The Effect of Ocular Demodex Colonization on Schirmer test and OSDI Scores in Newly Diagnosed Dry Eye Patients

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Objective: To determine whether ocular *Demodex* colonization results in differences in Schirmer test scores and Ocular Surface Disease Index (OSDI) questionnaire values in individuals with dry eye disease (DED) diagnosed for the first time.

Method: Eighty-eight adults aged 40 to 68 years who were admitted to Ophthalmology outpatient clinic for routine ophthalmological examination or presbyopia examination and diagnosed with DED for the first time and who do not have any chronic disease were included in the study. All the patients were asked to complete the OSDI, which is widely used for assessing dry eye symptom severity and vision-related functioning. The Schirmer test was performed, and then two eyelashes were taken from the inferior eyelids of each eyes. After saline (0.09% NaCl) was added to the sample, it was quickly taken to the microbiology laboratory, which is located next to the Ophthalmology policlinic. The sample was evaluated by a parasitologist experienced in *Demodex*.

Results: One hundred sixty-eight eyes of 84 patients were included in the study. Average Schirmer test score was 2.1±0.5, the OSDI questionnaire score was 61.82±10.95, and the mean age was 55.36±8.74 years in patients who had *Demodex* colonization (n=30), whereas the average Schirmer test score was 6.6±0.9 score, OSDI questionnaire score was 40.96±12.73, and the mean age was 49.12±6.87 years in patients without *Demodex* colonization (n=58). It has been observed that dry eye patients with *Demodex* colonization had a higher mean age (*P*: 0.001), higher mean OSDI score (*P*: 0.001), and lower average Schirmer test score (*P*: 0.001) compared with those without *Demodex*. The significant relationship between lower Schirmer test score and higher OSDI rates and occurrence of *Demodex* infestation continued after adjusting for mean age values (*P*=0.012; *P*=0.035).

Conclusion: It was determined that the presence of ocular *Demodex* colonization was associated with the average Schirmer test scores, OSDI scores, and age values in patients with newly diagnosed DED. Demodex quantity was found increased in older aged patients, but the significant relationship between lower Schirmer test score and higher OSDI rates and *Demodex* infestation persisted even after controlling the mean age values. Supporting these findings with large-numbered and randomized-controlled studies will help in clarifying the association of the Demodex infestation with etiopathogenesis of dry eye.

Key Words: Schirmer 1 test—Ocular demodex—Dry eye.

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Dry eye disease (DED) is one of the most common eye diseases that affect the quality of life of individuals because of symptoms such as ocular discomfort, foreign body sensation, itching, and pain. In community-based studies, prevalence varies widely from study to study and ranges from 5% to 35%.[1–3] Factors considered to play a role in the occurrence of the disease are particularly inflammation, aging, hormonal changes, smoking, ocular surgery, drugs, allergens, low humidity, high room temperature, and using a contact lens.[4]

Demodex folliculorum and *Demodex brevis* are two distinct *Demodex* species that are the most common ectoparasites of human. They feed on epidermal skin cells and sebum, so they are commonly found in the hair follicles and sebaceous glands of the cheeks, nose, chin, and periocular areas.[5] The *Demodex* agents are determined to be associated with dermatological diseases such as rosacea, acne, perioral dermatitis,[6,7] and inflammatory ocular diseases such as blepharitis[8–11] and chalazia.[12–14] It has been known that *Demodex* mites especially *D. brevis* may cause dry eye symptoms through meibomian gland dysfunction and inflammation.[11,15,16] However, some researchers suggest that *Demodex* mites are not pathogenic because these mites are frequently seen in asymptomatic individuals particularly elderly people.[9,17,18]

In recent years, the relationship between ocular *Demodex* colonization and ocular surface conditions have been investigated for clarifying pathogenicity of *Demodex*.[15,19,20] The aim of this study is to determine whether ocular Demodex colonization results in differences in Schirmer test scores and Ocular Surface Disease Index (OSDI) values in individuals with newly diagnosed DED.

