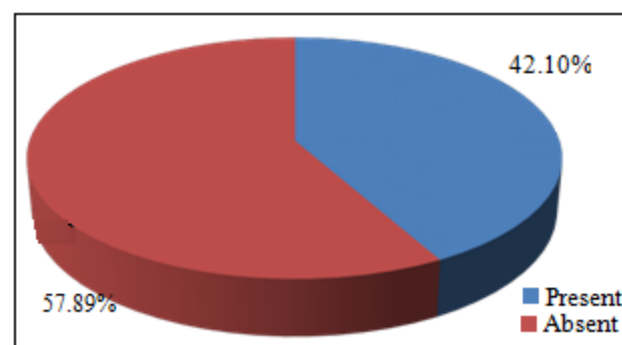


Figure 1: Shows distribution of Ocular Involvement in RA Patients

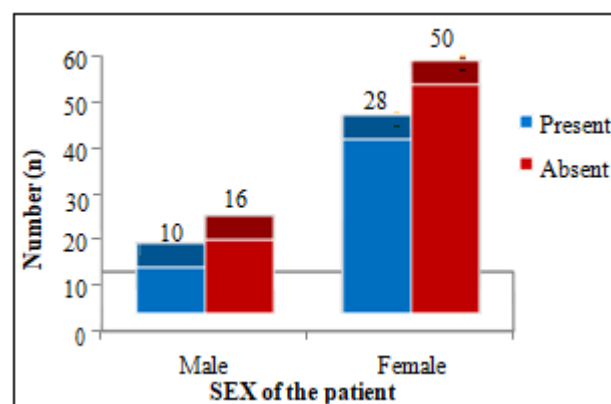


Figure 2: Shows Sex distribution in Patients with Ocular Manifestations of RA

FIGURE 1 shows ocular involvement in 48 (42.10%) patients of the 114 patients RA in this study, FIGURE 2 shows female preponderance with 38 (43.18 %) of 88 female

cases with male: female ratio is 1:3.8

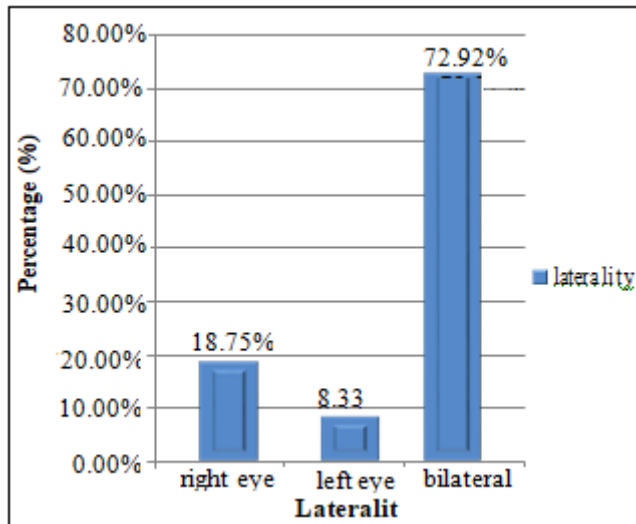


Figure 3: shows laterality in patients with ocular manifestations of RA

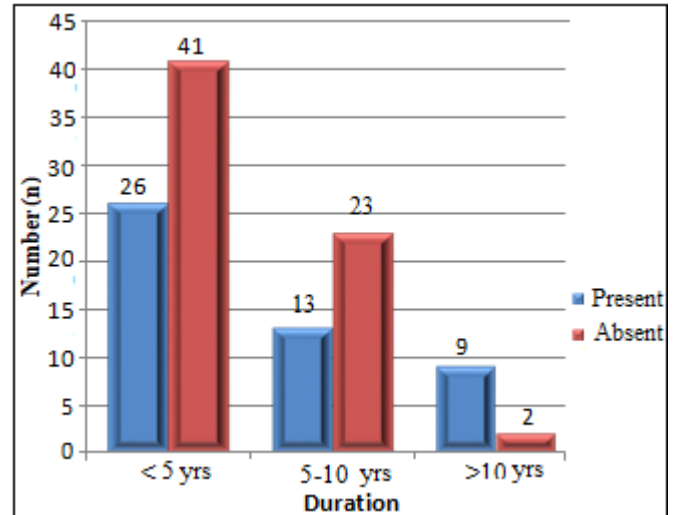


Figure 4: Ocular Manifestation in relation to duration of the disease

FIGURE 3 shows bilateral involvement more common i.e. 35 (72.92 %) and FIGURE 4 shows highest incidence in those cases who had > 10 years duration of the disease comprising of 9 (81.81 %) of the cases.

