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Evaluation of the incidence of Demodex in eyelashes in rosacea patients with ocular involvement

Oküler tutulumu olan rozase hastalarında kirpikte Demodeks insidansının değerlendirilmesi

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Abstract

Background and Design: Demodex, a mite, is known to influence the etiopathogenesis of rosacea, pityriasis folliculorum, pustular folliculitis, perioral granulomatous dermatitis, hyperpigmented patch, and chronic blepharitis. This study aimed to investigate the relationship between Demodex, which is increasingly important in the pathogenesis of rosacea, and ocular rosacea.
Materials and Methods: A total of 103 rosacea patients with ocular involvement (ocular rosacea) and 140 volunteers without facial dermatosis were included in the study as the control group. Written and verbal consent was obtained from the participants. A total of five eyelashes were pulled from the upper and lower eyelids of one or both eyes of the patient group and control group, using forceps, and the presence of Demodex was examined by the epilation method and standard superficial skin biopsy method from the face. Under a light microscope, ≥1 and ≥5 Demodex per cm^2 in the eyelashes and face were evaluated as positive, respectively.
Results: Of the 103 patients, 27 (26.2%) had conjunctivitis, 77 (74.8%) had blepharitis, 1 (1%) had hordeolum, and 24 (23.3%) had meibomian gland dysfunction. The eye examination findings of the control group were normal. The Demodex incidence rates were 84.5% and 29.3% in the patient group and control group, respectively. Of the 103 patients with rosacea accompanied by ocular rosacea, Demodex mites were present in the eyelashes and face of 51 patients (49.6%), only in the eyelashes in 26 (25.2%), and only in the face in 10 (9.7%). No Demodex mites were present on both eyelashes and face in 16 (15.5%) patients.
Conclusion: The results of this study show that Demodex positivity was detected at a higher rate in the eyelashes and face in patients with rosacea compared with the controls. Demodex may play an important role in the pathogenesis of rosacea and ocular rosacea.
Keywords: Demodex, ocular rosacea, eyelash

Öz

Amaç: Bir akar olan Demodeks'in rozase, pitiriyazis folikülorum, püstüler folikülit, perioral granülomatöz dermatit, hiperpigmente yama ve kronik blefaritin etiyopatogenezinde rolü olduğu bilinmektedir. Bu çalışmada rozase patogenezinde gün geçtikçe önemi artan Demodeks'in oküler tutulum ile ilişkisini araştırmak amaçlanmıştır.
Gereç ve Yöntem: Oküler tutulumu olan 103 rozase tanılı hasta ve herhangi fasiyal dermatozu olmayan 140 gönüllü birey kontrol grubu olarak çalışmaya dahil edildi. Katılımcıların yazılı ve sözlü onamı alındı. Hasta ve kontrol grubunun tek veya her iki gözünün üst ve alt göz kapağından toplamda 5 adet kirpik pens yardımı ile çekilerek epilasyon yöntemiyle, yüz bölgesinden ise standart yüzeysel deri biyopsi yöntemiyle Demodeks varlığına bakıldı. Işık mikroskobunda, kirpikte cm^2'de 1 ve daha fazla, yüzde cm^2'de 5 ve daha fazla Demodeks görülmesi pozitif olarak değerlendirildi.
Bulgular: Yüz üç hastanın 27'sinde (%26,2) konjonktivit, 77'sinde (%74,8) blefarit, 1'inde (%1) hordeolum, 24'ünde (%23,3) meibomian bez disfonksiyonu bulunmaktaydı. Kontrol grubundaki bireylerin hepsinin göz muayene bulguları normaldi. Hasta grubunda Demodeks görülme