METHOD

This observational cross-sectional study was conducted between September 2017 and January 2018 at the Ahi Evran University Education and Research Hospital Ophthalmology outpatient clinic. Adults aged 40 to 68 years who were diagnosed with DED or showed dry eye symptoms without a diagnosis of disease or the first time during routine ophthalmological examinations or presbyopia examination were included in the study. Patients with visual acuity of ≤20/20 in ophthalmologic examination and any ocular or systemic disease according to patient's detailed history were not included in the study.

Ahi Evran University Education and Research Hospital and university ethics committee approvals were obtained for the study. The study was conducted in accordance with the Helsinki Declaration on Good Clinical Practice, and informed consent was obtained from all patients.

Clinical Evaluation and Measures

Although there is no common diagnostic criterion of DED, its diagnosis is based on a good patient history, self-reports, and standard tests for assessing tear film stability and tear production.[21] In our study, the diagnosis of DED was evaluated using the OSDI and Schirmer test in addition to detailed history of patients with dry eye symptoms by an experienced ophthalmologist. Patients less than 5 mm/min wetting in the Schirmer test were included.

Ocular Surface Disease Index

Ocular Surface Disease Index is a questionnaire to evaluate DED patients' complaints in the past 2 weeks. It measures the severity of symptoms, functional problems, and environmental triggers and consists of 12 questions. It has been psychometrically tested as adequate for use in measuring severity of DED. It enables a quick assessment of the symptoms of ocular discomfort consistent with dry eye and their consequences on vision-related functioning. Each answer is scored on a 5-point scale, resulting in a total OSDI score ranging from 0 (no symptoms) to 100 (maximum symptoms). High scores indicate increased symptom severity.[22]

The Schirmer Test

The Schirmer test is based on the measurement of wetness 5 min after insertion of the filter paper into the conjunctiva. Five millimeter and 10 mm are the recommended cutting values. The disadvantage is that the test can be affected by room humidity and heat.[21]

Collection of *Demodex*

Two eyelashes were taken from the inferior eyelids of each two eyes, and the sample was immediately brought to the microbiology laboratory in the slides by pouring two drops of saline (%0.09 NaCl solutions) for analysis by the relevant specialist. At least one per four eyelashes was required to be included in the *Demodex*-positive group. Lid hygiene and tea tree oil lid shampoos, with literature information to be effective in treatment,[23,24] were recommended to all patients with *Demodex* infestation.

Statistical Analysis

For the data evaluation, 15.0 version of the Statistical Package for the Social Sciences (SPSS) program was used. Kolmogorov–Smirnov normality test was performed. Schirmer test score (P=0.11), OSDI score (P=0.13), and age (P=0.35) were found to be normally distributed. Groups were compared using independent sample t test in terms of variables those showed normal distribution. The difference in gender and presence of *Demodex* between the groups was assessed by the chi-square test. Descriptive statistics (number of *Demodex*) are shown as mean–SD and minimum–maximum or frequencies. Mean age variable was adjusted by one-way analysis of covariance. Statistical significance was accepted as $P<0.05$.

RESULTS

Demodex-positive group consisted of 30 patients, and 16 of them were male and 14 were female. *Demodex*-negative group consisted of 54 patients; 29 of them were male and 25 were female. The mean age of *Demodex*-positive group was 55.36±8.7 years, whereas the mean age of *Demodex*-negative group was 49.12±6.8 years. Number of *Demodex* was 94 in 352 eyelashes of 88 patients. Mean *Demodex* number was 2.68±2.5, and minimum value was "1" and maximum value was "11" in *Demodex*-positive group.

Demodex colonization in positive group was found to have an average Schirmer test score of 2.1±0.52 and OSDI questionnaire score of 61.82±10.95, whereas in patients without *Demodex* colonization, the average Schirmer test score was 6.6±0.9 and the OSDI questionnaire score was 40.96±12.73. There was no significant difference in the presence of *Demodex* between genders (P=0.957). The presence of ocular *Demodex* colonization was found to be associated with a statistically significant decrease in Schirmer test scores (P=0.001) and a statistically significant increase in OSDI questionnaire scores (P=0.001) and age (P=0.001) in patients with newly diagnosed DED. The significant relationship between lower Schirmer test score and higher OSDI rates and occurrence of *Demodex* infestation continued after adjusting for mean age values (P=0.012; P=0.035); Table 1).

