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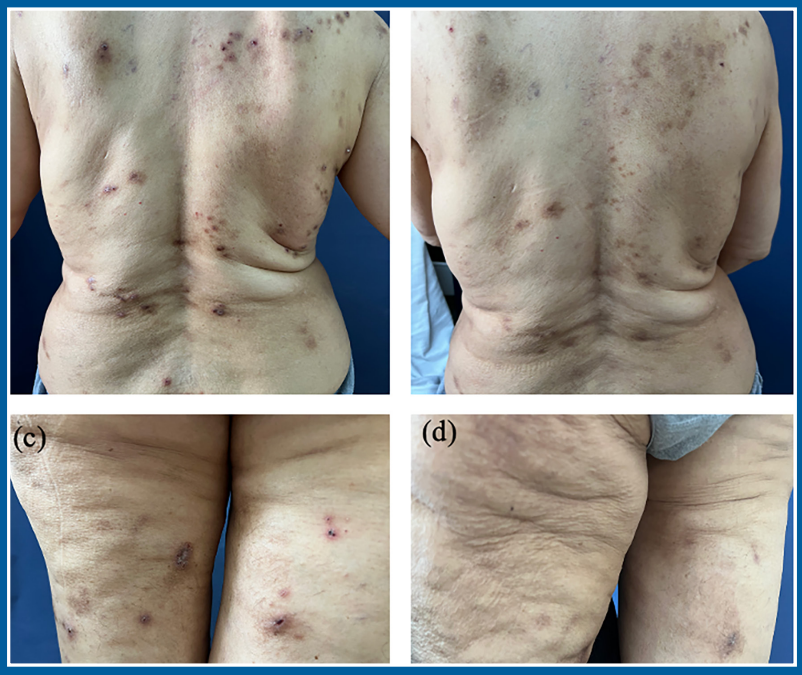

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Original Article

From Pediatrics to Adults: Evaluating Peripheral Globule Characteristics in Melanocytic Nevi and Their Clinical Implications

Dilara İlhan Erdil[1], Ayşe Esra Koku Aksu[2], Vefa Aslı Turgut Erdemir[3], Duygu Yamen[2], Cem Leblebici[4], Asude Kara Polat[5]

[1]Clinic of Dermatology, University of Health Sciences Türkiye, Ankara Etlik City Hospital, Ankara, Türkiye
[2]Clinic of Dermatology, University of Health Sciences Türkiye, İstanbul Training and Research Hospital, İstanbul, Türkiye
[3]Department of Dermatology, İstanbul Medeniyet University Faculty of Medicine, İstanbul, Türkiye
[4]Clinic of Pathology, University of Health Sciences Türkiye, İstanbul Training and Research Hospital, İstanbul, Türkiye
[5]Clinic of Dermatology, Memorial Hospital, İstanbul, Türkiye

Abstract

Aim: Melanocytic nevi in children and adults can differ in growth rate, melanoma risk, and dermoscopic pattern. Peripheral globules (PGs) are common in both groups while being usually benign in pediatric patients and may increase melanoma risk in adults. We aimed to compare baseline and 12-month follow-up, characteristics of melanocytic lesions with PGs (MLPGs) in adult and paediatric age groups.

Materials and Methods: A total of 170 MLPGs were evaluated morphologically; histopathological findings were reviewed when lesions were excised. Of these, 148 MLPGs had 12-month follow-up images and were analysed for changes in size, global pattern, and PGs.

Results: At baseline, MLPGs in adults most commonly showed a homogeneous pattern, whereas MLPGs in children predominantly displayed a globular pattern. The distribution of PGs did not differ between age groups ($P > 0.05$). Adult nevi PG were more atypical ($P = 0.001$), whereas pediatric nevi PG were more regular ($P = 0.001$). After 12 months, no significant changes were observed in adults, while dynamic changes occurred in the paediatric group. Complete regression of PGs was more frequent in pediatric lesions ($P = 0.046$).

Conclusion: MLPGs show distinct age-related behaviour: in adults, lesions remain largely stable while exhibiting more atypical PGs, whereas in children lesions evolve dynamically and PGs regress more frequently.