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oranı %84,5 iken, kontrol grubunda bu oran %29,3 idi. Oküler tutulumun eşlik ettiği rozasesi olan 103 hastanın 51'inde (%49,6) kirpik ve yüzde, 26'sında (%25,2) sadece kirpikte, 10'unda (%9,7) sadece yüzde Demodeks akarı mevcutken 16 (%15,5) kişide hem kirpikte hem yüzde Demodeks akarı görülmedi.
Sonuç: Bu çalışmadan elde edilen bulgular, kontrol grubuna göre rozaseli hastalarda göz tutulumunda kirpikte ve yüzde yüksek oranda Demodeks pozitifliği saptandığını, rozase ve oküler rozase patogenezinde Demodeks'in önemli rol oynayabileceğini göstermektedir.
Anahtar Kelimeler: Demodeks, oküler rozase, kirpik

Introduction

Demodexes are mites from the Demodicidae family of the prostigmata suborder of the arachnida class[1]. It was first described by Jacob Henle in 1841 and classified as a mite by Carl Gustav Theodor Simon in 1842[2-4]. In humans, only two species, Demodex folliculorum (DF) and Demodex brevis (DB), localized in pilosebaceous units, have been identified[5]. While DF is mostly located in the infundibular part of the hair follicles and eyelashes, singly or in groups, DB is located singly in deeper sebaceous glands, within the ducts, and in the meibomian glands[5,6].

In humans, Demodexes are found in body areas where the sebaceous glands are dense, such as the outer ear, chest, mons pubis, and gluteal region, especially in the T-region of the face[7,8]. Transmission occurs by direct human-to-human contact[9].

Although Demodexes are thought to have a role in the etiopathogenesis of rosacea, pityriasis folliculorum, pustular folliculitis, perioral granulomatous dermatitis, and hyperpigmented patch, it is also believed to have an important role in the etiology of chronic blepharitis[10]. Thus, this study aimed to investigate the incidence of Demodex mites, which is becoming increasingly important in the pathogenesis of rosacea, and its relationship with ocular rosacea.

Materials and Methods

A total of 103 rosacea patients with ocular involvement aged >18 years and 140 volunteers with no facial dermatosis and ocular signs, who consented to the Demodex investigation, were included in the study. A total of five eyelashes were removed from the upper and lower eyelids of one or both eyes of the patient group and control group using forceps through the epilation method. The density of Demodex invasion was measured by taking a sample from the area where the lesion was most intense, especially from the forehead, cheek, or chin, where the parasite was most common, using the standard superficial skin biopsy method.

The study was approved by the Ankara Training and Research Hospital Local Ethics Committee (approval number: 0588, date: 25.03.2015). All participants signed an informed consent form. Standard superficial skin biopsy is a non-invasive method that allows the examination of the follicle contents along with the corneal layer of the skin. In this method, an area of 1 cm^2 was drawn on the microscope slide with a ruler. The other unscratched side of the slide was wiped with ether or alcohol to remove artifacts. One drop of cyanoacrylate was applied to the marked area. The slide was adhered to the skin area where the agent was desired to be investigated. After approximately 1 min, the slide was slowly removed. Then, 2-3 drops of immersion oil or glycerin were dropped on the material area of the slide and covered with a coverslip. For the detection of Demodex in the eyelashes, a total of five eyelashes were plucked from the upper and lower eyelids of one or both eyes using forceps. A sample was taken on the slide, and 2-3 drops of immersion oil or glycerin were dripped onto the material area of the slide and covered with a coverslip. The marked area was scanned at x10 and x40 magnifications of the microscope. Demodex density was calculated by counting the parasites in the marked area. Studies have reported that demodicosis is diagnosed if there are >5 mites per cm^2 in the face and ≥1 mites in the eyelashes[11-15].

Statistical Analysis

Data analysis was conducted with IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA), at 95% confidence level. Independent samples t-test was used when continuous variables were compared in the patient and control groups. For categorical variables, Pearson's chi-square and Fisher's exact chi-square test were used to compare the groups. The p value calculated as a result of the analysis was compared with the 0.05 value, and if the p value was less than the significance coefficient of 0.05, a relationship existed between the variables.