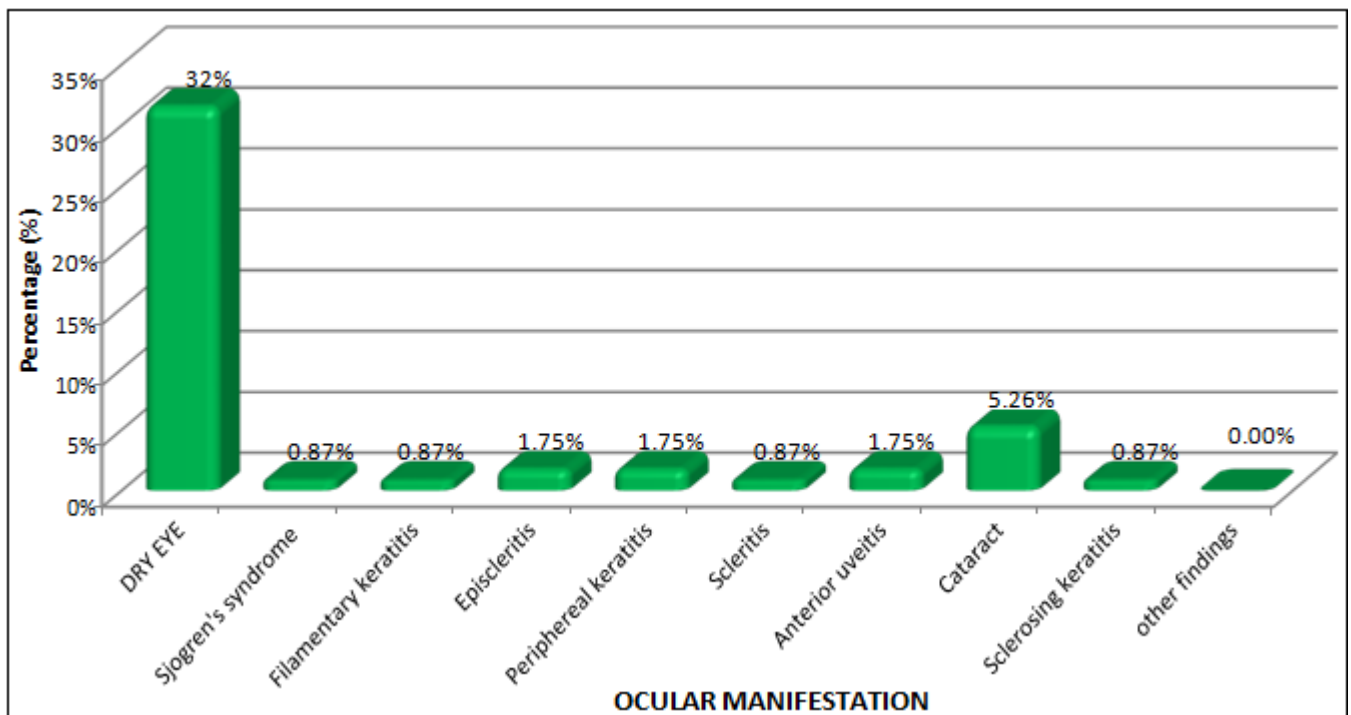
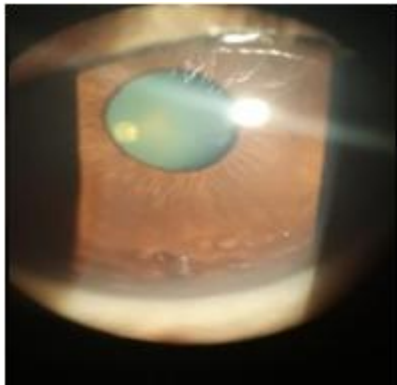