Keywords: Dermoscopy, melanocytic nevi, pediatrics, pathology, skin neoplasm

Introduction

Pediatric and adult melanocytic nevi may differ in terms of their pattern, growth rate, and presence of peripheral globules (PGs).[1,2] These differences are clinically significant, particularly in the assessment of melanoma risk, where age-related changes in nevi characteristics are evident.[3] PGs manifest as small brown globules in the periphery of the lesion and have been associated with centrifugally growing junctional and dermal melanocytes, as observed through reflectance confocal microscopy (RCM).[4] PGs are frequently observed in pediatric patients who present evident nevogenesis and active growth; these lesions are generally considered benign. In adults, however, the incidence of PGs decreases, and PGs are rarely associated with melanoma findings.[5] Therefore, the presence of PGs in pediatric patients can lead to unnecessary anxiety and excisions despite their benign nature. In our study, we aimed to evaluate and compare the pattern, diameter, and

Address for correspondence: Dilara İlhan Erdil, MD, Clinic of Dermatology, University of Health Sciences Türkiye, Ankara Etlik City Hospital, Ankara, Türkiye
Email: dilara2021@gmail.com
ORCID ID: 0000-0002-9303-1409

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PG morphology and evolution of melanocytic lesions with PGs (MLPGs) in pediatric and adult age groups.

Materials and Methods

Study Design and Data Extent

Patients who presented to the dermatology department between January 2010 and April 2022 underwent whole-body nevus examination and received a clinical diagnosis of MLPGs, were included in the study. A total of 53 patients with MLPGs who had indications for videodermoscopic follow-up were included. These patients were monitored for factors such as the number of nevi, atypical appearances of multiple nevi, or a personal and/or family history of melanoma or dysplastic nevus. The included patients had a total of 170 MLPGs on the trunk. Nevi from facial or extremity/acral regions containing PGs were not included because of their variable patterns. The demographic characteristics of the patients, baseline MLPG patterns, PG morphologies, and histopathological examination results were recorded. The changes in nevus diameter during the follow-up were measured in millimeters along the longest axis. MLPGs were classified into the following patterns: globular, globular-homogeneous, homogeneous, homogeneous-reticular, globular-reticular and reticular. Detailed assessments of the PGs, including their evolution and morphology, were recorded. PGs were classified as either focal or circumferential and further categorized as typical or atypical on the basis of shape and color uniformity, arrangement and regularity, (single or multiple rims of globules). MLPGs that met the melanoma criteria or exhibited significant PGs morphological abnormalities were excised. Patients without follow-up data due to excision, and those missing any data, were excluded from follow-up assessments. In the second evaluation, a total of 148 nevi from 47 patients were included in the study. This study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Türkiye, İstanbul Training and Research Hospital (approval number: 120, date: 08.04.2022). Patients provided informed consent. Patient files and photographs were retrospectively reviewed using medical records from hospitals and videodermoscopy databases. A FotoFinder dermoscope (FotoFinder Systems GmbH, Bad Birnbach, Germany) was used to capture the dermoscopic images.

Statistical Analysis

Statistical analyses were conducted using SPSS version 25.0. The normality of the variable distributions was assessed via the Shapiro-Wilk test. Descriptive analyses included the mean, standard deviation, median, minimum, and maximum values. For variables that followed a normal distribution, an independent samples t-test was used to evaluate differences between two groups. Categorical variables are presented as frequencies and percentages. Relationships between categorical variables were examined via the Fisher-Freeman-Halton exact test. When an expected frequency is less than 5, the Fisher-Freeman-Halton test is used to ensure accurate statistical analysis. *P* values less than 0.05 were considered statistically significant.

Results

Patient Characteristics

A total of 170 nevi from 53 patients with MLPGs were included in the study. According to the baseline data for these 170 MLPGs, adult nevi accounted for 59.4% of the total nevi, whereas pediatric nevi accounted for 40.6%. There was no significant difference in nevus distribution by sex ($P > 0.05$). The mean age of the adult patients was 31.1±10.8 years, whereas the mean age of the pediatric MLPG patients was 12.8±3.8 years. Only nevi on the trunk were included in the study, and MLPGs on the face and extremities were excluded. The average total nevi count was 76.41 for adults and 48.66 for pediatric patients. Patients were categorized according to the number of nevi, as shown in the Table 1.