Results

A total of 103 patients diagnosed with rosacea with ocular involvement were included in the study, and 140 consenting volunteers with normal eye examination findings and no facial dermatosis were included as the control group. In the patient group, 74 (71.8%) were female and 29 (28.2%) were male; in the control group, 86 (61.4%) were female and 54 (38.6%) were male. The female-to-male ratio was 2.55/1 in the patient group, whereas it was 1.59/1 in the control group. There was no statistically significant difference between the patient and control groups in terms of female/male ratio (Pearson chi-square test; p= 0.091). The age distribution ranged from 19 to 84, with a mean of 50.47±14.77 years, in the patient group and between 18 and 78, with a mean of 38.81±15.38 years, in the control group. When the mean age of the patient and control groups were compared, the mean age of the patient group was found to be statistically significantly higher. (T-test on independent samples; p<0.0001).

The distribution of Demodex presence in the patient and control groups according to the age groups is shown in Table 1. The findings of this study revealed no significant difference between the age groups for the patient and control groups in terms of Demodex positivity in the eyelashes and face (Fisher's exact test; p=0.292, p=0.694). Demodex positivity in the patient and control groups by sex is analyzed in Table 2. No significant difference was found between sexes and rate of Demodex positivity in the eyelashes and face in the patient and control groups (Fisher's exact test; p=0.102, p=0.050).

The relationship between eye examination findings and the presence of Demodex in patients with rosacea with ocular involvement is shown in Table 3.

Table 1. Distribution of Demodex positivity in the patient and control groups according to age groups

		Demodex positivity in the eyelashes and on face (number of people)	Demodex positivity in the eyelashes (number of people)	Demodex positivity in the face (number of people)	No Demodex in the eyelashes and face (number of people)	p
Patient group	≤25 years	1 (16.6%)	1 (16.6%)	1 (16.6%)	3 (50.0%)	0.292
	26-35 years	4 (50.0%)	2 (25.0%)	1 (12.5%)	1 (12.5%)	
	≥36 years	46 (51.6%)	23 (25.8%)	8 (8.9%)	12 (13.4%)	
Control group	≤25 years	0 (0.0%)	3 (9.0%)	6 (18.2%)	24 (72.8%)	0.694
	26-35 years	2 (5.6%)	2 (5.6%)	5 (13.8%)	27 (75.0%)	
	≥36 years	5 (7.0%)	11 (15.4%)	7 (9.8%)	48 (67.8%)	

Table 2. Distribution of Demodex positivity in the patient and control groups by sex

		Demodex positivity in the eyelashes and face (number of people)	Demodex positivity in the eyelashes (number of people)	Demodex positivity in the face (number of people)	No Demodex in the eyelashes and face (number of people)	p
Patient group	Female	34 (45.9%)	17 (23.0%)	10 (13.5%)	13 (17.5%)	0.102
	Male	17 (58.6%)	9 (31.0%)	0	3 (10.3%)	
Control group	Female	3 (3.5%)	14 (16.3%)	13 (15.1%)	56 (65.1%)	0.050
	Male	4 (7.4%)	2 (3.7%)	5 (9.3%)	43 (79.6%)	

Table 3. Relationship between eye examination findings and Demodex positivity in rosacea patients with ocular involvement

		Demodex positivity in the eyelashes and face (number of people)	Demodex positivity in the eyelashes (number of people)	Demodex positivity on face (number of people)	No Demodex in the eyelashes and face (number of people)	p
Conjunctivitis	None	36 (47.4%)	20 (26.3%)	7 (9.2%)	13 (17.1%)	0.830
	Have	15 (55.6%)	6 (22.2%)	3 (11.1%)	3 (11.1%)	
Blepharitis	None	9 (34.6%)	4 (15.4%)	3 (11.5%)	10 (38.5%)	0.003*
	Have	42 (54.5%)	22 (28.6%)	7 (9.1%)	6 (7.8%)	
Meibomian gland dysfunction	None	37 (46.8%)	21 (26.6%)	8 (10.1%)	13 (16.5%)	0.872
	Have	14 (58.3%)	5 (20.8%)	2 (8.3%)	3 (12.5%)	
Hordeolum	None	51 (50.0%)	25 (24.5%)	10 (8.5%)	16 (15.7%)	0.505
	Have	0 (0.0%)	1 (100%)	0 (0.0%)	0 (0.0%)	

