Original Article

The Relationship of Demodex Density with Acne Severity

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Abstract

Introduction: Demodex (D.) mites play a role in the etiology of many dermatological diseases. **Objectives:** The aim of this study was to reveal the relationship between acne severity (mild, moderate, and severe acne) and Demodex density in patients with acne vulgaris and compare this with the healthy population. **Materials and Methods:** In total 150 patients with acne vulgaris and 60 healthy individuals were evaluated. Patients diagnosed with acne vulgaris were divided into three groups as mild, moderate, and severe. The gender, body mass index, history of diabetes mellitus, smoking, alcohol use, tea and coffee consumption, usage frequency of moisturizer, facial cleanser and concealer, and skin type (dry/sensitive, mixed, and oily) were recorded. Demodex density was measured by using the standard superficial skin biopsy method. **Results:** Demodex infestation was observed in 40 (26.6%) of the acne patients and 13 (21.6%) of the healthy control group. The Demodex infestation was observed in 16 (32%) of the mild acne group, 15 (30%) of the moderate acne group, and 9 (18%) of the severe acne group; there was no significant difference between the control group and severity of acne. In patients with acne, being over 25 years of age 2.6-fold, sensitive-dry skin type 7.4-fold, and obesity 4.06-fold increased risk of Demodex infestation. **Conclusion:** In this study, we did not detect an increased incidence of Demodex, including disease severity, in patients with acne vulgaris. However, we showed that the density of Demodex was increased in those aged 25 years and older, obese patients, and those with sensitive-dry skin in patients with acne.

Keywords: Acne vulgaris, mites, obesity

Introduction

Demodex mites most frequently colonize the eyelids, forehead, nose, nasolabial folds, cheek, and chin.[1] Up to 80–90% of humans may harbor the Demodex organism but rarely causes clinical symptoms.[1,2] However, there are publications in the literature that Demodex mites play a role in the etiology of many dermatological and ocular disorders. Cutaneous diseases of the pilosebaceous unit caused by Demodex mites can be a primary skin disease or an exacerbation of inflammatory dermatoses such as papulopustular rosacea, facial folliculitis, acne vulgaris, and chronic blepharitis.[1,3,4]

Acne vulgaris is a multifactorial disease of the pilosebaceous unit that frequently affects adolescents and young adults.[5] Hyperseborrhea, disseborrhea, altered keratinization of the pilosebaceous duct, *Cutibacterium acnes* (C. acnes), and inflammation play a role in the pathophysiology of acne.[6] Demodex mites can cause perifollicular inflammation via protease and lipase enzymes and can contribute to the development of acne lesions by causing follicle occlusion and secretion of inflammatory cytokines.[7]

In this study, we aimed to reveal the relationship between acne severity (mild, moderate, or severe acne) and Demodex density in patients with acne vulgaris and compare this with the healthy population. In addition, we aimed to reveal the effects of sociodemographic characteristics and diet type on Demodex density.

Materials and Methods

Patients who applied to the outpatient clinic of dermatology and gave consent to participate by filling out a questionnaire were included in the study. In total

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150 patients with acne vulgaris and 60 healthy individuals were evaluated. Patients diagnosed with acne vulgaris were divided into three groups as mild, moderate, and severe according to the Global Acne Severity Scale (GASS), and 50 patients were included in each group.[8]

The gender, body mass index (BMI), history of diabetes mellitus, smoking, alcohol use, tea-coffee consumption (daily or less often), usage frequency of moisturizer, facial cleanser and concealer, and skin type (dry/sensitive, mixed, or oily) were recorded by the questionnaire. If the frequency of application of the facial cleansing product was more than once a day, it was considered as frequent use, moderate use once a day, and infrequent use less than once a day. If the frequency of application of moisturizer and concealer was more than once a day, it was considered as frequent use, moderate use once a day, and infrequent use less than once a day.

Nutritional style (Mediterranean diet, protein-based diet, vegetarian diet, and American-style diet) was also evaluated.

