Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/g6508655

OCULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS – A CASE SERIES ANALYSIS

Dr. K. Roshitha Gagarin[1], Dr. M. Krithika[2*], Dr. T. Prem Sai[3], Dr. C. M. Kalavathy[4]

[1]Junior resident, Department of Ophthalmology, Tagore Medical College, Chennai
[2*]Assistant Professor, Department of Ophthalmology, Tagore Medical College, Chennai
[3]Assistant Professor, Department of Ophthalmology, Tagore Medical College, Chennai
[4]Professor, Head of Department, Department of Ophthalmology, Tagore Medical College, Chennai

***Corresponding author:** Dr. M. Krithika
*Assistant Professor, Department of Ophthalmology, Tagore Medical College, Chennai, Tamil Nadu, India, Email ID: Krits7171122@gmail.com

Abstract
Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder primarily affecting joints,but it can also involve extra-articular manifestations, including cardiac, eyes, skin, pulmonary, renal, skeletal. Aim of our study is to evaluate the ocular manifestations of rheumatoid arthritis. The cases included patients of varying diseases, duration and severity, exhibiting ocular symptoms. The results show that dry eye syndrome being most common, followed by episcleritis and scleritis, peripheral ulcerative keratitis, anterior necrotizing scleritis without inflammation (scleromalacia perforans) and complications occurring post treatment with oral steroids. This caseseries presents an analysis of ocular manifestations in patients with RA, highlighting the diverse range of ocular complications associated with disease. This gives the importance of regular ophthalmic evaluations in RA patients to detect and manage ocular complications early, providing better outcomes and improving quality of life.

Keywords: Rheumatoid arthritis; ocular manifestations; keratoconjunctivitis sicca; dry eyes; peripheral ulcerative keratitis; episcleritis; scleritis; steroid induced cataract; hydroxychloroquine induced maculopathy; Rheumatoid factor; Schirmer's test

INTRODUCTION

Rheumatoid arthritis is the most common, chronic, progressive, systemic inflammatory disease of unknown aetiopathogenesis causing symmetrical destructive polyarthritiswith multiple articular and extra-articular manifestations including skin, heart, pulmonary, renal, skeletal, circulatory and ocular systems. [(1) (2)] It is antibody such as anti-cyclic citrullinated peptide(anti-CCP) mediated autoimmune disease that primarily affects small joints. [(3)] It affects up to 1- 3% of global population, with middle aged female preponderance with HLA-DR 4 association. [4, 5]

Ocular manifestations include keratoconjunctivitis sicca (KCS) (dry eye syndrome), scleritis, episcleritis, corneal changes like acute corneal melting, stromal keratitis, corneal thinning, peripheral ulcerative keratitis (PUK) & retinal vasculitis. Among all these dry eyes is the first most common ocular manifestation, second being the scleritis and episcleritis.
KCS being is the most associated ocular manifestation seen is caused due to dysfunction of lacrimal

gland, accessory lacrimal gland, meibomian gland and thereby decreasingthe tear production leading to foreign body sensation, grittiness. [5] Episcleritis being the second common manifestation occurs due to the inflammation of episcleral vessels which is self-limitingand recurrent condition, causing acute redness, photophobia and discomfort. Seen in 4%-10% of RA patients, is of two forms such as simple and nodular. Among the two forms, simple is more common compared to nodular. [6] Scleritis is the inflammation of the sclera characterized by pain,discomfort, occurring in two forms such as anterior and posterior. Anterior is again subdivided into diffuse, nodular, necrotizing with inflammation and necrotizing without inflammation (scleromalacia perforans). Posterior scleritis which is not visible clinically, requires an ultrasonography, in which a characteristic T-sign due to the fluid under Tenon's capsule is seen. Difference between episcleritis and scleritis is done by instillation of 2.5% phenylephrine leadingto the blanching of superficial episcleral vessels seen in episcleritis and the deeper scleral vesselsdoesn't blanch in case of scleritis. [7] PUK is inflammation of the peripheral cornea which is a destructive inflammatory condition in which cornea meltdown develops in juxta-limbal location,potentially leading to corneal perforation causing loss of vision, which is characterized by pain, tearing, blurring of vision. [8]

Rheumatoid factor (RF), anti-CCP antibody or both may be seen in 50-80% approximately.Patients with RA may also have positive ANA antibody, and raised CRP and ESR values which are helpful in diagnosis of RA. [9]

Management of RA is by NSAIDS such as ibuprofen naproxen, Glucocorticoids (GCS) such as prednisolone, dexamethasone, Disease-modifying Antirheumatic drugs (DMARDS) which include methotrexate (MTX), hydroxychloroquine (HCQ), sulfasalazine. [10] Prolonged treatment with steroids and HCQ also causes ocular toxicity in the form of **Bull's eye** maculopathy, lens opacities [11]

This study was done to report the ocular manifestations of nine patients with rheumatoid arthritis as a case series.

