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Original article

Ocular Complications in Rheumatoid Patients at Damietta Governorate: Correlation with Age, Gender and Disease Activity

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ABSTRACT

Background: Ocular complications are one of the well-recognized extra-articular complications of rheumatoid arthritis [RA]. The most common ocular complications of RA are Keratoconjunctivitis sicca, episcleritis, scleritis, marginal thinning of the cornea with keratolysis, stromal corneal opacities with peripheral vascularization, and iridocyclitis. The ocular complications were found to be significantly higher in patients with long duration of RA.

Aim of the work: This study was conducted to determine the common ocular complications that occur with RA and to determine the correlation of this complications with age, gender, duration, and activity of RA.

Patients and methods: Tow hundred eyes of one hundred patients [males and females] with symptomatic evidence of RA were studied. All patients subjected to full clinical evaluation, laboratory assessment, plain X-ray hand and detailed ocular examination [visual acuity, slit lamp, fundus examination and Schirmer's test].

Results: Our research showed that 47.0% of the studied cases were aged from 41 to 60 years old, 93.0% of them were females, 57.0 % of them had RA more than 2 years [longstanding RA] and 40.0 % of them had ocular complications. The most common eye complications among the studied cases were dry eye, episcleritis, and scleritis [28.5 %, 4.0 %, and 3.0 % respectively].

Conclusion: RA patients have a higher risk of ocular complications. Eye examination should be included as a routin for RA patients to facilitate early diagnosis and management of ocular complications.

Keywords: Rheumatoid arthritis; Disease activity; Disease severity; Ocular complications; Correlations.

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INTRODUCTION:

Rheumatoid arthritis [RA] is a chronic systemic autoimmune disease of unknown etiology that has articular and extra-articular manifestations, including ophthalmic involvement [1]. The clinical course of eye disease may be quite variable. Early diagnosis of eye disease in RA patient is very important since it permits the early management of potentially serious sight-threatening complications. The presence of the eye disease may also be an indicator of systemic disease activity[2-4]**.** However, ocular involvement particularly in severe dry eye, may exist independently from severe articular disease and should be evaluated in all RA patients regardless of extra-ophthalmic manifestations[5-6].

PATIENTS AND METHODS

Patients: This study included 200 eyes of 100 RA patients [males and females] who attended to the outpatient clinic of the departments of ophthalmology and rheumatology, AL-Azhar University Hospital, Damietta, Egypt. The patients were diagnosed according to ACR criteria 1987[7] or ACR/EULAR 2010 criteria, which of these the patients fulfill.

All patients were recruited from Damietta, Al-Azhar University Hospital, from February 2018 and January 2019. The patients selected randomly. Randomization based on a single sequence of random assignments [simple Randomization]. The protocol of this study was approved by the local ethics and research committee of Al-Azhar Faculty of Medicine [New Damietta], and informed consent was signed by all patients before inclusion in this study.

Exclusion criteria:

1. Presence of other autoimmune systemic disorders like systemic lupus erythematosus, graft versus host disease, and any immunosuppressive disorders.

2. Radiation history 3. Drug-induced eye Sid effect as hydroxychloroquine induced maculo-pathy. 4. Age less than 18 years 5. Age more than 60 to exclude age-related eye diseases like posterior vitreous detachment [PVD] and nuclear sclerosis.

Methodology

1-**History and clinical examination**: The age, sex, duration of RA and demographic data were initially collected from the patient. History of the eye symptoms was obtained. Clinical examination was done to confirm RA diagnosis.

2-**laboratory investigation**: Erythrocyte sedimentation rate [ESR], C - reactive protein [CRP], rheumatoid factors [RF], anti-CCP antibody level was detected using ELISA test[8]**.**

Disease activity score [DAS28] calculated by 28 joints examination for [swelling and tenderness] and ESR [DAS 28 by ESR] were calculated for all the patients to categorize the patients into low DAS28 [less than 3.2], moderate DAS28 [between 3.2 and 5.1] and high DAS28 [more than 5.1].

All patients divided into two groups, according to RA duration: [group A] early RA [less than 2 years]] and [group B] late or longstanding RA [more than 2 years].

3-Imaging: X-rays both hands posterior/ anterior [PA] view was done in all patients.

4- Eye assessment: A detailed anterior segment examination using slit lamp was done to detect episcleritis, scleritis, and corneal changes.

Schirmer's test, ocular staining score and tear film break-up time were done for diagnosis of dry eye. Posterior eye segment manifestations were detected by fundus examination. Ocular examination in every patient was done with torchlight and slit lamp bio microscopy. Schirmer's test was done by using Whatman filter paper. Tear film break-up time was done by using fluorescein stain to assess lacrimal function.