Demodex density is considered as the number of parasites per surface area. Accordingly, the detection of ≥5 Demodex mites in a 1 cm² area is considered as infestation. Demodex density was measured in all patients and controls from the clinically most suspicious area for Demodex using the standard superficial skin biopsy (SSSB) method which is a noninvasive method. In the healthy control group, samples were taken from the areas of the most oily skin (forehead, cheek, chin, etc.). In the SSSB method, the place from where the sample will be taken is cleaned with alcohol and a drop of cyanoacrylate adhesive is applied on the slide, and the adhesive surface of the slide is pressed against the patient's skin for about 1 min. A drop of immersion oil is dripped onto the sample, the coverslip is closed and examined under a microscope with 10× and 40× objectives. With this method, adult, larva, nymph, and egg forms of mites are investigated and the number of Demodex mites seen in a 1 cm² area is recorded.

The inclusion criteria for the study were not to have received topical or oral acne and rosacea treatment in the last six months, to be over 18 years old, and to have consented to participate.

Statistical analysis

The SPSS 23.0 statistical package program was used in the analysis of the data. The descriptive statistics of the evaluation results were given as numbers and percentages for categorical variables, and as mean, standard deviation (sd), minimum (min), and maximum (max) for metric variables. The conformity of the measurement data to the normal distribution was examined with the one-sample Kolmogorov-Smirnov test. In the comparisons of the measurement data of two independent groups, the Student *t*-test was used when the normal distribution condition was met, the Mann-Whitney U-test was used when the normal distribution condition was not met. The chi-square test was used to analyze the differences between the categorical ratios. In addition, factors that may be associated with Demodex infestation in acne patients were evaluated using logistic regression analysis in multivariate analyses. The interactions of the variables with each other were evaluated with the correlation matrix. The enter method was used when the variables were included in the models. The Hosmer-Lemeshow test was used to evaluate the fit of the models, and the Nagelkerke R^2 was used to evaluate the explanatory power. Odds ratio (OR) values were presented with a 95% confidence interval (CI) and the statistical significance level was taken as $P < 0.05$.

Results

A total of 210 people, including 150 patients with acne and 60 control group, were included in our study. The age range of the population was between 18 and 46 years. The mean age was 24.39 ± 6.139. Sociodemographic data of acne and control group are summarized in Table 1.

The Demodex infestation was observed in 40 (26.6%) of the acne patients and 13 (21.6%) of the healthy control group. Although Demodex infestation was more common

Table 1: Sociodemographic data of acne and control group

	Acne *n* = 150	Control *n* = 60	*P*–value
Gender, female, *n* (%)	119 (79.3)	44 (73.3)	0.363
Age, ≥25years, *n* (%)	59 (39.3)	33 (55)	**0.039**
Demodex infestation, *n* (%)	40 (26.6)	13 (21.6)	0.568
Facial cleanser, *n* (%)			0.182
Rare	111 (74)	45 (75)	
Moderate	27 (18)	14 (23.3)	
Frequent	12 (8)	1 (1.6)	
Moisturizer, *n* (%)			0.098
Rare	118 (78.6)	47 (78.3)	
Moderate	16 (10.6)	11 (18.3)	
Frequent	16 (10.6)	2 (3.3)	
Concealer, *n* (%)			0.264
Rare	118 (78.6)	49 (81.6)	
Moderate	21 (14)	10 (16.6)	
Frequent	11 (7.3)	1 (1.6)	
Skin type, *n* (%)			0.072
Dry/sensitive	12 (8)	9 (15)	
Mixed	87 (58)	39 (65)	
Oily	51 (34)	12 (20)	
Smoking , *n* (%)	20 (13.3)	11 (18.3)	0.284
Alcohol consumption, *n* (%)	16 (10.6)	5 (8.3)	0.239
Daily coffee consumption, *n* (%)	55 (36.6)	21 (35)	0.875
Daily tea consumption, *n* (%)	103 (68.6)	40 (66.6)	0.870
Diabetes mellitus, *n* (%)	4 (50)	4 (50)	0.229
Obesity, *n* (%)	13 (8.6)	9 (15)	0.212

in acne patients, the difference was not statistically significant (P = 0.568). The Demodex infestation was observed in 16 (32%) of the mild acne group, 15 (30%) of the moderate acne group, and 9 (18%) of the severe acne group; there was no significant difference between the control group and severity of acne (P = 0.229). Demodex density was also not associated with acne severity.

