Demodex mites among solid organ transplant recipients: a cross-sectional study

Adriana Marquardt-Feszler[1], Jakub Ruszkowski[2], Karolina Cekała[1], Maria Alicja Dębska-Ślizień[2], Beata Imko-Walczuk[1]

[1]Dermatology and Venereology Outpatient Clinic, Copernicus, Independent Public Healthcare Centre, Gdansk, Poland
[2]Department of Nephrology, Transplantology and Internal Diseases, Faculty of Medicine, Medical University of Gdansk, Poland

Adv Dermatol Allergol 2025; XLII (1): 89–95
DOI: https://doi.org/10.5114/ada.2024.145198

Abstract

Introduction: *Demodex* mites (DM) are pathogenic parasites that in some people cause demodicosis. It is widely discussed which groups of patients are more prone to develop the disease.
Aim: To evaluate the prevalence of DM in a population of solid organ transplant recipients (SOTRs) in comparison to immunocompetent controls.
Material and methods: A total of 225 SOTRs were tested for DM by 2 methods: microscopic evaluation of scrapings of the face and by dermoscopic examination of the face. Additionally, a group of 95 patients, who do not have any immunosuppression history, were asked to volunteer as controls. Every patient in study group was examined for face symptoms and had his medical history reviewed.
Results: The prevalence of positive *Demodex* test was not significantly different among SOTRs comparing to controls (21 positive results among SOTRs (9.3%) vs. 6 positive controls (6.3%), (p = 0.38)), but there was a numerically higher rate in SOTRs population. Patients treated with tacrolimus had a higher odds ratio of a positive *Demodex* test when compared to those treated with cyclosporine A (p = 0.046). Skin symptoms were characterized by relatively high negative predictive values (91.0–93.7%). Itch had the best balance between sensitivity and specificity, whereas exfoliation had the highest diagnostic accuracy.
Conclusions: In our study, demodicosis does not occur more often among SOTRs than in the general population. Notably, itch and exfoliation are symptoms of the greatest diagnostic value in demodicosis diagnosis. Patients receiving tacrolimus had a higher prevalence of a positive *Demodex* test when compared to those treated with cyclosporine A.

Key words: demodicosis, *Demodex* mites, organ transplantation, rosacea, immunosuppression.

Introduction

Demodex mites (DM) are widespread microscopic, elongated mites of normal hair follicles and sebaceous glands. They are considered the most common permanent ectoparasites of humans [1–3]. We can distinguish two species of DM among the human race: *Demodex folliculorum* and *Demodex brevis*. *D. folliculorum* is more prevalent than *D. brevis* [1]. It is mostly settled in the follicular infundibulum, while on the contrary *D. brevis* is regularly located in the deeper sebaceous and meibomian glands [1, 2, 4, 5]. DM have the ability to reside anywhere on the skin, although are most usually found in areas with the highest number of sebaceous glands including the nose, nasolabial folds, eyelids, cheek, forehead and neck [1, 2, 5, 6].

DM have been found in approximately all age, racial and geographical groups and their presence is in most people of no consequence [3, 7, 8]. Chen and Plewig presented in 2014 a classification that divides human demodicosis into two variants: primary and secondary, which have different manifestations [7].

Primary disease relates to some factors where one of them is absence of previous or coexisting inflammatory dermatoses like acne, rosacea or perioral dermatitis. Another specification is abnormal increase in mite colonization, which should be recognized from the active lesions at the time of examination. What is more, remission of the demodicosis should only be a result of adequate treatment with topical or systemic acaricides/arachnicides, but not with antibiotics possessing anti-inflammatory effects, such as tetracycline, doxycycline or macrolides [7, 9]. Primary demodicosis is characterized by late onset, in most cases after the age of 40 and particularly in the elderly population. It usually affects

Address for correspondence: Beata Imko-Walczuk MD, PhD, Dermatology and Venereology Outpatient Clinic, Copernicus, Independent Public Healthcare Centre, Powstańców Warszawskich 1/2, 80-101 Gdansk, Poland, e-mail: bimko@wp.pl
Received: 25.07.2024, **accepted:** 3.10.2024, **online publication:** 19.11.2024.

the face, typically periorificial areas (perioral, perinasal or periocular) with asymmetric distribution, grouped in an irregular shape with satellite lesions within one affected area. Primary demodicosis is being follicle bound and in most cases asymptomatic or mildly pruritic. The skin manifestation includes papulopustules, pityriasis folliculorum, nodulocystic changes with different intensity of inflammation. Infected patients usually do not present classical clinical manifestations of rosacea like erythema, transient flushing or telangiectasias [7].