*P<0.05

Table 4. Relationship between dermatological examination findings and Demodex in the group with rosacea

		Demodex positivity in the eyelashes and face (number of people)	Demodex positivity in the eyelashes (number of people)	Demodex positivity in the face (number of people)	No Demodex in the eyelashes and face (number of people)	p
Erythema	None	1 (10.0%)	5 (50.0%)	2 (20.0%)	2 (20.0%)	0.020*
	Have	50 (53.8%)	21 (22.6%)	8 (8.6%)	14 (15.1%)	
Telangiectasia	None	4 (57.1%)	1 (14.3%)	0 (0.0%)	2 (28.6%)	0.652
	Have	47 (49.0%)	25 (26.0%)	10 (10.4%)	14 (14.6%)	
Papules and pustules	None	14 (46.7%)	6 (20.0%)	5 (16.7%)	5 (16.7%)	0.451
	Have	37 (50.7%)	20 (27.4%)	5 (6.8%)	11 (15.1%)	
Phymatous changes	None	42 (48.3%)	20 (23.0%)	9 (10.3%)	16 (18.4%)	0.191
	Have	9 (56.2%)	6 (37.5%)	1 (6.2%)	0 (0.0%)	
Extrafacial involvement	None	42 (51.2%)	22 (26.8%)	5 (6.1%)	13 (15.9%)	0.150
	Have	9(42.9%)	4 (19.0%)	5 (23.8%)	3(14.3%)	
Facial edema	None	45 (48.4%)	25 (26.9%)	8 (8.6%)	15 (16.1%)	0.406
	Have	6 (60.0%)	1 (10.0%)	2 (20.0%)	1 (10.0%)	

*P<0,05

While no significant difference was found regarding Demodex positivity between those with and without conjunctivitis, meibomian gland dysfunction, and hordeolum, the Demodex positivity rate was significantly higher in patients with blepharitis than in those without blepharitis (Fisher's exact test; p=0.003).

The relationship between the dermatological examination findings and Demodex positivity in the patient group is shown in Table 4. Of the 103 patients, 93 (90.2%) had erythema, 96 (93.2%) had telangiectasia, 73 (70.8%) had papulopustules, 16 (15.5%) had phymatous changes, 21 (20.3%) had extrafacial involvement, and 10 (9.7%) had facial edema.

Demodex mites were detected in 50 (53.8%) patients with erythema both in the eyelashes and in the face, in 21 (22.6%) only in the eyelashes, in 8 (8.6%) only in the face. No mites were detected in the face and eyelashes in 14 (15.1%) of patients. Statistically significantly more Demodex positivity was found in the face and eyelashes in those with erythema than in those without erythema (Fisher's exact test; p=0.020).

Demodex mites were detected in both the eyelashes and face 47 (49.0%) of those with telangiectasia, only in the eyelashes in 25 (26.0%), and only in the face in 10 (10.4%). No mites were detected in the face and eyelashes in 14 (14.6%) of patients. There was no statistically significant difference in the face and eyelashes Demodex density between those with and without telangiectasia (Fisher's exact test; p=0.652).

