



BURDEN OF OCULAR MANIFESTATIONS IN PATIENTS OF RHEUMATOID ARTHRITIS IN TERTIARY CARE CENTRE OF KUMAON REGION , UTTARAKHAND.

Ophthalmology

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ABSTRACT

Rheumatoid arthritis is a chronic systemic inflammatory disease marked by a symmetric, peripheral polyarthritis. It is associated with various extra-articular organ manifestations including subcutaneous nodules, pericarditis, major cutaneous vasculitis, ocular manifestations, hematological abnormalities etc. The well documented ocular manifestations of RA include kerato-conjunctivitis sicca , anterior uveitis, episcleritis, scleritis, scleromalacia perforans, peripheral ulcerative keratitis, corneal filamentary keratitis, retinal vasculitis. The Aim of our study was to identify the rheumatoid arthritis patients with ocular involvement presenting at tertiary care centre of Kumaon region of Uttarakhand. We examined 97 patients with diagnosis of RA. The ocular examination included; best corrected visual acuity, slit lamp examination, Schirmer's test, tear break-up time, indirect ophthalmoscopy and fundus photography in patients with retinal involvement. In this study, the most common manifestation associated with RA was keratoconjunctivitis sicca followed by filamentary keratitis (7.86%) and uveitis (7.86%), scleritis (5%), episcleritis (3%). The least common was panophthalmitis (0.1%). Ocular manifestation among RA patients was found to be very common, i.e. 91.75% (89 cases, out of which 62 were females).

KEYWORDS

Rheumatoid Arthritis, Keratoconjunctivitis Sicca, Retinal Vasculitis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease, marked by a symmetric, peripheral polyarthritis.¹ It has been associated with a number of extra-articular organ manifestations, such as fatigue, subcutaneous nodules, pericarditis, pleuritis, major cutaneous vasculitis, peripheral neuropathy, ocular manifestations, glomerulonephritis, hematological abnormalities.²⁻⁷ It is an autoimmune disorder but the etiology of this disease is still unknown.^{5,6,8-10}

Rheumatoid arthritis affects middle age women three times more often than the men in a percentage of 0.5% - 2% of the general population.

The well documented ocular manifestations of RA include keratoconjunctivitis sicca (dry eye syndrome), anterior uveitis, episcleritis (episcleral nodulosis), scleritis, scleromalacia perforans, peripheral ulcerative keratitis, corneal filamentary keratitis.¹² There are few rare complications associated with RA, such as, granular opacities with peripheral vascularisation of corneal stroma,¹³ marginal furrows of cornea,¹⁴ choroiditis,¹⁵ optic neuritis,^{16,17} disc and macular edema due to posterior scleritis, retinal vasculitis,^{6,18,19} secondary retinal detachment.²⁰

Keratoconjunctivitis sicca (dry eye disease) , the most commonly found ocular sign in the patients of RA. The associated symptoms and signs are foreign body sensation , conjunctival hyperaemia (red eye), burning sensation of the eyes , ocular pain and blurred vision.

Episcleritis is mild , self limiting , recurrent disease. Occurs in two forms: the simple episcleritis and the nodular episcleritis. The simple (diffuse) episcleritis is more common.

Scleritis is common in patients of rheumatoid arthritis. Scleritis may be diffuse, nodular, or necrotizing. Necrotizing scleritis with inflammation is the most destructive.^{22,26} In addition to the ocular findings in non-necrotizing scleritis, avascular areas of the sclera or necrosis may also be seen, surrounded by scleral edema. Scleritis has a gradual onset with a deep, boring pain which may radiate into cheek, eyebrows and temples, blurring vision and photophobia, tender nodules over the sclera.^{27,28} Corneal disease is most commonly associated with keratoconjunctivitis sicca but it can be an isolated complication.^{22,23} Keratitis symptoms include, pain with photophobia, foreign body sensation, redness , watering and decreased vision. Uveitis (anterior uveitis, intermediate uveitis, posterior uveitis chorioretinitis, panuveitis), these are the several forms of intra-ocular inflammation. Involvement

of retina primarily is very rare in patients of rheumatoid arthritis. However cases of retinal vasculitis, bilateral choroidal nodules and secondary retinal detachment have been reported earlier.²⁰

Aim of our study was to present the frequency of ocular involvement in cases of rheumatoid arthritis in kumaon region of Uttarakhand.