The Demodex infestation was statistically significantly higher over the age of 25 years when compared to the participants under 25 years old (P = 0.001).

A comparison of the sociodemographic characteristics of acne patients under and over the age of 25 is presented in Table 2.

Demodex positivity was observed in 17 (18.7%) of the acne patients under 25 years old and 23 (39%) of those over 25 years old, and a statistically significant difference was observed (P = 0.008). Of the acne patients under the age of 25, 24 (26.4%) were in the mild acne group, 30 (32.9%) were in the moderate acne group, and 37 (40.6%) were in the severe acne group. Acne severity was statistically significantly higher under the age of 25 (P = 0.029) years.

The comparison of sociodemographic and clinical characteristics of patients with and without Demodex in patients with acne is summarized in Table 3. The Demodex infestation was significantly higher in the sensitive-dry skin type (P = 0.003).

Among the acne patients, 40% of those with Demodex infestation and 20.9% of those without Demodex infestation use facial cleansing products. This rate is statistically significantly higher in acne patients with Demodex (P = 0.043). In addition, no statistically significant difference was observed between the acne groups with and without Demodex in terms of smoking, alcohol use, and, tea and coffee consumption.

There was no significant difference in diet between the control group and the acne group (P = 0.446) and between

Table 2: Comparison of sociodemographic characteristics in acne patients under and above 25 years old

	<25 years n = 91	≥25 years n = 59	P-value
Gender, female, *n* (%)	68 (74.7)	51 (86.4)	0.100
Demodex infestation, *n* (%)	17 (18.7)	23 (39)	**0.008**
Facial cleanser, *n* (%)			0.117
Rare	71 (78)	40 (67.8)	
Moderate	16 (17.6)	11 (18.6)	
Frequent	4 (4.4)	8 (13.6)	
Moisturizer, *n* (%)			0.972
Rare	71 (78)	47 (79.6)	
Moderate	10 (11)	6 (10.2)	
Frequent	10 (11)	6 (10.2)	
Concealer , *n* (%)			0.499
Rare	72 (79.1)	46 (78)	
Moderate	14 (15.4)	7 (11.9)	
Frequent	5 (5.5)	6 (10.1)	
Skin type, *n* (%)			0.124
Dry/sensitive	4 (4.4)	8 (13.5)	
Mixed	54 (59.3)	33 (55.9)	
Oily		18 (30.5)	
Smoking, *n* (%)	16 (17.6)	4 (6.8)	0.081
Alcohol consumption, *n* (%)	11 (12.1)	5 (8.5)	0.595
Daily coffee consumption, *n* (%)	36 (39.6)	19 (32.2)	0.390
Daily tea consumption, *n* (%)	62 (68.1)	41 (69.5)	1.000
Diabetes mellitus, *n* (%)	1 (1)	3 (5.1)	0.300
Obesity, *n* (%)	9 (9.9)	4 (6.8)	0.568
Acne severity, *n* (%)			**0.029**
Mild	24 (26.4)	26 (44.1)	
Moderate	30 (32.9)	20 (33.9)	
Severe	37 (40.6)	13 (22)	

Table 3: The comparison of sociodemographic and clinical characteristics of patients with and without demodex in patients with acne

