RESEARCH ARTICLE

Dry eye disease and high disease activity score (DAS-28) in rheumatoid arthritis: An underrated combination

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Abstract

Objective: To determine the association of dryness of eyes with rheumatoid arthritis severity.

Method: The cross-sectional, observational study was conducted at the Jinnah Medical College Hospital, Karachi, from December 2020 to May 2021, and comprised adult patients of either gender with rheumatoid arthritis who were diagnosed on the basis of clinical and serological investigations. Data was collected using a structured pre-tested questionnaire. Ocular Surface Disease Index questionnaires with Tear Film Breakup Time were used to assess the severity of dry eyes. Disease Activity Score-28 with erythrocyte sedimentation rate was used to assess the severity of rheumatoid arthritis. Association between the two was explored. Data was analysed using SPSS 22.

Results: Of the 61 patients, 52(85.2%) were females and 9(14.8%) were males. The overall mean age was 41.7±12.8 years, with 4(6.6%) aged <20 years, 26(42.6%) aged 21-40 years, 28(45.9%) aged 41-60 years and 3(4.9%) aged >60years. Further, 46(75.4%) subjects had sero-positive rheumatoid arthritis, 25(41%) had high severity, 30(49.2%) had severe Occular Surface Density Index score and 36(59%) had decreased Tear Film Breakup Time. Logistic Regression analysis showed there were 5.45 times higher odds of having severe disease among the people with Occular Surface Density Index score >33 (p=0.003). In patients with positive Tear Film Breakup Time, there were 6.25 higher odds of having increased disease activity score (p=0.001).

Conclusion: Disease activity scores of rheumatoid arthritis were found to have strong association with dryness of eyes, high Ocular Surface Disease Index score and increased erythrocyte sedimentation rate.

Keywords: Rheumatoid arthritis, Tear film breakup time, Disease activity score-28, Dry eye, Ocular surface disease index. (JPMA 73: 275; 2023) **DOI: https://doi.org/10.47391/JPMA.5558**

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Introduction

The ocular surface needs a tear film covering the whole surface of the eye in order to maintain its health and protective function. Dry eye is a multifactorial disease in which tears and ocular surface are accompanied with the characteristic symptoms of discomfort, visual disturbance and tear film instability as well as increased permeability of tear film and ocular surface inflammation.[1,2]

Among the patients with dry eye syndrome, some patients are complicated with systemic immune diseases. The prevalence of dry eyes in primary Sjogren's syndrome (SS), systemic lupus erythematosus (SLE), and rheumatoid arthritis (RA) are the highest in systemic immune diseases. These autoimmune diseases are caused by infiltration of lymphocytes and plasma cells in salivary and lacrimal glands which play a major role in glandular destruction that causes dry eyes. The dry eye symptoms and signs of such patients are often more serious, the treatment effect is poorer, and the prognosis is not ideal.[3,4]

When compared to the incidence of dry eye in the general population, which ranges 5-17%, the incidence among RA individuals is substantially greater (19-31%).[1] Recent studies show that the pathogenesis of dry eye is similar to the other extra-articular complications of RA which includes mucosal autoimmune disease.[5] It is speculated that the degree of dry eye may also change with the systemic conditions, due to the influence of systemic immune response. The current study was planned to determine the association of dry eye withe RA severity.

Patients and Methods

The cross-sectional, observational study was conducted at the Jinnah Medical College Hospital, Karachi, from December 2020 to May 2021. After approval from the institutional ethics review committee, the sample was raised using non-probability, consecutive sampling technique.

Those included were adult patients of either gender diagnosed RA on the basis of serological and clinical investigations who were negative for anti-Ro and anti-La

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antibodies. Those excluded were patients with comorbidities, including thyroid disease, vitamin A deficiency and diabetes mellitus (DM). Patients who had a history of alcohol abuse and smoking, those with a history of skin allergies and taking treatment for dry skin, patients taking the antidepressants, antihistamine, beta blockers, and accutane and other retinoids for the preceding 6 months were also excluded. Besides, patients currently taking ocular topical treatment, or had previous ocular surgical treatment or were on treatment in the preceding six months, and patients with history of ocular trauma or using contact lens in the preceding 6 months were excluded as well.