MATERIAL AND METHODS

97 consecutive patients of rheumatoid arthritis, irrespective of their age and sex, attending ophthalmology clinic of Sushila Tiwari Memorial Hospital , Haldwani, from November 2017- November 2019, were evaluated for various ocular lesions and a detailed history was taken and thorough ocular examination was done. The ocular examination included; best corrected visual acuity, slit lamp examination, Schirmer's test, tear break-up time, indirect ophthalmoscopy and fundus photography in patients with retinal involvement.

OBSERVATIONS AND RESULTS

In this cross sectional study of 97 patients , the cases were within the age range of 14-85 years. RA is found to be more common in females than males.

In our study of 97 patients 72 were females and 25 were males, i.e 74% and 26% respectively.

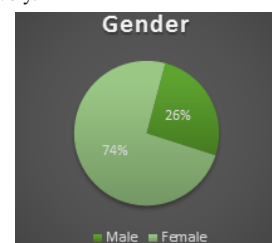


Figure 1. showing gender distribution in rheumatoid patients.

The maximum number of patients presented with ocular symptoms were in the group of 1-5 years of disease activity.

The most common systemic disease presenting in the RA patients was found to be Hypertension followed by Secondary Sjogren and Tuberculosis.

Table1 PRESENTING SYMPTOMS

	Symptoms	Male	Female	Total
1	No	2	11	13
2	Dryness, FBS	8	43	51
3	Redness	7	10	17
4	Diminision of vision	11	26	37
5	Photophobia	3	3	6
6	Discharge	2	0	2
7	Pain	5	8	13

In the above table, there were thirteen patients who had no ocular symptoms. According to the above mentioned data the most common symptoms with which the RA patients presented was Dryness and Foreign body sensation, followed by diminision of vision (DOV).

Table 2- OCULAR MANIFESTATIONS

	Ocular Manifestations	Male	Female	Total
1	Keratoconjunctivitis Sicca (KCS)	12	47	59
2	Peripheral Ulcerative Keratitis (PUK)	2	1	3
3	Filamentary keratitis	2	5	7
4	Episcleritis	0	3	3
5	Scleritis	3	2	5
6	Uveitis	5	2	7
7	Panophthalmitis	0	1	1
8	Retinal lesions	3	1	4
	Total	27	62	89

The table 2, showing the incidence of ocular manifestation among RA patients is very common, i.e. 91.75% (89 cases, out of which 62 were females,) out of which Keratoconjunctivitis Sicca (dry eye) is the most commonly found ocular manifestation (66.29%). The second most common ocular manifestations were found to be filamentary keratitis(7.86%) and uveitis (7.86%). The least common was panophthalmitis (0.1%). The incidence of retinal lesions was found to be 4% among the patients having ocular involvement.

DISCUSSION

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease, the cause of which has not been known. The extra-articular involvement of organs such as the skin, heart, lungs, and eyes is significant,^{3,4,5,18} and is present in 10-20% of patients, with more frequent association in seropositive patients.⁷

In the present study 97 patients with diagnosis of rheumatoid arthritis were included. Detailed ophthalmological examination under slit lamp biomicroscopy was done. The tests for dry eye disease were performed in all the patients with or without any presenting symptoms. The tests included schirmer's test and TBUT (flourescein tear film breakup time), and the values were noted for each test and then graded into severity of dry eyes using the TFOS-DEWS 2 (TFOS (Tear Film & Ocular Surface Society Dry Eye Workshop 2) classification system. The slit lamp examination of each patient was performed to look for entities like episcleritis, scleritis, keratitis etc, and fundus examination of every patient was done by direct and indirect ophthalmoscopy for any noted retinal and optic nerve involvement. The ocular lesions were noted and categorized according to the age of the patient , gender , treatment and duration of disease process, and also association with other systemic diseases.

