Ocular Manifestations in Rheumatoid Arthritis Patients - A Hospital Based Cross Sectional Study

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ABSTRACT

BACKGROUND

The prevalence of rheumatoid arthritis (RA) in India is 0.28% to 0.7%, 15-45% of patients with RA develop ocular manifestations. Ocular disabilities can be reduced with timely interference by an ophthalmologist. Keratoconjunctivitis sicca (Sjogren's syndrome) is the most common ocular association of RA. This study was done to find out various ocular manifestations in rheumatoid arthritis patients.

METHODS

A cross sectional study was conducted among the patients attending the rheumatology clinic at Government Medical College, Trivandrum. Patients in the age group of 18-60 years were screened and further evaluated at regional institute of ophthalmology, Trivandrum. Screening for RA was done using the American Rheumatism Association criteria. A complete ophthalmic examination was done for those who satisfied the criteria. The various ocular manifestations in RA are described and presented as proportions.

RESULTS

Ocular manifestation was found in 38% of total patients attending the rheumatology clinic. There were 54 females (80.5%) and 13 males (19.4%). Age group mainly affected were in 46-50 yr (17.9%). The duration of rheumatoid arthritis ranged from few months to 25 years. Keratoconjunctivitis sicca was the commonest manifestation found, detected in 22(84%) patients, episcleritis was noted in two patients (7.6%), scleritis in 1 patient (3.8%) and marginal furrowing in 1 patient (3.8%).

CONCLUSIONS

In this clinic-based study there was a high proportion (38%) of ocular involvement in RA and hence it is essential to include ophthalmic evaluation as a routine in RA patients. The most common manifestation was keratoconjunctivitis sicca followed by episcleritis, diffuse anterior scleritis and marginal corneal furrowing.

KEY WORDS

Rheumatoid Arthritis, Keratoconjunctivitis Sicca, Ocular Manifestations, Scleritis, Episcleritis

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BACKGROUND

Rheumatoid arthritis is mainly characterized by inflammation of the lining, or synovium, of the joints. It can lead to long–term joint damage, resulting in chronic pain, loss of function and disability. RA has a worldwide prevalence of 1%.[1,2,3] The average age of onset is in the fourth to fifth decade of life,[4] with a three times greater predilection in women than in men.[5] It can have devastating systemic and ocular effects. The diagnosis of the disease is made on the basis of clinical criteria (ACR).

15-45% of patients with RA develop ocular manifestations.[2,3,6] These include

Episcleritis	-	Episcleritis
		Simple
		Nodular
		Episcleral Nodules
Sclera	-	Anterior Scleritis
		Non necrotizing – Nodular/Diffuse
		Necrotizing with inflammation
		Necrotizing without inflammation
		(Scleromalacia perforans)
		Posterior scleritis
Cornea	-	Keratoconjunctivitis sicca (KCS)
		Sclerosing keratitis
		Acute stromal keratitis
		Limbal guttering
		Keratolysis
		Peripheral ulcerative keratitis
		Bank keratopathy
		Cornea verticellata
		(Secondary to NSAIDS or chloroquine)
		Peripheral corneal infiltrates
		(Secondary to gold compounds)
Lens	-	Cataract formation
		Lens deposits
		(Secondary to gold compounds)
Choroid	-	Choroidal effusion
		Ciliochoroidal detachment
Retina	-	Exudative retinal detachment
		(Secondary to posterior scleritis)
		Retinal microangiopathy and infarction
		Bull's eye maculopathy
		(Secondary to chloroquine)
Extra Ocular Muscles	-	Extra ocular muscle palsies
		Brown's syndrome
Miscellaneous	-	Blepharoconjunctivitis