METHODOLOGY:

This is a cross-sectional observational case series of nine patients who presented to the Department of Ophthalmology in a tertiary care hospital in southern India between May 2024 andAugust 2024 with signs and symptoms of various ocular lesions. A detailed ocular evaluation including visual acuity by Snellen's, intraocular pressure (IOP) by Non-contact tonometer (NCT), slit lamp bio microscopy of anterior segment and dry evaluation was done which includes Schirmer's 1 test without anaesthesia and Tear Fim Breakup Time (TBUT) by fluorescein stain and fundus examination by indirect ophthalmoscopy was done.

Case SeriesCase 1

A 30-year-old female presented with redness in left eye in the past 2 weeks. She is a known case of rheumatoid arthritis for 6 months and on regular medication. On examination, her visual acuityis 6/6 in both eyes. On slit lamp examination, sectoral congestion with dilated episcleral vessels with nodule present nasally in the left eye. (Fig 1) Right eye was normal. On investigations, RF ispositive with raised CRP with normal ESR and been diagnosed with Left eye Nodular Episcleritis and was commenced on Left eye topical Loteprednol Etabonate twice daily for a week andfollowed by tapering dose.

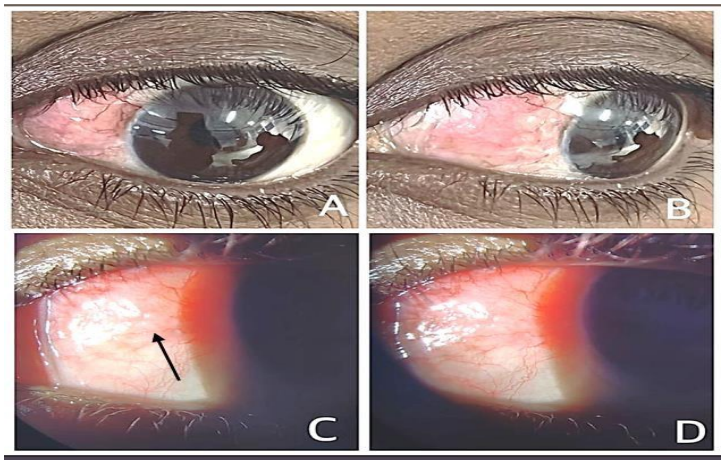

Fig 1: (A) and (B) showing sectoral congestion nasally in left eye; (C) and (D) depictsslit image of the nodule.

Case 2

A 70-year-old female presented with complaints of diminished vision in both eyes, more in right eye from the past 1 year. She is a known case of rheumatoid arthritis for past 10 years and is on oral hydroxychloroquine (HCQ) 200mg and oral prednisolone 5mg, with Hallux valgus (Fig 2C),having RF positive and raised CRP. Her best corrected visual acuity was CFCF and 6/36 in right and left eyes respectively. Her IOP was normal in both eyes. On evaluation of anterior segment, lens showed Right eye Mature cataract and Left eye NS III. B-Scan was done and was normal in both eyes. On dry eye evaluation, her Schirmer's test 1 and TBUT were abnormal in both eyes (Fig 2A & 2B) suggestive of Moderate Dry eyes in both eyes. Patient underwent cataract surgery in Right eye with post op vision 6/9 and started her on topical steroid with tapering doses postoperatively and artificial tear substitutes in both eyes for dry eye.