Secondary demodicosis may occur early in life and present a more diffuse facial distribution or truncal involvement with more widespread inflammation and symptoms including pustules/papules, erythema and/or telangiectasias. Skin lesions connected with an unusual increase of DM, which occur among patients with other well-known skin or systemic diseases are categorized as secondary demodicosis. Papulopustular rosacea and perioral dermatitis are named most often as underlying diseases [7]. It is frequently mentioned in the literature to occur in immunosuppressed patients [7].

The pathogenesis of human demodicosis remains largely unclear. The critical point seems to be a transition from the noninflammatory initial stage of disease to an inflammatory demodicosis. To understand host-parasite immunological relations we should know when and how DM initiate the inflammation process. It is uncertain if demodicosis is initiated more by an overreacting host immune response or by an enormous amount of DM as observed in the scabies.

Recognition and diagnosis of demodicosis depends often on the experience of the dermatologist and clinics often have different diagnostic methods to reveal DM. The method that is mentioned most often in the literature is a count of more than 5 mites per cm^2 identified from lesions by way of 'standardized skin surface biopsy' (SSSB) [7, 10]. It has also been suggested that two consecutive SSSBs enable confirmation of diagnosis with even higher sensitivity and specificity [11]. Another popular method to detect DM infestation is direct microscopic evaluation (DME) that involves extraction of sebaceous glands' ducts with a scalpel and then examination of the sample under microscope. The test is positive when there are more than 5 mites per cm^2 of the examined skin. In a study conducted by Yun *et al.*, DME is said to be a more sensitive method than SSSB, especially in patients with a more diffuse pattern or rosacea [12]. However, in patients with the T-zone pattern (forehead, nose and chin distribution), SSSB was confirmed to be more sensitive [12]. New diagnostic techniques such as dermoscopy, confocal laser scanning microscopy or high-definition optical coherence tomography show encouraging results, although there are only preliminary studies. The precision, validity and clinical practicability of these methods should be determined [7].

The possible therapy of demodicosis is up to now based on single case reports and poorly evidence based. The treatment of choice is purely acaricidal ivermectin. However, topical use of other acaricides, such as permethrin 5%, benzyl benzoate 10–25%, crotamiton 10%, lindane 1% or malathion 0 5%, has been accepted for the treatment of scabies, recent evidence for the efficiency of these acaricides in the treatment of demodicosis is very limited [7]. On the one side, most cases of demodicosis manifested as rosacea can be cured with systemic low-dose tetracycline or macrolide antibiotics, topical azelaic acid 15–20% or topical metronidazole 0.75–2%. On the other side it is uncertain whether that treatment is a reason of mainly anti-inflammatory or also in part acaricidal effects [7, 13].

The discussion about prevalence of demodicosis among solid organ transplant recipients (SOTRs) is, to this moment, based on a few case reports and smaller group studies. The results of studies based on patients under immunosuppression show often opposite results and conclusions. The present study was conducted to investigate pervasiveness of DM in SOTRs.

Aim

The aim of the study was to evaluate the prevalence of *Demodex* mites in a group of SOTRs in comparison to an immunocompetent control group. We also planned to find factors that are associated with the presence of demodicosis in organ transplant population.

Material and methods

Study design

The study was conducted between December 2018 and September 2022 in the Copernicus Dermatology and Venerology Outpatient Clinic in Gdansk, Poland. Every adult after organ transplantation was, after obtaining informed consent, included in the study and referred for *Demodex* test. The only exclusion criterion was age under 18. Additionally, adult patients of the same Clinic that did not have any immunosuppression history, were asked to participate voluntarily in the study as controls after giving informed consent.

The diagnostic method involved direct microscopic evaluation and dermoscopic examination of the face. Both study and control groups were referred for *Demodex* test in the same laboratory. In the test, an area of about 1 cm^2 of the skin of the face was scrabbed to obtain epithelium and glands' content. Among patients with skin symptoms, samples were taken from lesions, otherwise the scrapings were obtained from the T zone-area where DM are likely to be found. The scrapings were first put and prepared with 10% potassium hydroxide (KOH) solution with 20% dimethyl sulfoxide (DMSO) on glass microscope slides. The samples were then studied under optical microscope (×10, ×20). More than 5 organisms per

sample was counted as positive test. Every test was conducted by experienced laboratory diagnosticians. Dermoscopic examination of the skin of the face was performed by a dermatologist to find signs of demodicosis as *Demodex tails* and *Demodex folliculorum* openings [14].