	Demodex positive (n = = 40)	Demodex negative (n = 110)	P-value
Gender, female, *n* (%)	31 (77.5)	88 (80)	0.820
Age, ≥25 years, *n* (%)	17 (42.5)	74 (67.3)	**0.008**
Smoking, *n* (%)	3 (7.5)	17 (15.5)	0.280
Alcohol consumption, *n* (%)	4 (10)	12 (10.9)	1.000
Daily tea consumption, *n* (%)	29 (72.5)	74 (67.3)	0.691
Daily coffee consumption, *n* (%)	12 (30)	43 (39)	0.343
Facial cleanser, *n* (%)			
Rare	24 (60)	87 (79.1)	**0.043**
Moderate	10 (25)	17 (15.5)	
Frequent	6 (15)	6 (5.4)	
Moisturizer, *n* (%)			0.804
Rare		88 (80)	
Moderate	5 (12.5)	11 (10)	
Frequent	5 (12.5)	11 (10)	
Concealer, *n* (%)			0.319
Rare	29 (72.5)	89 (80.9)	
Moderate	6 (15)	15 (13.6)	
Frequent	5 (12.5)	6 (5.4)	
Skin type, *n* (%)			**0.003**
Dry/sensitive	8 (20)	4 (3.6)	
Mixed	18 (45)	69 (62.7)	
Oily	14 (35)	37 (33.6)	
Acne severity, *n* (%)			0.229
Mild	16 (40)	34 (30.9)	
Moderate	15 (37.5)	35 (31.8)	
Severe	9 (22.5)	41 (37.2)	
Diabetes mellitus, *n* (%)	1 (2.5)	3 (2.7)	1.000
Obesity, *n* (%)	8 (20)	14 (12.7)	0.204

Table 4: Linear regression analysis

	Odds ratio (95% CI)	*P*-value
Age, ≥25 years	2.686 (1.176–6.138)	**0.019**
Gender, female	1.528 (0.574–4.061)	0.396
Skin type, dry/sensitive	7.404 (1.849–29.656)	**0.005**
Skin type, mixed	3.799 (0.885–16.306)	0.072
Acne severity, severe	0.655 (0.223–1.920)	0.440
Acne severity, moderate	0.972 (0.377–2.506)	0.953
Obesity	4.068 (1.130–14.642)	**0.032**

Hosmer Lemeshow Test $P = 0.723$ Nagelkerke R^2:**19%**, Omnibus tests of model *P*: 0.003.

CI = confidence interval

the groups with and without Demodex in patients with acne ($P = 0.312$).

Linear regression analysis was performed to identify possible risk factors for Demodex infestation in acne patients. Linear regression analysis was presented in Table 4. Being over 25 years old, sensitive-dry skin type, and obesity were observed as risk factors for Demodex infestation in acne patients. In patients with acne, being over 25 years of age 2.6-fold, sensitive-dry skin type 7.4-fold, and obesity 4.06-fold increased risk of Demodex infestation.

Discussion

In this study, we found the prevalence of Demodex in acne patients to be 26.6%, similar to healthy volunteers. In addition, we did not find a relationship between acne severity and the presence of Demodex. In literature, Demodex mites have been considered to be possibly related to many kinds of facial dermatoses, such as papulopustular rosacea, facial folliculitis, and chronic blepharitis.[4,7]

Demodex mites specifically penetrate the keratinocytes lining the pilosebaceous follicles and feed on sebum and cellular proteins obtained by protease in salivary enzymes.[7] The enzymatic process, which starts with the lipase enzymes that Demodex uses in the digestion of lipids and microorganisms, may lead to the deterioration of the follicular epithelium and cause perifollicular inflammation.[7] Demodex mites can also cause mechanical blockage of the follicle opening, a granulomatous foreign body reaction, and a host immune response causing inflammatory changes.[7] Although all these suggest that Demodex parasites are involved in the etiopathogenesis of acne, there are different study results in the literature regarding the relationship between acne vulgaris and Demodex.

In two studies comparing the relationship between acne and Demodex in literature; the prevalence of Demodex was reported as 11.8% and 15.38%, these rates were lower compared with our study.[9,10] Contrary to our study, Akçınar *et al.* [11] reported a higher prevalence of Demodex as 42.6% in acne patients, and showed that Demodex positivity could be a risk factor for the development of acne vulgaris.

