Dermatology Practical & Conceptual

Facial Dermatoses in Patients With Blepharitis: a Cross-sectional Prospective Analysis

Semih Güder[1], Şafak Çulfa[2]

1 Department of Dermatology, Medical Faculty, Bezmialem Vakif University, Adnan Menderes Bulvarı, Fatih/Istanbul, Turkey
2 Department of Ophthalmology, Medical Faculty, Bezmialem Vakif University, Adnan Menderes Bulvarı, Fatih/Istanbul, Turkey

Key words: facial dermatoses, blepharitis, demodicosis, rosacea, seborrheic dermatitis

Citation: Güder S, Çulfa S. Facial dermatoses in patients with blepharitis: a cross-sectional prospective analysis. *Dermatol Pract Concept.* 2022;12(3):e2022113. DOI: https://doi.org/10.5826/dpc.1203a113

Accepted: November 23, 2021; **Published:** July 2022

Funding: None.

Competing interests: None.

Authorship: Conceptualization: S.G.; Ş.Ç.; Data collection: Ş.Ç, S.G.; Writing of the manuscript: S.G., Ş.Ç.; Manuscript editing and revision: S.G., Ş.Ç.

Corresponding author: Semih Güder, MD, Department of Dermatology, Medical Faculty, Bezmialem Vakif University, Adnan Menderes Bulvarı, Fatih/Istanbul, Turkey. E-mail: semihguder@gmail.com Tel: +905056655518

ABSTRACT

Introduction: The relationship between facial dermatoses and blepharitis has been known for a long time.

Objectives: We aimed to investigate the frequency of accompanying facial dermatoses in patients with blepharitis and their relationship with the severity of blepharitis.

Methods: In this cross-sectional study, 95 patients with blepharitis were examined for attending facial dermatoses. The type of blepharitis, the severity of blepharitis, and the degree of dry eye were determined in the patients. Dermoscopic and microscopic examinations were used in the diagnosis of facial dermatoses. The history of allergic rhinitis was questioned because Demodex species frequently accompany blepharitis, facial dermatoses, and allergic rhinitis patients. Mann-Whitney U test was used compare 2 independent groups. In comparing categorical variables, Pearson chi-Squared, Fishere Exact, and Fisher-Freeman-Holton tests were used.

Results: At least 1 facial dermatosis was detected in 84.2% patients, and we did not see any facial dermatosis in 15.8% ones. No patients had acne, which is one of the most common facial dermatoses. The most common facial dermatosis detected in our patients was facial demodicosis (57.9%). It was followed by seborrheic dermatitis (22.1%) and rosacea (12.6%), respectively. In addition, 2.1% of the patients had atopic eyelid dermatitis, 23.2% had a history of allergic rhinitis, and 63.2% had ocular demodicosis.

Conclusions: It is essential to perform dermatological examinations of all patients with blepharitis in terms of accompanying facial dermatoses and their early diagnosis.

Introduction

Blepharitis is a multifactorial inflammatory condition of the eyelids that occurs in less than 1% of the general population. It is classified as anterior blepharitis and posterior blepharitis according to the eyelash margin of the affected area. Affected individuals may complain of irritation as eyelid itching, burning sensation, watering-epiphora, eyelid crusting, foreign-body sensation, a feeling of heavy eyelids, and photophobia and blurring vision. Rarely blepharitis may lead to keratopathy, corneal ulceration, permanent changes of eyelid morphology, and result in decreased vision. Blepharitis is commonly categorized by anatomical location. Anterior blepharitis may occur in seborrheic or non-seborrheic types and is associated with increased eyelid commensals such as Staphylococcus epidermidis and Staphylococcus aureus [1,2].

However, posterior blepharitis is secondary to structural changes and occlusion of the meibomian gland orifices [2,3]. Blepharitis generally occurs due to underlying skin diseases such as seborrheic dermatitis (SD), atopic dermatitis (AD), rosacea, or facial demodicosis (FD) [2,4,5].

In anterior blepharitis, bacterial antigen, exotoxins, and delayed cell-mediated immune hypersensitivity leading to an inflammatory cascade. Infectious blepharitis is characterized by hyperemia, edema, scaling, and telangiectasia of the anterior lid margin. Severe cases are complicated with poliosis, madarosis, eyelid hypertrophy, and corneal scars. Recurrent hordeola are often related to staphylococcal strains in infectious blepharitis [6].

In posterior blepharitis cases, inflammation of the posterior lid margin induces Meibomian gland dysfunction (MGD). Terminal duct obstruction due to hype-rkeratinization reduces glandular secretion and causes tear film abnormalities. Evaporative tear disorders are mostly seen in patients with MGD and are reasons for patients complaints [7].

Seborrheic blepharitis more effecting sebaceous gland Zeis than meibomian glands has less inflammation than staphylococcal blepharitis but is characterized by more oily scaling. Some patients with seborrheic blepharitis show MGD [8].

Ocular complications such as eyelid dermatitis, blepharitis, conjunctivitis, cataract, keratoconus are seen in patients with atopic dermatitis [2,9]. In the report of the North American contact dermatitis study group, the frequency of atopic eyelid dermatitis was reported to be around 13% [10]. Every patient with blepharitis and conjunctivitis should be questioned about the history of atopy. Because it is common in these patients [11].

Rosacea is a progressive facial inflammatory dermatosis that may be associated with systemic diseases. Ocular surface changes such as blepharitis and conjunctivitis are seen in patients with rosacea [12,13].

The parasitic infection Demodex blepharitis is a chronic inflammatory disease caused by Demodex mites, affecting the eyelid margin and ocular surface. The worldwide incidence of ocular Demodex infestation is around 13%-70%. In addition, the presence of Demodex in the eyelashes of 18% of healthy individuals in the 2nd and 3rd decades is reported [5,14]. The rate of Demodex infestation increases with age and is seen in almost all people over 70 years of age [13,15-17].

Demodex mites have also been hypothesized to play a role in the etiology of posterior blepharitis [18]. Infestation along the posterior margin is a reason for obstruction of gland orifices [15]. Demodex's nutritional source is follicular and glandular epithelial cell sebum [19]. Demodex folliculorum infestation causes anterior blepharitis. Mites deposit their eggs on the base of the eyelashes, and keratin and epithelial cell deposits accumulate, forming cylindrical dandruff, the pathognomonic sign of demodicosis. Mites are in clusters around eyelashes and skin [20,21]. Demodex brevis penetrate the meibomian glands causing gland obstruction and dysfunction inducing marginal blepharitis. They are seen one by one in glands [21,22].

