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Investigation of Factors Associated with Gut Microbiota in *Demodex*-associated Skin Conditions

Demodeks ile İlişkili Deri Hastalıklarında Bağırsak Mikrobiyotasına İlişkin Faktörlerin Araştırılması

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ABSTRACT

Objective: This study describes the relationships of factors related to gut microbiota and skin conditions associated with *Demodex*, including demodicosis, rosacea, and perioral dermatitis.

Methods: A total of 113 patients from Dokuz Eylül University Hospital Dermatology Department answered a cross-sectional questionnaire. They consisted of 42 cases of *Demodex*-related skin diseases and 71 healthy controls. Demographic data and medical history, dietary and lifestyle habits, and gastrointestinal symptoms were recorded. Statistical analysis included descriptive statistics, chi-square tests, Fisher's Exact tests, independent samples t-tests, and logistic regression methods.

Results: Our findings identified alcohol consumption [odds ratio (OR)=11.13, 95% confidence interval (CI): 4.11-17.22, p<0.01] and smoking (OR=10.32, 95% CI: 2.47-21.57, p<0.01) as strong risk factors for *Demodex*-related conditions. Low water intake (0-1 liter per day) (OR=3.39, 95% CI: 2.08-5.57, p=0.03) and infrequent exercise (less than 1 hour per week) (OR=4.87, 95% CI: 2.70-12.54, p=0.02) were also significant risk factors. Additional factors associated with increased *Demodex* risk included reduced bowel movements (OR=2.71, 95% CI: 1.45-4.06, p=0.01) and higher pet ownership (OR=2.85, 95% CI: 2.13-4.27, p=0.03). Although vegetarian and high-fat diets showed some associations, they were not independently significant.

Conclusion: This study demonstrates key environmental and lifestyle factors, such as low water intake, infrequent exercise, reduced bowel movements, higher pet ownership, alcohol consumption, and smoking, that are significantly associated with *Demodex*-related skin conditions. These factors, related to gut microbiota, may provide valuable insights for managing these skin conditions and suggest promising directions for future research.

Keywords: *Demodex*, gut microbiota, rosacea, skin conditions, gut-skin axis

ÖZ

Amaç: Bu çalışma, demodikoz, rosacea ve perioral dermatit gibi *Demodeks* ile ilişkili deri hastalıklarına ve bağırsak mikrobiyotasına bağlı faktörlerin ilişkilerini tanımlamaktadır.

Yöntemler: Dokuz Eylül Üniversitesi Hastanesi Dermatoloji Bölümünden toplam 113 hasta kesitsel bir anketi yanıtladı. Bu hastalar, 42 *Demodeks* ile ilişkili deri hastalığı olgusu ve 71 sağlıklı kontrol grubundan oluşmaktaydı. Demografik veriler, tıbbi geçmiş, beslenme ve yaşam tarzı alışkanlıkları ve gastrointestinal semptomlar kaydedildi. İstatistiksel analizler, betimleyici istatistikler, ki-kare testleri, Fisher'ın kesin testleri, bağımsız örneklem t-testleri ve lojistik regresyon yöntemlerini içerdi.

Bulgular: Bulgularımız, alkol tüketimini [olasılık oranı (OO)=11,13, %95 güven aralığı (GA): 4,11-17,22, p<0,01) ve sigara içmeyi (OO=10,32, %95 GA: 2,47-21,57, p<0,01) *Demodeks* ile ilişkili hastalıklar için güçlü risk faktörleri olarak belirlemiştir. Düşük su tüketimi (0-1 litre gün başına) (OO=3,39, %95 GA: 2,08-5,57, p=0,03) ve seyrek egzersiz (haftada 1 saatten az) (OO=4,87, %95 GA: 2,70-12,54, p=0,02) de önemli risk faktörleri olarak bulunmuştur. Artmış *Demodeks* riskiyle ilişkili diğer faktörler arasında azalmış bağırsak hareketleri (OO=2,71, %95 GA: 1,45-4,06, p=0,01) ve yüksek evcil hayvan sahipliği (OO=2,85, %95 GA: 2,13-4,27, p=0,03) bulundu. Vejetaryen ve yüksek yağlı diyetlerin bazı ilişkiler gösterdiği görülmüş olmasına rağmen, bağımsız olarak anlamlı bulunmadı.