Before referring to *Demodex* test, the study population was examined by a dermatologist with focus on such face symptoms as presence of erythema/telangiectasias (E/T), papules or pustules (P/P), itch or exfoliation of the skin of the face. Additionally, dermoscopic examination was performed to find any precancerous lesions, skin cancers and dermoscopic signs of demodicosis as mentioned above. The medical history was reviewed for the date of transplantation, organ transplanted, history of dialysis (haemodialysis [HD] and/or peritoneal dialysis [PD]), pre-emptive transplantation in kidney transplant recipients (KTRs), reason for transplantation, immunosuppression at the time of *Demodex* test and dermatological examination. Data on doses of immunosuppressants were not collected in the study. Dermatological history was reviewed for 5 years before *Demodex* test or for the time after transplantation in patients transplanted in the last 5 years. In the group of 225 SOTRs, in 4 patients we did not manage to get dialysis history.

Statistical analysis

Data were collected using Microsoft Excel 2010. Acquired data were read and cleaned using R version 4.2.3 and the following libraries: *plyr* 1.8.9, *dplyr* 1.1.3, *readxl* 1.4.3 using RStudio 2023.06.0. Statistical analyses were conducted in Statistica software version 13.0 (Statsoft, Poland) and jamovi 2.4.8.

Because of non-normal distribution of both age and time between transplantation and *Demodex* test, continuous variables were expressed as medians with interquartile ranges (IQR). The categorical variables were expressed as absolute numbers and percentages. In the case of proportion of patients with a positive *Demodex* test, 95% confidence interval for a proportion was estimated using modified Wald method.

The differences in the demodicosis occurrence between SOTRs and the control group, as well as between SOTR subgroups (kidney only vs. other SOTRs), were tested using unadjusted logistic regression models. Association between immunosuppressive therapy and the occurrence of demodicosis was also tested using logistic regression models: both unadjusted and confounder-adjusted models. Using a directed acyclic graph, we identified age and time between transplantation and *Demodex* test as confounders in these analyses. Diagnostic value of symptoms in the diagnosis of *Demodex* mites was tested against *Demodex* test as a "gold standard" test using *meddecide* 0.0.2 module in jamovi.

When comparing continuous variables, the differences between two groups were tested using Mann-Whitney *U*-test. The threshold for statistical significance for this study was $p < 0.05$.

Results

Description of participants

A total of 225 consecutive adult solid organ transplant recipients (SOTRs) were included in the study. SOTRs primarily consist of only kidney transplant recipients ($n = 204$; 90.7%). Among them, 121 (59.3%) patients had a history of haemodialysis, 32 (15.7%) patients used PD in the past, another 20 (9.8%) patients had a history of both HD and PD, whereas 31 kidney recipients (15.2%) were transplanted preemptively. The "other SOTRs" group consists of liver transplant recipients ($n = 8$; 38.1%), heart transplant recipients ($n = 8$; 38.1%), lung transplant recipients ($n = 2$; 9.5%), both kidney and liver/heart/lung recipients (one case each). Additionally, we recruited 95 controls that were not treated with immunosuppressants. The clinical characteristics of both study and control groups are presented in Table 1.

Table 1. Characteristics of study participants

Characteristic	All SOTRs	Kidney only recipients	Other SOTRs	Control group
n	225	204	21	95
Male, *n* (%)	144 (64.0)	130 (64.0)	14 (63.6)	30 (31.6)
Age [years] median (IQR)	60 (49–67)	59 (47.8–67.0)	62 (57.0–67.0)	60 (44.5–73.0)
Number of transplantations, n (%)				
One	199 (88.4)	181 (88.7)	18 (85.7)	–
Two	22 (9.8)	19 (9.3)	3 (14.3)	–
Three	4 (1.8)	4 (2.0)	0	–
Time between transplantation and *Demodex* test [years], median (IQR)	8 (3–14)	8 (3.75–14.0)	7 (1.0–10.0)	–

SOTRs – Solid Organ Transplant Recipients.