Demodex species are also a common etiological factor for AR and blepharitis. The frequency of facial Demodex, which is thought to be a facilitating factor in patients with AR, was found to be 40% on average [5, 3,24].

Dermoscopy is a good diagnostic tool in common facial dermatoses. Demodex tails and Demodex follicular openings are frequently observed in facial demodicosis. Dotted vessels and fine yellowish scales in seborrheic dermatitis, linear veins in a polygonal network, and follicular pustules in rosacea are diagnostic clues [25].

Objectives

We planned this study to investigate the frequency of SD, AD, rosacea, and demodicosis, which are skin diseases that frequently affect the face and are thought to play an essential role in the etiology of blepharitis. We hypothesized that performing dermatological examinations of all patients with chronic blepharitis may be necessary for the early diagnosis and treatment of facial dermatoses.

Methods

The local ethics committee reviewed and approved the study (protocol ID: 2021/900/88), and written informed consent was obtained from all participants. The study was carried out according to the principles in the Declaration of Helsinki.

Patient Selection and Procedures

A total of 95 patients diagnosed with chronic blepharitis in our ophthalmology clinic and undergoing dermatological

evaluation on the same day were included in the study. The patients were examined for facial dermatoses, and a dermoscopic examination was performed. The history of allergic rhinitis was questioned because Demodex species frequently accompany blepharitis, facial dermatoses, and allergic rhinitis patients. In terms of accompanying demodicosis, skin scraping, standardized skin surface biopsy (SSSB), and eyelash sampling were performed. The duration of blepharitis and facial dermatoses, and the history of allergic rhinitis, were recorded.

Dermoscopic Evaluation

The dermoscopic evaluation was performed by using a handheld dermoscope (DermLite DL200HR; 3Gen, Inc.) at ×10 magnification (polarized light). Images were recorded directly by the smartphones attached magnetically to the dermoscope. We performed dermoscopic examination with two methods. First, we performed a classical dermoscopic examination (Figure 1, A,B,C. In this method, we placed the dermoscope probe vertically on the cheek skin. Second, our new lateral dermoscopic technique; makes demodex tails more prominent. We put the dermoscope horizontally on the cheek skin and then examined it by pinching between the index finger and the dermoscope (Figure 1, D,E,F, Figure 2).

Microscopic Eyelid Demodex Examination

Three eyelashes were taken from the eyelids of both eyes, prepared by glycerine-type separation, and evaluated under a light microscope (Olympus,) at ×40 and ×100 magnification. At least 3 Demodex folliculorum in each eyelash was considered as Demodex infestation (Figure 3) [26].

Evaluation of Tear Production

The Schirmer test was used to evaluate tear production in patients. Test strips were designated "L" and "R" for the left and right eyes, respectively. Afterward, each strip was bent at a 90-degree angle. The patient was told to look up, and the lower eyelid of the patient was pulled down. The curved end of the test strip was placed between the palpebral conjunctiva and the bulbar conjunctiva. This procedure was also done for the other eye. After both strips were seated, the patient was asked to close their eyes for five minutes gently. After five minutes, the test strips were removed. A score of more than 10 mm was considered normal. A score between 5mm and 10mm was graded as mild insufficiency, and a score of less than 5mm was graded as severe insufficiency [27].

Evaluation of the Severity of Seborrheic Dermatitis

The Seborrheic Dermatitis Area and Severity Index (SEDASI) scale developed by Micali et al. were used to assess the severity of seborrheic dermatitis [28].

Demodicosis Classification and Evaluation of the Density of Facial Demodex

Demodicosis was classified as follows: rosacea-like demodicosis, pityriasis folliculorum, Demodex dermatitis, spinulosus of the face, and pustular folliculitis [29]. Skin samples were taken from the right cheek of the patients using the SSSB method. A microscope slide with cyanoacrylate adhesive is pressed onto the lesion. After 30 seconds, the sample was removed from the skin. The sample was covered with a coverslip and examined by light microscopy at x10, x40, and x100 magnification in immersion oil. The total number of viable parasites in a sample was used to assess Facial Demodex severity and density (FDS): 0-5 per cm^2, 1+ density, 5-10 per cm^2, 2+, 10-15 per cm^2, 3+, 15-20 per cm^2, 4+ and >20.5 per cm^2 was classified as 5+ [30].

Rosacea Classification and Evaluation of the Clinical Severity (RCS)

The classification and scoring system of the American National Rosacea Society (NRS) was used for the type and severity of rosacea [31].

Bleraphyte Classification and Scoring of Severity

The Uludağ Ocular Demodicosis Clinical Scoring system (UODS) was used to evaluate the severity of blepharitis. According to this score, if there is at least one stinging, burning, itching, and pain complaint, 1 point is given; otherwise, 0 points were awarded. A score of 1 was given for anterior or posterior blepharitis, and 2 points were given if both were present. One point for long-term use of drops containing preservatives (eg glaucoma drugs); 2 points were given if there was a systemic or local disease other than blepharitis that would cause dry eye. It was given 1 point if there was an epithelial defect and 2 points if it presented with keratitis. The presence of cylindrical dandruff was given 2 points [32].

Statistical Analysis

The SPSS 25.0 (IBM Corporation) program was used in the analysis of the variables. The conformity of univariate data to normal distribution was evaluated with the Shapiro-Wilk Francia test, while homogeneity of variance was assessed with the Levene test.

The Mann-Whitney U test was used together with Monte Carlo results to compare two independent groups with each other according to quantitative data. In the comparison of more than two groups according to quantitative data, Kruskal-Wallis H test and Jonckheere-Terpstra test were used together with Monte Carlo results, and Dunn tand Tukey tests were used for post-hoc analyses. Kendall tau-b and Spearman rho tests were used to examining the correlations of the variables with each other.

