(International Print/Online Journal)

SJIF IMPACT FACTOR: 6.829
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 9, Issue 2 , Page No: 225-237
March-April 2026

IJMSCR

Integrating Clinical Symptoms and Objective Tests to Compare Dry Eye Burden in Rheumatoid Arthritis and Normal Populations

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Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Background: Dry Eye Disease (DED) is a multifactorial ocular surface disorder characterized by tear film instability, hyperosmolarity, inflammation, and neurosensory abnormalities. Rheumatoid arthritis (RA), a chronic systemic autoimmune condition, is strongly associated with secondary Sjögren's syndrome and various ocular manifestations, including DED.

Aim: To compare the burden of dry eye between patients with rheumatoid arthritis and healthy controls using both symptom-based assessment and objective diagnostic tests.

Methods: A cross-sectional study was conducted at a tertiary care centre involving 67 RA patients and 67 age- and sex-matched controls. Detailed ocular history, clinical examination, McMonnies dry eye questionnaire, Schirmer's tests (with and without anaesthesia), Tear Break- Up Time (TBUT), fluorescein staining, and lissamine green staining were performed.

Results: A significantly higher prevalence of dry eye was observed in RA patients. Significant associations were noted between subjective symptoms and objective tests, except fluorescein staining. The severity of dry eye and associated diagnostic markers increased in correlation with longer RA duration.

Conclusion: RA patients experience a higher burden of dry eye than normal populations. Combined use of symptom-based tools and objective tests provides a more accurate assessment of DED and should be included in routine RA management

Keywords: Dry Eye Disease (DED), Rheumatoid arthritis, Schirmer's test, Tear Break-Up Time (TBUT), fluorescein staining

Introduction

Dry eye disease (DED), also known as dry eye syndrome (DES) or keratoconjunctivitis sicca (KCS) is characterized by ocular irritation and visual disturbance resulting from alterations of the tear film and ocular surface.1 According to International Dry Eye Workshop (DEW 2), " Dry eye is multifactorial disease of ocular surface characterized by a loss of homeostasis of the tear film and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage and neurosensory abnormalities play etiological roles"1-2 Millions of people worldwide suffer from DED, and its prevalence rises with age, exposure to the environment, systemic illnesses, and drug usage. According to studies, the prevalence of dry eye varies between 5 and 16% in Western people and between 27 and 33% in Asian ones.2

Prevalence estimates are complicated by the lack of consistent diagnostic criteria and the use of both subjective and objective indicators. Symmetric, peripheral polyarthritis is a hallmark of RA, a chronic inflammatory illness with an unclear aetiology. This kind of chronic inflammatory arthritis is the most prevalent.2 Because it is a systemic disease, RA may result in a variety of extraarticular manifestations, including fatigue, subcutaneous nodules, lung involvement, pericarditis, vasculitis, hematologic abnormalities, peripheral neuropathy and ocular involvement. Eyes in particular are one of the most common sites of involvement in rheumatoid arthritis. Moreover, RA has a tendency to develop scleritis, episcleritis, corneal ulcers and dry eye syndrome. Nearly 11–31% of people have eye complications. Dry eye is often the most prevalent kind of ocular involvement. Approximately 10% of people with RA develop secondary Sjogren's syndrome 6.3 Because it is an autoimmune disease, it disrupts the immune system and contributes to the pathophysiology of dry eye, which combines immune and neurohormonal factors that change the production of tears from the lacrimal gland and initiates an inflammatory cascade on the ocular surface involving both cellular and soluble mediators.

There are various studies done in past to evaluate prevalence of Dry eye in rheumatoid arthritis patients and in general population,