Baseline Dermoscopy Features

With respect to morphology, 80.2% of PGs were circumferential, 62.4% were regular, and 73.3% had a typical appearance in the adult population. In the pediatric population, 87% of the PGs were circumferential, 89.9% were regular, and 95.7% had a typical appearance. The PGs in the adult group had significantly more atypical appearances ($P = 0.001$), and the pediatric PGs were more regular in appearance ($P = 0.001$). Figure 1 presents examples of nevi with various morphological characteristics.

Histopathological Findings

In adults with excised nevi, the most common diagnosis was dysplastic nevus (11.9%), followed by compound nevus (7.9%), junctional nevus (6.9%), and malignant melanoma (3%). The melanoma patients were aged 30, 37, and 71 years. No malignant melanoma was detected in the pediatric age group. The most common diagnosis in pediatric patients with excised nevi was dysplastic nevus (4.3%), followed by compound and junctional nevus (2.9% each) and Spitz nevus (1.4%). No significant difference was found between the adult and pediatric age groups in terms of diagnosis ($P > 0.05$). Table 1 presents the clinical features of 170 MLPGs in adult and pediatric patients.

Longitudinal Dermoscopic Changes

After the MLPGs that were initially excised or had missing follow-up data were excluded, 148 MLPGs from 47 patients were included. The average age of the adults was 29.07 years, whereas the average age of the pediatric patients was 12.8 years. The initial MLPG size was 4.66 mm in the adult age group and 4.3 mm in the pediatric age group. At 12 months, the average MLPG size was 5.31 mm for adults and 5.07 mm for the pediatric group. No significant difference was found between baseline and 12-month MLPG sizes in either age group. In adults, the most common patterns were homogeneous (53%), homogeneous-reticular (22.9%), and reticular (16.9%), whereas, in the pediatric age group, the most common patterns were globular (58.5%), reticular (16.9%), and homogeneous (12.3%). Homogeneous and homogeneous-reticular nevi were significantly more common in adults (P = 0.001), whereas globular and globular-homogeneous nevi were significantly more common in pediatric patients (P = 0.0001, P = 0.0050). At the 12-month evaluation, the number of nevi with homogeneous-reticular and reticular patterns increased in both age groups. Additionally, in the pediatric age group, the number of nevi with a globular pattern decreased, whereas the number of nevi with a globular-homogeneous pattern increased.

With respect to morphology, in the adult age group, 84.3% of PGs were circumferential, 68.7% were regular, and 80.7% had a typical appearance. In the pediatric age group, 86.2% of the PGs were circumferential, 89.2% were regular, and

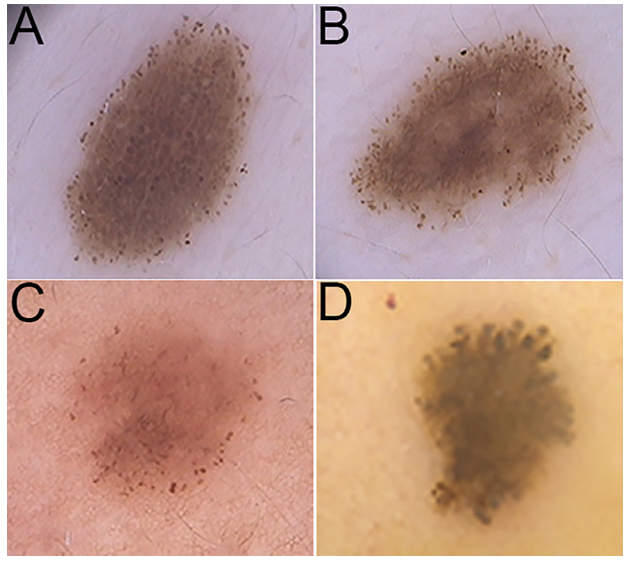

Figure 1. (A) Circumferential, regular (single rim), typical peripheral globules. (B) Circumferential, irregular (double rim), typical peripheral globules. (C) Focal, irregular, typical peripheral globules (dysplastic nevus). (D) Focal, irregular, atypical peripheral globules (melanoma *in situ*)