A total of 72 females and 25 males were included in this study , thus a sex (F/M) ratio of 2.8:1 . Our study showed that majority of the patients with RA were in their fourth and fifth decades which comprised i.e. 43 cases (37 females and 6 males).

The most common symptoms with which the RA patients presented in the eye opd was Dryness and Foreign body sensation (51 cases). 13 out of 97 patients had no ocular symptom (13.4%).

In the present study the, the incidence of ocular manifestation among RA patients was found to be very common, i.e. 91.75% (89 cases, out of which 62 were females). In the study by Charanya et al , it was found to be 52%⁴⁸ , whereas in study by reddy et al it was only 39%.¹¹

In the table 2 , it has been shown that the most common ocular manifestation in rheumatoid arthritis patients was keratoconjunctivitis sicca (66.29% out of patients with ocular involvement). The incidence of keratoconjunctivitis sicca is between 11.6% to 50% in literature.⁵⁴⁻⁵⁶

The second most common ocular manifestations ,in this study were found to be filamentary keratitis(7.86%) and uveitis (7.86%). The least common was panophthalmitis (0.1%).

Episcleritis was diagnosed in only 3 (3%) patients of rheumatoid arthritis in this study. All the patients diagnosed with episcleritis were females.

Scleritis was present in 5 (5%) patients. Nodular scleritis was present in one patient while diffuse scleritis was present in four (4) cases.

The retinal involvement was found in 4 patients of the total 97 patients. One patient was of retinal vasculitis , 2 patients were of retinal haemorrhage and one patient of secondary exudative retinal detachment. The incidence of cataract formation was also found to be high in the patients taking steroid treatment for rheumatoid arthritis. In our study , 47 patients out of 97 had cataract (29.18%). Out of these 47 patients, 27 patients were receiving long term oral corticosteroids and 11 of them had developed bilateral posterior subcapsular cataract. The intraocular pressure was normal in all of them. The study by Reddy et al had 9 cases of posterior subcapsular cataract bilaterally who were on long term oral steroids treatment¹¹, and this observation has been also well documented by Oglesby et al⁵¹ and Williamson et al.⁵²



IMAGE 2- EPISCLERITIS

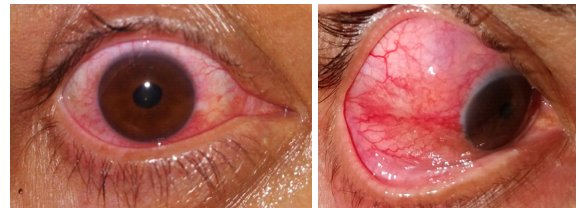


IMAGE 3&4- DIFFUSE SCLERITIS



IMAGE 5- CIRCUMCORNEAL CONGESTION IN CASE OF IRIDOCYCLITIS

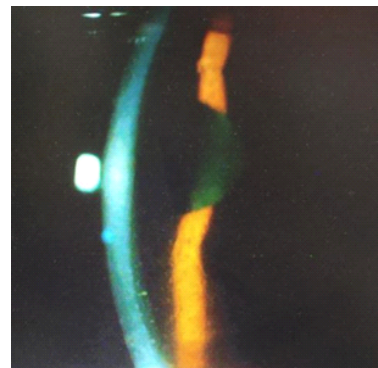


IMAGE 6- KP's & CELLS IN AC



IMAGE 7- SEQUELAE OF PUK WITH CORNEAL PERFORATION & IRIS PROLAPSE



IMAGE 8 - FUNDUS PICTURE OF A CASE OF PANUVEITIS WITH RETINAL VASCULITIS

CONCLUSION

In a study of 97 cases of rheumatoid arthritis 89 patients were found to be having various ocular lesions. The following conclusions can be drawn from the study.