1. Tandon R et al.(2020)4 concluded that prevalence of Dry eye is more in high altitude, i.e. 54 % as compared to army soldiers who were recently posted there and the difference was statistically significant ($p < 0.005$).
2. A study by Titiyal J S et al. (2018) found that prevalence of dry eye is 32 % in Delhi population where in Age group of 21-40 years was more affected.5
3. Bhatt K et al.(2023) studied 500 patients to detect prevalence of dry eye and they found that prevalence of dry eye was around overall 18% in their study population and it was 36.1% in patients with age > 70 years. Females were more affected.6
4. There is one study from Sri Lanka done in South Asian population on computer vision syndrome where Ranasinghe P et al. (2016) have found dry eye as one of the commonest symptom with a prevalence of 31.1% among general population.7
5. Vignesh AP et al.(2015) studied the comparison of prevalence and severity of dry eye in patients with rheumatoid arthritis and without rheumatoid arthritis in the Indian populations. Among 84 adult patients with RA and 84 controls, they found that 27.3% with rheumatoid arthritis had dry eyes based on the Schirmer test as compared to 12% in age- and sex-matched controls. 22.62% patients with RA had a tear film breakup time of < 10 seconds on slit-lamp examination, compared to 9.52% patients without RA. The difference in the mean wetting ($p = 0.003$) and mean tear film breakup time ($p < 0.001$) between RA and non-RA patients was statistically significant. Ocular symptoms had a limited correlation with the results of these tests. The study concluded that patients with RA in the Indian population have a significantly higher prevalence and severity of dry eye when compared to age- and sex-matched controls.8

Even though RA and DED are known to be related, there is frequently little link between symptoms and objective evidence of dry eyes. While some individuals with severe DED may be asymptomatic due to decreased corneal sensitivity, many report substantial ocular pain despite normal test findings.

Given these differences, a more accurate diagnosis can be obtained by combining objective tests like TBUT, Schirmer's, and ocular staining with subjective evaluations like the McMonnies Questionnaire.

In order to evaluate the dry eye burden of RA patients with that of normal persons, this study incorporates both clinical symptoms and objective measurements, providing important information to the Indian community, where there is a dearth of literature.

Materials And Methods

Study Design And Setting

A cross-sectional comparative study was conducted in the Outpatient department of Ophthalmology, Deenanath Mangeshkar Hospital and Research Centre, Pune.

The study spanned nine months and included two groups:

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Group 1: 67 patients diagnosed with Rheumatoid Arthritis.

Group 2: 67 age- and sex-matched controls without RA.

Sample Size Calculation

A sample size of 67 per group was calculated based on prior prevalence data showing an 11% increase in dry eye occurrence among RA patients compared to controls, with 80% power and α = 0.05

Formula used for sample size estimation

$$[\ Pa\ (1-Pa)/k + Pb\ (1-Pb)]\ (Z_{1-\alpha}$$

Where, $(Pa-Pb)2$

1. n=Sample size in each group (k=1; equal sample size in 2 groups)
2. proportion in group a, Pa = 0.13(13%) & proportion in group b, Pb=0.02(2%)
3. α is Type I error =5%; zα =1.64 one sided
4. β is Type II error, 1−β is power; z1−β=0.84 for 1−β=80%
5. effect size= (Pa−Pb) = ± 0.11 (11%)

Inclusion Criteria

1. Ophthalmology Treatment Naïve Adults diagnosed with RA (Group 1)
2. Ophthalmology Treatment Naïve Age- and sex-matched non-RA individuals (Group 2)
3. Consent to participate.

Exclusion Criteria (for both Group 1 and Group 2)

1. Connective tissue disorders other than RA diagnosed by Rheumatologist
2. Use of contact lenses previously for the last 3 months.
3. Ocular Refractive or Cataract or Pterygium surgery within 6 months
4. Systemic medications known to cause dry eye (antihistamines, HRT etc.)
5. Computer professionals, chronic smokers, and professional drivers
6. Ocular surface disorders not related to DED

History Taking

A detailed systemic and ocular history was collected. RA duration, systemic treatments, prior ocular symptoms, and comorbidities were documented.