Table 1. Clinical characteristics and comparisons of nevi with peripheral globules in pediatric and adult age groups

		Adult nevi (n = 101)		Pediatric nevi (n = 69)		
		n	%	n	%	*P*
Female		15	48.4	9	40.9	[b]0.59
Male		16	51.6	13	59.1	
Age, avg ± SD/min.-max.		31.16±10.80	18-71	12.79±3.75	5-17	[a]0.0001
Number of total nevi, avg ± SD/min.-max.		76.41±64.54	8-323	48.66±29.14	5-96	
Number of total nevi	1-10 nevi	2		3		
	10-50 nevi	10		8		
	50-100 nevi	10		11		
	> 100 nevi	9		0		
Peripheral globule distribution	Focal	20	19.8%	9	13.0%	[b]0.250
	Circumferential	81	80.2%	60	87.0%	[b]0.250
Peripheral globule regularity	Regular	63	62.4%	62	89.9%	[b]0.001*
	Irregular	38	37.6%	7	10.1%	
Peripheral globule morphology	Atypical	27	26.7%	3	4.3%	[b]0.001*
	Typical	74	73.3%	66	95.7%	
Histopathological results	Atypical pigmented Spitz nevus	1	1.0%	0	0.0%	[c]0.795
	Compound nevus	8	7.9%	2	2.9%	[c]0.671
	Dysplastic nevus	12	11.9%	3	4.3%	[c]0.640
	Junctional nevus	7	6.9%	2	2.9%	[c]0.607
	Malignant melanoma	3	3.0%	0	0.0%	[b]0.492
	Spitz nevus	0	0.0%	1	1.4%	[b]0.205

[a]: Independent samples t-test, [b]: Exact chi-square test, [c]: Fisher-Freeman-Halton exact test, *: Statistically significant
Min.: Minimum, Max.: Maximum, SD: Standard deviation, Avg: Average

95.4% had a typical appearance. While adult PGs were significantly more atypical ($P = 0.008$), pediatric PGs were significantly more regular ($P = 0.003$). Most PGs completely regressed in both age groups (48.2% vs. 64.6%, respectively). Complete regression was significantly more common in the pediatric age group, whereas a decrease in PG number was more common in the adult age group (30.1% vs. 13.8%). An increase in PG number was relatively rare in both age groups (6% vs. 4.6%). Table 2 summarizes the changes in patterns and morphological features of the 148 MLPGs that were monitored in this study.

Discussion

This comparative study reveals a marked age-related contrast in MLPGs: in adults PGs are more often atypical and lesions remain homogeneous and stable over 12 months, whereas in children the globules are usually regular, regress more frequently, and lesions change dynamically.

The presence of PGs is associated with horizontal growth in nevi, with MLPGs growing at a rate of 0.25 mm²/month before stabilizing. According to Bajaj et al.[6], MLPGs take an average of 58.6 months to stabilize, and PGs are lost during this phase. The MLPGs also have an average size of

Table 2. Comparison of adult and pediatric nevi with peripheral globules after 12 months of follow-up