1. Ocular involvement in rheumatoid arthritis is very common in the kumaon region of Uttarakhand. (91.75%)
2. Keratoconjunctivitis Sicca is the most common ocular manifestation associated with RA in the Kumaon region of Uttarakhand. (60.8%)
3. The frequency of the ocular lesions is related to the duration of arthritis.
4. Routine ophthalmic examination may help to detect the early onset of ocular lesions in patients of rheumatoid arthritis.

REFERENCES

1. E. William St. Clair, Ankoor Shah, Anthony S. Fauci, Carol A. Langford, Harrison's Rheumatology, 4th edition, chapter 6, Rheumatoid arthritis, pg no. 89.
2. Zlatanovic G, Veselinovic D, Cekic S, Zivkovic M, Dordevic-Jocić J, Zlatanovic M. Ocular manifestation of rheumatoid arthritis-different forms and frequency. *Bosn J Basic Med Sci* 2010; 10:324-327.
3. Felson DT, Anderson JJ, Boers M. American College of Rheumatology. Preliminary definition of improvement in rheumatoid arthritis. *Arthritis Rheum* 1995; 38:727-735
4. Turesson C, O'Fallon WM, Crowson CS, Gabriel SE, Matteson EL. Extra-articular disease manifestations in rheumatoid arthritis: incidence trends and risk factors over years. *Ann. Rheum Dis* 2003; 62:722-727
5. Sahaçin-Meka V, Rexhepi S, Manxhuka-Kërliu S, Rexhepi M. Extraarticular manifestation of seronegative and seropositive rheumatoid arthritis. *Bosn. J Basic Med Sci* 2010; 10(1):27-31
6. Lilleby V, Gran JT. Systemic rheumatoid arthritis: Tidsskr Nor Laegeforen 1997; 117(29):4223-4225
7. Goronzy JJ, Weyand CM. Developments in the scientific understanding of rheumatoid arthritis. *Arthritis Res Ther* 2009; 11(5):249
8. Sobrin L, Kim EC, Christen W, Papadakis T, Letko E, Foster CS. Infliximab therapy for the treatment of refractory ocular inflammatory disease. *Arch Ophthalmol* 2007; 125(7):895-900
9. Sainz de la Maza M., Foster C.S., Jabbur N.S. Scleritis associated with rheumatoid arthritis and with other systemic immune-mediated diseases. *Ophthalmology* 1999; 106(7):1281-1286
10. Fong LP, Sainz de la Maza M, Rice BA, Kupferman AE, Foster CS. Immunopathology of scleritis. *Ophthalmology* 1991; 98(4):472-479
11. Reddy SC, Gupta SD, Jain IS, Deodhar SD. Ocular manifestations of rheumatoid arthritis. *Indian J Ophthalmol* 1977; 25:20-6.
12. Duke Elder, S. and Leigh A.G. 1955, *System of Ophthalmology*, Part II, 1037. St. Louis, C.G., Mosby Co.
13. Stanworth, A. 1951, *Trans. Ophth. Soc. U.K.*, 71, 130.
14. Brown, S.I. and Grayson, M. 1968, *Arch. Ophth.*, 79, 563
15. Kimura, S.J., Hogan, M.J., Connor, G.R. and Epstein, W.V. 1966, *Trans. Amer. Ophth. Soc.* 64, 291
16. Jain, I.S., Gupta, and Sehgal, V.N. 1964, *Orient. Arch. Ophth.* 2, 138.
17. Chadwic, A.J. and Rosen, E.S. 1968, *Amer. J. Ophth.* 65, 784
18. Cimmino MA, Salvarani C, Macchioni P, et al. Extra-articular manifestations in Italian patients with rheumatoid arthritis. *Rheumatol Int* ; () : - []
19. Kanski JJ. *The eye in systemic disease*. Butterworths London
20. Hard, C.R., Snyder, W.B., and Ziff, M. 1970, *Amer. J. Med.* 48, 273.
21. Diamantis Almaliotis, Marina Zakalka, Antony Gerofotis, Kleopas Chatzigeorgiou, Maria Efsthathiou, Michael Daniilidis, Vasileios Karampatakis. *Open Journal of Ophthalmology*, 2016, 6, 170-175 Ocular Manifestations in Rheumatoid Arthritis.