Subjective Dry Eye Assessment

McMonnies Dry Eye Questionnaire9 was administered to all participants. Scores categorized patients as:

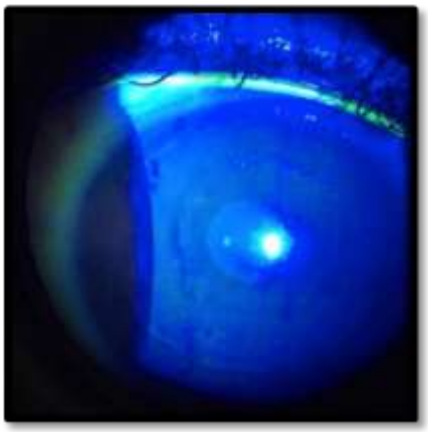
1. <10: Normal
2. 10–20: Moderate dry eye
3. >20: Severe dry eye

Clinical Examination

1. Visual acuity using Snellen chart
2. Slit-lamp biomicroscopy for lids, conjunctiva, cornea
3. Tear meniscus height assessment
4. Debris presence in tear film

Objective Dry Eye Tests

1. Tear Break-Up Time (TBUT)1,2
   a. Fluorescein strip instilled without anesthesia
   b. First appearance of a dry spot measured
   c. <10 seconds = abnormal



2. Schirmer's Test1,2

   Performed using Whatman 41 filter paper strips.

   • Without anesthesia: Basal and reflex tearing
   o <10 mm/5 min = abnormal
   • With anesthesia: Basal secretion
   o <5 mm/5 min = abnormal
3. Ocular Surface Staining1,2

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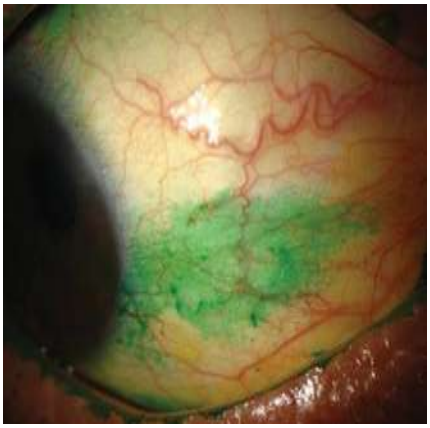
Both fluorescein and lissamine green dyes were used and graded using SICCA Ocular Staining Score.

Fluorescein staining10

- 0 = 0 dots
- 1 = 1–5 dots
- 2 = 6–30 dots
- 3 = >30 dots Positive if >5 dots

Lissamine green staining10

- 0 = 0–9 spots
- 1 = 10–32
- 2 = 33–100
- 3 = >100 Positive if ≥10 spots



Definition of Dry Eye1,2

A diagnosis was made if:

One or more symptoms (often/constant) and

One or more abnormal objective tests Or

Positive objective tests even if asymptomatic

Statistical Analysis

Data was analyzed using SPSS 20.0.

Continuous variables: Mean ± SD

Categorical variables: Percentage, Chi-square test

p-value <0.05 considered significant

Results

This cross-sectional study was carried out in total 134 patients,67 in each group, i.e. group 1(patients with rheumatoid arthritis) & group 2(patients without rheumatoid arthritis), attending Deenanath Mangeshkar Hospital, Pune, satisfying the inclusion and exclusion criteria.

During the 9 months enrollment period, patient's systemic history with respect to rheumatology was noted. These patients underwent complete ophthalmic examination including visual acuity, detailed anterior segment examination had done under slit lamp. Condition of lids noted, conjunctiva, cornea evaluated in detail. Then all patients underwent subjective and objective tests for dry eye.

Results were recorded and analyzed between two group. Group 1- included patients with rheumatoid arthritis Group 2- included patients without rheumatoid arthritis.

Table 1: frequency distribution in both groups based on age (in years)

Age group	**Group**		**Total**	**p-value**
	Group 1	**Group 2**		
≤ 50	29	35	64	
51 - 60	28	19	47	
> 60	10	13	23	0.296
Total	67	67	134	