Glaucoma ocular disabilities can be reduced with timely interference by an ophthalmologist. The present study is undertaken to describe the various ocular manifestations and their incidence. Keratoconjunctivitis Sicca (Sjogren's syndrome) is the most common ocular association of RA.[7,8,9] It is clinically evident in 20-50% of patients with RA, particularly in women (90%). It may be an early or presenting manifestation of RA. KCS appears in RA as a result of decreased secretion of tears from the main and accessory lacrimal glands. Histopathologic examination of lacrimal and salivary glands in Sjogren's syndrome reveals infiltration and replacement of normal lacrimal and salivary glandular structures by lymphocytes causing atrophic and cirrhotic changes in the lacrimal glands and reduction in the middle layer of the precorneal tear film. Patients complain of foreign body sensation, burning, itching, excessive mucus production, and a sensation of dryness or paradoxical tearing, all of which intensify in dry and smoky environment. The typical signs observable on evaluation includes a diminished marginal tear strip, superficial punctuate keratopathy (SPK), and ocular surface epitheliopathy; Rose Bengal staining generally reveals a horizontally oriented diamond pattern in the interpalpebral fissure. The consequence of the dryness is epithelial keratopathy most often seen in the interpalpebral fissure where fine epithelial erosions develop that stain with fluorescein. In KCS conjunctival goblet cells are stimulated to increase secretion of mucus, filamentous keratitis, in which a dialysis of corneal epithelium in the form of twisted filaments tied up to the cornea by one part with coverings of mucin is a particularly painful condition because blinking moves the filaments, tugging of the epithelial attachments and tending to strip off further epithelium. It is not clear whether the mucus manifestations are the result of simply an increase in mucus secretion (or an abnormal mucus), or to mucus precipitation because of the disturbed balance of components in the tear. KCS may progress to stromal ulceration, and corneal perforation. After KCS, scleritis is the most common ocular manifestation of RA.[10] Although it may be an initial sign of rheumatoid disease it typically presents many years after the onset of RA and often at the time when joint inflammation is in remission. Scleral inflammation in RA may extend to adjacent structures and may cause keratitis, anterior uveitis, glaucoma, cataract, retinal, choroidal and optic nerve changes and motility disturbance. Patients with rheumatoid scleritis have more advanced joint disease and more extraarticular manifestations than do rheumatoid patients without scleritis. The occurrence of scleritis is often a harbinger of worsening systemic disease and warrants re-evaluations of the existing medical therapy in these patients. The 3 year mortality rate of patients with scleritis associated with RA is 36 to 45%, if not aggressively treated with immunosuppressive therapy.

Simple episcleritis is more common in patients with RA. The presence of subconjunctival nodules that are mobile over the sclera differentiates nodular episcleritis from simple episcleritis. The episcleritis in the RA patients was relatively mild in all instances with an incidence of 0.17% in RA. Patients usually complain of hot, prickly or foreign body like sensation. Tenderness may be present localized to the inflamed area. Unlike typical idiopathic episcleritis, it did generally require the use of a systemic NSAID for resolution.

Corneal lesions- Corneal disease in patients with RA can be an isolated complication but it is most commonly associated with keratoconjunctivitis sicca or a form of anterior scleritis. The spectrum of disease may include keratitis, sclerosing keratitis, and peripheral or paracentral ulcerative keratitis. The drying effects of keratoconjunctivitis sicca leads to devitalized epithelial cells and punctuate epithelial erosion. Acute keratitis has been identified in 30 to 70 percent of patients with scleritis or episcleritis associated RA. Keratitis associated with scleritis may be acute (acute stromal keratitis and keratolysis) or sclerosing. It is marked by an inflammatory cell infiltrate that may result in corneal scarring, ulceration, or melting. It may occur as an isolated

finding, following previous episode of scleritis even in the setting of previous successful scleritis treatment with immunosuppressive agent. Acute stromal keratitis can manifest as stromal opacities at any level in the cornea with companying stromal oedema. The opacities may coalesce if left untreated. Overlaying epithelium may breakdown with the development of peripheral ulcerative keratitis. Vascularization and thinning of the cornea may occur as well. Many of these findings may resolve with appropriate treatment and resolution of accompanying scleritis.