Sonuç: Bu çalışma, düşük su tüketimi, seyrek egzersiz, azalmış bağırsak hareketleri, yüksek evcil hayvan sahipliği, alkol tüketimi ve sigara içme gibi *Demodeks*-ilişkili deri hastalıkları ile önemli ölçüde ilişkili olan çevresel ve yaşam tarzı faktörlerini göstermektedir. Bağırsak mikrobiyotası ile ilişkili bu faktörler, bu deri hastalıklarının yönetiminde değerli bilgiler sunabilir ve gelecekteki araştırmalar için umut verici yönler önerebilir.

Anahtar Kelimeler: *Demodeks*, bağırsak mikrobiyotası, rosacea, deri hastalıkları, bağırsak-deri ekseni

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Türkiye PARAZİTOLOJİ Dergisi

INTRODUCTION

Demodex mites are microscopic ectoparasites that mainly inhabit the hair follicles of mammals (1). In humans, two species are common: *Demodex folliculorum* and *Demodex brevis,* often called eyelash or face mites (1). Generally, they exist in small numbers, without visible problems. However, when overpopulated or penetrating deeper into the skin, they can cause pityriasis folliculorum, rosacea, and perioral dermatitis (2-6).

Demodex folliculorum resides in facial skin, and its overgrowth causes itching, redness, and scaling of the face. This condition is described as demodicosis (7). Rosacea, a chronic inflammatory disorder of the central face (8), often initiates with transient facial redness that may progress into fixed erythema and papules, pustules, and telangiectasia (8). This condition is most commonly seen in persons between 30 and 50 years of age and may also present with eye symptoms (8). Perioral dermatitis is another chronic inflammatory condition characterized by red papules and vesicles around the mouth, nose, and eyes; women were predominantly affected between the ages of 16 to 45 years (9).

Recent studies have established the critical role of gut microbiota in the maintenance of skin health and in modulating immune responses (10,11). Diversity in short-chain fatty acids produced by gut microbiota might affect the composition of skin microbiota and hence influence cutaneous immune responses (11-13). Besides, perturbations in gut microbiota have been shown to weaken skin barrier functions and lead to skin disorders through systemic inflammation (10,11).

Treatments for diseases such as rosacea (14), perioral dermatitis (15), and demodicosis (16) typically involve a strategy of reducing *Demodex* mites and minimizing environmental factors like sun exposure and spicy diet. A rising body of evidence points to the role of factors influencing gut microbiota -for example, dietary habits, lifestyle, and medical history- that might also impact the course of these skin diseases (17-22), but the data are still limited.

In this regard, this study investigates the possible relationships between several factors, including medical history, lifestyle, eating habits, and gastrointestinal symptoms related to gut microbiota, with *Demodex*-associated skin conditions, including demodicosis, rosacea, and perioral dermatitis. The identification of these relationships will be useful in attaining better management for those suffering from these diseases.

METHODS

Study Design and Participants

We carried out a cross-sectional web-based survey among adults who had been diagnosed with demodicosis, rosacea, or perioral dermatitis at Dokuz Eylül University Hospital's Dermatology Department within the past two years. Participants were recruited through a screening process and invited to complete a web-based survey. The study included a total of 113 participants, comprising 42 patients with the aforementioned conditions and 71 healthy controls.

Inclusion criteria for the patient group were adults with a confirmed diagnosis of demodicosis, rosacea, rhinophyma, or perioral dermatitis based on ICD-10 codes as determined by a dermatologist. Exclusion criteria included individuals under 18 years old, pregnant or lactating women, those with a history of malignancy or who were undergoing chemotherapy or radiotherapy, individuals with prior gastrointestinal surgery, those with severe infectious or immunosuppressive diseases, and those with significant cognitive impairments.

Ethical approval for the study was obtained from the Dokuz Eylül University Ethics Committee (approval number: 2024/20-20, date: 05.06.2024).

Data Collection

Participants who consented to join the study were given access to an anonymous web-based survey via a provided link. Informed consent was required at the start of the survey, and only the responses from participants who completed the entire survey were included in the analysis.

The survey gathered a variety of information, including demographic details such as age and sex, along with data on dermatological diagnoses to confirm conditions like demodicosis, rosacea, rhinophyma, or perioral dermatitis. Additionally, participants provided information about their medical history, current medications, family history of autoimmune diseases, and any known allergies.

The survey also collected details about dietary habits and lifestyle factors, such as alcohol and tobacco use, exercise routines, and the use of nutritional supplements. Furthermore, participants reported their psychological stress levels and any gastrointestinal symptoms they experienced.