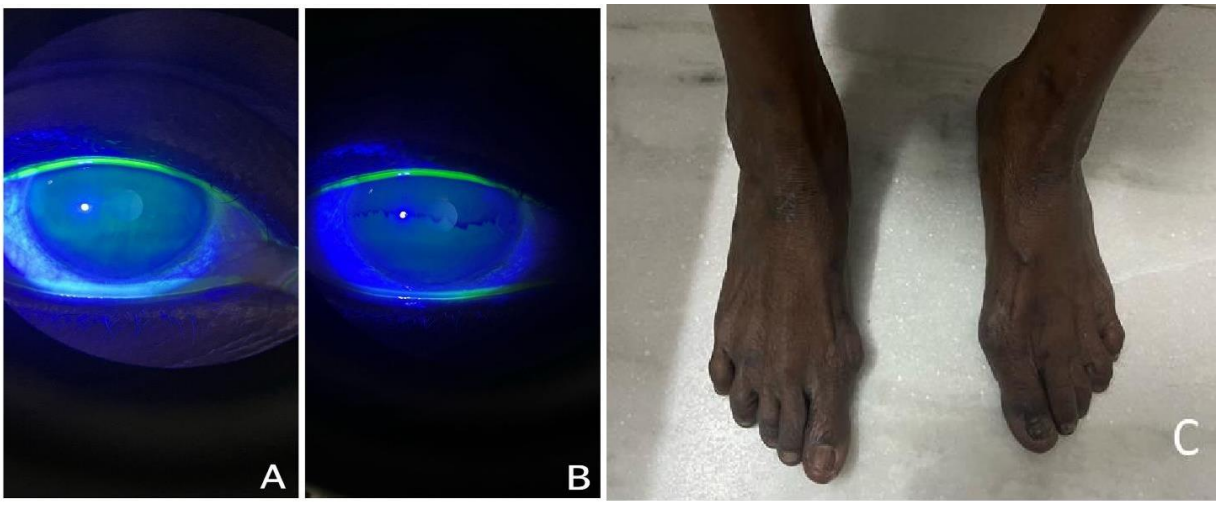

Fig 2: (A) TBUT test at the beginning; (B) appearance of dry spot at 6 Sec; (C) hallux valgus inboth legs.

Case 3

A 62-year-old female presented with repeated episodes of redness in the right eye for the past 6 months. Her best corrected visual acuity is 6/36 and 6/9 in right and left eyes respectively. Known case of RA for the past 10 years and was on regular medication. On slit lamp evaluation, scleral thinning is seen with clear cornea, festooned pupil and complicated cataract in right eye (Fig 3) indicative of old uveitis and left eye is pseudophakic. Patient also gives history of joint pains and back pains and on investigations RF was positive with raised ESR & CRP. Diagnosed as Right eye Scleromalacia Perforans and referred to Rheumatologist for further evaluation.

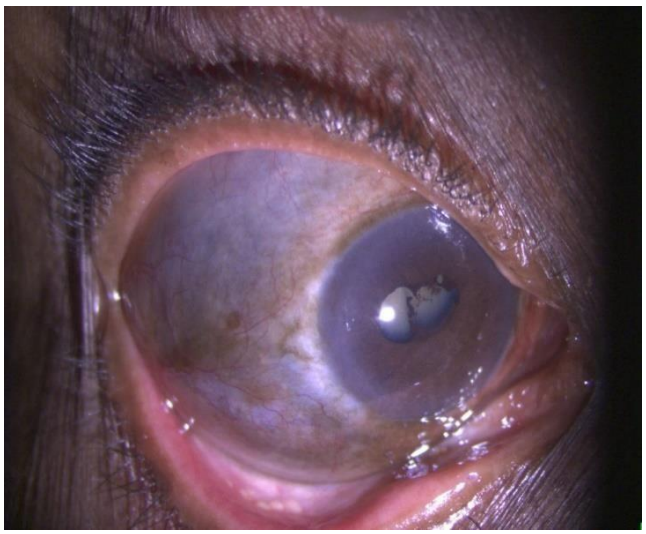

Fig 3: Right eye showing scleral thinning with clear cornea with festooned pupil.

Case 4

A 23-year-old female presented with 4 days history of intolerable pain and redness in left eye. Similar episodes of redness in left eye were seen 3 months ago which resolved on using topical eyedrops. Known case of rheumatoid arthritis. Her best corrected visual acuity was 6/6 and 6/12 in right and left eyes respectively. On slit lamp evaluation, left eye showed temporal congestion. (Fig 4A) On dilated fundus examination, left eye fundus showed Internal Limiting Membrane (ILM) folds (Fig 4C) and Right eye was within normal limits. B-scan of Left eye showed T-sign (Fig 4B) & OCT macula done shows retinal folds with normal foveal contour, (Fig 4D) suggestiveof Left eye Posterior Scleritis. Started her on Left eye topical Prednisolone acetate 1% 4 times a day for a week with tapering doses and oral steroids.