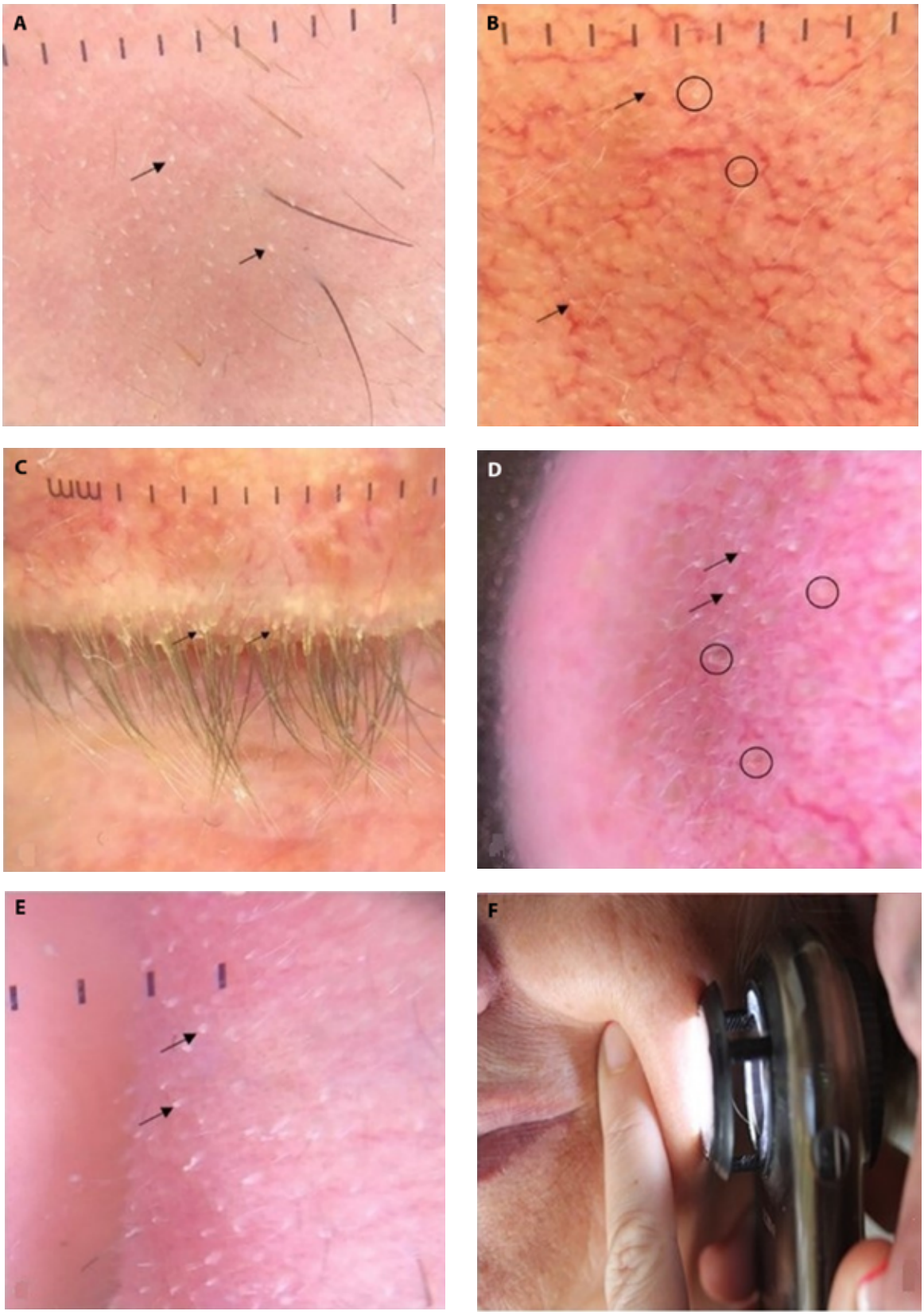

Figure 1. Dermoscopic findings of facial demodicosis (FD). (A)Pityriasis folliculorum on the right cheek area of a young man. The white yellowish structures are Demodex tails (arrows). (B) Cheek area of middle-aged woman. The white yellowish structures are Demodex tails (arrows), and Demodex follicular openings (black circles) are seen. Reticular dilated vessels are remarkable in the patient with a history of intermittent steroidal cream use. (C) Diffuse eyelash demodicosis in an elderly man; white yellowish structures are Demodex tails (arrows); increased vascularity less pronounced possibly due to age-related atrophy. (D and E) Dermoscopy of the cheek region of 2 different patients, lateral dermoscopic examination technique. In the patient on the left, Demodex follicular openings (black circles) and reticular dilated vessels are observed in addition to Demodex tails (arrows). (F) Lateral dermoscopic technique for FD.