Statistical Analysis

Descriptive statistics, including the mean, standard deviation, frequencies, and percentages, were calculated. Categorical variables were analyzed using chi-square (χ^2) tests and Fisher's Exact tests, while independent samples t-tests were used for continuous variables. Logistic regression analysis was performed to evaluate the impact of various risk factors on the diagnosed conditions. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. A p-value of less than 0.05 considered statistically significant. All analyses were performed using SPSS version 22.0.

RESULTS

Among patients, 73.8% had rosacea, 14.3% had perioral dermatitis, and 9.5% had demodicosis. Age and gender distributions between the control and patient groups were similar (p=0.08 and p=0.06, respectively) (Table 1).

Regarding clinical characteristics, patients had significantly fewer weekly bowel movements compared to controls (5.12±2.41 vs. 7.41±3.79; p=0.02). Additionally, controls had a higher prevalence of known allergies compared to patients (40.8% vs. 21.4%; p=0.01) (Table 1).

There were no significant differences between the control and patient groups regarding immunosuppressing conditions, significant stress or life events, or known infections (all p>0.05). However, patients reported significantly higher levels of physical intensity or fatigue compared to controls (p=0.04). No participants had a history of inflammatory bowel disease or family history of it (Table 2).

Comparing gastrointestinal symptoms, no significant differences were found between groups in terms of constipation, post-meal bloating, abdominal pain, gallbladder issues, and reflux (Table 3). Patients, however, reported higher regular medication use

Table 1. Comparison of demographic and clinical measurements between patients with dermatologic conditions related to *Demodex* and controls

Measure	Control (n=71) mean ± SD	Patients (n=42) mean ± SD	p-value
Age	33.66±12.25	38.21±13.82	0.08
Sex			0.06
- Male	37 (52.1%)	14 (33.3%)	
- Female	34 (47.9%)	28 (66.7%)	
Clinical characteristics			
Comorbidities	24 (33.8%)	15 (35.7%)	0.94
Medication for other diseases	16 (22.5%)	11 (26.2%)	0.92
Annual antibiotic use	1.85±1.95	1.45±1.66	0.19
Average annual diarrhea episodes	9.18±15.01	10.83±5.72	0.51
Average weekly bowel movements	7.41±3.79	5.12±2.41	**0.02***
Stress severity	2.25±0.67	2.19±0.59	0.37
Medical history			
Duration of breastfeeding (months)	12.26±9.14	11.50±9.22	0.54
Delivery method			**0.03***
- Vaginal delivery	44 (62.0%)	31 (73.8%)	
- Cesarean section	27 (38.0%)	11 (26.2%)	
Autoimmune disease	9 (12.7%)	2 (4.8%)	0.13
Autoimmune disease in family	20 (28.2%)	9 (21.4%)	0.44
Known allergy	29 (40.8%)	9 (21.4%)	**0.01***
Family history of allergy	19 (26.8%)	14 (33.3%)	0.12

*: p<0.05 indicates significant differences, SD: Standard deviation

Table 2. Clinical characteristics related to immunity

Characteristic	Control (n=71)	Patients (n=42)	p-value
Immunosuppressing conditions or medications	1 (1.4%)	0 (0.0%)	0.92
Significant stress or life events	21 (29.6%)	11 (26.2%)	0.77
Physical intensity/fatigue	24 (33.8%)	17 (40.5%)	**0.04***
Known infections (HIV, hepatitis, syphilis)	2 (2.8%)	1 (2.4%)	0.92

*: p<0.05 indicates significant differences, HIV: Human immunodeficiency virus

compared to controls (p=0.04). Post-antibiotic diarrhea incidence was similar in both groups (p=0.93).

Regarding dietary habits, there were no significant differences between groups in weekly consumption of vegetables, probiotic foods (such as homemade yogurt, pickles, and vinegar), fiber-rich foods, fermented foods, sugary foods, packaged foods, and processed foods (Table 4). However, a carbohydrate-based diet was more prevalent among controls, while a vegetarian diet and a high-fat diet were more common among patients, with these differences being statistically significant (p=0.04).