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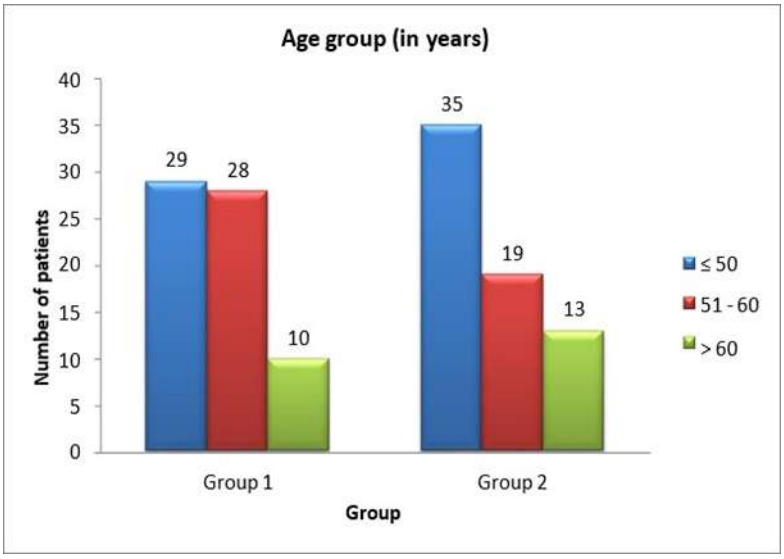

Graph 1 frequency distribution in both groups based on age (in years)

The above table and graph show 29 patients with age ≤ 50,28 in 51-60 and 10 in >60 in group 1 with and the mean age is 52.22±7.933, and 35 patients with age ≤ 50, 19 in 51-60 and 13 in >60 in group 2 with the mean age is 52.01±9.04.

Table 2: Frequency distribution in both groups based on gender

Gender	Group		Total	p-value
	Group 1	Group 2		
Male	4	4	8	0.999
Female	63	63	126	
Total	67	67	134	

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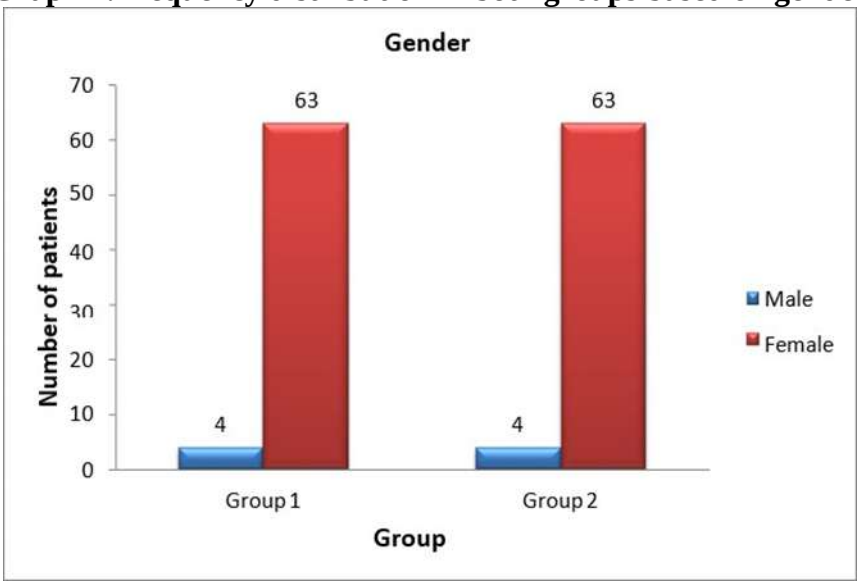
Graph 2: frequency distribution in both groups based on gender



Above table and graph shows, in both groups, out of total 67 patients 4 were males and 63 were females.

Table 3: Results of subjective and objective tests between group 1 and group 2

		Group		Total	p-value
		Group 1	Group 2		
McMonnies questionnaire score	< 10	41	58	99	0.001
	≥ 10	26	9	35	
Tear Meniscus Height	Normal	55	67	122	< 0.001
	Abnormal	12	0	12	
TBUT (in seconds)	< 10	38	21	59	0.005
	≥ 10	29	46	75	
Schirmer's without anaesthesia (in mm)	< 10	20	5	25	0.002
	≥ 10	47	62	109	
Schirmer's with anaesthesia (in mm)	< 5	16	2	18	< 0.001
	5 - 10	19	12	31	
	> 10	32	53	85	