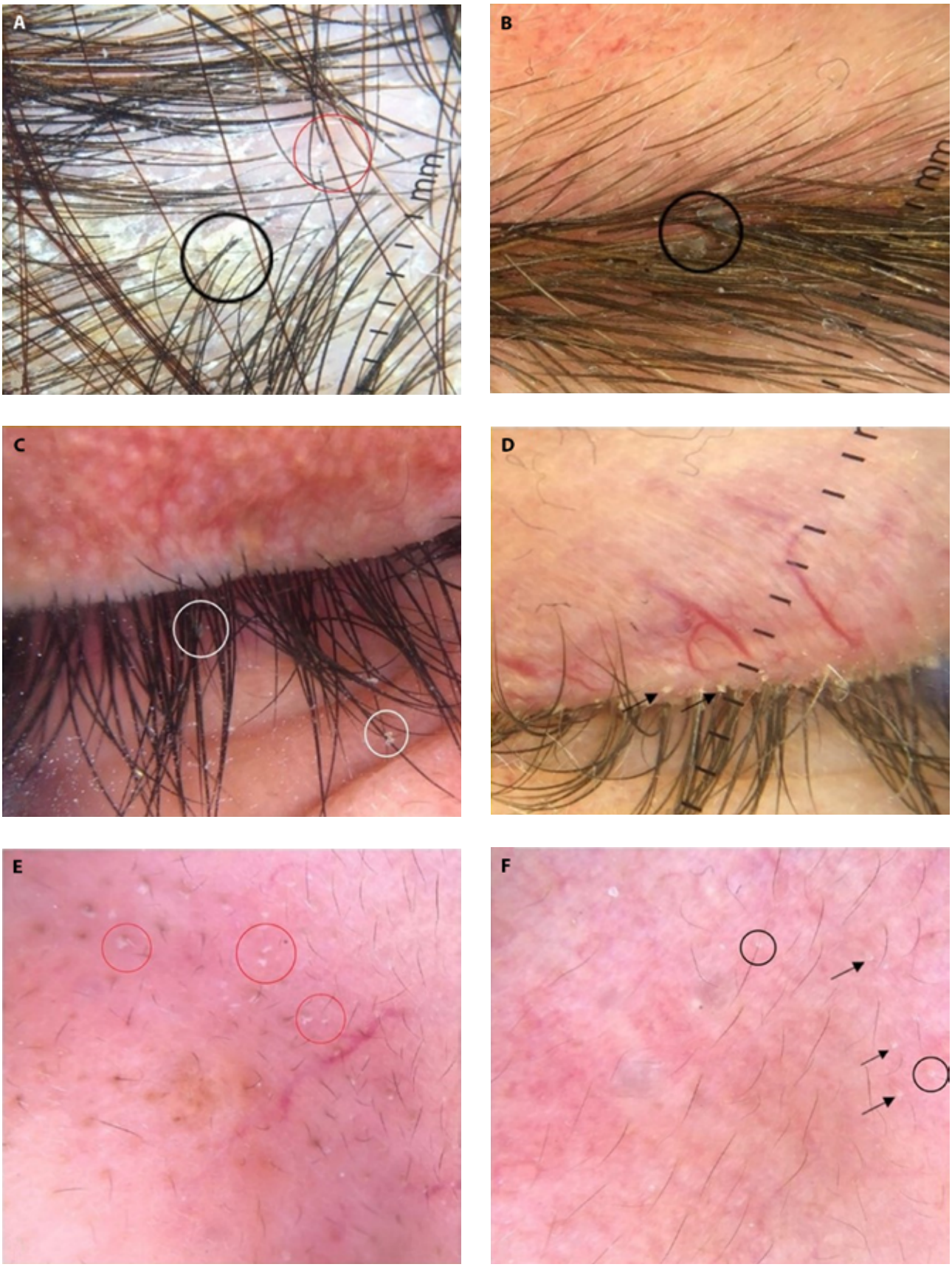

Figure 2. Dermoscopic findings of seborrheic dermatitis (SD). (A) Interfollicular pale erythema (red circle) and oily scale (black circle) in the scalp region. (B) Oily scale on eyebrows (circle) (C) Eyelash of the patient with SD. Thin scales (white circles) attached to the eyelashes are seen (no accompanying Demodex). (D) Eyelash demodicosis in a patient with SD. The white yellowish structures are Demodex tails (arrows), and dilated, and arborized vessels are visible. (E) A dermoscopic view of the nasolabial fold. Fine white nonspecific scales are seen (circles). (F) Dermoscopic view of the cheek of a patient with SD accompanied by facial demodicosis. Demodex follicular openings (circles) and Demodex tails (arrows) are visible.

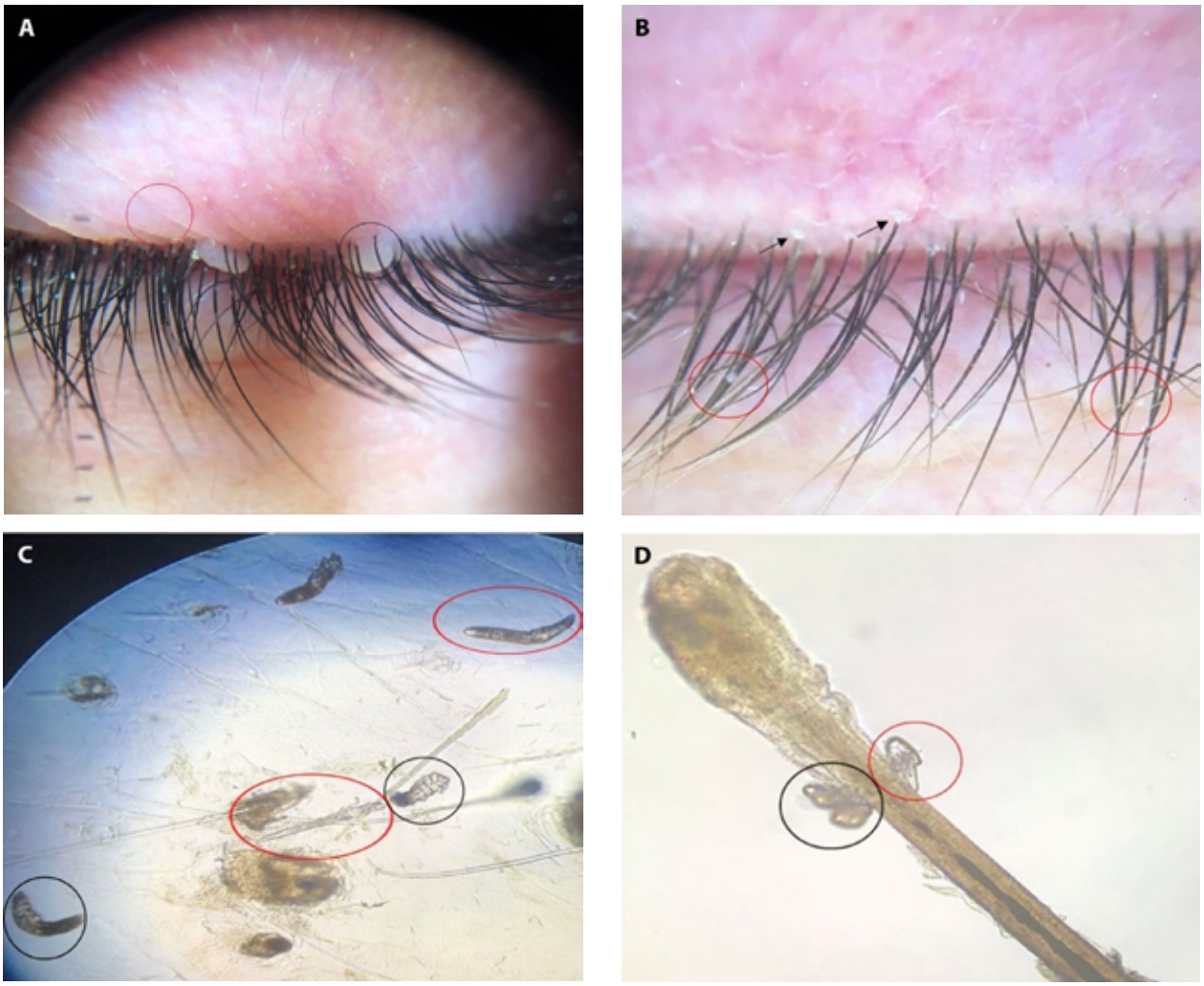

Figure 3. The appearance of eyelid and eyelashes of a patient with atopic eyelid dermatitis and allergic rhinoconjunctivitis; microscopic views of facial and ocular demodicosis. (A) A middle-aged man with atopic eyelid dermatitis, presumably secondary to scratching trauma. Prominent skin lines (red circle) and polypoid structures (black circles) are seen. (B) Eyelashes of the patient with allergic rhinoconjunctivitis. The white yellowish structures are Demodex tails (arrows). Thin white scales wrapped around the lashes are also observed (circles). (C) Microscopic view of Demodex folliculorum (black circles) and its larvae (red circles) appear on standardized skin surface biopsy (SSSB) (×40). (D) Microscopic view of the eyelash: Demodex folliculorum eggs (black circle) and larvae (red circle) (×40).