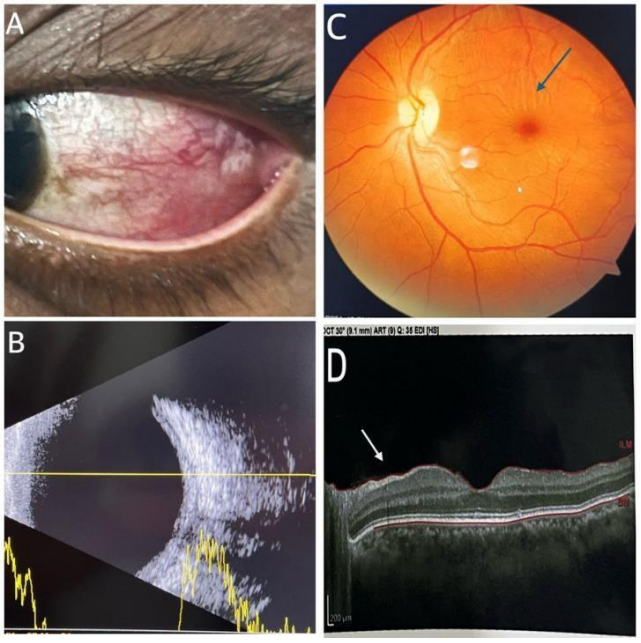

Fig 4 (A) shows temporal congestion; (B) shows T sign of left eye; (C) fundus image of left eye with ILM folds radiating from fovea; (D) OCT of left eye showing retinal folds

Case 5

A 42-year-old male presented with recurrent redness in right eye associated with mild pain, photophobia, watering for the past 2 days. His visual acuity was 6/6 in both eyes. Newly diagnosed Rheumatoid arthritis with RF positive and raised CRP. On evaluation, diffuse congestion with

dilated episcleral vessels is seen in right eye. (Fig 5) Fundus examination is normal in both eyes. Diagnosed as Right Eye Simple Episcleritis and started him on topical Flurometholone and Tobramycin eyedrops 4 times a day for 5 days in tapering doses. Rheumatology was consulted and was commenced on oral prednisolone 5mg.

Fig 5: Right eye showing engorged episcleral vessels

Case 6

A 59-year-old female presented with history of diminution of vision in both eyes for past 2 years. Her best corrected visual acuity was 6/12 and 6/9 in right and left eyes respectively. Known case of type 2 diabetes mellites for past 1 year and on regular medication and rheumatoid arthritis for the past 6 years and on regular oral hydroxychloroquine (HCQ) 200mg. History of having morning stiffness and joints paints in metacarpophalangeal joints with RF positive with raised ESR. On evaluation, her anterior segment was within normal limits. Both eyes foveal reflex was dull. On further evaluation OCT showed foveal thinning with central foveal thickness of 196mm and 206mm in right and left respectively (Fig 6) suggestive of HCQ induced maculopathy. Rheumatologist consultation is advised for alternate treatment due to HCQ induced maculopathy.

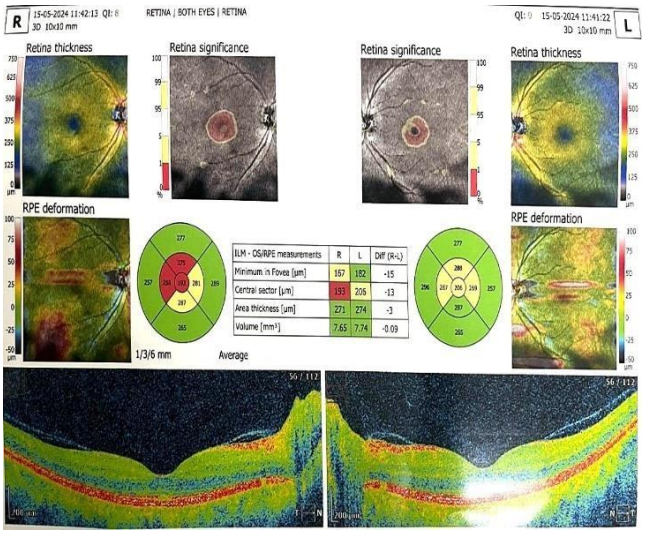

Fig 6: Both eye OCT RNFL showing central foveal thinning

Case 7

A 45-year-old female presented with complaints of diminution of vision in both eyes, for the past 3 years. Her best corrected visual acuity was 6/18 and 6/36 in right and left eye respectively. Known case of rheumatoid arthritis for the past 20 years and on oral chloroquine 200mg and oral prednisolone 5mg once daily. On slit lamp examination, lens shows steroid induced posterior subcapsular cataract (PSC) (Fig 7) in both eyes (LE>RE). She is advised to undergo both eyes cataract surgery post rheumatologist clearance.

