



MULTICENTRE PROSPECTIVE STUDY ON DRY EYES IN PERIPHERAL DISTRICT REFERRAL HOSPITAL

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ABSTRACT

Aim of Study: To identify the causes of dry eyes from patients who have attended our Out-Patient Department of Ophthalmology of the Peripheral District Head Quarters Hospital, kallakurichi and confirming the causes of their autoimmune and other related rheumatic Diseases associations from two referral Rheumatology Centres of Salem. **Introduction:** Dry eye disease is a chronic condition of the corneal surface marked by persistent symptoms of irritation or burning that can cause inflammatory damage to the cornea and conjunctiva if untreated. Common risk factors for this syndrome include advancing age, female sex, low humidity environments, systemic medications, and autoimmune disorders. **Materials And Methods:** All patients presented with dry eye symptoms include burning, foreign body sensation; itching, dryness and photophobia were recruited from Peripheral District Head Quarters Hospital, kallakurichi, Tamil Nadu State in a period of three years (March 2015 - February 2018). We did following tests as Schirmer Test, Tear film break up time (TBUT), Ocular straining score (OSS), atleast two must be positive for the initial working up diagnosis of dry eye syndrome. **Results:** In a total of 42 patients, five (12%) were males and 37 (88%) were females. Thirty (out of 42) patients had definite dry eye were included in the study. the prevalence of dry eye was 60% in males and 73% in females. The mean age of studied Dry eye patients was 45.40 ± 9.7 years. The mean duration of Dry eye was 4.69 ± 4.2 years. The mean DAS-28 was 5.27 ± 1.2 . RF was positive in 12 (40%) patients while anti SSA/Ro and anti SSB/La was negative in all patients. **Conclusion:** severity of dry eye is not correlated with activity of RA but with its duration. Dry eye cannot be excluded even in patients with only mild RA hence dry eyes should be always thought off in all cases of RA and further firmly insist that regardless of RA disease activity.

KEYWORDS :

INTRODUCTION:

Dry eye disease is a chronic condition of the corneal surface marked by persistent symptoms of irritation or burning that can cause inflammatory damage to the cornea and conjunctiva if untreated. Common risk factors for this syndrome include advancing age, female sex, low humidity environments, systemic medications, and autoimmune disorders. Recently, a hospital-based study from north India reported a prevalence rate of 32%, in which a majority of the patients were categorized with moderate to severe DED. Another study from south India reported an incidence rate of 1.46%. Rheumatoid Arthritis is the most common autoimmune disorder associated with dry eye. Dry eye is the most common ocular manifestation of RA.^{4,7} Dry eyes in rheumatoid arthritis patients may be a manifestation of secondary Sjogren's syndrome (SS). Ocular involvements, particularly dry eye, may present independently from severe articular disease and should be evaluated in all patients with RA regardless of articular disease.

MATERIALS AND METHODS

Forty-two patients presented with dry eye symptoms include burning, foreign body sensation; itching, dryness and photophobia were recruited from Peripheral District Head Quarters Hospital, kallakurichi, Tamil Nadu State in a period of three years (March 2015 - February 2018). Those patients with dry eye symptoms have been referred to the Department of Rheumatology, Government Mohan Kumaramangalam Medical College Hospital and to Akitha Hospital, the Centre of Excellence for Autoimmune Diseases, Salem and subjected them for further evaluations for identifying the autoimmune and rheumatism causes and to confirm the diagnosis. Exclusion criteria include any conditions associated with dry eye as Steven Johnson, pemphigus vulgaris, sarcoidosis, infections as hepatitis C virus (HCV) and human immunodeficiency virus (HIV), diabetes, contact lens wear, history of refractive corneal surgery and treatment with antidepressants and parasympatholytic drugs, chronic smokers. But for study, we have specifically included only RA,

primary and secondary Sjogren's syndrome.

This study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki. Ethical approval for the study was obtained from local ethics committee. Informed consent was obtained from the patients who have been included in the study.

Ophthalmologic Examination:

We did following tests to come to our clinical diagnosis of dry eye. Among three available tests such as Schirmer Test, Tear film break up time (TBUT), Ocular straining score (OSS), atleast two must be positive for the initial working up diagnosis of dry eye syndrome.

