

**OCULAR MANIFESTATIONS IN A SAMPLE OF SYRIAN PATIENTS WITH
RHEUMATOID ARTHRITIS; A CROSS SECTIONAL STUDY**Hashem Obaid Hassnah*¹ and Dr. Maysoun Kudsi²¹Sixth Year Medicine Student²Professor of Rheumatology Damascus University
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ABSTRACT

Background: Rheumatoid arthritis is the most frequent systemic disease affecting the joints and other organs such as the eyes. We aimed to evaluate the frequency and characteristics of ocular manifestation in patients with rheumatoid arthritis. **Methods:** All the study subjects underwent complete ophthalmological examination involving visual acuity assessment, examination of anterior and posterior eye segments, Schirmer's test, diameter and mobility of pupils, as well as eyeball mobility assessment of intraocular pressure. Demographics data, disease duration, age at diagnosis, treatment, ocular symptoms and history were registered. **Results:** The age of study group was 41.5 ± 10 years. 78.59% were females. Ocular manifestation was present in 31.14%. The most common manifestation of ocular injury was episcleritis (57.03%), while scleritis was diagnosed in 16.41%. The most affective factors that lead to the ocular manifestations were biological treatment, and diagnosis age. **Discussion:** The prevalence of ocular manifestation ranges between 39% and 66%, and it is increased with the disease duration. The most common manifestation of ocular involvement was dry eye, episcleritis, and scleritis. Uveitis is rare, occurring as a complication of scleritis, and as a complication of anti-TNF agents. Some studies showed that positive serum RF and ACPA significantly increased the risk of having more ocular manifestations, especially dry eyes. Studies experience that the ocular manifestations prevalence significantly more frequent among male patients, long disease duration and treatment with biologics and DMARDs. **Conclusion:** Ocular symptoms are relatively frequent complications of RA, and may result in irreversible changes in vision. Regular ophthalmological examinations are essential among RA patients.

KEYWORDS: rheumatoid arthritis, episcleritis, biological treatment, ocular manifestations.**INTRODUCTION**

Rheumatoid arthritis (RA) is a systemic immune disease that damages synovial joints. It can affect any organ including the eye.^[1]

Several forms of eye disease can occur in patients with RA, and the clinical course of the ocular disease may be quite variable.^[2]

Early diagnosis of ophthalmic disease in RA patient with RA is very important, since it permits the timely management of potentially serious sight-threatening complications.^[2,3]

Ocular manifestations in RA include keratoconjunctivitis sicca, episcleritis, scleritis, corneal changes, and retinal vasculitis.^[2-4]

The presence of ocular disease may be an indication of the disease activity. However, ocular involvement, in

particular severe dry eye, may exist independently from severe articular disease and should be evaluated in all RA patients.^[4,5]

Ocular disease is prevalent in established and long-standing systemic diseases; it may also be a presenting manifestation of RA, and it is highly probable that the ophthalmologist is the first to encounter these patients.^[2-5] The aim of our study was to present different ocular manifestations of RA and their frequency, and characteristics.

PATIENT AND METHODS**Study design and population**

A descriptive cross-sectional study was conducted at the Rheumatology Unit in Damascus Hospital, Damascus, Syria from January 2021 to January 2023. A total of 411 patients with rheumatoid arthritis diagnosed according to the 2010 ACR / EULAR criteria^[6] were enrolled in our study.

The sample size was calculated using the website (Raosoft.com) and it was (40) patients with a confidence interval level of (95%). The study was approved by the Ethical Committee of Faculty of Medicine, (BN53214, 2021), Syrian Private University, Syria.

Inclusion criteria: RA patient >18 years old who signed the confirmed consent.

Exclusion criteria: Patients above 60 year old, patients with history of infection, patient with other connective tissue diseases or overlap syndrome, previous eye diseases, surgery or trauma to the eye, hypertension, and diabetes mellitus.

Methods: Demographic and clinical characteristics were collected including: Age, gender and body mass index, RA duration, the present main complain, including the number of painful and swollen joints, duration of morning stiffness, and the patient's self-evaluation had also been asked and registered for patients.

Presence of eye symptoms such as pain, dryness, redness, photophobia, discharge, and blurred vision, medical history, treatment, clinical disease activity index (DAS28).^[7]

Physical examination

Clinical examinations of the body. Rheumatologic examination includes: the number of tender and swollen joints in patients.

Schirmer test was done to all patients and then all of them were examined by a same consultant

ophthalmologist by fundoscopy and slit lamp examination.

Laboratory tests included RF, ACPA, CRP and erythrocyte sedimentation rate.