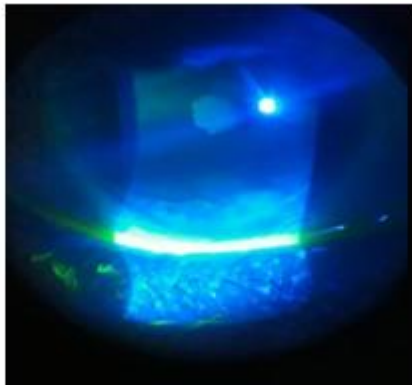
Figure 5: Shows different ocular manifestations in rheumatoid arthritis

FIGURE 5 shows distribution of various ocular manifestation among the 114 RA patients and dry eye was the most common manifestation occurring in 36 (31.57 %)

cases followed by cataract in 6 (5.26%) of cases.



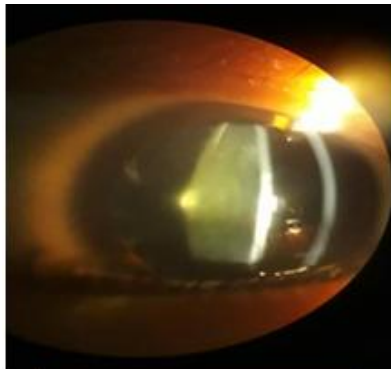
Filamentary keratitis



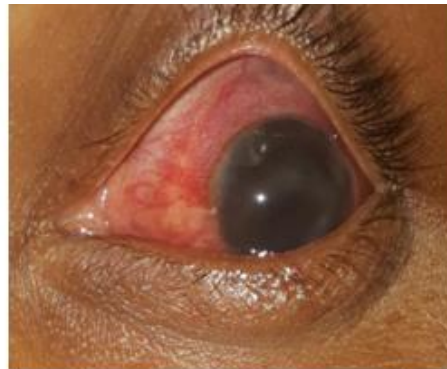
PUK



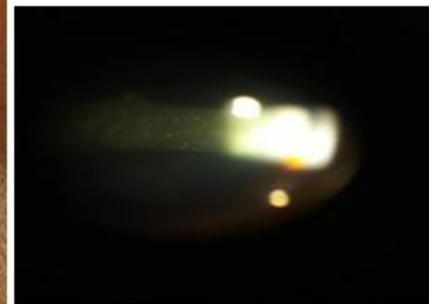
Episcleritis



PSC



Sclerosing keratitis



Uveitis



Posterior synechiae

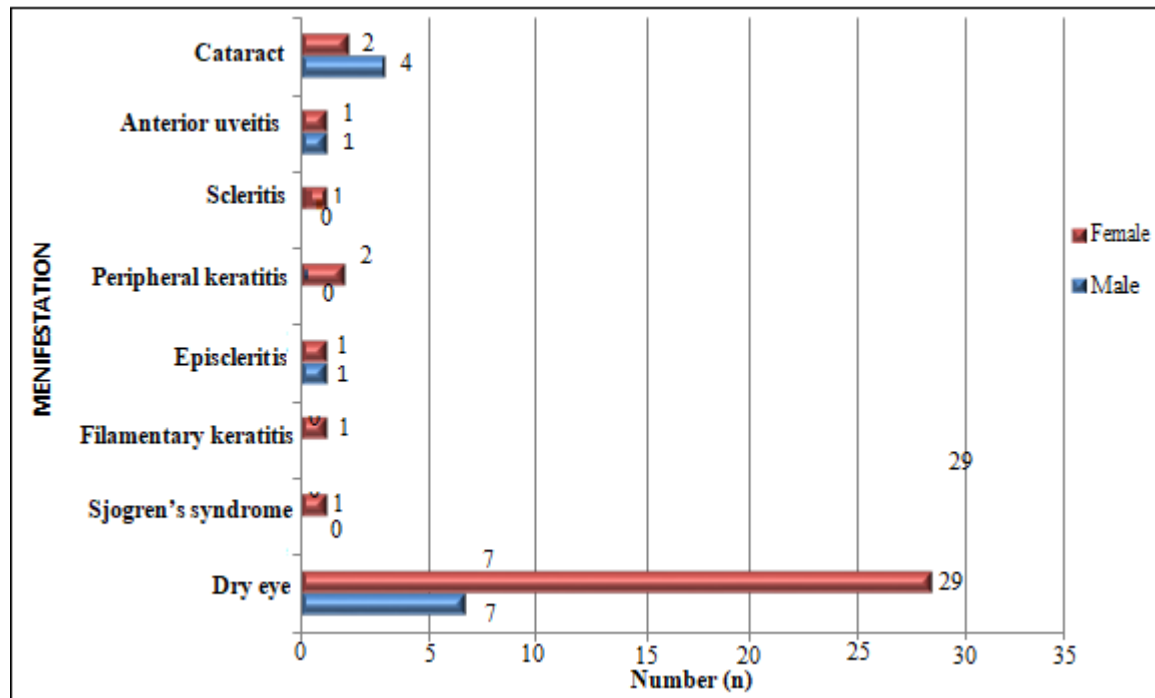


Figure 6: Graph Showing Sex Wise Distribution of Different Ocular Manifestations of RA