In comparing categorical variables, Pearson chi-Squared, Fisher exact, and Fisher-Freeman-Holton tests were tested with the Monte Carlo simulation technique, and column ratios were compared with each other and expressed according to Benjamini-Hochberg corrected P value results.

Quantitative variables were expressed as mean (± standard deviation), median (minimum/maximum), and median (percentile 25° / percentile 75°) in the tables, while categorical variables were shown as N (%). The variables were analyzed at 95% confidence level, and a P value less than 0.05 was considered significant.

Results

Demographic Data

Thirty-two (33.7%) of our patients were males, and 68 (66.3%) were femalse. The mean age of our patients was 46.58 (±14.78) years. The mean disease duration was 24.99 (±22.49) months. Ninety-one (95.8%) patients had anterior blepharitis, 22 (23.2%) had posterior blepharitis, and 18 (18.9%) had compound blepharitis. The mean UODS were 4.23 (±2.39). All our patients had at least 1 of the symptoms of eyelid itching, burning sensation, watering, eyelid crusting, feeling of heavy eyelids, and photophobia. We did not find keratitis in any of the patients (Table 1).

The mean Schirmer test values of the patients were 9.46 for the right eye and 9.77 for the left eye, and more than one-third of them had a severe dry eye (Table 1).

At least one facial dermatosis was detected in 84.2% of our patients, and we did not see any facial dermatosis in 15.8%. And none of our patients had acne, which is one of the most common facial dermatoses. The most common facial dermatosis detected in our patients was FD (57.9%). This was followed by SD (22.1%) and rosacea (12.6%), respectively. In addition, 2.1% of the patients had atopic eyelid dermatitis (AED), 23.2% had a history

Table 1. Blepharitis types and severity, Schirmer scores, facial dermatoses types, rates and severity, together with demographic data in our patients

	N	%
Male	32	33.7%
Female	63	66.3%
Schirmer right eye score		
Mild	29	30.5%
Moderate	24	25.3%
Severe	42	44.2%
Schirmer left eye score		
mild	33	34.7%
moderate	26	27.4%
Severe	36	37.9%
Facial demodicosis severity (FDS)		
0-5	4	4.2%
5-10	5	5.3%
10-15	16	16.8%
15-20	24	25.3%
>20	6	6.3%
Facial demodicosis	55	57.9%
Spinulosis of face	28	29.5%
Pityriasis folliculorum	6	6.3%
Rosacea like demodicosis	21	22.1%
Positive eyelash microscopy for Demodex	60	63.2%
Ocular demodicosis	60	63.2%
Seborrheic dermatitis	21	22.1%
Rosacea	12	12.6%
All facial dermatoses	80	84.2%
Positive cheek microscopy for Demodex	55	57.9%
Demodex tails	55	57.9%
Demodex follicular openings	35	36.8%
Demodex dilated capillaries	30	31.6%
History of allergic rhinitis	22	23.2%
Anterior blepharitis	91	95.8%
Posterior blepharitis	22	23.2%
Compund belpharitis	18	18.9%
Cylindiric scale	52	54.7%
Droplet usage	17	17.9%
Different xerophthalmia cause and keratitis	0	0.0%
Epithelial defect	7	7.4%
	N	**Median (min/max)**
Age	95	43 (24 / 82)
Blepharitis duration (m)	95	18 (2 / 96)
UODS	95	4 (2 / 15)
Seborrheic dermatitis duration (m)	21	60 (48 / 240)
SEDASI	21	16 (8 / 24)
Rosacea duration (m)	14	36 (24 / 72)
Rosacea clinical severity	14	6 (6 / 9)
Allergic rhinitis duration (m)	22	96 (60 / 360)
Schirmer right eye	95	8 (4 / 20)
Schirmer left eye	95	10 (5 / 20)

m = month; SD = Standard Deviation; SEDASI: Seborrheic Dermatitis Area and Severity Index; UODS = Uludağ Ocular Demodicosis Clinical Scoring system.

of allergic rhinitis (AR), and 63.2% had ocular demodicosis (OD) (Table 1).

Duration and Severity of Detected Facial Dermatoses

The patients had not previously applied to the dermatology outpatient clinic regarding this condition, and they had no complaints about this. Therefore, we could not calculate the FD time. The FDS was as follows: + in 4 patients (4.2%), ++ in 5 patients (5.3%), +++ in 16 patients (16.8%), ++++ in 24 patients (25.3%), 6 patients (6.3%) +++++ FD was present. The mean SD duration was 85.71 (±44.79) months. The mean SEDASI was 14.48 (±5.06). The mean disease duration of the patients with rosacea was 41.86 (±13.18) months, and the mean RCS was 7.29 (±1.54) (Table 1).

Relationships Between Duration and Severity of Blepharitis and Duration and Severity of Facial Dermatosis

There was no correlation between blepharitis duration, rosacea duration, SD duration, RCS score, SEDASI scores with blepharitis severity (UODS) in our patients. There was only a weak positive correlation between rosacea duration and UODS and between FDS score and UODS (P = 0.002 and P = 0.013, respectively) (Table 2).

Facial Dermatoses and History of Allergic Rhinitis Compared with the Severity of Blepharitis and Degree of Dry Eye.

In terms of the severity of blepharitis, the median value of the UODS score in the FD group was greater than the median value of the allergic rhinitis group (P = 0.026) and the median value of the SD group (P = 0.001), and it was statistically significant. There was no significant difference in the severity of blepharitis between patients with allergic rhinitis and patients with SD (P = 0.208). No significant correlation was found between patients with allergic rhinitis and patients with SD in terms of dry eye degree (P > 0.05) (Table 3).

However, there was a weak positive correlation between the presence of FD with Schirmer scores of the right and left eyes (r = 0.369 and 0.489, respectively), which was statistically significant (P = 0.027 and 0.002, respectively) (Table 4).

Anterior blepharitis was significantly higher in the FD group than in the SD and AR groups (P = 0.028) (Table 5).

We examined the rate of FD in facial dermatoses we detected. We observed a higher rate of FD, especially in patients with rosacea compared to other groups. FD was present in 66.7% of patients with rosacea and 47.6% of patients with SD. We found the incidence of FD to be quite low (22.7%) in patients with AR than in patients without AR. This difference was statistically significant (P < 0.001). We did not find a significant difference in the incidence of FD in patients with or without SD and with or without rosacea (respectively P = 0.280 and P = 0.510) (Table 6).