DISCUSSION AND CONCLUSION

In this study, adults aged 40 to 68 years admitted to policlinic for routine ophthalmological examination or presbyopia and showed dry eye symptoms were included. Study patients with and without ocular *Demodex* colonization were compared in terms of age, Schirmer test scores, and OSDI scores. Our main results demonstrate that there was a statistically significant increase in age and OSDI test scores and a significant decrease in Schirmer test scores in *Demodex*-positive group compared with *Demodex*-negative group. The significant relationship between lower Schirmer test score and higher OSDI rates and *Demodex* infestation continued after adjusting for mean age values.

In a study from Korea, the association of *Demodex* frequency with severity of ocular discomfort was investigated ; the number of *Demodex* showed a significant correlation with age, sex, and tear breakup time test (is used in DED diagnosis), but there was no significant relationship between *Demodex* quantity and the

TABLE 1. Demodex Groups Comparison

Demodex Positive (n: 30)	Demodex Negative (n: 54)	P
Male n=16 Female n=14	Male n=29 Female n=25	0.76[a]
Age: 55.36±8.74	Age: 49.12±6.87	0.001[b]
Schirmer 1 score: 2.1±0.5	Schirmer 1 score: 6.6±0.9	0.001[b]
OSDI score: 61.82±10.95	OSDI score: 40.96±12.73	0.001[b]

[a]Chi-square test.

[b]Independent t test.

OSDI, Ocular Surface Disease Index.

Schirmer test scores.[19] In another study from our country, two groups of healthy subjects without ocular complaints were evaluated; a significant increase in *Demodex* presence and *Demodex* quantity was detected in the group in which Schirmer test scores were above 5 mm/min compared with that in which Schirmer test scores were below 5 mm/min.[20] These studies and in addition our study shed light on the *Demodex* agent's association with dry eye parameters without blepharitis or any other ocular infectious condition.

Another finding of our study was that the mean age was significantly higher in the *Demodex*-positive group compared with the *Demodex*-negative group. In most studies comparing patients with ocular surface diseases such as blepharitis and dermatological diseases with healthy controls in terms of *Demodex* infestation, it has been detected that the presence of infection increased with age. In the study by Biernat et al,[25] it was found that a high mean number of mites were frequently seen in individuals older than 50 years. In another study, patients who were followed up in dermatology outpatient clinic for various skin problems were divided into 2 groups: 35 years and younger, and 36 years and older, and the presence of *Demodex* was examined. It was detected that the presence of *Demodex* was significantly higher in the elderly group.[26] In our study, there was a positive correlation between the number of *Demodex* and mean age in accordance with previous studies.

In the literature regarding *Demodex*, it has been seen that the number of eyelashes taken in studies varies from only two eyelashes from each eyelid of each eyes to four eyelashes from each eyelid.[19,27] We have taken four eyelashes in total, two from each eye, and this may be a limitation. We aimed to demonstrate the presence of *Demodex* rather than *Demodex* number, and we thought that it would create a serious comfort problem for the patient. An important limitation of our study is the small sample size. The OSDI self-report scale used in our work may cause reporting bias. Another limitation is that different tests used to evaluate dry eye signs could be applied.

As a result of this study, it has been observed that the presence of ocular *Demodex* colonization was associated with a statistically significant decrease in Schirmer test scores and a statistically significant increase in OSDI questionnaire scores in patients with newly diagnosed DED. The significant relationship between lower Schirmer test score and higher OSDI rates and *Demodex* infestation continued after adjusting for mean age values. The individuals included in the study consisted of patients who had applied for routine eye examination and whose main complaint was not dry eye. So, determining *Demodex* infestation as a factor in the occurrence and progression of DED with multifactorial etiopathogenesis, it will contribute to the early treatment and prevention of the progression of DED. We believe that this finding may be important in improving the quality of life of the patients and making the disease later symptomatic if supported by large-numbered, randomized-controlled studies.

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