		Adult nevi (n = 83)		Pediatric nevi (n = 65)		
		Avg ± SD	Median (IQR)	Avg ± SD	Median (IQR)	*P*
Age		29.07±7.95	28 (11)	12.79±3.75	13.5 (4.5)	[a]0.0001*
Baseline average size		4.66±1.76	4.35 (2.13)	4.3±1.93	3.7 (2.75)	[a]0.247
12-month average		5.31±1.73	5 (1.95)	5.07±2.02	5 (2)	[a]0.452
		n	%	n	%	
Sex	Male	13	52.0%	13	59.1%	[b]0.626
	Female	12	48.0%	9	40.9%	
Baseline pattern	Globular	6	7.2%	38	58.5%	[b]0.0001*
	Globular + homogeneous	0	0.0%	6	9.2%	[c]0.005*
	homogeneous	44	5.,0%	8	12.3%	[b]0.001*
	homogeneous + reticular	19	22.9%	2	3.1%	[c]0.001*
	Reticular	14	16.9%	11	16.9%	[b]0.993
12-month follow-up pattern	Globular	4	4.8%	22	33.8%	[b]0.001*
	Globular + homogeneous	0	0.0%	11	16.9%	[c]0.001*
	Globular + reticular	0	0.0%	1	1.5%	[c]0.439
	homogeneous	43	51.8%	11	16.9%	[b]0.001*
	homogeneous + reticular	20	24.1%	4	6.2%	[b]0.003*
	Reticular	16	19.3%	16	24.6%	[b]0.434
Peripheral globule distribution	Focal	13	15.7%	9	13.8%	[b]0.819
	Circumferential	70	84.3%	56	86.2%	[b]0.758
Peripheral globule regularity	Regular	57	68.7%	58	89.2%	[b]0.003*
	Irregular	26	31.3%	7	10.8%	
Peripheral globule morphology	Atypical	16	19.3%	3	4.6%	[b]0.008*
	Typical	67	80.7%	62	95.4%	
Change in peripheral globules	Increased	5	6.0%	3	4.6%	[b]0.707
	Same	13	15.7%	11	16.9%	[b]0.836
	Decreased	25	30.1%	9	13.8%	[b]0.020*
	Disappeared	40	48.2%	42	64.6%	[b]0.046*

[a]: Independent sample t-test, [b]: Exact chi-square test, [c]: Fisher-Freeman-Halton exact test, *: Statistically significant
Avg: Average; SD: Standard deviation, IQR: Interquartile range

4.10 mm, with nevi that are still growing are smaller. In our study, the average nevus size was 4.66±1.7 mm in adults and 4.3±1.9 mm in pediatric patients, indicating that MLPGs are generally small. Another study reported that PG nevi grow at an average rate of 0.16 mm²/month, independent of age, sex, or location.[7] Similarly, in our study, no difference in growth rate was found between the pediatric and adult groups, even though there was a significant increase in nevus size from baseline to follow-up.

When age and PG morphology were evaluated in our study, most MLPGs exhibited circumferential, typical, and regular globules. There were clear age-related differences in PG morphology, with pediatric patients showing significantly more regular, typical PGs than adult patients. However, no significant difference was found between the two age groups in terms of the presence of circumferential or focal globules, which is an important criterion in melanoma detection according to previous studies.[8] All melanomas in our study occurred after age 30 and exhibited suspicious PGs. The observed PGs in the patients with melanoma were all atypical and irregular; in one patient, the PGs were circumferential, whereas in the other two patients, they were focal. In a study of melanomas with PGs, 63.4% occurred in individuals aged 30-50 years, whereas 31.7% occurred in those over 50 years. The presence of atypical globules was identified as a risk factor for melanoma.[9] In a study monitoring 154 high-risk melanoma patients, the following criteria were considered for excision: asymmetry in two axes, the presence of PGs in less than 25% of the circumference with a history of less than 1 year, reappearance of PGs, and irregular size, shape, or color of PGs.[10] PG morphology may vary, and completely circumferential typical globules (single rim or tiered) are less likely to be found in melanoma. Conversely, atypical or asymmetrically distributed PGs increase the risk of melanoma. Even when PGs are present in melanoma patients, at least two melanoma-specific structures accompany the PGs.[8]

The prepubertal age group typically exhibits a dominant globular pattern, whereas the reticular pattern becomes prevalent in adulthood. Globular nevi are most common in pediatric patients, but the prevalence decreases to 0.9% in older age groups, whereas reticular nevi are the predominant pattern after age 30.[3] In our study, pattern modifications during follow-up were more frequently observed in the pediatric age group than in the adult age group. In addition, the transition from globular nevi to reticular nevi was not observed in the pediatric age group. According to cohort studies conducted in adolescents, the rate of transformation from reticular to globular nevus patterns was only 1%, whereas the opposite change occurred in 4% of cases. Although these transformations are rare, an increase in reticular nevi and a decrease in globular nevi were observed over the monitoring period. This finding supports the previously reported concept of dual nevogenesis. In childhood, globular nevi develop from dermal melanoblasts, whereas in adulthood, mature melanocytes in the epidermis create a reticular pattern, primarily due to ultraviolet exposure.[4,11-13] Similar trends were observed in our study, suggesting that MLPGs exhibit age-dependent distribution patterns comparable to those of nevi without PGs.