Ocular surface lesions were detected by using Rose Bengal and fluorescein staining. Dry eye diagnosis was based on the American-European Consensus Criteria for Sjögren's syndrome which includes presence of connective tissue disorder, duration of eye dryness >3 months, Van Bijsterveld score ≥4 , tear film break-up time <10 seconds .

Schirmer's test [without anesthesia] ≤5 mm/5 minutes

5- **Statistical methods**: The collected data were organized, tabulated and statistically analyzed, using Statistical Package for Social Science [SPSS] version 16 [SPSS Inc., Chicago, USA], running on IBM compatible computer with Microsoft ® Windows 7 Operating System. Frequency and percentage were used, chi-square and Fisher exact tests was used for testing the significance of observed differences between studied patients. The level of significance was adopted at $p < 0.05$.

RESULTS

Demographic data of the patients: -Most of our patients [47.0%] were aged from 41 to 60 years old, [83.0%] of them were females, [57.0 %] of them had RA more than 2 years [longstanding RA] , 45.0 % of them had high disease activity score[DAS28 ESR] and 46.0 % of patients had ocular complications[34 of them had bilateral eye affection and 12 of them had unilateral eye affection] Table [1].

Frequency of ocular complications among the patients: 80 of 200 eyes [40.0 %] of examined eyes had ocular complications. The most common eye complications among the studied cases were dry eye [Fig. 1], episcleritis [Fig. 2], and scleritis [28.5 %, 4.0 %, and 3.0 % respectively], Table [2].

Correlation of ocular complications with the patient's age: The majority of ocular complications were among patients aged from 41 to 60 years [50.00 %], with significant difference [0.011], table [3].

Correlation of ocular complications with patient's sex: The Ocular complications among our patients were more in males than females [52.94 and 37.34 respectively] but not significant [0.09], table [4].

Correlation of ocular complications with RA duration: The majority of ocular complications were in group B, longstanding RA [56.14%], with significant difference [0.001] table [5].

Correlation of ocular complications with disease activity score [DAS28 ESR] of RA: Most of the patients with high DAS 28 ESR [86.66 %] had ocular complications, also 80.48 of patients with moderate DAS28ESR had ocular complications, but [57.14 %] of patients with lowDAS28 ESR had ocular complications, with significant difference [0.05], table [6]

Table [1]: Demographic data of the patients

characteristics	100 patients=200 eyes	%
Age		
From 20 to 30 years	16	16.0
From 31-40 years	37	37.0
From 41 to 60 years	47	47.0
Sex		
Male	17	17.0
Female	83	83.0
Duration of RA		
Less than 2 years RA]	43	43.0
More than 2years	57	57.0
DAS28 ESR		
Low DAS	14	14.0
Moderate DAS	41	41.0
High DAS	45	45.0
Number of examined eyes	200	100.0
Ocular complications among examined eyes	80 eyes	46.0 of patients
Laterality	bilateral = 34 %	unilateral = 12%

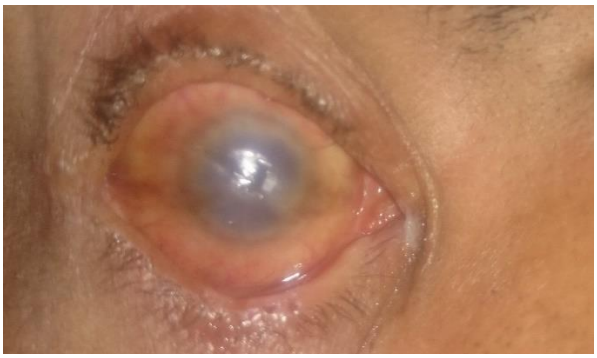

Figure [1]: Sever dry eye and corneal vascularization

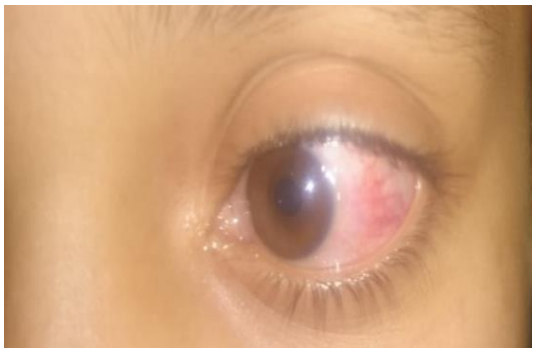

Figure [2]: Episcleritis.