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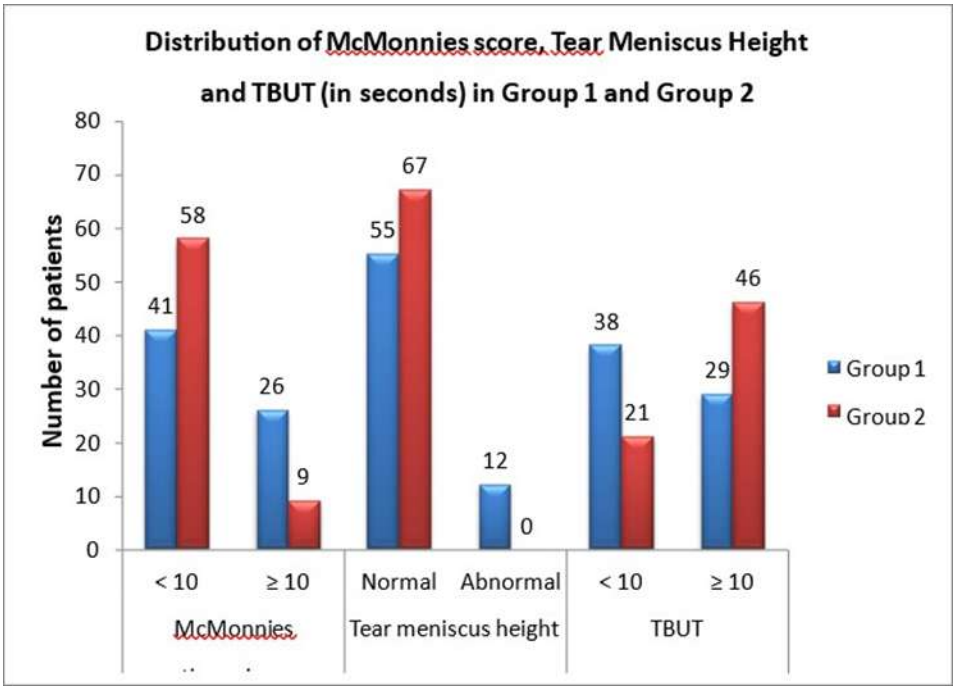
Lissamine green staining	0	32	55	87	< 0.001
	1	22	10	32	
	2	13	2	15	
Fluorescein staining	0	61	62	127	0.115
	1	6	1	7	

Graph 3: Results subjective and objective tests between group 1 and group 2



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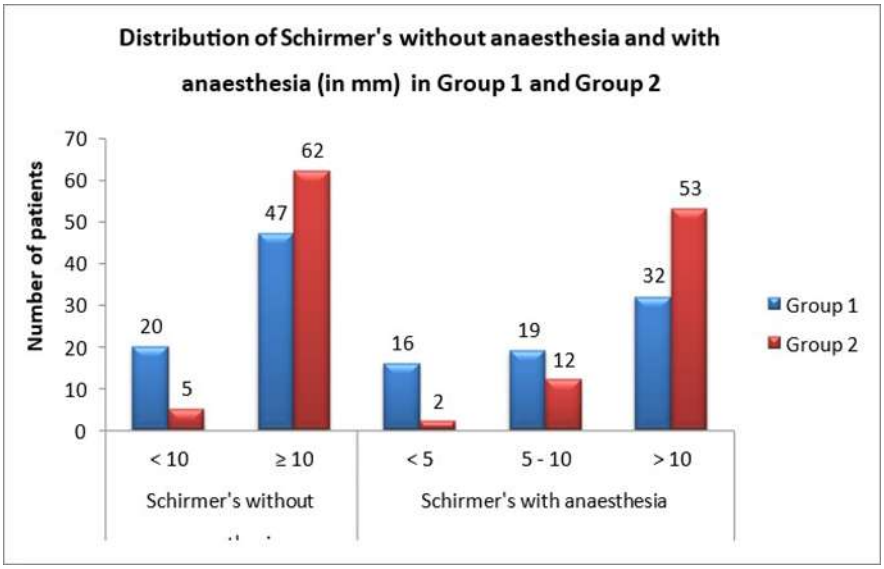
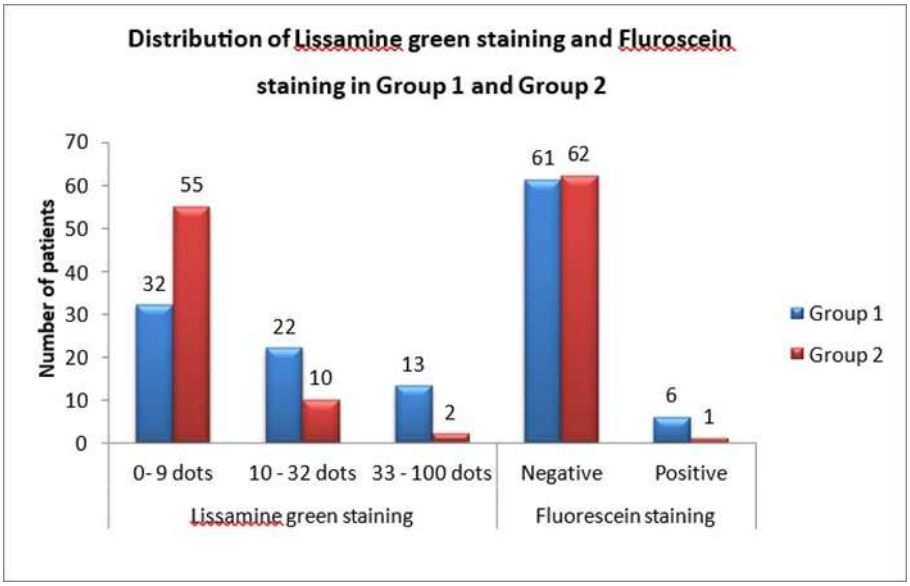
Graph 3.1: Distribution of McMonnies score, Tear Meniscus Height and TBUT (in seconds) in Group 1 and Group 2