The analysis of lifestyle characteristics revealed several significant differences between the healthy controls and patients (Table 5). Alcohol consumption was notably higher among patients (61.9% vs. 32.4% in controls, p<0.01), as was tobacco use (69.0% vs. 52.1% in controls, p<0.01). Pet ownership was also more common among patients (35.7% vs. 19.7% in controls, p=0.02). Patients consumed less water daily, with 23.8% drinking 0-1 liter compared to 14.1% of controls (p=0.01). Moreover, patients engaged in less physical activity, with 52.4% reporting no exercise versus 26.8% of controls (p=0.01). There was a borderline significant difference in the proportion of patients who reported regularly getting adequate sleep (54.8% vs. 43.7% of controls, p=0.04), though sleep problems were similarly reported in both groups (p=0.89).

The most frequently used supplements among patients were vitamin D, multivitamins, omega-3, vitamin B12, magnesium, iron, zinc, and protein powder. No significant differences were found between patients and controls regarding the use of these supplements (all p>0.05).

In multivariate analysis (Table 6), alcohol consumption exhibited a strong association with *Demodex*-related skin conditions, with an OR of 11.13 (95% CI: 4.11-17.22, p<0.01). Smoking also had a significant association, with an OR of 10.32 (95% CI: 2.47-21.57, p<0.01).

Lack of regular exercise (less than 1 hour per week) was a notable risk factor, with an OR of 4.87 (95% CI: 2.70-12.54, p=0.02). Low

Table 3. Digestive characteristics

Digestive characteristics	Control (n=71)	Patients (n=42)	p-value
Constipation	22 (31.0%)	14 (33.3%)	0.68
Post-meal bloating	32 (45.1%)	22 (52.4%)	0.24
Abdominal pain	21 (29.6%)	15 (35.7%)	0.17
Gallbladder issues	4 (5.6%)	2 (4.8%)	0.91
Reflux	21 (29.6%)	14 (33.3%)	0.18
Regular medication use	9 (12.7%)	10 (23.8%)	**0.04***
Post-antibiotic diarrhea	10 (14.1%)	6 (14.3%)	0.93

*: p<0.05 indicates significant differences

Table 4. Examination of nutritional characteristics

Nutritional characteristics: Weekly frequency of consumption	Control (n=71) mean ± SD	Patients (n=42) mean ± SD	p-value
Vegetables	3.11±0.69	3.07±0.89	0.78
Homemade yoghurt, pickles, vinegar	2.39±1.10	2.69±1.07	0.17
Fiber-rich foods	0.70±0.72	0.90±0.82	0.18
Fermented foods	0.66±0.67	0.60±0.66	0.61
Sugary food consumption	0.86±0.87	0.71±0.83	0.39
Packaged food consumption	0.56±0.71	0.33±0.57	0.08
Processed foods	0.17±0.53	0.24±0.53	0.51
Nutritional habit definition			
Mediterranean diet	29 (40.8%)	18 (42.9%)	**0.04***
Meat-based diet	21 (29.6%)	13 (31.0%)	
Carbohydrate-based diet	20 (28.2%)	6 (14.3%)	
Vegetarian diet	0 (0.0%)	3 (7.1%)	
High-fat diet	1 (1.4%)	2 (4.8%)	

*: p<0.05 indicates significant differences, SD: Standard deviation

water intake (0-1 liter per day) had an OR of 3.39 (95% CI: 2.08-5.57, p=0.03), indicating its importance.

Pet ownership was also significantly associated with increased risk, with an OR of 2.85 (95% CI: 2.13-4.27, p=0.03). Fewer bowel movements per week were associated with an OR of 2.71 (95% CI: 1.45-4.06, p=0.01). Known allergies did not significantly impact the outcome (p=0.11), while vegetarian and carbohydrate-dominant diets showed no significant associations after adjustment (p=0.62 and p=0.51, respectively).

DISCUSSION

This study investigates the associations between gut microbiota-related factors and *Demodex*-associated skin conditions. Pathophysiology of rosacea, a prototypical condition among *Demodex*-related skin conditions, characterized by immune system imbalances and inflammation, is linked to variations in skin microbiota, such as increased *Proteobacteria* and *Firmicutes* (23). Although studies on gut microbiota's role in rosacea are limited, differences in bacterial genera like *Acidaminococcus* and