Table [2]: The frequency of eye complication in RA patients

Ocular complications	No	%
Dry eye [Keratoconjunctivitis sicca] [KCS]	57	28.5
Episcleritis	8	4.0
Scleritis	6	3.0
corneal neovascularization	4	2.0
Sclerosing keratitis	3	1.5
Iritis [anterior uveitis]	2	1.0
Total	80 eyes	40.0%

Table [3]: Relation between ocular complications with the patient's age

Ocular complications	Age						P
	From 20 to 30 years [16P=32E]		from 31- 40 years [37P=74E]		from 41 to 60 years [47P=94E]		
	No	%	No	%	No	%	
Dry eye [KCS]	5	15.6	19	25.67	33	35.10	0.08(NS)
Episcleritis	1	3.125	2	2.70	5	5.31	0.66(NS)
Scleritis	0	0.00	2	2.70	4	4.25	0.46(NS)
Peripheral Corneal vascularization	1	25.0	1	25.0	2	50.0	0.83(NS)
Sclerosing keratitis	0	0.0	1	33.33	2	66.67	0.68(NS)
Iritis	0	0.0	1	50.0	1	50.0	0.81(NS)
Total	7	21.87	26	35.13	47	50.00	0.011*

NS = Not significant *= Significant

Table [4]: Relation between ocular complications with patient's sex

Ocular complications	Sex				P
	Male [17P=34E]		Female [83P=166]		
	No	%	No	%	
Dry eye [KCS]	11	32.35	46	27.71	0.58 (NS)
Episcleritis	2	5.88	6	3.61	0.53 (NS)
Scleritis	2	5.88	4	2.40	0.28(NS)
Peripheral corneal neovascularization	1	2.94	3	1.80	0.66(NS)
Sclerosing keratitis	1	2.94	2	1.20	0.44(NS)
Iritis [anterior uveitis]	1	2.94	1	0.60	0.21(NS)
Total	18	52.94	62	37.34	0.09 (NS)

NS = Not significant

Table [5]: Relation between ocular complications with RA duration

Ocular complications	RA duration				P value
	[Group A] 43 P= 86 E		[Group B] [57 P= 114 E]		
	No	%	No	%	
Dry eye [KCS]	10	11.62	47	41.22	<0.001*
Episcleritis	2	2.32	6	5.26	0.29 (NS)
Scleritis	2	2.32	4	3.50	0.62 (NS)
Peripheral corneal neovascularization	1	1.16	3	2.63	0.46 (NS)
Sclerosing keratitis	1	1.16	2	1.75	0.73 (NS)
Iritis [anterior uveitis]	0	0.00	2	1.75	0.21 (NS)
Total	16	18.60	64	56.14	<0.001*

NS = Not significant *= Significant

Table [6]: Relation between of ocular complications with [DAS28 ESR] of RA

Ocular complications	DAS28 ESR						p
	Low [14]		Moderate [41]		High [45]		
	No	%	No	%	No	%	
Dry eye [KCS]	7	50.00	24	58.53	26	57.77	0.92(NS)
Episcleritis	1	7.14	3	7.31	4	8.88	0.95(NS)
Scleritis	0	0.00	2	4.87	4	8.88	0.43(NS)
Peripheral corneal neovascularization	0	0.00	2	4.87	2	4.44	0.71(NS)
Sclerosing keratitis	0	0.00	1	2.43	2	4.44	0.67(NS)
Iritis [anterior uveitis]	0	0.00	1	2.43	1	2.22	0.84(NS)
Total	8	57.14	33	80.48	39	86.66	0.05*

NS = Not significant *= Significant

DISCUSSION

Rheumatoid arthritis [RA] is a chronic autoimmune disease of articular and extra-articular features. The most prominent features of RA are Joint pain, swelling and limited joint mobility. The course of the disease differs greatly between the patients. Some patients have a mild disease and some patients have progressive joint destruction and disability. Besides articular symptoms, RA can be associated with extra-articular features, including ophthalmic involvement[1]. Eye complications were found in 46 % of our study population.

Reddy et al.[9] found the incidence of eye complications in RA were 39% in100 patients. Also, Vignesh and Srinivasan[10] found the incidence of eye manifestations in RA were 39% of 196 patients. The incidence in our study slightly elevated from the previous studies, this may be due to the geographic difference.

The most common eye complications in our patients are dry eye [28.5%] and this agrees with Vignesh and Srinivasan[10] in their study found the incidence of dry eye was 28%. Also Punjabi et al.[11] reported that 27.3% of RA patients had dry eye in an Indian population, but Bettero et al.[12], reported secondary Sjögren's syndrome in 12.1% of the population with RA and Reddy and Rao[13] in there study found the incidence of dry eye was 16.6 %.