Study tools

1-2010 ACR / EULAR criteria (6) for the diagnosis of RA

2-Disease Activity Score28 (7) for assessment of disease activity, as: remission; DAS 28<2.6, mild; DAS=2.6-3.2, moderate; DAS=3.2-5.1, and severe; DAS>5.1.

DAS28: is based on:

- Number of tender palpable joints.
- Number of swollen joints.
- Patient's assessment of the pain severity (90-100)
- The value of CRP or ESR

Statistical analysis

Statistical software (SPSS version 22, IBM, USA), and Excel 2010 were used for analysis. Kolmogorov-Smirnov test was used to assess the normal distribution of continuous variables. Continuous variables were reported as mean ±SD, and categorical variables as frequencies and percentages. P value < 0.05 was considered statistically significant.

RESULTS

Descriptive data

The age of study group ranged between 20-59 years with a mean of 49.25±17.155(11-97) years. 323(78.59%) RA patients out of 411 were females, and meanwhile 88(21.41%) RA patients were males (Figure-1)

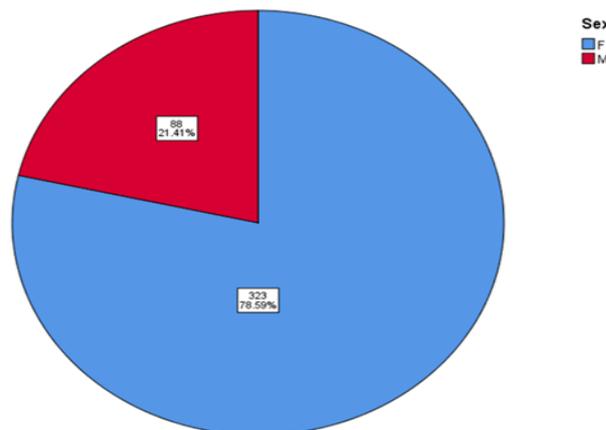


Figure-1: Male and female distribution.

350(85.2%) of patients were married, 61(14.8%) of patients were single.

Table1 showed the comorbidities in our sample patients

Table 1: Comorbidities percent.

		Responses		Percent of Cases
		N	Percent	
Medical history	Hypertension	49	11.5%	11.9%
	Diabetes	27	6.4%	6.6%
	Asthma	7	1.6%	1.7%
	cardiac illness	3	0.7%	0.7%

	kidney failure	2	0.5%	0.5%
	hepatitis B	1	0.2%	0.2%
	None	335	78.8%	81.5%
	Thalassemia	1	0.2%	0.2%
Total		425	100.0%	103.4%

We have 159 had the diagnosis for less than 5 years and 4.40% of them had the eye manifestation, and 108 patients had the diagnosis for 5-10 years and 20.95% of them had ocular manifestation, and 34 patients had the

diagnosis for 10-15 years and 64.70% of them had the ocular manifestation, and 100 patients had the diagnosis for more than 15 years and 83.00% of them had ocular manifestation (Table-1).

Table-2:

Number of patients	Disease duration, years	Percent of ocular manifestation,%
159	<5yrs.	4.40%
118	5-10yrs.	20.95%
34	10-15yrs	64.70%
100	>15yrs.	83.00%

A positive serum for RF was obtained in 349(84.9%) of patients. While a positive ACPA was found in 398(96.8%) patients. ESR was elevated in 399(97.1%) of patients, meanwhile CRP was elevated in 398(92.7%) of patients.

Table 2, and 3 showed the treatment of our patients. About a third of patients ((43.1%) were treated with biologics.

Table 3: Treatment.

				Percent of Cases
		N	Percent	
Drugs	hydroxy chloroquine	76	7.9%	18.5%
	methotrexate	289	29.9%	70.3%
	Levo	5	0.5%	1.2%
	sulfasalazine	88	9.1%	21.4%
	NSAIDS	372	38.5%	90.5%
	corticosteroid	132	13.7%	32.1%

Table 4: Biologic treatment.

	Frequency	Percent	Valid Percent	Cumulative Percent
Yes	177	43.1	43.1	43.1
No	234	56.9	56.9	100.0
Total	411	100.0	100.0	

Ocular manifestation was present in 128 patients (31.14%) of patients, in 91(28.17%), of females, and in 37 of males (Figure-2)

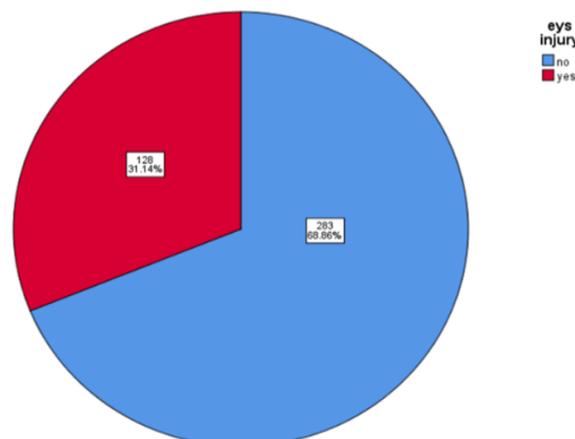


Figure-2: Ratio of ocular injury in our sample.