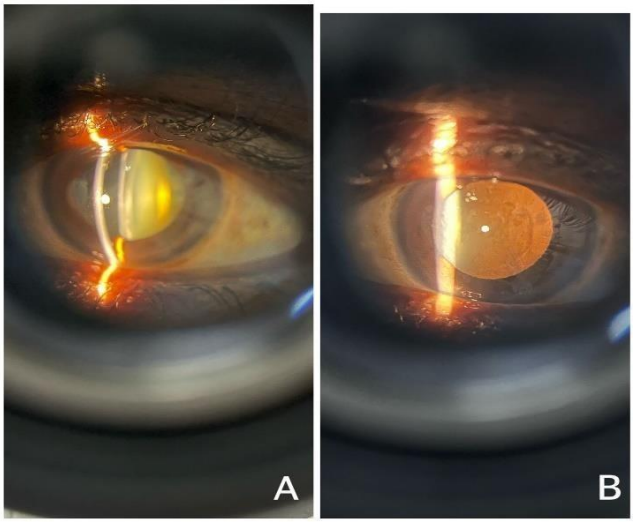

Fig 7: Slit lamp image showing Left eye Posterior subcapsular cataract

Case 8

A 35-year-old female came with complaints of foreign body sensation, grittiness in both eyes in the past 6 months. She is a known case of rheumatoid arthritis since 1&1/2 years with no systemic signs and using over the counter medications on and off. On examination, her best corrected visual acuity was 6/9 in both eyes. On slit lamp examination, her cornea showed diffuse superficial punctate keratitis (Fig 8A) on staining with fluorescein in both eyes and rest of the anterior segment was within normal limits. Based on her symptoms, dry evaluation was done consisting of Schirmer's test 1 showing Both eyes <5mm in 5 min and TBUT showed Right eye 2 Sec and Left eye 6 Sec. (Fig 8B) Undilated fundus is seen and normal in both eyes. On investigations, RF factor was positive and raised ESR with normal C-Reactive protein, was diagnosed with Both eyes Severe Dry Eyes and been treated with topical 0.5% Carboxymethyl Cellulose 4 times a day and Both eye topical Hydroxypropyl methylcellulose eye ointment at night for a month. Referred to Rheumatologist for further evaluation.

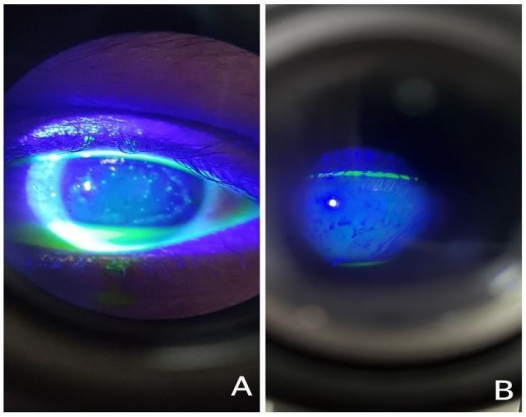

Fig 8: (A) showing superficial punctate keratitis on cornea stained with fluorescein stain seen under cobalt blue light; (B) showing appearance of dry sports at 6sec

Case 9

A 70-year-old female presented to the OPD with a history of pain, photophobia, redness, occasional watering in both eye for the past 15 days. Known case of rheumatoid arthritis for the past 14 years, having metacarpophalangeal joint pains and pain in knee joints & was on medication. History of usage of over-the-counter topical eyedrops for 7 days and found no change in symptoms. Her best corrected visual acuity was 6/36 and 6/24 in right and left eye respectively. On slit lamp evaluation, both eyes showed diffuse congestion with peripheral corneal thinning and superficial vascularization

seen temporally (Fig 9) suggestive of Both eyes Peripheral Ulcerative Keratitis. Started her on topical steroids and antibiotics and asked to come for follow up.

