

Evaluation of Dry Eye Symptoms Among Individuals with Rheumatoid Arthritis

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ABSTRACT

Background: Around 25% of patients with rheumatoid arthritis presented with dry eye conditions leading to episcleritis and scleritis in 0.17% of patients causing permanent vision deterioration.

Purpose: To compare tear film stability parameters between rheumatoid arthritis patients and healthy subjects and the relationship with disease activity score (DAS-28) in rheumatoid arthritis patients.

Materials and Methods: A comparative study was conducted at the Pakistan institute of medical sciences (PIMS). The sampling technique was purposive sampling. Healthy subjects and patients with rheumatoid arthritis were included. Patients with any Ocular abnormalities and systemic illnesses were excluded. Disease activity score (DAS-28) was calculated by erythrocyte sedimentation rate test (erythrocyte sedimentation rate), C-reactive protein (C - reactive protein), and rheumatoid factor (RF). For dry eyes, ocular surface disease Index (OSDI), tear film breakup time (TFBT), Schirmer test, corneal sensitivity, and Fluorescein staining were assessed using questionnaires and physical examination.

Results: The tear breakup time was low for rheumatoid arthritis ($p < 0.0001$). The mean OSDI score was in the mild dry eye disease grade. ($p < 0.0001$) the mean C - reactive protein and erythrocyte sedimentation rate was significantly higher for the rheumatoid patients. ($p < 0.0001$). No association was reported between disease activity and ocular dryness.

Conclusion: There was no significant association between disease activity and the ocular parameters. However, RF and anti-CCP positivity was found to be more in dry eye disease with raised erythrocyte sedimentation rate and C - reactive protein.

Keywords: Rheumatoid Arthritis; Schirmer's Test; C-reactive Protein

Abbreviations: PIMS: Pakistan Institute of Medical Sciences; RF: Rheumatoid Factor; OSDI: Ocular Surface Disease Index; RA: Rheumatoid Arthritis; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; TBUT: Tear Break up Test; IOD: Inflammatory Ocular Disease

Introduction

Rheumatoid arthritis (RA) is one of the conditions faced mostly by females than males. It is a condition of joints causing inflammation of the synovia. The incidence of RA among Pakistanis and the United Kingdom-based Pakistanis came out to be 0.14% and 0.3%, respectively. This causes a lot of disability in walking and restricts a person's routine work causing a rise in the burden on the economic status of a country. The inability or disability contributes to the burden of disease and increases the number of disability life years in any country [1]. Rheumatoid arthritis (RA) is reported among 5 per 1000 people. Over the last two years, considerable improvement has been made regarding disease pathophysiology and effective treatment strategies. Early identification and management of rheumatoid arthritis can prevent or slow joint damage in up to ninety percent of the patients. In addition, outcomes have improved by using disease-modifying anti-rheumatic drugs [2]. The most frequent complaints registered include limitation of movement, pain in doing the activity, or swelling of the joints causing pain. The early diagnosis remains quite difficult due to a lack of information regarding the history of the patients and their related examination and tests which may indicate the disease [3]. Individual awareness is vital along with the reinforcement of disease management by the doctors.

The more the management is delayed the more there are chances that the disease will spread to other organs causing more severe disease-related issues than in earlier stages. Rheumatoid arthritis can affect a lot of other organs besides the joints. In the eyes, it may cause keratitis or scleritis, in the lungs it may present as rheumatoid nodules, in the heart, it may lead to pericardial inflammation and it may also involve blood vessels and cause inflammation [4]. If the treatment is started early, the disease progress is slowed down, and many patients achieve remission. The patients can cure easily and rapidly if the treatment is initiated at the right time [5]. Dry eye is a condition that involves the disruption of tear film normal structure and quantity the lacrimal unit is generally made up of the lacrimal gland, cornea, Meibomian generating glands, eyelids, and goblet cells [6]. Around twenty-five percent of individuals with rheumatoid arthritis also have ophthalmic complaints. Several risk factors may lead to dryness including natural aging causing malfunction of the unit of tear film production, a reduction in male hormones, external ocular disorders and diseases (e.g., HSV keratitis), systemic inflammatory diseases (e.g., rheumatoid arthritis), or surgeries and techniques may induce dry eyes. Sometimes the trigeminal nerve is disrupted [7]. Dryness of the eyes may lead to dryness of the cornea and may lead to ulcers or perforation.