Table 2. Relationships between duration and severity of facial dermatosis with blepharitis severity.

	UODS	
	r	P
FDS	0.255	0.013
RCS	0.149	0.566
SD duration	0.262	0.148
SEDASI	0.275	0.133
Rosacea duration	0.706	0.002
Allergic rhinitis duration	0.111	0.518

Kendall tau b test, Spearman rho test.
FDS = facial demodicosis severity; r = Correlation Coefficient; RCS = Rosacea clinical severity; SD = seborrheic dermatitis; SEDASI = Seborrheic Dermatitis Area and Severity Index; UODS = Uludağ Ocular Demodicosis Clinical Scoring system.

Table 3. Relationships between facial dermatoses and history of allergic rhinitis with the severity of blepharitis.

	UODS	
	Median (q1 / q3)	P
		0.001
Allergic rhinitis (A)	3 (2 / 4)	P (A-B) = 0.208
Seborrheic dermatitis (B)	2 (2 / 3)	P(A-C) = 0.026
Facial demodicosis (C)	4 (4 / 5)	P(B-C) = 0.001

Kruskal-Wallis H test (Monte Carlo); Post Hoc test: Dun test.
AR = allergic rhinitis;FD = facial demodicosis; q1 = 25°percentile; q3 = 75° percentile;. SD = seborrheic dermatitis; UODS = Uludağ Ocular Demodicosis Clinical Scoring System Blepharitis severity score.

Table 4. Relationships between facial dermatosis and history of allergic rhinitis, with the degree of dry eye.

	Allergic Rhinitis		Seborrheic Dermatitis		Facial Demodicosis	
	r	P	r	P	r	P
Schirmer right eye score	-0.204	0.466	0.324	0,332	0.369	0.027
Schirmer left eye score	-0.312	0.257	0.324	0.332	0.489	0.002
SEDASI	-	-	0.106	0.757	-	-
FDS	-	-	-	-	-0.080	0.643

FDS = facial demodicosis severity; r = Spearman rho test correlation coefficient; SEDASI = Seborrheic Dermatitis Area and Severity Index.

Table 5. The relationship between blepharitis type and severity parameters and facial dermatoses.

	Allergic Rhinitis (N = 15)	Seborrheic Dermatitis (N = 11)	Facial Demodicosis (N = 36)	P
	N (%)	N (%)	N (%)	
Anterior blepharitis				0.028
None	2 (13.3) [C]	2 (18.2) [C]	0 (0.0)	
Yes	13 (86.7)	9 (81.8)	36 (100.0) [AB]	
Posterior blepharitis				0.545
None	10 (66.7)	9 (81.8)	29 (80.6)	
Yes	5 (33.3)	2 (18.2)	7 (19.4)	
Compound blepharitis				0.280
None	12 (80.0)	11 (100.0)	29 (80.6)	
Yes	3 (20.0)	0 (0.0)	7 (19.4)	
Cylindric scale				<0.001
None	12 (80.0) [C]	10 (90.9) [C]	9 (25.0)	
Yes	3 (20.0)	1 (9.1)	27 (75.0) [AB]	
Droplet usage				0.019
None	9 (60.0)	11 (100.0) [A]	31 (86.1) [A]	
Yes	6 (40.0) [BC]	0 (0.0)	5 (13.9)	
Different xerophthalmia cause				-
None	15 (100.0)	11 (100.0)	36 (100.0)	
Yes	0 (0.0)	0 (0.0)	0 (0.0)	
Epithelial defect				0.368
None	15 (100.0)	11 (100.0)	32 (88.9)	
Yes	0 (0.0)	0 (0.0)	4 (11.1)	

Fisher freeman Halton test (Monte Carlo). [A] expresses significance according to AR group, [B] expresses significance according to SD group, [C] expresses significance according to FD group, [AB] expresses significance according to AR and SD group, [BC] expresses significance according to SD and FD group

Table 6. Frequency of facial demodicosis in facial dermatoses and patients with allergic rhinitis.

	Seborrheic Dermatitis		Allergic Rhinitis		Rosacea	
	None	Yes	None	Yes	None	Yes
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Facial Demodicosis						
None	29 (39.2)	11 (52.4)	23 (31.5)	17 (77.3)	36 (43.4)	4 (33.3)
Yes	45 (60.8)	10 (47.6)	50 (68.5)	5 (22.7)	47 (52.6)	8 (66.7)
P	0.280 [a]		<0.001 [a]		0.510 [a]	

a: Pearson Chi-Square Test (Monte Carlo).

Conclusions

This study aimed to investigate the frequency of accompanying facial dermatoses in patients with blepharitis and whether there is a relationship between the severity of dermatoses and the severity of blepharitis. As a result of our research, we found that patients with blepharitis mostly have facial inflammatory dermatosis.

We detected at least one facial dermatosis in most of our wastes. This may suggest that a common factor plays a role in the etiopathogenesis of facial dermatoses and blepharitis. For example, many studies suggest that Demodex infestation, which plays a role in the etiology of facial dermatoses, is associated with rosacea and SD [16,33,34].

A similar immunopathogenesis in these disease groups may also be responsible for the association of facial dermatoses and blepharitis. The presence of STAT-1 gene mutations that cause a primary immunodeficiency, which is blamed especially in the etiology of rosacea, Demodicosis, blepharitis, or the emergence of Demodicosis, SD and rosacea in secondary immunodeficiency cases may be a consociate etiopathogenetic factor [35-38].

We thought that the treatment of blepharitis might be triggering facial dermatoses due to the coexistence of facial dermatoses and blepharitis. However, we found the duration of facial dermatosis to be much longer than the duration of blepharitis. For example, as the duration of rosacea increased, the severity of blepharitis increased ($P = 0.002$). Therefore, blepharitis may actually develop as a result of a chronic facial inflammatory process. We think that the duration of FD is also long in our patients, but prospective studies are needed to explain this.

Both the severity of blepharitis and the degree of dry eye were higher in patients with FD compared to patients with SD and AR. The association of ocular Demodex infestation with dry eye is known [39,40]. This may be related to the presence of OD in the vast majority (85.5%) of our patients with FD, and thus our study supported the presence of dry eye symptoms in patients with OD.