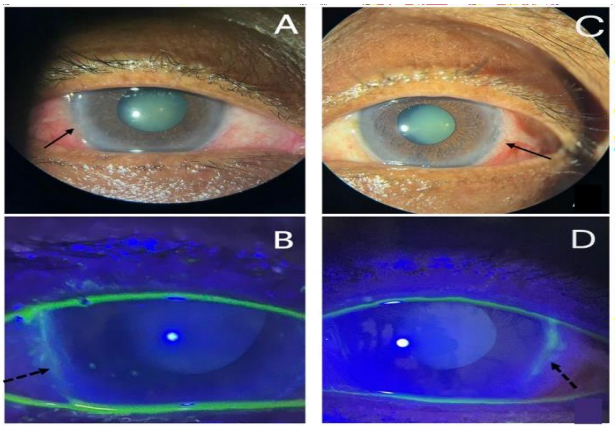

Fig 9: (A) & (B) showing temporal corneal thinning at 9 O' clock position in Right eye before andafter staining with fluorescein depicted by arrow and dotted arrow respectively; (C) & (D) showing temporal corneal thinning at 3 O' clock position in Left eye before and after staining with fluorescein depicted by arrow and dotted arrow respectively.

Among the nine cases, we have 8 females and 1 male with 2 cases in 3rd decade, 1 in 4th decade,2 in 5th decade, 1 in 6th decade and 3 cases in 7th decade. We have 2 cases of episcleritis, one being simple and the other is nodular, 2 cases of scleritis, one is scleromalacia perforans and the other is posterior scleritis, 2 cases of dry eyes, others are the PUK, steroid induced cataract, HCQ induced maculopathy shown in Table 1. As all these patients are known cases of RA but case1, 4, and 8 donot have any systemic signs. Dry eye severity was graded as mild, moderate, severe based on DryEyes Workshop II (DEWS II) on Schirmer's test and TBUT. Rheumatologist consultation is advised accordingly. Line of management depends on the severity of symptoms, duration of the symptoms and surgery in case of cataract and rheumatologist consultation accordingly.

Table 1: Demographics, Clinical Presentations, Lab Investigations of patients in our case series

Case No	Age gender	Symptoms	Duration of symptom	Ophthalmic Diagnosis	Ocular Diagnostic Test		Systemic Signs	Systemic Diagnostic Test		
					Schirmer's I (5 mins)	TBUT (10 sec)		RF	CRP	ESR
1	30/F	Redness in LE	2 weeks	LE Nodular Episcleritis	RE 30 mm LE 35 mm	BE 12 Sec	NIL	15 IU/ML	10 mg/L	13 mm/hr
2	70/F	Diminution of vision in BE	1 year	RE Mature Cataract LE NS III	RE 8 mm LE 7 mm	BE 6 Sec	Hallux valgus in both big toes	29 IU/ML	7.5 mg/L	15 mm/hr
3	62/F	Redness in RE	6 months	RE Scleromalacia Perforans	-	-	Joint pains and back pain	21 IU/ML	8.2 mg/L	33 mm/hr
4	23/F	Redness, Pain in LE	4 days	LE Posterior Scleritis	BE 35 mm	BE 17 Sec	NIL	10 IU/ML	3.57mg/L	25 mm/hr
5	42/M	Recurrent Redness in RE	2 days	RE Simple Episcleritis	BE 35 mm	RE 15 Sec LE 12 Sec	Pain in small joints	35 IU/ML	9 mg/L	13 mm/hr
6	59/F	Diminution of vision in BE	2 years	HCQ Induced maculopathy	RE 20 mm LE 17 mm	BE 11 Sec	Joint pains in metacarpophalageal joints, Morning stiffness	29 IU/ML	3.1 mg/mL	31 mm/hr
7	45/F	Diminution of vision in BE, LE>RE	3 years	Steroid Induced PSC	RE 33 mm	RE 12 Sec LE 15 Sec	Joint pains in wrist and knee	31 IU/ML	9.2 mg/mL	19 mm/hr
8	35/F	Foreign body sensation, grittiness in BE	6 months	BE Severe Dry Eyes	BE <5 mm	RE 2 Sec LE 6 Sec	NIL	23 IU/ML	2.57 mg/mL	34 mm/hr
9	70/F	Pain, redness, photophobia, occasional watering in BE	15 days	BE PUK	-	-	Metacarpophalangeal joint pains & knee joint pains	34 IU/ML	11.52 mg/mL	18 mm/hr