Supportive medicine and surgical procedures to cover the affected portion help relieve the pain and recover some of the visual acuity [8]. Dry eye conditions are troublesome for the patient. They not only irritate but also hamper the vision. Usually eliminating the primary

cause helps relieve the symptoms. Artificial tears and softeners help in relieving the dry eye condition [9]. Hence, it was suggested that special consideration shall be done to patients with rheumatoid arthritis to get diagnosed earlier and managed properly by doctors at earlier stages of dry eye conditions in systemic immune-related [10].

Objectives

- To compare the parameters of tear film stability between rheumatoid arthritis patients and age/gender-matched healthy subjects.
- To investigate tear film stability parameters with disease activity score (DAS-28) in rheumatoid arthritis patients.

Methodology

A comparative study was done at the Pakistan Institute of Medical Sciences from February 2023 to August 2023. A purposive sampling technique was used. The sample size was calculated with the help of the computer program Pass 15.0. Ethical approval was obtained for conducting this research. Written Informed consent was taken from all participants before data collection and procedure. Group sample sizes of a minimum of 47 subjects in the rheumatoid arthritis group and 47 subjects in the Healthy were included. The group achieves 90.267% power to reject the null hypothesis of equal means when the population means the difference is $\mu_1 - \mu_2 = 5.3 - 6.5 = -1.2$ with a standard deviation for both groups of 1.8 and with a significance level (alpha) of 0.050 using a two-sided two-sample equal-variance t-test. Patients were selected from the rheumatology ward of the Pakistan institute of medical Sciences (PIMS) according to the inclusion and exclusion criteria. Participants were guided about the proceeding of the study; written consent was taken from the participants or their guardians. Disease activity score (DAS-28) Was calculated based on a clinical and biochemical parameter by a Rheumatologist which included erythrocyte sedimentation rate test (ESR), rheumatoid factor (RF), and C-reactive protein (CRP).

In addition, for dry eyes, ocular surface disease index (OSDI), Schirmer test, tear film breakup time (TFBT), corneal sensitivity, and Fluorescein staining were assessed using questionnaires and physical examination.

Clinical Grading of Dry Eye

Normal eyes were defined as the eye having average tear quality and quantity in which the tear stability grading was "0". While Dry eye disease was defined as Schirmer test result will be low, i.e., 5mm wetting of the paper after 5 minutes. The Schirmer's test was graded as, Grade 0 (normal) 0-10 mm, Grade 1(mild): 5-10 mm, Grade 2(moderate): 3-4 mm, Grade3 (severe) 0-2 mm [11]. Tear Break up Test (TBUT) less than 10 secs was considered abnormal, and Grade As: Grade0 (normal): > 10 sec normal, Grade1 (fair): 6.1-10 sec fair, Grade2 (moderate): 3.1-6 sec moderate, Grade 3(poor):<3sec poor

[12]. The Ocular Surface Index (OSDI) demonstrates sensitivity and specificity in ruling out ocular surface dryness in individuals. The criteria used for the Grading were 0-12 score, normal; 13-22 score, mild; 23-32 score, moderate; and 33-100 score, severe [12]. Data analysis was done using descriptive statistics. The means were compared using a T-test, and the Chi-square test was used to compare frequencies.

Statements and Declarations

The authors don't have any conflict of interest or financial disclosure. The authors did not receive support from any organization for the submitted work. No funding was received to assist with the preparation of this manuscript. No funding was received for conducting this study. No funds, grants, or other support were received.

Results

A total of 94 individuals were enrolled in the study. Individuals were divided into two groups based on the presence or absence of rheumatoid arthritis. Group A had rheumatoid patients (n=47, 50%), while Group B had healthy individuals (n=47, 50%). Rheumatoid factors and anti-CCP levels were not found among healthy individuals. Showed the parameters of dry eye disease and DAS-28 score among the two groups. Showed the comparison of ocular dry eye parameters with the disease activity score revealed no association between the degree of ocular dryness and the intensity of the disease activity in rheumatoid patients. The Frequency of DED in healthy individuals and rheumatoid arthritis. Overall results revealed that the activity of rheumatoid arthritis in the patients did not contribute to the alteration of dry eye parameters; however, compared to healthy adults, dry eye condition was higher in rheumatoid arthritis individuals. Among the rheumatoid arthritis patients, the frequency of dry eye disease was found to be higher in the patients showing positivity for anti-CCP as compared to the ones showing only RF positivity. The frequency of DED and its association with RF and anti-CCP. Showed the frequency of dry eye disease in rheumatoid patients; it shows how the frequency is more in individuals with Anti-CCP. This warrants further research to see the correlation between the levels of anti-CCP and the positivity of dry eye syndrome and parameters of ocular hydration.