After taking informed consent from the subjects, data was collected using a pre-designed proforma. The calculation of Disease Activity Score-28 with erythrocyte sedimentation rate (DAS-28-ESR) score was done and on the same day the patient was assessed for Tear Film Breakup Time (TBUT) after which the Ocular Surface Disease Index (OSDI) score was worked out.[6-9]

Data was analysed using SPSS 22. Quantitative data was presented as mean and standard deviation. Qualitative data was presented as frequencies and percentages. Data was further assessed using t-test and Chi-square test, while logistic regression analysis was also run. P<0.05 was considered statistically significant.

Results

Of the 158 patients assessed, 61(38.6%) were included; 52(85.2%) females and 9(14.8%) males (Figure 1). The overall mean age was 41.7±12.8 years, with 4(6.6%) aged <20 years, 26(42.6%) aged 21-40 years, 28(45.9%) aged 41-60 years and 3(4.9%) aged >60 years. Demographic and clinical data was noted in detail (Table 1). In terms of ESR values, majority had ESR >20 (Figure 2). TBUT time (Figure 3) and OSDI score (Figure 4) were also noted.

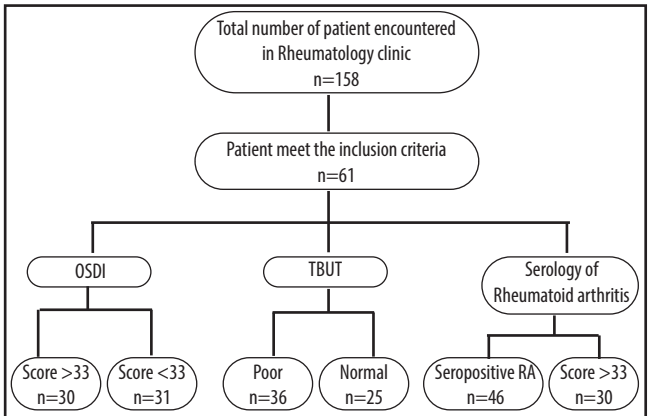

Figure-1: Study flowchart.
OSDI: Ocular surface disease index, TBUT: Tear film breakup time, RA: Rheumatoid arthritis.

Further, 46(75.4%) subjects had sero-positive RA, 25(41%) had high severity, 30(49.2%) had severe OSDI score and 36(59%) had decreased TBUT (Table 2).

Table-1: Characteristics of RA patients with dry eye.

Characteristics	n (%)
Age (years)	
< 20	4 (6.6)
21-40	26 (42.6)
41-60	28 (45.9)
More than 60	**3 (4.9)**
Gender	
Male	9 (14.8)
Female	52 (85.2)
Marital status	
Single	10 (16.4)
Married	51 (83.6)
Status of patient	
Outpatient	61
Monthly income In rupees	
< 20,000	10 (16.4)
21,000-40,000	31 (50.8)
41000-60,000	15 (24.6)
61,000-80,000	3 (4.9)
More than 80,000	2 (3.3)
Smoker	
Yes	1 (1.6)
No	60 (98.4)
Family history of Autoimmune disease	
Yes	16 (26.2)
No	45 (73.8)
Previous history of dry eyes	
Yes	7 (88.5)
No	54 (11.5)
Duration of disease	
< 1 year	15 (24.6)
1-5 years	28 (45.9)
5-10 years	9 (14.8)
More than 10 years	9 (14.8
Raised ESR	
Yes	13 (21.3)
No	48 (78.7)

RA: Rheumatoid arthritis, ESR: Erythrocyte sedimentation rate.