22. Patel, S.J. and Lundy, D.C. (2002) Ocular Manifestations of Autoimmune Disease. 66.
23. Fuerst, D.J., Tanzer, D.J. and Smith, R.E. (1998) Rheumatoid Diseases. *International Ophthalmology Clinics*, 38, 47-80.
24. Shizato, M., Yamamoto, J., Hirata, C.E., Goldberg, C.A., Yoshinari, N.H. and Bonfa, E. (2008) Eye Disease in a Patient with Rheumatoid Arthritis. *Vogt-Koyanagi-Harada Syndrome and Rheumatoid Arthritis*
25. del Castillo, B.J.M., Diaz-Valle, D., Pato, E., Abad, L.C. and Alejandre, N. (2008) Articular Diseases and Uveitis. *Anales del Sistema Sanitario de Navarra*, 31.
26. McGavin, D.D., Williamson, J., Forrester, J.V., Foulds, W.S., Buchanan, W.W., Dick, W.C., et al. (1976) Episcleritis and Scleritis. A Study of Their Clinical Manifestations and Association with Rheumatoid Arthritis. *British Journal of Ophthalmology*, 60, 192-226
27. Harper, S.L. and Foster, C.S. (1998) The Ocular Manifestations of Rheumatoid Disease. *International Ophthalmology Clinics*, 38, 1-19.
28. Galor, A. and Thome, J.E. (2007) Scleritis and Peripheral Ulcerative Keratitis. *Rheumatic Disease Clinics of North America*, 33, 835-854
29. Kenyon KR: Decision-making in the therapy of external eye disease. Noninfected corneal ulcers. *Ophthalmology*, 89:44-51 1982 6280121
30. Staggos, N. (2002) *Clinical Ophthalmology*, 16, 444-445
31. Lowder, C.Y. and Char, D. (1984) H. UVEITIS—A Review. *Western Journal of Medicine*, 140, 421-432.
32. Marmor, M.F., Kellner, U., Lai, T.Y., Lyons, J.S. and Mieler, W.F. (2011) American Academy of Ophthalmology. Revised Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy. *Ophthalmology*, 118, 415-422
33. McGavin DD, Williamson J, Forrester JV, Foulds WS, Buchanan WW, Dick WC, et al. Episcleritis and scleritis. A study of their clinical Charanya, et al.: Ocular Manifestation in Rheumatoid Arthritis *International Journal of Scientific Study* | November 2015 | Vol 3 | Issue 8 66 manifestations and association with rheumatoid arthritis. *Br J Ophthalmol* 1976; 60:192-226.
34. Moss SE, Klein R, Klein BE. Prevalence of and risk factors for dry eye syndrome. *Arch Ophthalmol* 2000; 118:1264-8
35. Kotaniemi KM, Salomaa PM, Sihto-Kauppi K, Säilä HM, Kauppi MJ. An evaluation of dry eye symptoms and signs in a cohort of children with juvenile idiopathic arthritis. *Clin Ophthalmol* 2009; 3:271-5.
36. Watson PG, Hayreh SS. Scleritis and episcleritis. *Br J Ophthalmol* 1976; 60:163-91
37. Jabs DA, Mudun A, Dunn JP, Marsh MJ. Episcleritis and scleritis: Clinical features and treatment results. *Am J Ophthalmol* 2000; 130:469-76.
38. Vignesh AP, Srinivasan R. Ocular manifestations of rheumatoid arthritis and their correlation with anti-cyclic citrullinated peptide antibodies. *Clin Ophthalmol* 2015; 9:393-397.