Table 5. Examination of lifestyle characteristics

Lifestyle characteristic	Control (n=71)	Patients (n=42)	p-value
Alcohol consumption	23 (32.4%)	26 (61.9%)	**<0.01***
Tobacco use	37 (52.1%)	29 (69.0%)	**<0.01***
Regularly getting adequate/quality sleep	31 (43.7%)	23 (54.8%)	**0.04***
Sleep problems	28 (39.4%)	16 (38.1%)	**0.89**
Keeping pets at home	14 (19.7%)	15 (35.7%)	**0.02***
Daily water consumption			
0-1 liter	10 (14.1%)	10 (23.8%)	**0.01***
Liters	35 (49.3%)	18 (42.9%)	
More than 2 liters	26 (36.6%)	14 (33.3%)	
Weekly exercise duration (hours)			
None	19 (26.8%)	22 (52.4%)	**0.01***
1 hour	16 (22.5%)	5 (11.9%)	
Hours	27 (38.0%)	12 (28.6%)	
4-6 hours	9 (12.7%)	3 (7.1%)	

*: p<0.05 indicates significant differences

Megasphaera in rosacea patients suggest a potential connection via the gut-skin axis (24,25).

Our study identified alcohol consumption as the strongest risk factor for rosacea (RR=11.13, 95% CI: 4.11-17.22, p<0.01), consistent with a meta-analysis showing a 4.17-fold increased risk of phymatous rosacea among alcohol drinkers (95% CI =1.76-9.91) (26). While the exact mechanism linking alcohol and rosacea remains unclear, potential pathways include direct effects of alcohol metabolites on skin vasculature and indirect effects on both the skin and gut microbiomes (19,20).

Our study showed a significant association between smoking and rosacea (OR=10.32, 95% CI: 2.47-21.57, p<0.01). However, the relationship between smoking and *Demodex*-related conditions is complex and potentially paradoxical. While some studies suggest smoking might initially reduce rosacea symptoms (potentially through vasoconstriction, anti-inflammatory effects, and skin barrier disruption) (17), it could ultimately contribute to *Demodex* proliferation and rosacea development through its impact on the skin, immune system, and gut microbiota (18). This complexity is highlighted by research indicating that former smokers may have an increased risk of rosacea compared to active smokers (17).

Our study identified that infrequent bowel movements (three or fewer weekly) were significantly associated with 2.71 times the risk of *Demodex*-related dermatological conditions (95% CI: 1.45-4.06, p=0.01). This finding aligns with the understanding that constipation, often linked to bacterial overgrowth in the gut (27), can influence skin health. Treating bacterial overgrowth has been shown to improve rosacea symptoms (28), suggesting a potential pathway through which reduced bowel movements and associated gut microbiome changes could contribute to *Demodex*-related skin conditions.

Our study identified that infrequent exercise (less than 1 hour per week) as a significant risk factor for *Demodex*-related skin disorders (OR=4.87, 95% CI: 2.70-12.54, p=0.02). The literature on exercise and rosacea is limited, but a cross-sectional study with 110 rosacea patients found that increased muscle mass, a

Table 6. Identification of multiple risk factors

Variable	Univariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Alcohol	1.61 (1.10-2.12)	**<0.01***	11.13 (4.11-17.22)	**<0.01***
Smoking	1.45 (0.94-1.96)	**<0.01***	10.32 (2.47-21.57)	**<0.01***
Lack of regular exercise (<1 hour/week)	1.43 (0.92-1.94)	**<0.01***	4.87 (2.70-12.54)	**0.02***
Low water intake (0-1 L/day)	1.17 (0.66-1.68)	**0.02***	3.39 (2.08-5.57)	**0.03***
Pet ownership	1.28 (0.77-1.79)	**0.03***	2.85 (2.13-4.27)	**0.03***
Weekly bowel movements (3 and less)	1.21 (0.89-1.56)	**0.01***	2.71 (1.45-4.06)	**0.01***
Known allergy	0.63 (0.38-1.04)	**<0.01***	0.46 (0.18-1.19)	0.11
Vegetarian diet	1.07 (0.56-1.58)	**0.04***	0.61 (0.14-4.33)	0.62
Carbohydrate-dominant diet	0.92 (0.41-1.43)	**0.04***	0.93 (0.22-2.35)	0.51
Regular medication use	1.02 (2.55-3.57)	**0.02***	0.94 (0.57-3.64)	0.44
Normal delivery method	1.05 (2.64-3.66)	**0.03***	0.96 (0.48-2.82)	0.74
Experiencing physical fatigue	1.01 (2.51-3.53)	**0.03***	0.99 (0.77-1.17)	0.16

*: p<0.05 indicates significant differences, OR: Odds ratio, CI: Confidence interval

proxy for regular exercise, was associated with reduced rosacea severity (29). It has been suggested that insufficient exercise may contribute to the development of rosacea by altering the gut microbiome and disrupting immune function, thereby increasing susceptibility to skin disorders (30). However, more comprehensive research is needed to draw reliable conclusions about the effects of exercise and muscle mass on *Demodex*-related conditions. This is especially important because microbiota, which can have significant immune effects throughout the body, is influenced by various personal factors such as urban versus rural living, geographical location, alcohol and tobacco use, stress, mental health status, and exercise (31).