Systemic Examination:

All our study patients are fully evaluated with their history of dry eyes and its durations, other related sicca symptoms like dry mouth, dry vulvovaginal areas, and did proper ophthalmic and physical examinations of small and large joints. The suspected RA cases assessed with DAS 28 (Disease Activity Score) for the swollen, tender joints and with bed side test of ESR (Erythrocyte Sedimentation Rate) and applied visual analog scale for pain etc.

DAS is 3.2 or less -mild disease activity,
3.2 to 5.1 - moderate disease activity
more than 5.1 -high disease activity.
less than 3.2 or below 2.6 RA under remission

Laboratory Investigations:

ESR(mm/h),
Rheumatoid factor (RF)
C-reactive protein (CRP)
ANA
Anti SSA/Ro and anti SSB/La anti-bodies

Minor Salivary Gland Biopsy (MSGB)

Done for moderate to severe dry eyes.

Histopathologically studied for number glands, looked for the presence and number of lymphocytic foci (focus score) in each patient sample. One lymphocytic focus is defined as a group of >50 lymphocytes and considered for the diagnosis of Sjogren Syndrome when the focus score more than 1 per 4mm²

RESULTS:

In a total of 42 patients, five (12%) were males and 37 (88%) were females. Thirty (out of 42) patients had definite dry eye were included in the study. Three (10%) patients were males and 27 (90%) were females. Thus, the prevalence of dry eye was 60% in males and 73% in females.

The mean age of studied Dry eye patients was 45.40 ± 9.7 years. The mean duration of Dry eye was 4.69 ± 4.2 years. The mean DAS-28 was 5.27 ± 1.2. RF was positive in 12 (40%) patients while anti SSA/Ro and anti SSB/La was negative in all patients. Table 1 shows the demographic, clinical and laboratory data of Dry eye patients.

Table 1. The Characteristics Of All Our Study Groups Of Dry Eye Patients With RA

Status and Characteristics	Total No of Dry eye patients (n = 30)
Age, in years with mean (SD)	45.40±9.7
Male, n (%)	3 (10%)
Female, n (%)	27 (90%)
Duration of RA, years, mean (SD)	4.69±4.2
Tender joints, mean (SD)	11.77±9.02
Swollen joints, mean (SD)	2.73±2.4
DAS-28, mean (SD)	5.27±1.2
ESR first hour, mm/h, mean (SD)	46.73±21.4
RF, number (%)	12 (40%)
Anti SSA/Ro, number (%)	0 (0%)
Anti SSB/La, number (%)	0 (0%)

Table 2. Showing Patient's With Dry Eye Test Results.

Dry eye basic Tests	Dry eyes patients with RA (n=30)		
	Results	Number of pts	percentage
Schirmer test	5-10mm	21	70%
	<5mm	9	30%
TBUT	5-10s	15	50%
	<5s	15	50%
OSS	<3	26	86.7%)
	≥3	4	13.3%)

Table 3. Correlation Between Ocular Tests In Relation To Disease Activity Score And Different Clinical And Laboratory Data.

Clinical Exam	Schirmer test		TBUT		OSS	
	r	P-values	r	P-values	r	P-values
DAS-28	0.155	0.4	0.332	0.07	0.181	0.3
Tender joints	0.160	0.4	0.352	0.06	0.324	0.08
Swollen joints	-	0.4	0.016	0.9	-	0.8
Duration of RA (years)	0.616	<.0001*	0.198	0.3	0.523	.003*
ESR	0.114	0.5	0.206	0.3	0.273	0.1
RF	0.059	0.8	0.082	0.7	0.080	0.7

*statistically significant

Table 4. Characteristics Severe Dry Eye With RA And Had MSGB Procedure.

Category	Patient 1	Patient 2	Patient 3	Patient 4
Result of biopsy	Focus score <1	Within normal	NSCS	Focus score <1
Age in years	40	50	61	49
Sex	Female	Female	Female	Female

Duration of RA	8	10	6	20
Tender joints	10	0	4	20
Swollen joints	6	0	3	2
DAS 28	5.96	3.47	5.10	4.33
ESR first hour, mm/h	65	80	70	28
RF	Positive	Positive	Negative	Negative
Anti SSA/Ro	Negative	Negative	Negative	Negative
Anti SSB/La	Negative	Negative	Negative	Negative
Schirmer test, mm	<5	5-10	5-10	<5
TBUT, s	5-10	<5	<5	<5
OSS	>3	>3	>3	>3

NSCS: nonspecific chronic sialadenitis; RA: rheumatoid arthritis; DAS: disease activity score; ESR: erythrocyte sedimentation rate; RF: rheumatoid factor; TBUT: tear film break up time; OSS: ocular staining scores.