The eye involvement was unilateral in 79 patients and bilateral in 49 patients.

Dry eye was found in 150(36.5%) of patients, burning sensation was found in 140 (34.1%) of patients, Foreign body sensation was found in 90 (21.9%) of patients, painful eye was found in 81(19.7%) of patients, itchy eye was found in 104(25.3%), of patients, redevye in 106(25.8%) of patients, photophobia was found in 110(26.8%), of patients.

All patients were examined by the same ophthalmologist.

The most common manifestation was episcleritis, which was found in 85 patients (20.2%), while scleritis was diagnosed in 29(6.9%) of patients, glaucoma was present in one patient, while retinitis was present in 10 (2.4%) patients. KCS was present in 5(1.2%) patients. There were no patients with necrotizing scleritis among our sample. scleromalacia of cornea was not present in our patients (Table 4, and Figure 3).

Table-5:

		Responses		Percent of Cases
		N	Percent	
Eyes injury type	Scleritis	29	6.9%	7.1%
	Episcleritis	85	20.2%	20.8%
	KCS	5	1.2%	1.2%
	Retinitis	10	2.4%	2.4%
	Glaucoma	1	0.2%	0.2%
	Cataract	8	1.9%	2.0%

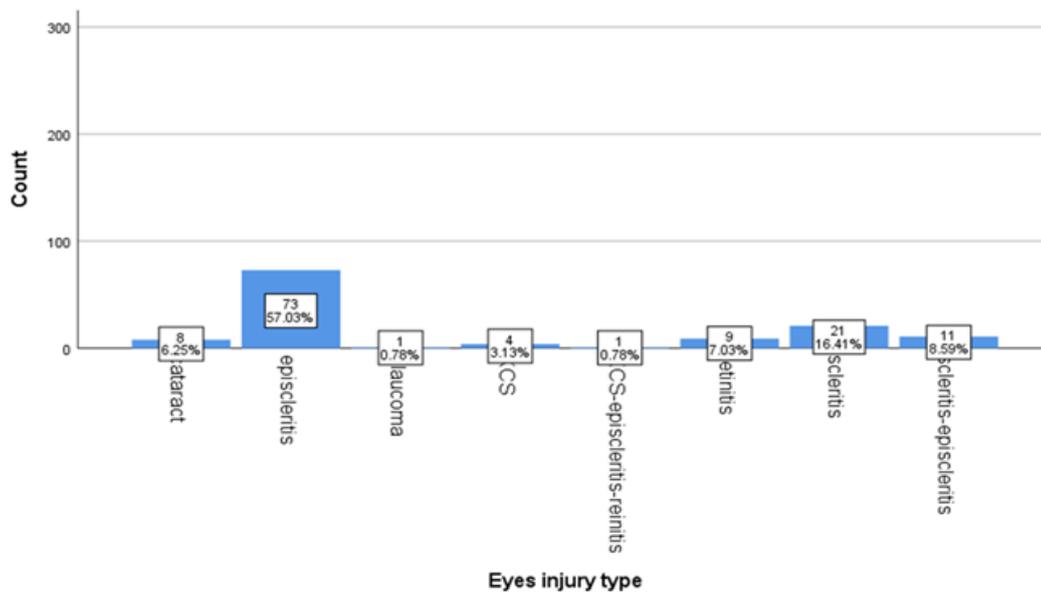


Figure-3: Ocular manifestations.

Analytical data

To study the effect of each of the predictor variables on the risk of having ocular manifestation, a multiple logistic regression model was used. Age and age at diagnosis, sex, comorbidities, duration of disease, and treatment with biologic DMRADs and steroids were included in the logistic model as predictors.

The diagnosis age had a strong significance, the more the diagnosis age is older, the higher ratio of ocular manifestations is rising (Table-5):

There was no relation between age, sex, duration of disease, laboratory tests (ESR, CRP), and treatment with DMRADs and ocular manifestation. Meanwhile there was a significant correlation between diagnosis age, comorbidities, and treatment with biologics and ocular involvement (Table-5, table-6, table-7, and table 8 respectively)

Table-6:

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	213.754 ^a	4	.000	.000	
Likelihood Ratio	224.439	4	.000	.000	
Fisher's Exact Test	220.845			.000	
Linear-by-Linear Association	167.476 ^b	1	.000	.000	.000
N of Valid Cases	411				

Comorbidities had a strong association with ocular manifestations. Results are based on nonempty rows and columns in each innermost sub-table. a. More than 20% of cells in this sub-table have expected cell counts less

than 5. Chi-square results may be invalid. The minimum expected cell count in this sub-table is less than one. Chi-square results may be invalid (Table-6).