A meta-analysis by Zhao *et al.*[12] concluded that acne vulgaris was also significantly associated with Demodex infestation, but not as close as in rosacea. Aktaş Karabay *et al*. [7] showed that Demodex infestation rates were higher in patients with rosacea, acne vulgaris, and seborrheic dermatitis than in controls, additionally rates were significantly higher in the rosacea group. On the other hand, Okyay *et al.* [13] showed no significant difference observed between D. folliculorum prevalence and between the group with acne or without acne and between the types of acne as in our study.

Zhao *et al.* [14] concluded that Demodex prevalence increases with age, oily or mixed skin sebaceous hyperplasia appears to favor Demodex proliferation, and Demodex infestation may be associated with acne vulgaris. They reported that age, skin type, and skin disease independently correlate with Demodex infestation. Also, having a Demodex infestation for oily or mixed skin has increased Demodex 2.1-fold more than those for dry or neutral skin. The same study concluded that for oily or combination skin, sebaceous hyperplasia appears to favor Demodex proliferation and Demodex infestation may be associated with acne vulgaris.[14] In our study different from Zhao *et al.* [14], the frequency of Demodex was found to be higher in acne patients with sensitive-dry skin, and having a sensitive-dry skin type was found to be associated with 7.4-fold increased Demodex infestation in patients with acne. We think that additional cosmetic products that can be used in sensitive dry skin types can be a food source for Demodex.

Akçınar *et al*.[11] found that cigarette smoking did not influence the positivity and density of Demodex in the adolescent and postadolescent acne group; alcohol consumption was related to Demodex positivity in the postadolescent acne group, but not in the adolescent acne group.[11] In another study, Okyay *et al*.[13] showed that D. folliculorum was significantly more common in alcohol consumers and was more common in seborrheic skin. Similarly, in our study, the prevalence of Demodex was significantly higher in patients with postadolescent acne, we found being over 25 years of age was associated with 2.6-fold increased Demodex infestation in patients with acne. Also, we found that alcohol and smoking did not influence the positivity of Demodex.

Zhao *et al.*[14] and Dokuyucu *et al.*[15] found that gender was not statistically correlated with Demodex infestation as in our study. Yazısız *et al.*[5] did not found relationship between Demodex positivity and age, gender, number of baths per week, use of make-up materials, and use of shared towels.

We did not find any relation between the use of concealer and moisturizer and Demodex infestation. However, we showed that acne patients with Demodex infestation had a higher frequency of use of facial cleansing products than acne patients without Demodex infestation. This may be due to the search for the treatment of dry skin sensitivity and grating feeling due to Demodex.

In our study; we did not find any correlation in tea-coffee consumption in acne patients when compared with controls and between acne patients with and without Demodex consumption, which are the triggers of rosacea disease, which has been shown to be associated with Demodex infestation in the literature.

Dokuyucu *et al.*[15] reported that Demodex positivity was significantly higher in obese patients. Some authors suggested that poor blood glucose regulation, obesity, and metabolic syndrome all increase the susceptibility to D. folliculorum mite infestation.[11] Although no difference was observed between the acne and control groups in terms of obesity and dietary habits in this study, we concluded that being obese was associated with a 4.06-fold increase in Demodex infestation in patients with acne.

Limitations of the study

The number of participants included in this study is small. Since it is a cross-sectional study, the determination of the products used according to the skin types depends on the patient's definition, and before and after the products used could not be fully evaluated.

Conclusion

In our study, we did not detect an increased incidence of Demodex, including disease severity, in patients with acne vulgaris, however, we showed that the density of Demodex was increased in those aged 25 years and older, obese, and those with sensitive-dry skin in patients with acne. According to the results of our study, we can suggest that patients with acne should be investigated in terms of Demodex in patients with symptoms such as facial sensitivity and dryness. However, studies with larger numbers of patients are needed to refine the evidence value of these results.

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Conflicts of interest

There are no conflicts of interest.

Author's contribution

Conception or design of the work: AF and LBS; data collection: AF, LBS, and OK; data analysis and interpretation: AF, LBS, and DAA; critical revision of the article: AF, LBS, DAA, and OK. Final approval of the version to be published: AF and LBS.

Data availability statement

The data that support the findings of this study are available from the corresponding author.

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