Low water intake (0-1 liter per day) was significantly associated with 3.39 times the risk of having *Demodex*-related cutaneous disease (95% CI: 2.08-5.57, p=0.03), highlighting its importance. The protective effect of water consumption in *Demodex*-related skin conditions could be attributed to its role in maintaining skin hydration and normal physiological processes (32,33). Studies have shown that low skin moisture correlates with higher mite density, though results have not always been significant (34). Water intake is also a critical factor influencing gut microbiota (35), which may indirectly affect skin microbiota diversity and resistance to diseases.

Pet ownership was significantly associated with *Demodex*-related skin disorders in our multivariate analysis (OR=2.85, 95% CI: 2.13-4.27, p=0.03). While *Demodex* mites are common in animals and can cause demodicosis, they are not typically transmissible to humans through normal contact (36). A study involving 96 healthy volunteers found no significant relationship between pet ownership and the presence of *Demodex* mites (36). The increased risk observed in our study may not solely be related to the direct effect of having pets on *Demodex* mites. Numerous findings have identified relationships between the microbiota characteristics of pet owners and their pets (37). For example, one study found that patients with rosacea who also had higher rates of pet ownership exhibited gut microbiome dysbiosis, with a significant decrease in the abundance of *Ruminococcaceae* and *Blautia* and an increase in *Prevotellaceae*. This suggests that environmental factors like pet ownership might contribute to microbial imbalances that influence *Demodex* proliferation and inflammation, rather than direct mite transmission (38).

This study observed a higher frequency of *Demodex*-related skin conditions in patients reporting vegetarian or high-fat diets, though these associations were not independently significant in multivariate analyses. Previous research has linked specific enterotypes, influenced by long-term dietary habits, to rosacea and other conditions (39). Differently from the reults of the present study, one study found a higher prevalence of carbohydrate-associated Enterotype III in rosacea patients (39), while fiber-rich, plant-based Enterotype II was less common (39). However, the study also noted Enterotype I, associated with animal products and saturated fats, as most prevalent in both patient and control groups, wich they concluded as potentially because of regional common dietary patterns (39).

The lack of significant dietary associations in our study might be attributed to our single-center design and limited sample size, potentially restricting dietary variations. Additionally, the inconsistencies observed across the literature underscore the complex interplay of factors influencing diet's impact on skin health, emphasizing the need for more standardized research methodologies. Future research on cutaneous *Demodex* and dietary habits should incorporate rigorous, objective assessment methods to clarify the potential links between environmental factors and these conditions.

Study Limitations

This retrospective study has inherent limitations. Recall bias may have influenced survey responses, and the relatively small sample size could limit statistical power, potentially obscuring the impact of environmental factors. Despite these limitations, this study offers valuable preliminary findings regarding the connection between gut microbiota and *Demodex*-associated skin conditions, informing future research directions.

CONCLUSION

This study uncovers important links between gut microbiota-related factors and *Demodex*-associated skin conditions. Key findings include the strong association of alcohol consumption

with *Demodex* disorders, likely due to its effects on the skin and gut microbiomes. Smoking is also linked, though its effects on *Demodex* and rosacea are complex. The research highlights the significance of hydration and physical activity, with low water intake and lack of exercise identified as risk factors. Additionally, reduced bowel movements and higher pet ownership are associated with increased risk. Future research should involve larger, diverse populations and objective dietary assessments to better understand the interplay between environmental factors, gut microbiota, and *Demodex*-related conditions, potentially leading to improved management and therapeutic strategies for affected individuals.

*Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Dokuz Eylül University Ethics Committee (approval number: 2024/20-20, date: 05.06.2024).

Informed Consent: Informed consent was required at the start of the survey, and only the responses from participants who completed the entire survey were included in the analysis.