Demodex mites were detected in 37 (50.7%) patients with papulopustules both in the eyelashes and in the face, in 20 (27.4%) only in the eyelashes, in 5 (6.8%) only in the face. No mites were detected in the face and eyelashes in 11 (15.1%) of patients. No significant difference was found between those with and without papulopustular lesions in terms of Demodex density in the eyelashes and face (Fisher's exact test; p=0.451). Demodex mites were found in both the eyelashes and face in 9 (56.2%) patients with phymatous changes, in the eyelashes in 6 (37.5%), and only in the face in 1 (6.2%). No significant difference was noted in the face and eyelash Demodex density between those with and without phymatous changes (Fisher's exact test; p=0.191).

Demodex mites were detected in both eyelashes and face in 9 (42.9%) patients with extrafacial involvement, in the eyelashes in 4 (19.0%), and in the face in 5 (23.8%). No mites were detected in 3 (14.3%) patients. No significant difference was found in the face and eyelash Demodex density between those with and without extrafacial involvement (Fisher's exact test; p=0.150).

Demodex mites were detected in both eyelashes and face in 6 (60.0%) patients with facial edema, only the eyelash in 1 (10.0%), and only the face in 2 (20.0%). No mites were detected in 1 (10%) patient. No significant difference was found in the eyelash and facial Demodex density between those with and without facial edema (Fisher's exact test; p=0.406).

The presence and distribution of Demodex in the patient and control groups are reported in Table 5. While the Demodex rate in the patient group was 84.5%, it was 29.3% in the control group. Of the 103 patients with rosacea with ocular involvement, Demodex mites were present in both eyelashes and face in 51 (49.6%), only in the eyelashes in 26 (25.2%), and only in the face in 10 (9.7%). Demodex mites were not detected in both eyelashes and face in 16 (15.5%) patients. In the control group of 140 people, Demodex mites were present in the eyelashes and face in 7 (5%) people, only in the eyelashes in 16 (11.4%), and only in the face in 18 (12.9%). Demodex mites were not seen in both the eyelashes and face in 99 (70.7%) people. Significantly higher Demodex positivity rate was found in the eyelashes and face in the patient group than in the control group (Pearson chi-square test, p=0.001).

Discussion

The DF and DB species of the Demodicidae family, which have been to play important roles in triggering of rosacea and papulopustular lesions, are also present in the human body[5]. Primary demodicosis begins with itching of the normal skin in the T-zone of the face, followed by an erythematous, scaly rash. Its major etiologic agent is DF[12,16]. Secondary demodicosis is characterized by a rash with symmetrical papules and pustules in the malar region. The major cause is DB[17]. Inattention to skin cleaning, intensive use of cosmetic products, and not washing these products directly which increased sebum production as in summer, oily skin, impaired immune system due to steroid use, and older age may cause increased pathogenicity in mites[18]. Regarding the Demodex incidence according to age, no mite is found in children, it is rarely seen in adolescents, and the incidence of mites increases with age[1,19-23]. In the present study, no significant difference was found between age groups for the patient and control groups in terms of Demodex positivity in the eyelashes and face (Fisher's exact test; p=0.292, p=0.694). However, the Demodex positivity rate in the eyelashes and face increased with age in the patient and control groups, similar to the literature. Although no significant difference was found, this finding supports the thesis that the increase in sebaceous activity with age increases the incidence of mites in older ages by creating a suitable environment for mite proliferation.

There are conflicting results regarding the relationship between sex and Demodex. Some studies have detected more parasites in men, that is, men may have higher risk for infestation because they are more active during the day, they have higher secretions of sebum and sweat, and they use less facial moisturizer than women[24,25]. However, other studies have shown a higher rate in women[21]. In the present study, when the

Table 5. Presence and distribution of Demodex in the patient group and control group

		Patient group (number of people)	Control group (number of people)	p
Demodex	Demodex positivity in the eyelashes and face	51 (49.6%)	7 (5%)	0.001*
	Demodex positivity in the eyelashes	26 (25.2%)	16 (11.4%)	
	Demodex positivity in the face	10 (9.7%)	18 (12.9%)	
	No Demodex in the eyelashes and face	16 (15.5%)	99 (70.7%)	

*P<0.05

patient and control groups were compared within themselves and with each other, no significant difference was found between sex and the incidence of Demodex (Fisher's exact test; p=0.102, p=0.050). The mite positivity rates in the eyelashes were high in men in the patient group and in women in the control group, although it was not significant.