Peripheral corneal ulceration is potentially devastating disorder consisting of a crescent shaped destructive inflammation at the margin of corneal stroma that is associated with an epithelial defect, presence of stromal inflammatory cells, and progressive stromal degradation and thinning. It may occur in association with necrotizing scleritis in inflamed or noninflamed eyes. Loss of stroma occurs in regions of clear cornea and may progress to descemetocele formation. Corneal and scleral stromal lysis with wound dehiscence has been described after cataract and strabismus surgery in patients with RA, often in patients with preoperative KCS. Rarely, cryoglobulins (complexes of RF and polyclonal IgG that precipitate at temperatures lower than 370C [98.60F] precipitate in the peri limbic circulation, leading to ulcers that can perforate the cornea with extrusion of the aqueous. Anterior uveitis accompanying episcleritis or scleritis is a common finding in RA but anterior uveitis alone probably has no higher incidence in adult RA patient than in general population.

We wanted to find out various ocular manifestations in rheumatoid arthritis.

METHODS

A cross -sectional study was conducted at the Rheumatology Clinic of Trivandrum Medical College during August 2005-April 2007. Diagnosis of rheumatoid arthritis was based on the 1988 Revised American Rheumatism Association Criteria.[10] 67 patients in the age group of 18-60 yrs were included in the study as per the criteria. All patients were subjected to a detailed examination, which included history taking as to, age, the duration of disease, treatment taken, other systemic illness and ocular complaints.

A detailed ocular examination was done using torch light and slit lamp. Detailed fundus examination was done to rule out maculopathy and any evidence of vasculitis using direct ophthalmoscope, 90 D and indirect ophthalmoscope. Lacrimal secretion was measured using Schirmer's test I and II using Whatmann filter paper No. 41. Lissamine green staining & TBUT was done in these cases.[11,12,13,14] Macular function was assessed using colour vision and Amsler's grid test. FFA, field analysis and B-Scan were ordered if necessary. RA patients when tested positive for above mentioned tests were considered as having ocular manifestations. Patients with ocular manifestations were given the standard treatment available. Ethical committee clearance was obtained from the Institution. Written informed consent was obtained from all the study participants.

Statistical Analysis

The data was coded, entered and analysed in MS Excel 4.0. The quantitative variables were expressed as mean and standard deviation. The qualitative variables were analysed and represented as proportion.

RESULTS

67 diagnosed rheumatoid arthritis patients were included in the study. The mean age of the study participants was 42.8 yrs, 46-50 yrs age group (17.9%) was the predominant group. Majority of the patients were females (80.59%).61.2% of the patients had ocular manifestations and 84% had keratoconjunctivitis sicca, followed by episcleritis 7.6%. Scleritis and marginal furrowing were less common with 3.8%.

Patients	Number (percentage) Total N=67 (100%)
Males	13 (19%)
Females	54 (80.59%)

Table 1. Gender Distribution of Study Participants

Age Groups (yrs)	Number (percentage) Total N=67 (100%)
21-25	5 (7.5%)
26-30	5 (7.5%)
30-35	7 (10.4%)
36-40	11 (16.4%)
41-45	8 (11.9%)
46-50	12 (17.9%)
51-55	9 (13.4%)
56-60	7 (10.4%)
61-65	2 (2.9%)
66-70	1 (1.5%)

Table 2. Age Distribution of Study Participants

Duration (yrs)	Number (percentage) Total N=67 (100%)
0-5	43 (64.2%)
6-10	16 (23.9%)
11-15	4 (5.9%)
16-20	2 (2.9%)
21-25	2 (2.9%)

Table 3. Distribution of Study Participants Based on Duration of Rheumatoid Arthritis