*Authorship Contributions

Concept: F.G., S.S., Design: F.G., S.S., Data Collection or Processing: S.S., E.A., Analysis or Interpretation: F.G., S.S., Ö.Ö., Ş.K., E.A., Literature Search: F.G., Writing: F.G., S.S., Ö.Ö., Ş.K., E.A.

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REFERENCES

1. Desch C, Nutting WB. *Demodex folliculorum* (Simon) and *D. brevis* akbulatova of man: redescription and reevaluation. J Parasitol. 1972; 58: 169-77.
2. Ayres S Jr, Ayres S 3rd. Demodectic eruptions (demodicidosis) in the human. 30 years' experience with 2 commonly unrecognized entities: *Pityriasis folliculorum* (*Demodex*) and acne rosacea (*Demodex* type). Arch Dermatol. 1961; 83: 816-27.
3. Bonnar E, Eustace P, Powell FC. The *Demodex* mite population in rosacea. J Am Acad Dermatol. 1993; 28: 443-8.
4. Forton F, Seys B. Density of *Demodex* folliculorum in rosacea: a case-control study using standardized skin-surface biopsy. Br J Dermatol. 1993; 128: 650-9.
5. Zhao YE, Peng Y, Wang XL, Wu LP, Wang M, Yan HL, et al. Facial dermatosis associated with Demodex: a case-control study. J Zhejiang Univ Sci B. 2011; 12: 1008-15.
6. Dolenc-Voljc M, Pohar M, Lunder T. Density of *Demodex* folliculorum in perioral dermatitis. Acta Derm Venereol. 2005; 85: 211-5.
7. Aumond S, Bitton E. Palpebral and facial skin infestation by *Demodex folliculorum*. Cont Lens Anterior Eye. 2020; 43: 115-22.
8. Van Zuuren EJ. Rosacea. N Engl J Med. 2017; 377: 1754-64.
9. Teng Y, Ren M, Ding Y, Yang X, Fan Y, Tao X. A Case of Perioral Dermatitis Successfully Treated with Abrocitinib. Clin Cosmet Investig Dermatol. 2023; 16: 3035-8.
10. O'Neill CA, Monteleone G, McLaughlin JT, Paus R. The gut-skin axis in health and disease: A paradigm with therapeutic implications. Bioessays. 2016; 38: 1167-76.
11. Salem I, Ramser A, Isham N, Ghannoum MA. The Gut Microbiome as a Major Regulator of the Gut-Skin Axis. Front Microbiol. 2018; 9: 1459.
12. Samuelson DR, Welsh DA, Shellito JE. Regulation of lung immunity and host defense by the intestinal microbiota. Front Microbiol. 2015; 6: 1085.
13. Kim YG, Udayanga KG, Totsuka N, Weinberg JB, Núñez G, Shibuya A. Gut dysbiosis promotes M2 macrophage polarization and allergic airway inflammation via fungi-induced PGE_2. Cell Host Microbe. 2014; 15: 95-102.
14. Trave I, Micalizzi C, Cozzani E, Gasparini G, Parodi A. Papulopustular Rosacea Treated With Ivermectin 1% Cream: Remission of the Demodex Mite Infestation Over Time and Evaluation of Clinical Relapses. Dermatol Pract Concept. 2022; 12: e2022201.
15. Tempark T, Shwayder TA. Perioral dermatitis: a review of the condition with special attention to treatment options. Am J Clin Dermatol. 2014; 15: 101-13.
16. Paichitrojjana A, Paichitrojjana A. Successful treatment of ivermectin refractory demodicosis with isotretinoin and permethrin cream. JAAD Case Rep. 2022; 26: 98-100.
17. Yuan X, Yin D. Association between rosacea and smoking: A systematic review and meta-analysis. Dermatol Ther. 2021; 34: e14747.
18. Capurso G, Lahner E. The interaction between smoking, alcohol and the gut microbiome. Best Pract Res Clin Gastroenterol. 2017; 31: 579-88.
19. Li S, Cho E, Drucker AM, Qureshi AA, Li WQ. Alcohol intake and risk of rosacea in US women. J Am Acad Dermatol. 2017; 76: 1061-7.e2.
20. Casafont Morencos F, de las Heras Castaño G, Martín Ramos L, López Arias MJ, Ledesma F, Pons Romero F. Small bowel bacterial overgrowth in patients with alcoholic cirrhosis. Dig Dis Sci. 1996; 41: 552-6.
21. Yuan X, Huang X, Wang B, Huang YX, Zhang YY, Tang Y, et al. Relationship between rosacea and dietary factors: A multicenter retrospective case-control survey. J Dermatol. 2019; 46: 219-25.
22. Rainer BM, Fischer AH, Luz Felipe da Silva D, Kang S, Chien AL. Rosacea is associated with chronic systemic diseases in a skin severity-dependent manner: results of a case-control study. J Am Acad Dermatol. 2015; 73: 604-8.
23. Murillo N, Aubert J, Raoult D. Microbiota of *Demodex* mites from rosacea patients and controls. Microb Pathog. 2014; 71-72: 37-40.
24. Nam JH, Yun Y, Kim HS, Kim HN, Jung HJ, Chang Y, et al. Rosacea and its association with enteral microbiota in Korean females. Exp Dermatol. 2018; 27: 37-42.
25. Sánchez-Pellicer P, Eguren-Michelena C, García-Gavín J, Llamas-Velasco M, Navarro-Moratalla L, Núñez-Delegido E, et al. Rosacea, microbiome and probiotics: the gut-skin axis. Front Microbiol. 2024;14:1323644.
26. Liu L, Xue Y, Chen Y, Pu Y, Zhang Y, Zhang L, et al. Alcohol consumption and the risk of rosacea: A systematic review and meta-analysis. J Cosmet Dermatol. 2022; 21: 2954-61.
27. Mares CR, Săsăran MO, Mărginean CO. The relationship between small intestinal bacterial overgrowth and constipation in children - a comprehensive review. Front Cell Infect Microbiol. 2024; 14: 1431660.
28. Parodi A, Paolino S, Greco A, Drago F, Mansi C, Rebora A, et al. Small intestinal bacterial overgrowth in rosacea: clinical effectiveness of its eradication. Clin Gastroenterol Hepatol. 2008; 6: 759-64.
29. Nam JH, Yang J, Park J, Seo JH, Chang Y, Ryu S, et al. Association between rosacea severity and relative muscle mass: A cross-sectional study. J Dermatol. 2019; 46: 11-7.
30. Zhu W, Hamblin MR, Wen X. Role of the skin microbiota and intestinal microbiome in rosacea. Front Microbiol. 2023; 14: 1108661.
31. Wegierska AE, Charitos IA, Topi S, Potenza MA, Montagnani M, Santacroce L. The Connection Between Physical Exercise and Gut Microbiota: Implications for Competitive Sports Athletes. Sports Med. 2022; 52: 2355-69.
32. Palma L, Marques LT, Bujan J, Rodrigues LM. Dietary water affects human skin hydration and biomechanics. Clin Cosmet Investig Dermatol. 2015; 8: 413-21.
33. Palma ML, Tavares L, Fluhr JW, Bujan MJ, Rodrigues LM. Positive impact of dietary water on in vivo epidermal water physiology. Skin Res Technol. 2015; 21: 413-8.