FIGURE 6 shows incidence of dry eye in female (80.55%) was much higher than males (19.44%) but cataract was seen more in males (66.67 %). Although very less in compared to dry eye, more severe manifestation like Sjogren's syndrome, filamentary keratitis, PUK, scleritis and sclerosing keratitis all were observed in females in this present study.

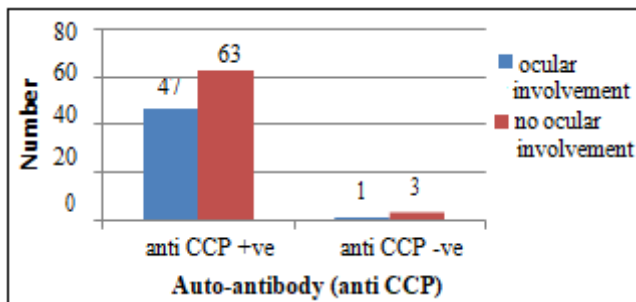


Figure 7: Role of Anti CCP Antibodies and Ocular Symptoms Typical of Rheumatoid Arthritis

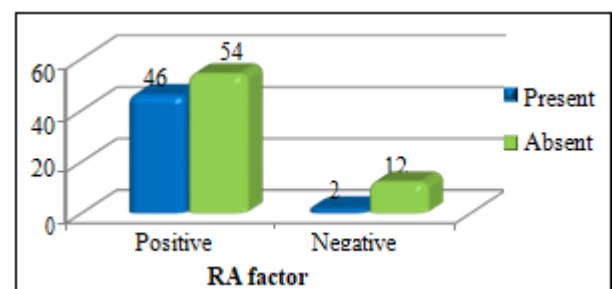


Figure 8: Graph Shows Relationship between RA Factor and Ocular Manifestation

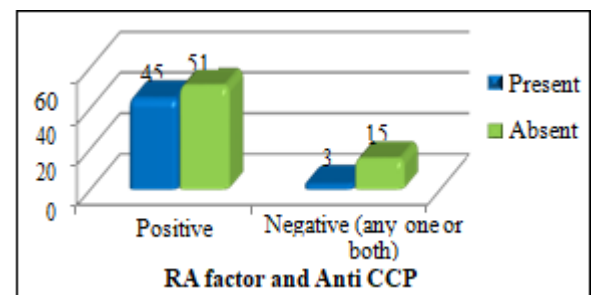


Figure 9: Shows relationship of ocular manifestation in RA with both RA factor and anti CCP antibody

FIGURE 7, 8 and 9 shows relationship of ocular manifestation with presence and absence of Anti CCP antibody and RA factor antibody