Graph 3.2 Distribution of Schirmer's without anaesthesia and with anaesthesia (in mm) in Group 1 and Group 2



Graph 3.3 Distribution of Lissamine green staining and Fluroscein staining in Group 1 and Group 2

The above table 3 and graph 3.1 shows that McMonnies was more than or equal to 10

i.e. positive for dry eye in 26 patients with RA i.e. case group (group 1) and in 9 patients without RA i.e. control group. And score was less than 10, in 41 and 58 patients in group 1 and 2 respectively.

Then tear meniscus height was abnormal in 12 patients from group 1 and normal in all subjects in group 2. TBUT score was less than 10 i.e. positive in 38 patients with RA and 21 in without RA. It was more than or equal to 10 in 29 and 46 patients in group 1 and group 2 respectively.

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The above table 3 and graph 3.2 shows that the Schirmer's test without anaesthesia value was less than 10 (positive) in 20 RA patients (group1), and 5 in control group (group 2), it was more than or equal to 10 in 47 and 62 in both groups respectively. Then it shows that among the 67 RA patients, value of Schirmer's test with anaesthesia was less than 5 (positive) in 16 and 5 to 10 (equivocal) in 19, it was in 2 and 12 patients respectively in group 2, and more than 10 was in 32 patients in group1 and 53 in group 2.8