When examining the rates of PG regression, we observed decrease in or the complete disappearance of PGs in both age groups. Considering that MLPGs stabilize over time and lose the associated PGs, a longer follow-up period could have increased the disappearance rates. When analyzed individually, the disappearance of PGs was more prevalent in the pediatric age group, whereas a reduction in PGs was more frequently observed in the adult age group. Interestingly, the overall rates of PG reduction and disappearance were similar, 78.3% in the adult group and 78.4% in the pediatric group, respectively. These rates are similar to findings reported in a study with an average follow-up of 25 months, which showed a 75% reduction in PGs.

Atypical and irregular features, which are associated with melanoma, were more frequently observed in adult MLPGs. This finding is consistent with the increased melanoma risk observed with age in MLPGs. In our study, PG morphology in both age groups generally showed benign characteristics and regressed or disappeared in the majority of cases within one year. The relationship between MLPGs and the frequency of melanoma in our study indicated that melanoma is rare and is detected in approximately 3% of adults. In a study evaluating MLPGs in high-risk patients, the melanoma rate was 1.9%.[10] Additionally, in an MLPG cohort of 121 lesion which received histopathological evaluation, no melanomas were observed.[6] In a different study evaluating MLPGs, a melanoma rate of 10% was observed, which is higher than previous findings.[9] In summary, although melanoma rates varied based on the age group included in the study and the presence of risk factors, the rates generally remained low. In one study, the number of patients who needed biopsy to detect one melanoma in the pediatric age group was 1,035.[14] These findings indicate that risk factors should be well characterized, especially in the pediatric age group, to decrease unnecessary skin excisions. According to the currently recommended management algorithm, which incorporates age and PG morphology, regular dermoscopic monitoring is recommended for individuals under 35 years of age. This is particularly important for lesions showing an organized rim of globules with a reticular, globular, or mixed central pattern, including PGs. In cases where nevi with PGs present two or more new atypical dermoscopic structures, advanced evaluation and follow-up with RCM are recommended. For

individuals between 35 and 55 years of age, surgical excision of any atypical dermoscopic structures is recommended. Even in the absence of melanoma-specific dermoscopic criteria, evaluation with RCM is advised. For individuals aged 55 and above, surgical excision is recommended for all patients.[5]

Study Limitations

The exclusion of high-risk nevi from follow-up because they were excised could introduce bias in parameters such as growth rate, pattern changes, and PG morphology. This potential bias represents a key limitation of our follow-up data.

Another significant limitation is that, since PGs are more common in younger populations, the average age of our adult patients was relatively young. As a result, we are limited in our ability to comment on older populations, where the risk of melanoma associated with PGs is significantly greater. Other limitations of this study are the small sample size and the retrospective design.

In conclusion, PG morphology changes with age, and higher-risk morphologies may be observed in adults. Larger studies that include older patients are needed.

Conclusion

Our study demonstrates that MLPG exhibit distinct age-related behaviors. In adults, MLPG are more likely to remain stable but can present with atypical and irregular features that may indicate a higher melanoma risk. In contrast, pediatric MLPG display dynamic changes with frequent regression of peripheral globules and generally benign characteristics. These findings highlight the importance of age-specific evaluation in the management of MLPG. Tailored follow-up strategies can help minimize unnecessary excisions in children while ensuring timely detection of suspicious changes in adults. Larger studies that include older patients are needed.

Ethics

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Türkiye, İstanbul Training and Research Hospital (approval number: 120, date: 08.04.2022).

Informed Consent: Patients provided informed consent.