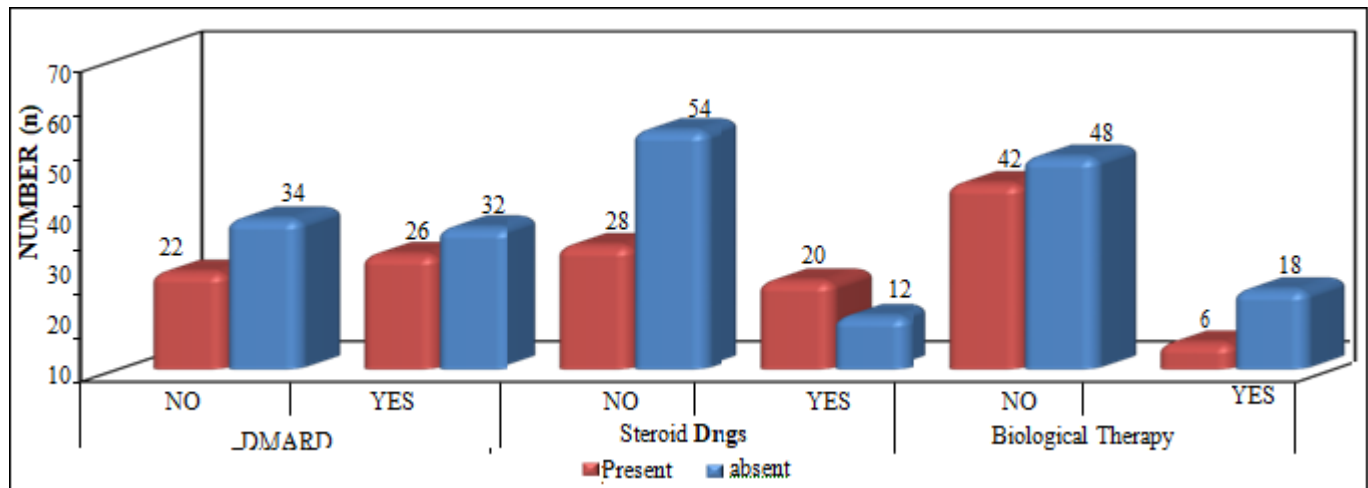


Figure 10: Different Drugs and Ocular Manifestations in RA Patients

FIGURE 10 shows a significant relationship between the use of steroid and ocular manifestation showed by p value of 0.00586. But there was no significant relationship in the DMARD alone group and the Biological therapy group of patients.

Age Distribution

Discussion

Maximum in of 40 -<50 years age grp i.e. 17 (35.41 %) followed by 30 -<40 years i.e. 13 (27.08%). Similar result was seen in study done by Zlatanovic et al. [3]

Sex Wise Distribution

38 (43.18%) of the female group had ocular manifestation unlike only 10 (38.46 %) of the male group with M : F ratio 1:3.8 and this goes with the study done by Zlatanovic et al and Markovitz E et al. [3], [4]

Duration of Rheumatoid Arthritis Disease

Ocular manifestation was seen in patients with >10 years of duration 9 (81.81 %) out of 11 patients so there is a relation with duration of the disease as observed in study done by Ammapati et al. [5]

Laterity of Ocular Involvement

Out of 48 patients with ocular manifestations 35 (72.92 %) had bilateral ocular involvement Reddy et al also found bilateral involvement more i.e. in 66 % than unilateral involvement. [6]

Ocular manifestations in Rheumatoid Arthritis Patients

- Present literature have documented incidence of ocular manifestations among RA patients ranging from 25 % to 39 %.
- Out of the 114 diagnosed cases of RA in the present study ocular
- Manifestation was found in 48 (42.10 %)
- Maximum in the age group of 40-<50 years but the more severe ocular manifestation like PUK, Scleritis and Sclerosing keratitis were found in the younger age group i.e. 30- <40 years

Study	Year	Ocular manifestation in RA patients (%)
Reddy et al ⁶	1977	39
Bhadoria et al ⁷	1989	21
Zlatanovic G ³	2010	27.2
Kumar et al ⁸	2013	66
Present study	2017-2018	42.10

Dry Eye

- Dry eye is reported as the most common ocular manifestation in RA in literature till date.
- It is thought to be caused by infiltration of lacrimal gland by T and B lymphocytes, leading to secondary atrophy of the gland and consequent decreasing production of tears
- In this study we found dry eye to be present in 31.5 % of the total 114 cases.

Studies	Year	Percentage of patients with dry eye (%)
Reddy et al ⁶	1977	29
Bhadoria et al ⁷	1989	17.7
Bettero et al ⁹	2008	29.8
Zlatanovic et al ³	2010	17.65
Markovitz et al ⁴	2011	85
Ammapati et al ⁵	2015	28
Present study	2017-2018	31.57

Sjogren's Syndrome

- A young female patient with Sjogren's syndrome was also recorded in our study. Bettero et al reported it in 12.1 % of population with RA. [9]

Cataract

- Prempal Kaur et al found it in 5 (3.5 %) patients and all as a complication clearly related to steroid therapy. [10] Ammapati et al and Reddy et al also reported it in their study. [5,6]
- In this study 6(5.26 %) patients presented with cataract. All of them were on steroids for RA.