34. Zeytun E, Tilki E, Doğan S, Mumcuoğlu KY. The effect of skin moisture, pH, and temperature on the density of *Demodex folliculorum* and *Demodex brevis* (Acari: Demodicidae) in students and staff of the Erzincan University, Turkey. Int J Dermatol. 2017; 56: 762-6.

35. Vanhaecke T, Bretin O, Poirel M, Tap J. Drinking Water Source and Intake Are Associated with Distinct Gut Microbiota Signatures in US and UK Populations. J Nutr. 2022; 152: 171-82.

36. Horváth A, Neubrandt DM, Ghidán Á, Nagy K. Risk factors and prevalence of *Demodex* mites in young adults. Acta Microbiol Immunol Hung. 2011; 58: 145-55.

37. Abdolghanizadeh S, Salmeh E, Mirzakhani F, Soroush E, Siadat SD, Tarashi S. Microbiota insights into pet ownership and human health. Res Vet Sci. 2024; 171: 105220.

38. Marson J, Berto S, Mouser P, Baldwin H. Association between Rosacea, Environmental Factors, and Facial Cutaneous Dysbiosis: A Pilot Study from the Largest National Festival of Twins. SKIN. 2021; 5: 487-95.

39. Guertler A, Hering P, Pacífico C, Gasche N, Sladek B, Irimi M, et al. Characteristics of Gut Microbiota in Rosacea Patients-A Cross-Sectional, Controlled Pilot Study. Life (Basel). 2024; 14: 585.