Footnotes

Authorship Contributions

Surgical and Medical Practices: D.İ.E., D.Y., C.L., Concept: D.İ.E., A.E.K.A., V.A.T.E., A.K.P., Design: D.İ.E., A.E.K.A., V.A.T.E., A.K.P., Data Collection or Processing: D.İ.E., A.E.K.A., V.A.T.E., D.Y., C.L., A.K.P., Analysis or Interpretation: D.İ.E., A.E.K.A., V.A.T.E., D.Y., C.L., A.K.P., Literature Search: D.İ.E., A.K.P., Writing: D.İ.E., A.E.K.A., V.A.T.E., A.K.P.

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Original Article

Contamination Fear Among Dermatology Residents: A Comparative Study

Kadir Küçük, Hanife Karataş, Selda Pelin Kartal

Clinic of Dermatology and Venerology, University of Health Sciences Türkiye, Ankara Etlik City Hospital, Ankara, Türkiye

Abstract

Aim: Depression, burnout, and obsessive-compulsive symptoms are common in physicians. This study aimed to examine the fear of contamination among dermatology residents compared to surgical residents and to highlight it as a workplace stress factor.

Materials and Methods: The fear of contamination in dermatology residents was investigated and compared with that of surgical residents. Participants were recruited from two tertiary hospitals in Ankara. Fear of contamination was measured using the Padua Inventory-Washington State University Revision and Contamination Cognition Scale.

Results: Female dermatology residents tended to score highly on the scales. They experienced contamination anxiety more frequently outside the workplace. The perception of not having training in contagious dermatological diseases and the tendency to research this topic are more common than previously thought. In regression analysis, carrying hand sanitizer, using it outside of the workplace, and experiencing similar levels of fear outside the workplace were risk factors for being in the high-scoring group. The practice of laying napkins on the toilet seat and holding the toilet brush with napkins was prevalent in all the units.

Conclusion: In general, residents are concerned about contamination and behavioral avoidance in hospitals. Female dermatologists are more susceptible to fear of contamination. In this situation, medical education is insufficient. It may be beneficial to assess individual perceptions before the start of the residency program. Managers should establish a safe and reliable environment and proper education to reduce anxiety and occupational stress among residents.

Keywords: Healthcare workers, fear of dirt and germs, obsessive-compulsive symptoms

Introduction

Physicians are more prone to depression and burnout than other workers.[1,2] There are studies indicating that obsessive-compulsive symptoms are more commonly observed in physicians.[3] In fact, this has been demonstrated in numerous studies conducted during the coronavirus disease-2019 (COVID-19) pandemic. Healthcare workers showed higher levels of obsessive-compulsive symptoms at the beginning of the pandemic.[4] Females and healthcare workers who felt psychological pressure during the pandemic had higher obsessive-compulsive symptom scores.[5] Obsessive-compulsive symptoms significantly increased during the pandemic compared to the pre-pandemic period.[6] The frequent occurrence of these symptoms even before the pandemic and their intensification in the presence of a contagious disease agent suggest that fear of contamination may represent a silent stressor in the professional lives of healthcare workers.

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Address for correspondence: Kadir Küçük, MD, Clinic of Dermatology and Venerology, University of Health Sciences Türkiye, Ankara Etlik City Hospital, Ankara, Türkiye,
Email: drkadirkucuk@hotmail.com
ORCID ID: 0000-0001-6633-2292

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First, this study aimed to examine the obsessional thoughts of dermatology residents on fear of contamination and to compare them with those of surgery residents. Second, it aimed to indicate the place of fear of contamination, as a stress factor among many other stress factors in the workplace.

Materials And Methods

Selection of Participants

With their informed consent, the study was conducted among residents working in two tertiary hospitals in Ankara (University of Health Sciences Türkiye, Ankara Etlik City Hospital and Gülhane Training and Research Hospital) to compare the fear of contamination in dermatology and surgery residents between January 2025 and June 2025.

The hospitals included in the study were selected because they have similar physical conditions and geographical proximity, and are located in the center of Ankara, serving a similar yet diverse patient population.