Some patients with blepharitis have a history of AR. Patients with AR also have Demodex infestation. It raises the question of whether there is a cross immune response between house mites and Demodex. However, no allergen cross-reactivity was detected between house dust mites and Demodex [41]. However, we did not associate the development of blepharitis in AR patients with Demodex because only one (6.7%) of our patients with AR had OD. Further clinical studies are needed to explain blepharitis and allergic rhinitis association.

We interpreted the reasons why we found anterior blepharitis more than posterior and compound blepharitis in the FD, SD, and AR groups. We detected cylindric scales in 80% of patients with OD. Since this finding is often associated with *D. folliculorum*, which causes anterior blepharitis, we may have seen anterior blepharitis possibly related to *D. folliculorum* much more in our patients with OD [15, 20, 21]. Since SD involves the Zeis glands more frequently, and anterior segment findings can be expected [8]. Therefore, we may have seen anterior blepharitis more frequently in our SD patients, as expected.

Main limitations of the study were thatthe information about the drugs used by the patients for blepharitis and their other diseases was not recorded and the lack of a control group.

We detected high rates of facial dermatosis in patients with blepharitis. For this reason, we think that it is essential for all patients diagnosed with blepharitis to be examined in dermatology clinics for facial dermatoses. Thus, we predict that the patient's quality of life will increase with the treatment of an early-detected facial dermatosis. Furthermore, we are becoming more and more aware that dermoscopy can be a helpful tool in the diagnosis of periocular diseases besides all skin diseases and facial dermatoses.

References

1. Bron AJ, Tiffany JM. The Evolution of Lid Margin Changes in Blepharitis. In: Lass JH, ed. *Advances in Corneal Research: Selected Transactions of the World Congress on the Cornea IV*. Boston, MA: Springer US; 1997:3-18.
2. Hsu JI, Pflugfelder SC, Kim SJ. Ocular complications of atopic dermatitis. *Cutis*. 2019;104(3):189-193. PMID: 31675394.
3. Arici C, Mergen B, Bahar Tokman H, et al. Investigation of the Demodex Lid Infestation with in Vivo Confocal Microscopy versus Light Microscopy in Patients with Seborrheic Blepharitis. *Ocul Immunol Inflamm*. 2021:1-5. DOI: 10.1080/09273948.2020.1857792. PMID: 33560183.
4. Auw-Haedrich C, Reinhard T. Chronische Blepharitis. Pathogenese, klinischer Verlauf und therapeutische Ansätze [Chronic blepharitis. Pathogenesis, clinical features, and therapy]. *Ophthalmologe*. 2007;104(9):817-826; quiz 827-828. DOI: 10.1007/s00347-007-1608-8. PMID: 17762935.
5. Yan Y, Yao Q, Lu Y, et al. Association Between Demodex Infestation and Ocular Surface Microbiota in Patients With Demodex Blepharitis. *Front Med (Lausanne)*. 20204;7:592759. DOI: 10.3389/fmed.2020.592759. PMID: 33251239. PMCID: PMC7672197.
6. Scheinfeld N, Berk T. A review of the diagnosis and treatment of rosacea. *Postgrad Med*. 2010;122(1):139-143. DOI: 10.3810/pgm.2010.01.2107. PMID: 20107297.
7. Obata H. Anatomy and histopathology of human meibomian gland. *Cornea*. 2002;21(7 Suppl):S70-S74. DOI: 10.1097/01.ico.0000263122.45898.09. PMID: 12484702.
8. Lindsley K, Matsumura S, Hatef E, Akpek EK. Interventions for chronic blepharitis. *Cochrane Database Syst Rev*. 2012;2012(5):CD005556. DOI: 10.1002/14651858.CD005556.pub2. PMID: 22592706. PMCID: PMC4270370.
9. Barankin B, Guenther L. Rosacea and atopic dermatitis. Two common oculocutaneous disorders. *Can Fam Physician*. 2002;48:721-724. PMID: 12046367. PMCID: PMC2214024.