Keratitis

- The peripheral cornea because of its close proximity to the limbal conjunctiva can subject to inflammatory response.
- As regards to corneal involvement, PUK was diagnosed in 2 (1.75%), filamentary keratitis in 1 (0.87%) similar to

Zlatanovic G [3] study but much lesser than in study by Lee et al.[11]

- A case of Sclerosing keratitis (SK) was observed in this study. Tong L et al. reported that tissue damage in sight threatening complications like scleritis, PUK, SK in RA is auto immune mediated.^[12]
- Squirrell et al concluded that RA associated PUK often has a poor visual outcome and may herald the transformation of a patient's RA into the systemic vasculitic phase^[13]

Uveitis

- Reddy et al and Ciurtin C et al observed anterior uveitis as a common finding in
- RA but in this study only 2 cases presented with it.^[6,14]
- Kumar et al determined 20 % of uveitis in their study on RA patients much higher than the present study.^[8]
- This may be due to smaller number of patients in this study but in RA, uveitis is rare, it can occur as a complication of scleritis in about 42 % especially with anterior scleritis.

Episcleritis and Scleritis

- McGavin et al studied 4,210 patients with RA and observed episcleritis in 0.17% and scleritis in 0.67% patients.[15] Reddy et al[6] reported episcleritis in 1% patients and Bhadoria et al in 0.93% patients.^[7]
- These studies were similar to the present study with episcleritis in 1.75 % and scleritis in 0.87 % cases but lesser than that reported by Ammapati et al [5] in 2015 (3% episcleritis and 2% scleritis) and Zlatanović G [3] in 2010 (5% episcleritis and 2% scleritis)

Relation of Ocular Manifestation with Disease Activity

- This study revealed that there was no statistically significant relationship with severity of the RA disease, estimated by DAS 28 score which is comparable to Zakeri et al study.^[16]
- While Gilbo et al in 2001 concluded that dry eye syndrome in RA patients reflect more disease activity and a relationship with ESR and number of painful joints^[17]

Relation of ocular manifestation with anti CCP and RA factor

- Ocular manifestations in Anti CCP +ve patients 47(42.72 %), RA factor +ve patients 46(46 %) and in both Antibody +ve patients 45(46.87 %).
- A significant co relation between the presence of both the antibodies and absence of both / any one shown by the p value - 0.0172.
- Pulido JS et al concluded that patients with both antibodies positive had more and worse ocular disease than sero negatives patients.^[18]
- Ammapati Paul et al also found strong association between Anti CCP antibodies and ocular manifestation in RA patients.^[5]

Relation of ocular manifestation with DMARD, and biological drugs

- Ocular manifestations were found in those patients on additional steroids with a significant correlation shown by p value i.e. 0.00586.

- Similar results were found in study Prempal Kaur et al.^[10]
- No such relationship was seen with the use of DMARD and Biological agents while Zlatanovic et al.^[3] study showed that DMARDs are necessary to improve tear production and to resolve severe ocular complications in RA patients.

5. Conclusion

- RA is one of the most common autoimmune diseases causing ocular manifestation causing varying degrees of ocular morbidity.
- In this study, 42.10 % cases had ocular manifestation with M: F ratio being 1:3.8 and the most common ocular manifestation was dry eye (31.57 %) followed by cataract (5.26 %).
- There were varied ocular presentations of RA and some were even sight threatening. So, every case need early and proper evaluation.
- Duration of the disease and steroid use were found to be major risk factors but the disease activity had no role
- Ocular manifestation in relationship to antibodies**(Anti CCP and RA factor)
 - Significant with the presence / absence of any one or/ and both the antibodies
 - Manifestations are more when both the antibodies are positive
 - Both antibody positive patients had more severe ocular involvement.
- So, collaborative efforts between the ophthalmologists and rheumatologists is important to effectively manage to prevent permanent irreparable loss of vision in RA patients.

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