	Number (percentage) Total N=67 (100%)
No. of patients having ocular manifestations	26 (38.8%)
No. of patients not having ocular manifestation	41 (61.2%)

Table 4. Distribution of Study Participants Based on Ocular Manifestations

Ocular Manifestations	Number (percentage) N=26 (100%)
Marginal furrowing	1 (3.8%)
Scleritis	1 (3.8%)
Episcleritis	2 (7.6%)
KCS	22 (84%)

Table 5. Distribution of Ocular Manifestations

DISCUSSION

A total of 67 rheumatoid arthritis patients attending the clinic were studied. There were 54 (80.59%) females and 13 (19.4%) males. Female: male ratio was 4.15:1. Similar female

predominance was noted in other studies also like Chandreskharan et al.[15] (4:1) and Narayanan et al.[16] (4:1). In this study age group of the study population ranges between 20-80 years with maximum number of patients in the age group of 46-50 years (17.9%). Mean age group in a study by Wanchu et al. was 41 years and mean age group in the study by Waters et al. was 45 years which showed concordance with the present study. The mean age in the present study was 42.48 years.

In this study population, duration of disease (RA) ranged between few months to 25 years. Mean duration of illness was 5.2 years 64.2% of patients had disease duration in the range of 0-5 years. Wanchu et al. had studied patients with disease duration of 5.3+4.1 years. In a study by Kalke et al. the mean duration was 5 years. In this study population, ocular manifestations were found in (38.8%) patients in the age group of 46-50 years (17.9%).

Ocular manifestations detected were keratoconjunctivitis sicca, episcleritis, diffuse anterior scleritis, and peripheral ulcerative keratitis. Comparing the present study with other studies in the table below:

Studies	Ocular Manifestations
Mody et al.[17]	31.7%
Reddy SC & Rao[18]	24.40 %
Bharodia et al.[14]	19.63%
Ashu et al.	21.81%
Present study	38%

Keratoconjunctivitis sicca was the commonest manifestation found, detected in (84%) patients. In a study by Shaw et al. incidence of severe dry eye was 5.55%. While 37.03 had borderline tear deficiency. A few of them had corneal epithelial lesions. All diagnosed patients were put on lubricant eye drops and were followed up. Reddy et al.[19] has found 29% of KCS in their study conducted at Hyderabad in India, Gilboe et al.[20] has found an incidence of 21%, while the study by by Bhadoria et al.[21] showed an incidence of 17.7% and the incidence of KCS in the study by Mastuo et al. was[22] 17.10 %. Most of these studies show concordance with our study and in all of them KCS was the commonest ocular manifestation. In the present study episcleritis was noted in two patients (7.6%). Shaw C et al. reported an incidence of 3.7% episcleritis in their study. Bharodia et al. had an incidence of 0.93% in their study.

Diffuse anterior scleritis was seen in 1 patient (0.03%). In a study by Matsuo et al. the incidence of scleritis was 0.9%

Marginal corneal furrowing was seen in 1 patient (0.03%). Reddy et al.[20] in this study has reported a case of marginal corneal furrowing.

Ocular Manifestation	Other Studies	Present Study
KCS	(29%) Reddy et al. (21%) Gioboe et al. (17.7%) Bhadoria et al. (17.10) Mastuo et al.	84%
Scleritis	(0.9%) Matsuo et al.	3.8%
Episcleritis	(3.7%) Shaw C et al.	7.6%
PUK	(0.03%). Reddy et al.	3.8%

CONCLUSIONS

The present study shows that there is a high incidence of ocular involvement in rheumatoid arthritis. Therefore, it is essential to include ophthalmic evaluation as a routine for rheumatoid arthritis patients to facilitate timely diagnosis so that appropriate management strategies can be employed to prevent ocular morbidity as all these patients may not be symptomatic. The most common ocular manifestation detected was keratoconjunctivitis sicca, followed by episcleritis, diffuse anterior scleritis and marginal corneal furrowing.

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