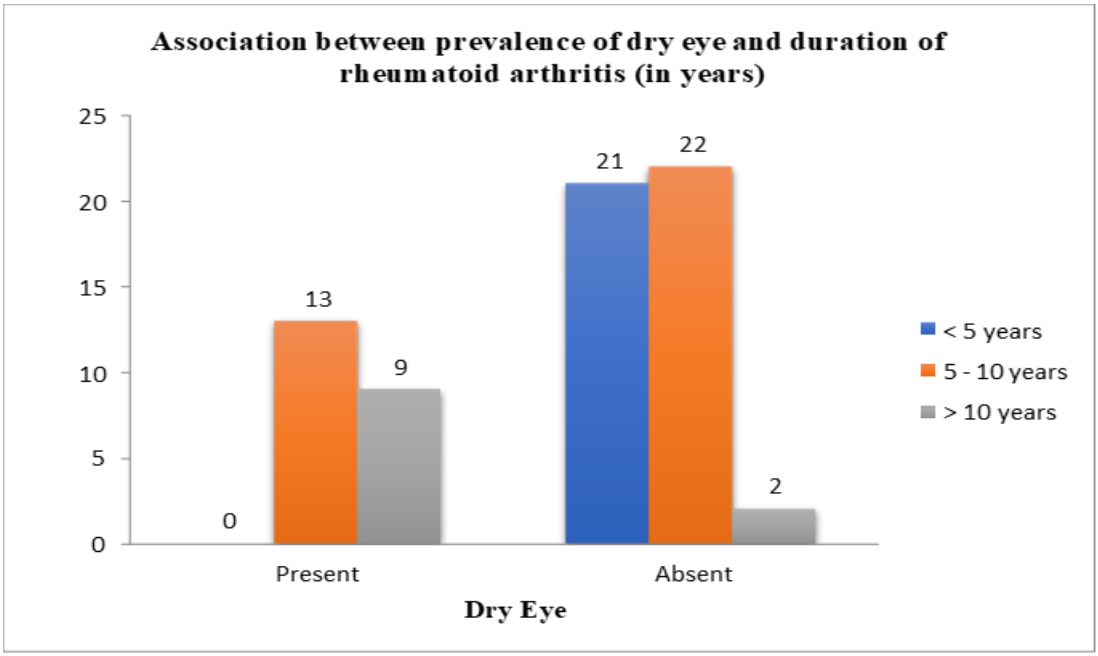
The above table 3 and graph 3.3 shows that there were 34 RA patients had negative lissamine staining, 22 had 10 to 32 dots and 13 had 33 to 100 dots so total 35 patients showed positive staining. In the control group, there is 55 patients had negative staining, 10 patients had 10 to 32 dots and 2 had 33 to 100 dots so 12 showed with positive staining.

It also showed that there was presence of fluorescein staining in 6 rheumatoid arthritis patients and 61 had no staining, while 66 patients in control group had no staining and only 1 was with positive staining.

Table 4 Association between prevalence of dry eye and duration of rheumatoid arthritis (in years)

Dry Eye	Duration			Total	p-value
	< 5	5 – 10	> 10		
Present	0	13	9	22	< 0.001
Absent	21	22	2	45	
Total	21	35	11	67	

Graph 4 Association between prevalence of dry eye and duration of rheumatoid arthritis (in years)



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Conclusion-The above table and graphs shows that there is an association between the duration of rheumatoid arthritis and prevalence of dry eye as the p value was less than 0.05.

Discussion

In this hospital based cross sectional study Group 1 included patients with Rheumatoid arthritis recruited from Rheumatology OPD and Group 2 included patients without Rheumatoid arthritis.

The study population included total 134 patients fulfilling inclusion and exclusion criteria divided into two groups i.e. 67 in each as group 1(case group) and group 2 (control group). There was an equal gender distribution in both the groups, i.e. 63 females and 4 males as age- sex matched control was needed, with mean age in group 1 was 52.22±7.933 and 52.01±9.04 in group 2. In group I, mean duration of RA was 7.29±4.64 years. Tandon R et al.(2020)4 stated that the older population and females were more likely to have dry eye among Indian patients attending tertiary care center.

The gender distribution of both groups in the current investigation was comparable (Table 2), guaranteeing that gender-related bias did not affect the results. This is significant since hormonal variables that affect tear production and ocular surface stability, including as androgen shortage and post-menopausal alterations, are known to make DED more frequent in females Stapleton F et al. (2017)11. As a result, the validity of the observed differences between the groups is strengthened by the matched distribution.

Scores ≥10, which indicate a high risk of dry eyes, were found to be substantially more common in RA patients (38.8%) than in controls (13.4%), according to a subjective assessment using the McMonnies questionnaire ($p = 0.001$).

This is consistent with previous research highlighting increased symptom load in RA as a result of lacrimal gland involvement, meibomian gland dysfunction, and chronic inflammation Turk MA et al. (2021)12. Because symptom-based reports are correlated with RA patients' quality of life, treatment-seeking behaviour, and disease severity, they have clinical significance.