Prevalence of positive *Demodex* test

Demodex test was positive in the case of 21 (9.3% (95% CI: 5.9–13.9%)) SOTRs patients. The prevalence of positive *Demodex* test did not significantly differ between SOTRs and the control group (6.3%; crude OR 1.52 (95% CI: 0.60–3.91), $p = 0.38$) nor between SOTR subgroups (9.3% and 9.5% in only kidney recipients and other SOTRs, respectively; crude OR 0.97 (95% CI: 0.21–4.51), $p = 0.97$).

Association between immunosuppressive therapy and result of the *Demodex* test

Since the difference in the prevalence of positive *Demodex* test between SOTRs and control groups was negligible, we hypothesized that the impact of used immunosuppression on *Demodex* infestation is rather limited. Notably, we found a differential relationship between the use of specific calcineurin inhibitors (tacrolimus (TAC) and cyclosporine A (CsA)) and the odds ratio of demodicosis. Among 145 patients treated with TAC, 18 (12.4%, 95% CI: 7.9 to 18.9%) were positive for DM, whereas only 3 (4.0%, 95% CI: 0.9 to 11.6%) patients treated with CsA were positive in the *Demodex* test. In multivariable analysis, patients treated with TAC had a higher odds ratio of a positive *Demodex* test when compared to those treated with CsA (adjusted OR = 3.73, 95% CI: 1.03–13.59, $p = 0.046$; details in Table 2). However, the certainty of the association is limited because of the wide confidence intervals.

We did not observe any difference in the number of used immunosuppressive drugs between patients with and without *Demodex* infestation (Mann-Whitney *U* test, $p = 0.91$). Moreover, the use of glucocorticosteroids (GC), azathioprine (AZA), mycophenolate mofetil (MMF), or mTOR inhibitors was not associated with positive *Demodex* test in our study (all $p > 0.05$, details in Table 3). This suggests that the risk of *Demodex* infestation in transplant patients is not influenced by the number or type of immunosuppressive medications other than calcineurin inhibitors (CNI) used in their treatment.

Table 2. Association between specific calcineurin inhibitors and a positive result of *Demodex* test

Variable	Model 1 ($\chi^2 = 4.62$, $p = 0.032$)		Model 2 ($\chi^2 = 8.11$, $p = 0.044$)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
CNI				
CsA	Reference	–	Reference	–
TAC	3.40 (0.97–11.94)	0.056	3.73 (1.03–13.59)	0.046

Model 1: crude association between CNI and Demodex test result. Model 2: association between CNI and Demodex test result adjusted for age and time between transplantation and Demodex test. In both models five patients treated without CNI were excluded. CI – confidence interval, CNI – calcineurin inhibitors, CsA – cyclosporine A, OR – odds ratio, TAC – tacrolimus.

Relation between symptoms and result of the *Demodex* test

Among all assessed symptoms, the most prevalent was erythema/telangiectasias among 72 patients (32.0% (95% CI: 26.0–38.5)). Thirty-seven patients (16.4% (95% CI: 11.9–21.9)) had papules/pustules (P/P); 36 (16.0% (95% CI: 11.5–21.5)) reported itch of the skin of the face and 20 (8.9% (95% CI: 5.5–13.4)) reported exfoliation. When *Demodex* test was treated as a "gold standard", all four symptoms were characterized by relatively low sensitivity to diagnose *Demodex* colonization (in all cases sensitivity was lower than 50%) and higher specificity (Table 4). Therefore, positive predictive values were low (up to 25% in the case of itch and exfoliation). However, the symptoms were characterized by relatively high negative predictive values (91.0–93.7%), which means the lack of these symptoms implies a high probability of a negative *Demodex* test. Itch had the best balance between sensitivity and specificity (Youden's J = 0.296 (95% CI: 0.032–

Table 3. Associations between other immunosuppressants and a positive result of *Demodex* test

Variable	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
	Model 1 ($\chi^2 = 0.15$, $p = 0.70$)		Model 2 ($\chi^2 = 3.34$, $p = 0.34$)	
GC	1.47 (0.18–11.80)	0.72	1.54 (0.19–12.64)	0.69
Antiproliferative agents				
Variable	Model 1 ($\chi^2 = 0.34$, p = 0.85)		Model 2 ($\chi^2 = 3.96$, p = 0.41)	
Absence	Reference	–	Reference	–
AZA	0.67 (0.07–6.38)	0.73	1.43 (0.12–16.47)	0.77
MMF	0.73 (0.25–2.14)	0.57	0.73 (0.25–2.17)	0.57
Variable	**Model 1 ($\chi^2 = 0.51$, $p = 0.47$)**		**Model 2 ($\chi^2 = 3.98$, $p = 0.26$)**	
mTORi	1.85 (0.38–8.95)	0.45	2.24 (0.44–11.41)	0.33