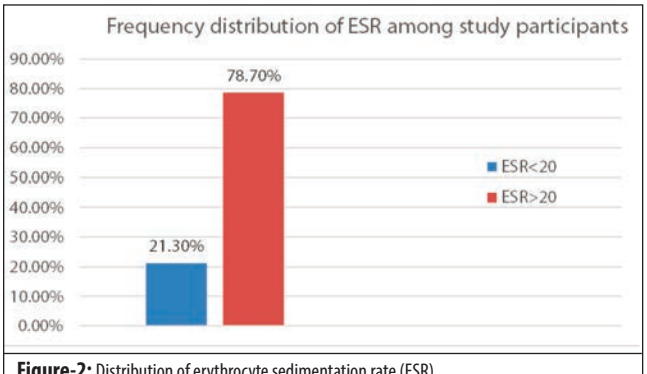

Figure-2: Distribution of erythrocyte sedimentation rate (ESR).

Table-2: Disease-specific characteristics.

Disease characteristics	n (%)
Serological status of RA patients	
Sero positive	46 (75.4)
Seronegative	15 (24.6)
DAS score	
Remission	5 (8.2)
low	10 (16.4)
Moderate	21 (34.4)
High	25 (41.0)
OSDI	
Normal	20 (32.8)
Mild	4 (6.6)
Moderate	7 (11.5)
Severe	30 (49.2)
TBUT	
Normal	25 (41)
Poor	36 (59)

Disease Activity Score (DAS) score: Remission <2.6, low 2.6-3.1, moderate 3.2-5.0, high >5.1. Ocular Surface Density Index (OSDI): Normal 0-12, mild 13-22, moderate 23-32, severe 33-100. Tear Film Breakup Time (TBUT): Nnormal >10 seconds, poor <10 seconds.

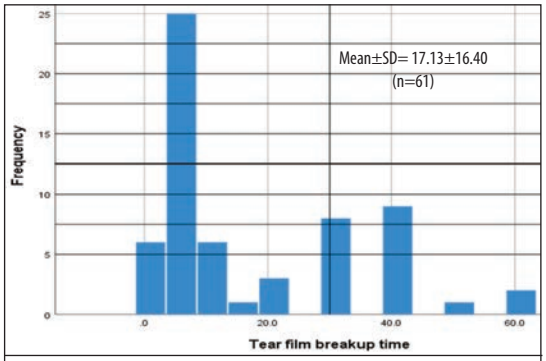

Figure-3: Frequencies of Tear film breakup time (TBUT).

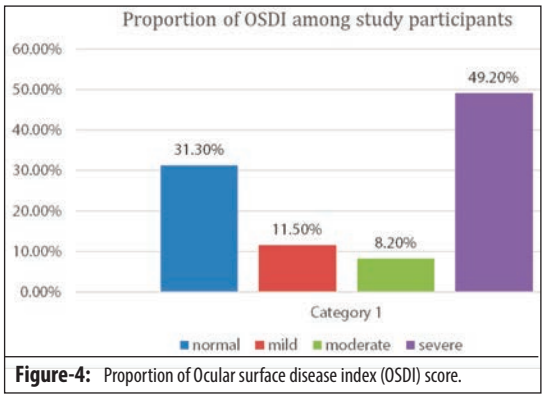

Figure-4: Proportion of Ocular surface disease index (OSDI) score.

Factors associated serological status of RA included dry eyes (Table 3).

There were 5.45 times higher odds of having severe disease among RA patients with OSDI score >33 (p=0.003). In patients with positive TBUT, there were 6.25 higher odds of having increased disease activity score (p=0.001) (Table 4).

Table-3: Factors associated with the serological status.

Characteristics	Sero-negative (n)	Sero-positive (n)	*p*-value	Odds Ratio	95% CI
Age (years)					
<40 years	06	24	0.411	1.255	0.752-2.093
>40 years	09	22			
Gender					
Female	11	41	0.416 [a]	1.183	0.130-1.917
Male	03	06			
Marital status					
Married	13	38	0.0429 [a]	3.079	1.355-26.69
Single	01	09			
Smoking status					
Smoker	00	01	1.00	0.767	0.667-0.882
Non Smoker	14	46			
Family History					
Negative	03	13	0.742	1.075	0.806-1.434
Positive		11	34		
Dry Eyes					
Yes	04	03	0.042 [a]	1.901	0.801-4.515
No	10	44			
DAS score					
Remission	03	07			
Low	01	06	0.090 [a]	0.653	0.354-1.621
Moderate	01	17			
Severe	09	17			
OSDI					
Normal	02	18			
Mild	01	03	0.363 [a]	0.256	0.874-1.352
Moderate	01	05			
Severe	09	21			
Duration of Disease					
<1 year	04	11			
2-5 years	06	22			
6-10 years	03	06	0.702 [a]	1.653	0.257-2.14
>10 years		01	08		
TBUT					
Normal	10	27	0.053 [a]	1.852	1.007-6.766
Poor	04	20			