Significant anomalies among RA individuals were also shown by objective measures. Twelve RA patients had aberrant tear meniscus height, a measure of aqueous tear volume, whereas all controls had normal tear meniscus height ($p < 0.001$). Autoimmune-mediated lacrimal gland infiltration and destruction, a characteristic of secondary Sjögren's syndrome linked to RA, is frequently associated with aqueous-deficient dry eye Baudouin C et al. (2016)13. The RA group had a considerably higher frequency of reduced tear breakup time (TBUT) ($p = 0.005$). According to the TFOS DEWS II pathophysiology model (Craig et al., 2017)4, low TBUT indicates tear film instability, one of the primary processes generating DED. Tear film evaporation has been linked to meibomian gland dysfunction and chronic systemic inflammation in RA. Ramos-Casals M et al. (2020).14

Schirmer's test values, both with and without anaesthesia, were markedly lower in RA patients ($p = 0.002$ and $p < 0.001$, respectively). Reduced Schirmer's values are consistent with lacrimal gland hypofunction in RA secondary to lymphocytic infiltration and autoimmune-mediated damage. Previous studies have similarly reported significantly reduced tear secretion in RA, especially in patients with longer disease duration. Vignesh AP et al.(2015)8

Lissamine green staining of the ocular surface revealed considerably more conjunctival staining in RA patients ($p < 0.001$). This suggests significant damage to epithelial cells and a lack of mucin, which frequently happens in long-term inflammatory conditions Bron AJ et al., (2017)15. i.e. Because mild-

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to-moderate illness accounts for a considerable part of patients or because corneal epithelial alterations manifest later than conjunctival changes, fluorescein staining did not significantly vary across groups.

The significant correlation between the prevalence of dry eyes and the lengthening of rheumatoid arthritis ($p < 0.001$) is one of the study's main conclusions. When compared to patients with shorter illness durations, those with RA lasting more than five years showed a significantly greater frequency of DED (Table 4). Chronic inflammatory infiltration and structural glandular damage are two ways that long-term RA is known to contribute to increasing lacrimal gland dysfunction Senolt L et al. (2019)16. This backs up suggestions that RA patients undergo routine eye screening, particularly after five years of illness.

The overall results are consistent with recent worldwide research showing that systemic inflammation, autoimmune processes, and related secondary Sjögren's syndrome considerably increase the incidence of DED in RA patients. Baudouin C et al. (2016)13 Because untreated DED in RA can result in visual problems, keratitis, and a worse quality of life, early identification and treatment are essential. Overall, the study's findings highlight how crucial it is to include routine ophthalmologic testing in the long-term care of RA patients. Early diagnosis is improved and thorough monitoring of ocular problems is ensured by the use of both subjective and objective diagnostic techniques.

Conclusion

The present study demonstrates a significantly higher prevalence of dry eye disease among patients with rheumatoid arthritis compared with age- and gender-matched healthy controls. Both subjective symptoms, as assessed by the McMonnies questionnaire, and objective clinical tests—including tear meniscus height, TBUT, Schirmer's tests, and lissamine green staining— showed marked abnormalities in the RA group. These findings highlight the multifactorial impact of RA on tear secretion, tear film stability, and ocular surface integrity. Moreover in our study(graph 4) and as shown in the literature a clear association was observed between increasing duration of rheumatoid arthritis and higher dry eye prevalence, suggesting that chronic inflammatory activity contributes progressively to ocular surface dysfunction.

Given the substantial ocular morbidity associated with dry eye disease, the study underscores the importance of routine ophthalmologic evaluation in individuals with rheumatoid arthritis. Early detection and timely management may prevent long-term complications, improve visual comfort, and enhance overall quality of life.

Thus, integrating dry eye screening into the standard care pathway for RA patients is strongly recommended.

Limitations

1. Single-centre study: The data were collected from one institution, which may limit the generalizability of the findings to broader populations or other geographic regions.
2. Modest sample size: Although 134 participants were included, a larger sample could provide greater statistical power and more robust subgroup analyses.
3. Cross-sectional design: Causal relationships between RA duration and dry eye severity cannot be established, as the study captures only one point in time.
4. Lack of advanced diagnostic tools: Objective tests such as tear osmolarity, meibography and ocular surface interferometry were not used, which may have provided more comprehensive tear film assessment.
5. Unmeasured confounding factors: Environmental influences, systemic medications (e.g., DMARDs, biologics), and comorbid autoimmune conditions may have

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affected tear film status but were not fully controlled.

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