Model 1: crude association between the immunosuppressant and the result of Demodex test. Model 2: association between the immunosuppressant and Demodex test result adjusted for age and time between transplantation and Demodex test. In the case of antiproliferative drugs, four patients treated with both AZA and MMF simultaneously were excluded in both models. AZA – azathioprine, CI – confidence interval, GC – glucocorticosteroids, MMF – mycophenolate mofetil, mTORi – mTOR inhibitors, OR – odds ratio.

Table 4. Diagnostic value of symptoms in the diagnosis of Demodicosis

Statistics	Symptom			
	Erythema/ telangiectasia	Exfoliation	Itch	Papules/pustules
Symptom presence, *n* [%]	72 [32.0 (26.0–38.5)]	20 [8.9 (5.5–13.4)]	36 [16.0 (11.5–21.5)]	37 [16.4 (11.9–21.9)]
Sensitivity, %	42.9 (21.8–66.0)	23.8 (8.2–47.2)	42.9 (21.8–66.0)	19.0 (5.4–41.9)
Specificity, %	69.1 (62.3–75.4)	92.6 (88.2–95.8)	86.8 (81.3–91.1)	83.8 (78.0–88.6)
Diagnostic accuracy, %	66.7 (60.1–72.8)	86.2 (81.0–90.4)	82.7 (77.1–87.4)	77.8 (71.8–83.0)
Positive predictive value, %	12.5 (5.9–22.4)	25.0 (8.7–49.1)	25.0 (12.1–42.2)	10.8 (3.0–25.4)
Negative predictive value, %	92.2 (86.7–95.9)	92.2 (87.6–95.5)	93.7 (89.2–96.7)	91.0 (85.9–94.6)
Proportion of false positives, %	30.9 (24.6–37.7)	7.4 (4.2–11.8)	13.2 (8.9–18.7)	16.2 (11.4–22.0)
Proportion of false negative, %	57.1 (34.0–78.2)	76.2 (52.8–91.8)	57.1 (34.0–78.2)	81.0 (58.1–94.6)
False discovery rate, %	87.5 (77.6–94.1)	75.0 (50.9–91.3)	75.0 (57.8–87.9)	89.2 (74.6–97.0)
False omission rate, %	7.8 (4.1–13.3)	7.8 (4.5–12.4)	6.3 (3.3–10.8)	9.0 (5.4–14.1)
Youden's J statistic	0.120 (–0.159 to 0.414)	0.165 (–0.036 to 0.430)	0.296 (0.032 to 0.571)	0.029 (–0.165 to 0.305)
Likelihood ratio of a positive test	1.388 (0.813–2.369)	3.238 (1.307–8.020)	3.238 (1.766–5.936)	1.178 (0.462–3.001)
Likelihood ratio of a negative test	0.827 (0.564–1.211)	0.822 (0.646–1.048)	0.659 (0.453–0.958)	0.966 (0.778–1.199)

Demodex test treated as a "gold standard" test. Values in round brackets represent 95% confidence intervals.

0.571); its inverse – called number needed to diagnose – is 3.38), whereas exfoliation had the highest diagnostic accuracy (86.2% (95% CI: 81.0–90.4%)).

Discussion

To our knowledge, this is the biggest study focusing on the significance of DM as an opportunistic infection in the population of SOTRs. Our study does not confirm that demodicosis is more common in the group of SOTRs. However, it shows some correlations and tendencies that may help in the diagnosis. These are only two studies conducted among SOTRs. Aydingöz *et al.* conducted a study among 30 kidney transplant recipients in which authors deny the correlation [15]. Although they repeated the study 4 years later with a change of method (instead of 1 SSSB, they took two SSSB samples), there was still no correlation found between incidence of DM and SOTRs in a group of 12 patients and 12 controls [16]. Chovatiya and Colegio, in 2016, in a case report presenting 4 patients with demodicosis after organ transplantation suggested that it may be a bigger problem than previously thought [17].