39. Safaa A. Abouda, Mohamed O. Abd Elkhaleka, Nagla H. Alyb, Enas A. Abd Elaleem. Ocular involvement and its manifestations in rheumatoid arthritis patients. *Delta Journal of Ophthalmology* 2017, 18:57-62
40. Punjabi OS, Adyanthaya RS, Mhatre AD, Jehangir RP. Rheumatoid arthritis is a risk factor for dry eye in the Indian population. *Ophthalmic Epidemiol.* 2006; 13(6):379-384.
41. Bettero RG, Cebrían RFM, Skare TL. [Prevalence of ocular manifestation in 198 patients with rheumatoid arthritis: a retrospective study]. *Arq Bras Oftalmol.* 2008; 71(3):365-369. Portuguese.
42. Tong L, Thumboo J, Tan YK, Wong TY, Albani S. The eye: a window of opportunity in rheumatoid arthritis? *Nat Rev Rheumatol.* 2014; 10(9):552-560.
43. Villani E, Galimberti D, Viola F, Mapelli C, Papa ND, Ratiglia R. Corneal Involvement in Rheumatoid Arthritis: An In Vivo Confocal Study. *Invest Ophthalmol Vis Sci.* 2008; 49(2):560-564.
44. Bhadoria DP, Bhadoria P, Sundaram KR, Panda A, Malaviya AN. Ocular manifestations of rheumatoid arthritis. *J Indian Med Assoc.* 1989; 87(6):134-135.
45. Ocular manifestations of rheumatoid arthritis and their correlation with anti-cyclic citrullinated peptide antibodies, ammapati Paul Pandian Vignesh renuka srinivasan Department of Ophthalmology, Jawaharlal institute of Postgraduate Medical education and research, Pondicherry, india, *Clinical Ophthalmology* 2015; 9:393-397
46. van Bijsterveld OP. Diagnostic tests in the Sicca syndrome. *Arch Ophthalmol* 1969; 82:10
47. Lemp MA, Hamill JR Jr. Factors affecting tear film breakup in normal eyes. *Arch Ophthalmol* 1973; 89:103
48. C. Charanya, Achanti Swathi, Siddharam Janti, R. Pandurangan, Post-graduate, Department of Ophthalmology, Chettinad Hospitals and Research Institute, Chennai, Tamil Nadu, India, Associate Professor, Department of Ophthalmology, Chettinad Hospitals and Research Institute, Chennai, Tamilnadu.
49. Smith VA, Hoh HB, Easty DL: Role of ocular matrix metalloproteinases in peripheral ulcerative keratitis. *Br J Ophthalmol.* 83:1376-1383 1999, 10574817
50. Stern ME, Schaumberg CS, Dana R, et al.: Autoimmunity at the ocular surface: Pathogenesis and regulation. *Mucosal Immunol.* 3:425-442 2010, 20485329
51. Olesby, R.B., Black, R.L., Sallmann, L. Ven., and Bunin, J.J. 1961, *Arch. Ophth.* 66, 519
52. Williamson, J., Paterson, R.W.W., Me Gavin, D.D.M., Jasani, M.K., Boyle, J.A., and Doig, W.M. 1969, *Brit. J. Ophth.* 53, 363.
53. Smith, J.L. 1957, *Amer. J. Ophth.* 43, 575.
54. Arnett FC, Edworthy SM, Bloch DA. The American Rheumatism Association revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988; 31:315-324
55. Goto E, Matsumoto Y, Kamoi M, Endo K, Ishida R, Dogru M. Tear evaporation rates in Sjögren syndrome and non-Sjögren dry eye patients. *Am J Ophthalmol* 2007; 144(1):81-85
56. Barr CC, Davis H, Culbertson WW. Rheumatoid scleritis. *Ophthalmol* 1981; 88:1269-1273.