*RE: Right Eye, LE: Left Eye, BE: Both Eyes, PSC: Posterior Subcapscular Cataract, PUK: Peripheral Ulcerative Keratitis, RF: Rheumatoid Factor, CRP: C-Reactive Protein ESR: Erythrocyte Sedimentation Rate

Discussion

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder primarily affecting the joints and the extra articular manifestations such as cardiac, pleuropulmonary, skin, eye, renal, etc. The ocular manifestations include keratoconjunctivitis sicca, episcleritis, scleritis, PUK, uveitis, retinal vasculitis. In a study done by M Gerosa et al [12] showed that female have 3 times higher risk in developing RA compared to males. In our series also, we have 8:1 of female: male ratio.

Several studies have reported the most common ocular manifestation of RA as keratoconjunctivitis sicca by Dammacco.R et al,[13] Dewi Gullelec et al,[14] Swathi singh et al,[15] SC Reddy et al [16] occurring due to the infiltration of lacrimal gland by T and B lymphocytes thereby decreasing the tear production. Thus, increasing the need of supplementation of lubricants to improve the quality of life. Episcleritis and scleritis being the second most common association found in studies done by Dewi Gullelec et al,[14] M S de la Maza et al, [17] concluding that scleritis is significantly associated with RA. Scleromalacia perforans, one of the types of anterior necrotizing scleritis without inflammation is seen almost after 10 years of history of RA as reported by Wu et al. [18] Thus, an appropriate and timely management is required as it is a potentially blinding condition. Long term oral therapy of steroids has shown the development of cataracts found by C.Furst et al,[19] M S de la Maza et al, [17] giving the importance of timely ocular examination. Mainstay of treatment being the DMARDS in RA have complications of developing changes like bull's eye maculopathy, foveal thinning reported in studies done by O Oderinlo et al [20] and ZS Hasan et al [21], foveal thinning shown in optical coherence tomography (OCT),other research must be done further for earlier detection of their toxicity and thereby definitely requiring the alternative management for RA. Table 2 shows the ocular manifestations of various studies.

Table 2: Frequency of ocular manifestations in RA in various studies

Author (year)	Sample size	Keratoconjunctivitis sicca	Episcleritis	Scleritis	PUK	PSC
Damacco.R[13] (2022)	489	29	6	5	2	NA
Dewi Guellec[14] (2020)	798	28	NA	NA	NA	NA
Swathi singh[15] (2022)	634	71	1	1.5	NA	NA
SC Reddy[16] (1977)	100	29	1	NA	NA	9
M S de la Maza[17] (2012)	500 Scleritis 85 Episcleritis	NA	3.5% had RA	6.4% had RA	NA	NA
C. Fürst[19] (1966)	113	NA	NA	NA	NA	6

PUK: Peripheral ulcerative keratitis, PSC: Posterior subcapsular cataract, NA: Not applicable

CONCLUSION

Ocular involvement in RA is common and can vary from mild dry eye to severe, vision threatening conditions. It Includes keratoconjunctivitis sicca, episcleritis, scleritis, corneal changes like corneal thinning, peripheral ulcerative keratitis. Women were more commonly affected. The longer the duration of RA the larger the number of extra ocular manifestations. Early signs of HCQ

maculopathy can be detected by OCT, thus ophthalmologists play an important role in RA patients, requiring OCT as a main tool to detect early HCQ toxicity. It is important to have regular ophthalmic examination. Our study represents the understanding of consequences of RA in eye and thereby highlighting need for regular eye checkup and the timely management in patients of RA.