There are also studies concerning demodicosis among patients under immunosuppression for reasons other than organ transplantation. A study among rheumatoid arthritis (RA) patients led by Ciftci *et al.* among 41 RA patients did not show any correlation between incidence and density of DM and immunosuppressed patients [1]. Yazisiz *et al.* in their study tested 93 patients with RA and 76 controls for DM. Although DM density was higher in the study group, the rate of infestation was similar in both groups. Additionally, use of any medication was not related to presence of DM [18]. In our study carried out in a much larger group of patients a possible correlation between use of tacrolimus and DM was found.

The importance of DM appears very often when discussing pathogenesis of rosacea. Rosacea is a common chronic inflammatory disease whose aetiology and pathogenesis is still not clear [19]. It affects face with erythema, papules/pustules, telangiectasias and recurrent flushing. Hu *et al.* in their research article try to summarize data about the role of, among others, DM in rosacea [19]. The mechanism remains controversial. On the one side, DM is said in many studies to be a stimulator of inflammation and to cause tissue degradation [20–22]. On the other side, studies also point that dysregulation in the immune system and skin barrier in rosacea may be a triggering factor for growth of DM [23]. In the review article in 2022 by Forton, the author points that there is growing evidence for the crucial role of DM in the inflammatory process in rosacea [24]. DM cause two opposite actions in the host's immune system: the defensive immune response to fight the pathogen and immunosuppressive action that boosts growth of mites even more. Chronic infectious stimulation causes dysfunction in T-cells response called T-cells exhaustion [25]. This reaction leads, together with immunosuppressive action, to higher production of vascular endothelial growth factor (VEGF) that results in better environment for DM to grow [24].

In our study, most of the patients reporting facial symptoms were negative for DM. However, itch and exfoliation were the two factors that were significantly

associated with the presence of DM. In a study conducted by Karincaoglu *et al.*, authors examined 67 patients with kidney failure [26]. The results show that patients on chronic dialysis have significantly higher density of DM (6.12/cm^2 vs. 0.31/cm^2). The authors mentioned also that patients with demodicosis reported pruritus more often, even though it was not statistically significant [26]. The observation was also confirmed in our study. Amitay-Laish *et al*. in their study retrospectively reviewed medical documentation of 28 patients under immunosuppression with demodicosis. Authors highlight that demodicosis may have diverse clinical presentations and clinicians should have it in mind when diagnosing facial eruptions in patients under immunosuppression [27].

The biggest limitation of our study is the *Demodex* test method that was dictated by the Clinic's testing standard. In order to obtain the highest possible sensitivity, we enriched the study with dermoscopic evaluation that is also mentioned as a useful tool to confirm the diagnosis [28–30]. Samples were obtained from the skin of the T zone or, in patients that presented symptoms that indicate demodicosis, from the lesions. Different localizations in patients' faces may suggest lack of method uniformity and another limitation, but at the same time we believe that it enabled to catch the areas with the biggest amount of DM in symptomatic patients and ensure their DM test to be positive.

The strength of our study is the number of included patients.

Conclusions

In our study, demodicosis does not occur more often among SOTRs than in the general population. However, there are some factors and symptoms that can indicate demodicosis. We suggest that practicians should consider *Demodex* test if patients after organ transplantation report itch or/and exfoliation of the skin of the face. In TAC treated patients the prevalence of demodicosis was higher as compared to CsA.

Funding

No external funding.

Ethical approval

The study was approved by the Bioethical Committee of the Medical University of Gdansk (NKBBN/156/2021).

Conflict of interest

The authors declare no conflict of interest.