Table-7:

		eyes injury
Medical History	Chi-square	13.950
	df	8
	Sig.	.083 ^{a,b}

Table-8:

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	139.349 ^a	1	.000	.000	.000
Continuity Correction	136.821	1	.000		
Likelihood Ratio	148.102	1	.000	.000	.000
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	139.010 ^c	1	.000	.000	.000
N of Valid Cases	411				

Table-9:

			Eye injury		Total
			Yes	No	
Biological treatment	Yes	Count	110	67	177
		% within biological treatment	62.1%	37.9%	100.0%
		% within eyes injury	85.9%	23.7%	43.1%
	No	Count	18	216	234
		% within biological treatment	7.7%	92.3%	100.0%
		% within eyes injury	14.1%	76.3%	56.9%
Total	Count	128	283	411	
	% within biological treatment	31.1%	68.9%	100.0%	
	% within eyes injury	100.0%	100.0%	100.0%	

Logistic Regression

Case Processing Summary			
Unweighted Cases		N	Percent
Selected Cases	Included in Analysis	411	100.0
	Missing Cases	0	.0
	Total	411	100.0
Unselected Cases		0	.0
Total		411	100.0

a. If weight is in effect, see classification table for the total number of cases.

Model Summary			
Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	414.001 ^a	.031	.048

a. Estimation terminated at iteration number 20 because maximum iterations has been reached. Final solution cannot be found.

DISCUSSION

RA affects middle age population with predominance of females(1), which is consisted with our results, as the mean age of our sample patient was 41.5±10 years, and 323(78.59%) of them were females.

The prevalence of ocular manifestation ranges between 39% and 66% according to different studies.^[8-10] It was 31.14% in our study, which is compatible with the previous studies.^[8-10] This difference may attribute to the different ethnic group, meanwhile we had only one ethnic in Syria.

The risk of occurring of ocular manifestations in RA is increased with the disease duration^[11], and this in concordance with our results.

Dry eye, as a symptom was found in 36.5%, followed by burning sensation was found in 34.1%, which is compatible with other studies.^[3,13]

The most common manifestation of ocular involvement was episcleritis, scleritis, retinitis, and KCS.^[8,14] Our results are concordance with some studies^[8,14], and different from others.^[9,15] This may be explained by different ethnic population and environmental factors.^[15]

The prevalence of keratitis in the current study was 1.2% patients closely similar to the study done by Kumar *et al.*^[8] Retinitis was found in 1.2% which is lower than by Kumar *et al.*^[8], and this may due to the smaller number of patients in our study.

Episcleritis prevalence in this study was 16.41%, which similar to Zlatanović *G, et al.*^[3], and different to Kumer, *etal.*^[8]

The most common type is simple episcleritis, in which there are intermittent bouts of moderate-to- severe inflammation that often recur at 1- to 3-month intervals. The episodes usually last 7-10 days and most resolve after 2-3 weeks. Prolonged episodes may be more

common in patients with associated systemic conditions.^[16]

Necrotizing scleritis with or without inflammation is much less frequent, and associated with systemic autoimmune disorders.^[16] There was no case of necrotizing scleritis in our study.

In rheumatoid arthritis, uveitis is rare, occurring as a complication of scleritis, and as a complication of anti-TNF agents that used as a treatment of RA.^[14,17,18]

Some studies showed that positive serum RF and ACPA significantly increased the risk of having more ocular manifestations, especially dry eyes^[12,19] which dis-agree with the results we obtained.

Zlatanović *et al*^[3], and Bettero *et al*^[13] studies that reported women were more affected than men, which is in concordance with ours, and this can be explained by different environmental and genetic factors between these populations.

Age, and sex showed no statistically significant association with ocular manifestations which disagreed with Reddy *et al.*^[9]

No available data to support correlation between ESR, and CRP with ocular eye manifestation in rheumatoid arthritis.

Regarding drug induced ocular manifestations in RA in the present study, the most common one is the cataract as complication of systemic glucocorticoids, which is slightly higher than that obtained by Hamied *et al.*^[20], the reason may due to different steroid dose and duration.

CONCLUSION

Extra-articular involvement of organs in RA is significant. Ocular manifestations involved with RA are episcleritis, scleritis, KCS, glaucoma, retinitis and cataract. The most common manifestation was episcleritis. Patients with biological treatment, and the

prolonged period of the illness have more risk to have ocular manifestations. We were the first study that correlated between ocular manifestation and the age of disease diagnosis.

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