10. Warshaw EM, Voller LM, Maibach HI, et al. Eyelid dermatitis in patients referred for patch testing: Retrospective analysis of North American Contact Dermatitis Group data, 1994-2016. *J Am Acad Dermatol.*. 2021;84(4):953-964. DOI: 10.1016/j.jaad.2020.07.020. PMID: 32679276.
11. Mannis MJ. Allergic blepharoconjunctivitis. *Postgrad Med*. 1989;86(4):123-129. DOI: 10.1080/00325481.1989.11704418. PMID: 2571142.
12. Woo YR, Cho M, Ju HJ, et al. Ocular Comorbidities in Rosacea: A Case-Control Study Based on Seven Institutions. *J Clin Med*. 2021;10(13):2897. DOI: 10.3390/jcm10132897. PMID: 34209731. PMCID: PMC8267744.
13. Kara YA, Çalış F, Gürel İ B. Ocular Manifestations of Patients With Cutaneous Rosacea With and Without Demodex Infection. *Cutis*. 2021;108(1):46-50. DOI: 10.12788/cutis.0289. PMID: 34397359.
14. Emre S, Aycan OM, Atambay M, Bilak S, Daldal N, Karincaoglu Y. What is the importance of Demodex folliculorum in Behçet's disease? *Turkiye Parazitol Derg*. 2009;33(2):158-161. PMID: 19598094.
15. Liu J, Sheha H, Tseng SC. Pathogenic role of Demodex mites in blepharitis. *Curr Opin Allergy Clin Immunol*. 2010;10(5):505-510. DOI: 10.1097/ACI.0b013e32833df9f4. PMID: 20689407. PMCID: PMC2946818.
16. Zhao Y-e, Peng Y, Wang X-l, et al. Facial dermatosis associated with Demodex: a case-control study. *J Zhejiang Univ Sci B*. 2011;12(12):1008-1015. DOI: 10.1631/jzus.B1100179. PMID: 22135150. PMCID: PMC3232434.
17. Rather PA, Hassan I. Human demodex mite: the versatile mite of dermatological importance. *Indian J Dermatol*. 2014;59(1):60-66. DOI: 10.4103/0019-5154.123498. PMID: 24470662. PMCID: PMC3884930.
18. Gao YY, Di Pascuale MA, Li W, et al. High prevalence of Demodex in eyelashes with cylindrical dandruff. *Invest Ophthalmol Vis Sci*. 2005;46(9):3089-3094. DOI: 10.1167/iovs.05-0275. PMID: 16123406.
19. Koo H, Kim TH, Kim KW, Wee SW, Chun YS, Kim JC. Ocular surface discomfort and Demodex: effect of tea tree oil eyelid scrub in Demodex blepharitis. *J Korean Med Sci*. 2012;27(12):1574-1579. DOI: 10.3346/jkms.2012.27.12.1574. PMID: 23255861. PMCID: PMC3524441.
20. Bhandari V, Reddy JK. Blepharitis: always remember demodex. *Middle East Afr J Ophthalmol*. 2014;21(4):317-320. DOI: 10.4103/0974-9233.142268. PMID: 25371637. PMCID: PMC4219223.
21. Coston TO. Demodex folliculorum blepharitis. *Trans Am Ophthalmol Soc*. 1967;65:361-392. PMID: 4229846. PMCID: PMC1310279.
22. Fromstein SR, Harthan JS, Patel J, Opitz DL. Demodex blepharitis: clinical perspectives. *Clin Optom (Auckl)*. 2018;10:57-63. DOI: 10.2147/OPTO.S142708. PMID: 30214343. PMCID: PMC6118860.
23. Arli C, Ozsan M, Gurkan E, Aycan Kaya O, Kokacya S. The Incidence of Demodex folliculorum in the Combination of Allergic Rhinitis and Diabetes Mellitus. *Iran J Parasitol*. 2019;14(3):459-464. PMID: 31673265. PMCID: PMC6815856.
24. Yengil E, Cevik C, Kaya OA, Taner M, Akkoca AN, Ozer C. Relationship between Demodex folliculorum and allergic rhinitis in adults. 2014;30:27-31.
25. Friedman P, Sabban EC, Cabo H. Usefulness of dermoscopy in the diagnosis and monitoring treatment of demodicidosis. *Dermatol Pract Concept*. 2017;7(1):35-38. DOI: 10.5826/dpc.0701a06. PMID: 28243492. PMCID: PMC5315038.
26. Zhang, AC, Muntz, A, Wang, MTM, Craig, JP, & Downie, LE. Ocular Demodex: a systematic review of the clinical literature. *Ophthalmic Physiol Opt* 2020;40:389–432. https://doi.org/10.1111/opo.12691
27. Brott NR, Ronquillo Y. Schirmer Test. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing2021.
28. Micali G, Dall'Oglio F, Tedeschi A, Dirschka T. A new proposed severity score for seborrheic dermatitis of the face: SEborrheic Dermatitis Area and Severity Index (SEDASI). *J Am Acad Dermatol*. 2017;76(6):Abstract18. Available from: https://www.jaad.org/action/showPdf?pii=S0190-9622%2817%2930575-3.
29. Segal R, Mimouni D, Feuerman H, Pagovitz O, David M. Dermoscopy as a diagnostic tool in demodicidosis. *Int J Dermatol*. 2010;49(9):1018-1023. DOI: 10.1111/j.1365-4632.2010.04495.x. PMID: 20931672.
30. Akçınar UG, Ünal E, Doğruman Al F. Demodex spp. as a possible aetiopathogenic factor of acne and relation with acne severity and type. *Postepy Dermatol Alergol*. 2018;35(2):174-181. DOI: 10.5114/ada.2018.75239. PMID: 29760618. PMCID: PMC5949547.
31. Wilkin J, Dahl M, Detmar M, et al. Standard grading system for rosacea: report of the National Rosacea Society Expert Committee on the classification and staging of rosacea. *J Am Acad Dermatol*. 2004;50(6):907-912. DOI: 10.1016/j.jaad.2004.01.048. PMID: 15153893.
32. Alver O, Kıvanç SA, Akova Budak B, Tüzemen N, Ener B, Özmen AT. A Clinical Scoring System for Diagnosis of Ocular Demodicosis. *Med Sci Monit*. 2017;23:5862-5869. doi: 10.12659/msm.907824. PMID: 29224027. PMCID: PMC5733813.
33. Aktaş Karabay E, Aksu Çerman A. Demodex folliculorum infestations in common facial dermatoses: acne vulgaris, rosacea, seborrheic dermatitis. *A*An Bras Dermatol. 2020;95(2):187-193. DOI: 10.1016/j.abd.2019.08.023. PMID: 32113677. PMCID: PMC7175027.
34. Karincaoglu Y, Tepe B, Kalayci B, Atambay M, Seyhan M. Is Demodex folliculorum an aetiological factor in seborrhoeic dermatitis? *Clin Exp Dermatol*. 2009;34(8):e516-e520. DOI: 10.1111/j.1365-2230.2009.03343.x. PMID: 19486039.
35. Molho-Pessach V, Meltser A, Kamshov A, Ramot Y, Zlotogorski A. STAT1 gain-of-function and chronic demodicosis. *Pediatr Dermatol*. 2020;37(1):153-155. DOI: 10.1111/pde.14011. PMID: 31637766.
36. Sáez-de-Ocariz M, Suárez-Gutiérrez M, Migaud M, et al. Rosacea as a striking feature in family members with a STAT1 gain-of-function mutation. *J Eur Acad Dermatol Venereol*. 2020;34(6):e265-e267. DOI: 10.1111/jdv.16241. PMID: 31991004.
37. Forrestel AK, Kovarik CL, Mosam A, Gupta D, Maurer TA, Micheletti RG. Diffuse HIV-associated seborrheic dermatitis - a case series. *Int J STD AIDS*. 2016;27(14):1342-1345. DOI: 10.1177/0956462416641816. PMID: 27013615.
38. Hachfi W, Slama D, Ben Lasfar N, et al. Demodicosis revealing an HIV infection. *New Microbes New Infect*. 2019 9;31:100525. DOI: 10.1016/j.nmni.2019.100525. PMID: 31388432. PMCID: PMC6676229.

39. Ayyildiz T, Sezgin FM. The Effect of Ocular Demodex Colonization on Schirmer test and OSDI Scores in Newly Diagnosed Dry Eye Patients. *Eye Contact Lens*. 2020;46 Suppl 1:S39-S41. DOI: 10.1097/ICL.0000000000000640. PMID: 31393313.
40. Hung KH, Tan HY, Chen HC, Yeh LK. Clinical characteristics and topographic findings of corneal ectasia in patients with symptomatic Demodex blepharitis. *Taiwan J Ophthalmol*. 2020;30;11(2):146-155. DOI: 10.4103/tjo.tjo_45_20. PMID: 34295620. PMCID: PMC8259524.
41. Sidenius KE, Hallas TE, Poulsen LK, Mosbech H. Allergen cross-reactivity between house-dust mites and other invertebrates. *Allergy*. 2001;56(8):723-733. DOI: 10.1034/j.1398-9995.2001.056008723.x. PMID: 11488665.