References

1. Zlatanović G, Veselinovic D, Cekic S, Zivkovic M, Dordevic-Jocic J, Zlatanovic M. Ocular manifestations of rheumatoid arthritis-different forms and frequency. Bosn J Basic Med Sci 2010;10:323-7
2. Ravulaparthi, Gayathri; Bandla, Bhavagna; Visala, N Venkata[1]. Ocular disease as the presenting sign of rheumatoid arthritis – An observational case series. Indian Journal of Ophthalmology 71(4):p 1647-1651, April 2023. | DOI: 10.4103/IJO.IJO_2765-22
3. Vignesh APP, & Srinivasan R. (2015). Ocular manifestations of rheumatoid arthritis and their correlation with anti-cyclic citrullinated peptide antibodies. Clin Ophthalmol 2015;9:393-7.
4. Grassi W, De Angelis R, Lamanna G, Cervini C. The clinical features of rheumatoid arthritis. Eur J Radiol. 1998 May; 27 Suppl 1:S18-24. doi: 10.1016/s0720-048x(98)00038-2.
5. Z.H. Eldaly et al./ The Egyptian Rheumatologist 42 (2020)
6. Bhamra MS, Gondal I, Amarnani A, Betesh S, Zhyvotovska A, et al. (2019) Ocular Manifestations of Rheumatoid Arthritis: Implications of Recent Clinical Trails. Int J Clin Res Trails 4: 139. doi: http://doi.org?10.153344/2456-8007/2019/139
7. Cunningham ET Jr, McCluskey P, Pavesio C, Wakefield D, Zierhut M. Scleritis. Ocul Immunol Inflamm. 2016;24 (1):2-5. doi: 10.3109/09273948.2016.1136190.
8. Gupta Y, Kishore A, Kumari P, Balakrishnan N, Lomi N, Gupta N, Vanathi M, Tandon R. Peripheral ulcerative keratitis. Surv Ophthalmol. 2021 Nov-Dec;66(6):977-998. doi: 10.1016/j.survophthal.2021.02.013.
9. Aletaha D, Smolen JS. Diagnosis and Management of Rheumatoid Arthritis: A Review. JAMA. 2018 Oct 2;320(13):1360-1372. doi: 10.1001/jama.2018.13103.
10. Radu A-F, Bungau SG. Management of Rheumatoid Arthritis: An overview. Cells. 2021; 10(11):2857. http://doi/org/10.3390/cells10112857
11. Jaichander, Roshan Christina; Thomas, Reji Koshy; Shobha, Vineeta[1]. A study to determine the effect of hydroxychloroquine (HCQ) on central corneal thickness (CCT) in patients with rheumatoid arthritis (RA). Indian Journal of Ophthalmology 72(2):p 270-274, February 2024. | DOI: 10.4103/IJO.IJO_3052_22
12. Gerosa M, De Angelis V,Riboldi P, Meroni PL. Rheumatoid arthritis: a female challenge. Womens Health (Lond). 2008 Mar;4(2):195-201. doi: 10.2217/17455057.4.2.195.
13. Dammacco R, Guerriero S, Alessio G, Dammacco F. Natural and iatrogenic ocular manifestations of rheumatoid arthritis: A systematic review. Int Ophthalmol 2022;42:689-711.
14. Guellec D, Cozien S, Ruyssen-Witrand A, Dieude P, Saraux A. Prevalence and clinical significance of extra-articular manifestations at diagnosis in the ESPOIR cohoty with recent-onsetarthritis. Semin Arthritis Rheum 2020;50:409-13.
15. Singh S, Das AV, Basu S. Ocular involvement in Sjogren syndrome: Risk factors for severe visual impairment and vision-threatening corneal complications. Am J Ophthalmol 2021;225:11-7.
16. Reddy SC, Gupta SD, Jain IS, Deodhar SD. Ocular manifestations of rheumatoid arthritis. Indian J Ophthalmol 1977;25:20.
17. Sainz de la Maza M, Foster CS, Jabbur NS. Scleritis associated with systemic vasculitis diseases. Ophthalmology 1995; 102:687-92.
18. Wu C, Yu H, Yen J, Tsai W, Liu H. Rare extra-articular manifestation of rheumatoid arthritis: scleromalacia perforans. Kaohsiung J Med Sci. 2005;21:233-5.
19. Fürst C, Smiley WK, Ansell BM. Steroid cataract. Ann Rheum Dis. 1966 Jul;25(4):364-8. doi: 10.1136/ard.25.4.364.
20. Oderinlo O, Bogunjoko T, Hassan AO, Idris O,Dalley A, Oshunkoya L, Odubela T. Normal

central foveal thickness in a thousand eyes of healthy patients in sub Saharan Africa using fourierdomain optical coherence tomography. Niger J Clin Pract. 2023 Mar;26(3):331-335. doi: 10.4103/njcp.njcp_318_22.

21. Hasan, Z., Mohammed, S., Abdelmohsen, F. (2019). Ocular Manifestations of Rheumatoid Arthritis and Complications of Hydroxychloroquine Treatment. The Egyptian Journal of HospitalMedicine, 77(3), 5148-5154. doi: 10.21608/ejhm.2019.52404.