References

1. Ciftci IH, Dundar U, Cetinkaya Z, et al. Demodex folliculorum in patients with rheumatoid arthritis. Acta Parasitol 2007; 52: 70-3.
2. Seyhan ME, Karincaoglu YK, Bayram N, et al. Density of Demodex folliculorum in haematological malignancies. J Inter Med Res 2004; 32: 411-5.
3. de Freitas Yamashita LSF, Cariello AJ, Geha NMA, et al. Demodex folliculorum on the eyelash follicle of diabetic patients. Arq Bras Oftalmol 2011; 74: 422-4.
4. Baima B, Sticherling M. Demodicidosis revisited. Acta Derm Venereol 2002; 82: 3-6.
5. Jansen T, Kastner U, Kreuter A, Altmeyer P. Rosacea-like demodicidosis associated with acquired immunodeficiency syndrome. Br J Dermatol 2001; 144: 139-42.
6. García Morrás P, Pérez Santos S, Longo Imedio I, et al. Rosacea-like demodicidosis in an immunocompromised child. Pediatr Dermatol 2003; 20: 28-30.
7. Chen W, Plewig G. Human demodicosis: revisit and a proposed classification. Br J Dermatol 2014; 170: 1219-25.
8. Lacey N, Kavanagh K, Tseng SCG. Under the lash: Demodex mites in human diseases. Biochem (Lond) 2009; 31: 2-6.
9. Aylesworth R, Vance JC. Demodex folliculorum and Demodex brevis in cutaneous biopsies. J Am Acad Dermatol 1982; 7: 583-9.
10. 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.
11. Forton FMN, De Maertelaer V. Two consecutive standardized skin surface biopsies: an improved sampling method to evaluate demodex density as a diagnostic tool for rosacea and demodicosis. Acta Derm Venereol 2017; 97: 242-8.
12. Lee JR, Chul H, Yun J, et al. Demodex mite density determinations by standardized skin surface biopsy and direct microscopic examination and their relations with clinical types and distribution patterns. Ann Dermatol 2017; 29: 137-42.
13. Clyti E, Nacher M, Sainte-Marie D, et al. Ivermectin treatment of three cases of demodecidosis during human immunodeficiency virus infection. Int J Dermatol 2006; 45: 1066-8.
14. Friedman P, Cohen Sabban E, Cabo H. Usefulness of dermoscopy in the diagnosis and monitoring treatment of demodicidosis. Dermatol Pract Concept 2017; 7: 35-8.
15. Aydingöz IE, Mansur T, Dervent B. Demodex folliculorum in renal transplant patients. Dermatology 1997; 195: 232-4.
16. Aydingöz IE, Dervent B. Demodex folliculorum in renal transplant patients revisited. Dermatology 2001; 203: 272-3.
17. Chovatiya RJ, Colegio OR. Demodicosis in renal transplant recipients. Am J Transplant 2016; 16: 712-6.
18. Yazisiz H, Çekin Y, Sezer İ, et al. Demodex species frequency and risk factors in patients with rheumatoid arthritis. Arch Rheumatol 2020; 35: 376-84.
19. Hu XM, Li ZX, Zhang DY, et al. Current research and clinical trends in rosacea pathogenesis. Heliyon 2022; 8: e10874.
20. Casas C, Paul C, Lahfa M, et al. Quantification of Demodex folliculorum by PCR in rosacea and its relationship to skin innate immune activation. Exp Dermatol 2012; 21: 906-10.
21. Margalit A, Kowalczyk MJ, Zaba R, Kavanagh K. The role of altered cutaneous immune responses in the induction and persistence of rosacea. J Dermatol Sci 2016; 82: 3-8.
22. Lazaridou E, Apalla Z, Sotiraki S, et al. Clinical and laboratory study of rosacea in northern Greece. J Eur Acad Dermatol Venereol 2010; 24: 410-4.

23. Foley R, Kelly P, Gatault S, Powell F. Demodex: a skin resident in man and his best friend. J Eur Acad Dermatol Venereol 2021; 35: 62-72.
24. Forton FMN. Rosacea, an infectious disease: why rosacea with papulopustules should be considered a demodicosis. A narrative review. J Eur Acad Dermatol Venereol 2022; 36: 987-1002.
25. Blank CU, Haining WN, Held W, et al. Defining 'T cell exhaustion.' Nat Rev Immunol 2019; 19: 665-74.
26. Karincaoglu Y, Seyhan ME, Bayram N, et al. Incidence of demodex folliculorum in patients with end stage chronic renal failure. Ren Fail 2005; 27: 495-9.
27. Amitay-Laish I, Solomon-Cohen E, Feuerman H, et al. Facial demodicosis in the immunosuppressed state: a retrospective case series from a tertiary referral center. Int J Dermatol 2022; 61: 1245-52.
28. Segal R, Mimouni D, Feuerman H, et al. Dermoscopy as a diagnostic tool in demodicidosis. Int J Dermatol 2010; 49: 1018-23.
29. Karadağ Köse Ö, Borlu M. Definition of videodermoscopic features of demodicosis. Int J Dermatol 2019; 58: 1153-9.
30. Kara Y, Özden H. Dermoscopic findings of rosacea and demodicosis. Indian J Dermatol 2021; 66: 165-8.