The most common complaints and findings in ocular rosacea are related to dry eyes triggered by inflammation and meibomian gland dysfunction. This situation quite favors the proliferation of Demodex mites[26-28]. In the literature, studies are investigating Demodexes in the eyelashes and face in patients with various ocular diseases. In most of the studies examining the relationship between Demodex and eye diseases such as blepharitis, meibomian gland dysfunction, chalazion, burning in the eyes, itching, foreign body sensation, conjunctival redness, and heaviness in the eyelids, a higher rate of Demodex positivity was found in the patient groups than in the control groups[29-38]. Other studies have found significant improvement in eye examination findings as a result of treatments for Demodex[37]. In a study conducted in 2020, Demodex was found in the eyelashes in all six family members all diagnosed with ocular rosacea[39]. In the present study, of the 103 patients, 27 (26.2%) had conjunctivitis, 77 (74.8%) had blepharitis, 1 (1%) had hordeolum, and 24 (23.3%) had meibomian gland dysfunction as ocular rosacea examination findings. The eye examination findings in the control group were normal. A significantly higher Demodex positivity rate was found in the eyelashes and face of patients with blepharitis than in those without blepharitis (Fisher's exact test; p=0.003). Although more Demodex was detected in both the eyelashes and face in patients with conjunctivitis, meibomian gland dysfunction, and hordeolum, it was not significant (Fisher's exact test; p>0.05). This situation might be related to the low number of patients. In some studies examining the relationship between Demodex and rosacea and its subgroups, the rate of Demodex positivity in was higher all rosacea subgroups than in the control group, but a significantly higher rate was found in the papulopustular type[40,41]. Data also indicate that extrafollicular localization in the dermis causes granulomatous rosacea with foreign body-like granulomatous reaction in patients with immunosuppressive status or people using steroids[5,42,43]. The relationship between dermatological examination findings and Demodex in the patient group is shown in Table 4. Accordingly, the Demodex positivity rate was higher all subgroups than in the control group, but a significant increase was detected only in the group with erythema.

Finally, in our study, when the patient group with ocular involvement and the control group were compared in terms of the presence of Demodex, without dividing them into subgroups, a significantly higher Demodex positivity rate was found in the eyelashes and face in the patient group than in the control group (Pearson chi-square test; p=0.001) (Table 5). This suggested that Demodex mites may have a role in the etiopathogenesis of ocular rosacea and that the treatment of Demodex may be beneficial for ocular findings. Although a few studies have examined both eyelash and facial Demodex positivity in ocular rosacea, the number of patients in existing studies was less than the number of patients in our study.

Study Limitations

In our study, the separation of patients into smaller subgroups based on the separate evaluation of eyelashes and facial Demodex by separating them into groups according to their examination findings negatively affected the significance of the results.

Conclusion

This study showed that Demodexes, which have been one of the factors that affect the etiology and clinical course of rosacea for years, may also play important roles in ocular rosacea. The importance of our findings and the relationship between ocular rosacea and Demodex will become clear in studies with larger patient groups.

Ethics

Ethics Committee Approval: The study was approved by the Ankara Training and Research Hospital Local Ethics Committee (approval number: 0588, date: 25.03.2015).

Informed Consent: Written and verbal consent was obtained from the participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Z.M., Concept: Z.M., Design: Z.M., N.B., E.Ş.Ö., H.M.E., Data Collection or Processing: Z.M., Analysis or Interpretation: Z.M., Literature Search: Z.M., N.B., F.Ö., Writing: Z.M.

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