Discussion

Dry eye disease is often reported among patients with rheumatoid arthritis with complications and discomfort-related complaints. A descriptive cross-sectional study conducted in Baghdad revealed that the prevalence of dry conditions was almost 27% in their sample. It was other added that among 103 individuals, dry eyes showed a positive association with ACPA (anti-citrullinated peptide antibody) (34.7%) and RF positivity (37%) This study is like our study, as the frequency of dry eye disease was found to be more in rheumatoid patients. Also, the patient with anti-CCP positivity showed drier eye conditions as compared to RF positivity.⁹ Another study supporting our results reported that tear break-up time was less in rheumatoid

arthritis patients. The reason was attributed to Meibomian gland dysfunction in rheumatoid arthritis individuals, leading to decreased tear break-up time and dry eye conditions. Contrary to the literature, the study results showed that the disease activity does not influence the severity of dry eyes. Similar to our results of a moderate score of tear break-up time noted among rheumatoid arthritis patients [13]. Contrary to our results, in another study, it was reported that dry eye prevalence was high among rheumatoid arthritis individuals ranging up to 48.5%. OSDI scores correlated with evaluative tests done for detecting the hydration of the eye. It was suggested that these tests were linked with a poor correlation between signs and indications in the primary stages.

No link was discovered between the individual's results for frequency of dry conditions in eyes and length of RA illness, rheumatoid factor, or arthritis disease activity [14]. Similarly, another study evaluating the inflammatory ocular disease (IOD) and extra-articular manifestations of rheumatoid arthritis revealed that dry eye syndrome (42%, $p = 0.024$) was higher than our results [8]. Similar to our results, a study reveals the diagnosis of dry eye disease utilized simple tests that needed to be done in routine. shimmer test score and anti-Ro or anti-La autoantibody status were observed for all patients. The tear osmolality, tear breakup time (TBUT), and corneal staining scores were compared. It was found that tear osmolality was increased with shorter TBUT, raised corneal staining score, and erythrocyte sedimentation rate c-reactive protein levels ($P < 0.05$) in patients with rheumatoid arthritis [15]. A similar study was done to assess the correlation of rheumatoid arthritis activity using the Disease Activity Score (DAS-28), C-reactive protein, and erythrocyte sedimentation rate. A Health Assessment Questionnaire. The results reflected that the disease activity did not correlate with eye dryness. ($P=0.036$). It was concluded that dry eye was the most frequent ocular manifestation in the study of patients having rheumatoid arthritis. However, the existence of dry eye disease was not correlated with disease activity. The study raised the importance of examining and diagnosing dry eyes in all patients regardless of the severity of the disease [16].

Conclusion

Dry eye is the most common ocular index in our investigated patients with rheumatoid arthritis. Eye involvement is present in approximately fifty percent of patients with rheumatoid arthritis. Dry eye disease presence is not connected with disease activity. Hence all patients with rheumatoid arthritis should be frequently examined for dry eye irrespective of disease severity. There was no significant association between disease activity and the ocular parameters. However, RF and anti-CCP positivity was found to be more in dry eye disease with raised erythrocyte sedimentation rate and C-reactive protein. Therefore, rheumatologists could use the OSDI questionnaire for screening for dry eye disease in individuals with rheumatoid arthritis. The presence of anti-CCP antibodies may denote dry eye disease and

be linked with rheumatoid arthritis disease activity. The presence of anti-CCP antibodies may denote dry eye disease and be linked with rheumatoid arthritis disease activity. Hence, frequent screening of individuals may help in early diagnosis and prevention of complications of dry eye disease.

Authors Contribution

Dr. Nida Amin writes the manuscript and reviews. Attiq Riaz, Ayesha Saeed and Nimra Fatima prepared results. Humaira malik collected data and done with statistical analysis.

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