Dry eye results from decreased secretion of tears from the lacrimal glands due to atrophic and cirrhotic changes. The combination of this disease with dryness of mouth is referred to as the sicca syndrome. When associated with RA or another connective tissue disorder, the resultant triad is known as Sjögren's syndrome[14].

Keratitis and corneal ulceration may develop in such patients if the disease is not treated early. The diagnosis of secondary Sjögren's was made based on the American-European Consensus Criteria for Sjögren's syndrome which was based on the duration of

symptoms, Schirmer's test, and positive vital dye staining of the eye surface. Tear film osmolality also correlates with dry eye activity.

Tong et al.[15] found that tear film osmolality correlated with the severity of dry eye score. So, more research is needed on the markers of the eye surface in RA. Tong et al at.[15] studied the immune markers that lead to dryness of the eye and correlated with a disease activity.

Villani et al.[16] found that immune-suppression modified the eye surface pathology in RA patients with secondary Sjögren's syndrome. Also, Villani et al.[17] found the corneal surface activity was more in patients with secondary Sjögren's.

The second eye complication in our patients was episcleritis[4.0 %]and this agrees with Reddy et al.[9], that in their study they found the incidence of episcleritis was 3.7 % in RA patients, and also agree with Vignesh and Srinivasan[10] that in their study they found the incidence of episcleritis was 3%. But, McGavin et al. [2] studied 4,210 RA patients and established the incidence of episcleritis was 0.I7%. Bhadoria et al.[18] reported episcleritis in 0.93% of the patients.

The episclera is a thin layer of tissue that lies between the conjunctiva and the sclera. Episcleritis is a common condition, characterized by painless eye redness, typically presenting as redness, irritation, and watering of the eye with preserved vision. Most cases of episcleritis respond well to topical therapy alone and do not threat the vision. Many cases of episcleritis require no treatment and typically resolve over a short time. The third eye complication in our patients was scleritis [3.0%] and this agrees with Vignesh and Srinivasan[10] that, found the incidence of scleritis was 2%. But Reddy et al. [9] found the incidence of scleritis was 0.9 % in RA patients and McGavin et al.[2] reported the incidence of scleritis was 0.67% in RA patients.

The scleritis can be isolated to the eye, but about half of the affected cases it occurs secondary to an auto immune disease, such as rheumatoid arthritis or Wegener's granulo-matosis. Although uncommon, scleritis is often extremely painful condition and can lead to threatening of the vision.Scleritis is three types: the most common type is diffuse scleritis. The second type is nodular scleritis, and the third type is necrotizing scleritis and it the most severe type. Scleritis may be the early manifestation of autoimmune diseases. Corneal neovascularization is the in-growth of new blood vessels from the pericorneal plexus into avascular corneal tissue as a result of oxygen deprivation[19].

Corneal transparency is dependent on maintaining avascularity of the cornea that required for optimal vision. If corneal transparency decreased the visual acuity will deteriorate. The Cornea is avascular in nature and the presence of vascularization, which can be deep or superficial, is always pathologically related[20].

Corneal neovascularization [CNV] is a condition that threats the vision and caused by any cause of inflammation. Common causes of CNV are infection, chemical injury, autoimmune conditions, post-corneal transplantation, and traumatic conditions. Other causes are trachoma, corneal ulcers, rosacea keratitis, interstitial keratitis, sclerosing keratitis, chemical burns, and wearing contact lenses for long time[21]. CNV may be Superficial and are usually occurred with wearing of contact lens for long time and may be deep and caused by chronic inflammation and anterior eye segment diseases[22].

CNV in our study represent [2.0 %] of RA patients but the previous researches did not detect this complication so we may be the first research detect this sight-threatening condition with RA. The majority of eye complications seen in our study were in longstanding RA [56.14%], with significant difference [0.001] which was comparable to Vignesh and Srinivasan[10] in which the duration of RA in the patients with vision-threatening conditions like sclerosing keratitis and PUK was 10.5 years. Bettero et al.[12] reported eye complications in the patients who had a long duration of RA.

Our study demonstrated that the eye complications of RA seen in patients with high DAS 28 ESR [86.66 %], also with moderate

DAS28 ESR [80.48%], but [57.14 %] of patients with lowDAS28 ESR had ocular complications, with significant difference [0.05]. McGavin et al.[2], Foster et al.[3] and Dana at al.[4], demonstrated that the eye complications of RA seen in patients with a more severe form of the disease, and often exacerbated with increased activity of the disease.

Conclusion and recommendation: This study indicates that eye involvement is very common and the need for close follow-up. The rheumatologists should get an ocular examination as a routine for all RA patients at diagnosis and then at periodic intervals for early detection of any ocular involvement.

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