CI: Confidence interval, DAS: Disease activity score, OSDI: Ocular surface disease index, TBUT: Tear film breakup time. [a] Fisher exact test performed: p<0.05 was considered significant

In terms of ESR values, majority had ESR >20 (Figure 2). TBUT time (Figure 3) and OSDI score (Figure 4) were also noted.

Discussion

Studies in the past have shown some controversies regarding the association of dryness of eye with RA severity.[10]

In the current study, 36 of 61 RA patients had dry eye, which was assessed with TBUT, which showed significant correlation with RA severity (DAS-28), and there was 6.7 times higher odds for high OSDI score to have increased DAS-28 score. Also, there was 5.5 times higher odds of increased ESR leading to increased DAS-28 score.

Table-4: Factors associated with severity of rheumatoid arthritis (RA) through logistic regression analysis.

Independent variables	DAS <5 (not-severe)	DAS >5 (severe)	Unadjusted Ratio Odds	Adjusted odds	*p*–value	95% Confidence Interval
Age (years)						
>40 years	20	11	1.585	2.578	0.025*	1.41-3.323
<40 years	22	08				
Gender						
Female	35	17	1.586	3.47	0.053*	3.25 -7.03
Male	7	2				
Marital status						
Married	33	18	3.556	5.87	0.01*	6.54-18.406
Single	9	1				
Income (PKR)						
<40,000	27	14	0.786	0.987	0.654	0.420-1.475
>40,000	15	5				
Duration						
>5 years	12	6	0.741	1.21	0.065	1.253-3.24
< 5 years	30	13				
OSDI						
>33	15	15	6.750	5.45	0.003*	3.94-24.054
<33	27	4				
TBUT						
Poor	20	16	4.987	6.25	0.001*	3.32-16.239
normal	22	3				
ESR						
>20	29	19	5.5	7.58	0.038*	5.10-27.49
<20	13	0				

CI: Confidence interval, DAS: Disease activity score, OSDI: Ocular surface disease index, TBUT: Tear film breakup time. [a] Fisher exact test performed: $p<0.05$ was considered significant.

Contrarily, a study concluded that there was no correlation between dry eye with DAS-28 scores.[11] However, the other study found positive correlation between duration of disease and dryness of eyes, while the current study found no such association. A study concluded that there was negative correlation for Schirmer test scores, duration of disease, relationship of DAS-28 score and ocular manifestation of RA.[12] Fujita et al. concluded that dryness of eyes can be seen in patients with or without Sjogren syndrome, but the relationship between disease severity and dryness of eye was not significant.[13] Another study said there was no significant association of eye dryness with RA severity.[14]

However, some studies reported some relationship between eye dryness and DAS-28 parameters.[15,16] These studies hypothesised that the positive results were due to a non-standard drug regime. In the current study as well, most patients were diagnosed late which delayed their treatment.

Dryness of eyes has been a major concern for rheumatologists while treating RA patients with multiple comorbidities. Eyes should always be examined especially in the patients with DAS-28 score of >5, starting with the screening of symptoms by using OSDI score and along with the confirmatory test TBUT (10s). Dry eye questionnaires and OSDI scores can also be used to screen and confirm the disease respectively.[4,17]

The current study has certain limitations, sample size was not calculated in this study and only those patients were enrolled in the study who fulfilled the inclusion criteria and visited during specified time of study. Due to limited resources, TBUT was used to confirm eye dryness when assessment with other modalities, like Schirmer test, Lissamine Green test and tear osmolarity test, would have given more specific results.

Conclusion

DAS-28 score of RA had a strong association with eye dryness, high OSDI score and raised ESR. RA patients should be screened for eye dryness.

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Conflict of Interest: None.

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