DISCUSSION

Dry eyes can be a symptom of Sjogren's syndrome and it is a common autoimmune disorder that's often associated with rheumatoid arthritis and else as separately with primary Sjogren syndrome or occasionally with other autoimmune diseases like systemic Lupus erythematosus (SLE), mixed connective tissue diseases (MCTD) and etc.

Dry eye diseases due to tears and ocular surface symptoms that often fail to correspond to diagnostic testing. It is a widespread problem that may often be overlooked since it is not a common cause of permanent visual morbidity. We often fail in picking up early cases of dry eye syndrome because clinical examinations were evaluated not by a same physician who have specifically interested in autoimmune diseases associations in these types of cases and also very many times they are not being examined in a standardized way. RA is a chronic inflammatory disease with extraarticular involvement. Eyes particularly are one of the most common sites of involvement in RA. According to the clinical observations, we expected that the disease activity might be positively correlated with dry eye and patients in the disease active stage might have more severe dry eye but the correlation between dry eye and RA disease showed controversy in previous studies. The disease assessment of RA can not only compare the effects of treatment at different stages of individuals but also help to assess the progress of disease. According to the clinical observations, we expected that the disease activity might be positively correlated with dry eye and patients in the disease active stage might have more severe dry eye. However, our results suggested that there was no much significant difference between the active or stable groups, except for the CFS. We assumed that in the beginning of the active stage in RA, the patients may have more serious dry eye condition. However, the patients in stable stage of RA showed similar severity of dry eye to those in active group. Detailed dry eye examinations should be paid to all the RA patients, as patients in the stable stage exhibited mild dry eye. In addition, these results were consistent with the study of Miho Fujita et al on the RA patients with non secondary Sjögren's syndrome. Schargus et al found that the disease activity and tear osmotic pressure showed a positive correlation.

In our study, there were 30 patients with dry eye. The severity of dryness measured by Schirmer test, TBUT and OSS didn't show significant correlation with RA activity assessed by DAS-28, tender and swollen joint count, ESR and RF. We also found that the duration of RA was significantly positively correlated with Schirmer test and OSS (p < .0001 and p 1 4 .003, respectively), but not with TBUT. Thus, longstanding RA patients were more susceptible to develop severe ocular dryness compared to early ones.

In these test, RF found to be positive in 5 males and 16 females.

CRP has positive high timers in 8 males and 21 females. ANTI-CCP found to be positive in 7 cases of RA. ANA IF positive only in 4 Cases. SSA positive in 4 and SSB was positive in only 3 cases.

In a study of El-Badawy et al.²³ DAS showed a statistically no significant correlation with clinical tests of dry eye included Schirmer's test, tear breakup time test and ocular surface fluorescein staining. They concluded that dry eye disease existence is not correlated with disease activity.

Many definitions have been proposed for diagnosis of dry eye. In dry eye workshop II (DEWS II), diagnosis of dry eye requires first screening of symptoms using dry eye questionnaire -five or ocular surface disease index and one positive confirmatory ocular tests including TBUT (<10 s), osmolarity and OSS [20]. In Asia Dry Eye Society, diagnosis of dry eye based on combination of symptoms questionnaires and unstable tear film (<5s) making diagnosis simpler.¹³ The previous two definitions don't include Schirmer test which is important for diagnosis of aqueous deficient dry eye in RA patients who expected to have SS. In our study, we noticed 5 (16.7%) RA patients had TBUT 5-10s despite their Schirmer was < 5mm. OSS is included in most of SS criteria. This study shows one (3.3%) RA patient had TBUT 5-10s despite the OSS > 3.

There are some limitations of this study. Most of Dry eye patients participated in this study were sever cases. Steroid therapy was not included to study its effect on dry eye symptom or sign. The relationship between conjunctival damage (not only OSS) and RA activity is a shortage in our study and need further research.

CONCLUSION

the severity of dry eye is not correlated with activity of RA but with its duration. Dry eye cannot be excluded even in patients with only mild RA hence dry eyes should be always thought off in all cases of RA and further firmly insist that regardless of RA disease activity.

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