Residents in obstetrics and gynecology, in plastic surgery, and from the two hospitals served as the comparison group. General surgery and urology residents were not included in the study group because, in their routine practice, they frequently consulted the dermatology department for infectious diseases, dermatological conditions, and sexually transmitted infections encountered during examination of the anogenital skin and mucosa. In contrast, in their daily practice, plastic surgeons, who more frequently examined the skin and mucosa, and obstetrics and gynecology residents, who routinely examined the anogenital skin, were prioritized as the comparison group among all surgical residents.

Residents with psychiatric disorders and those undergoing psychiatric treatment were excluded from the study. This is because existing psychiatric conditions may lead to extreme values in the psychometric scale scores, potentially affecting the overall means.

Fear of Contamination Measurement

In the research group, fear of contamination was measured using the Padua Inventory-Washington State University Revision (PI-WSUR) and Contamination Cognitions Scale (CCS). The PI-WSUR was revised by Burns et al.[7] based on the original scale established by Sanavio.[8] Translation into Turkish and a validity analysis were conducted by Yorulmaz et al.[9] The scale consisted of five subscales and 39 5-point Likert-type questions, scored between 0 (not at all), 1 (a little), 2 (quite a lot), 3 (a lot), and 4 (very much). The subscales were obsessive thoughts about harming oneself or others (7 items), obsessive impulses to harm self/other (9 items), checking compulsions (10 items), dressing/grooming compulsions (3 items), and contamination obsessions and washing compulsions (10 items).

CCS, developed by Deacon and Olatunji[10], is a 13-item scale associated often with patients' perception of contagious objects, and consists of two parts. The probability of contamination by contact with the object in the first part of the scale, and the threat perception regarding the possible consequences after contamination in the second part, are scored between 0 and 100 in each item. The points that could be obtained in each section ranged from 0 to 1300. It was translated into Turkish by İnözü and Eremsoy[11], and a validity analysis was conducted.

Along with these scales, the participants were given a form consisting of demographic data and other questions. The form was delivered to the participants via an Internet link sent via message and was filled electronically (Supplementary File 1).

The study received approval from the Scientific Research Evaluation and Ethics Committee of Ankara Etlik City Hospital (approval number: AEŞH-BADEK-2024-044, date: 31.01.2024).

Statistical Analysis

Descriptive statistics were used to analyze the demographic data. The chi-squared test was used to examine categorical data. In the chi-square analysis, categories with low frequencies within groups were either combined or analyzed separately in their original forms. The analyses were strengthened by including fewer than five categorical data points in similar groups. For multiple comparisons, the Fisher-Freeman-Halton test and the adjusted z-value significance level were used, along with the Bonferroni correction. The normality of the distribution was examined using the Kolmogorov-Smirnov, or Shapiro-Wilk tests. Averages were compared using an independent samples t-test or Mann-Whitney U test. The Kruskal-Wallis test or one-way ANOVA was used to compare the means between more than two groups. Further examination of intergroup comparisons was conducted using the Tukey or Games-Howell test, depending on the homogeneity of variances.

The participant group was divided into two low-score and high-score groups according to PI-WSUR and CCS scores, based on the study conducted by Deacon and Olatunji.[10] They divided PI-WSUR (COWC) and CCS into low- and high-score groups according to the average scores from healthy and patient groups.[9] Binary logistic regression analysis was performed with gender, age, department, working year, excluding those related to laying a napkin on the toilet seat and using the brush in the toilet, as well as other questions. Among the variables, those that violated the linearity assumption, as

determined by the Box-Tidwell test and variance inflation factor, were excluded. Univariate and multivariate regression analyses were performed using the enter method. Then, the significant variables and all other variables were included in the regression model using the backward stepwise likelihood ratio method. Statistical significance was set at $P < 0.05$.

Results

The survey was administered to 342 residents. A total of 112 volunteers participated in the study, and 15 were excluded from the analysis because they were diagnosed with a psychiatric illness or were taking psychiatric medication. Of the participants, 97 were included in the study, comprising 38 dermatology residents (39.2%) and 59 surgical residents (60.8%). Of the participating surgical residents, 14 (23.73%) were obstetrics and gynecology residents and 45 (76.27%) were plastic surgery residents. The mean age of participants was 28.08±2 in the dermatology department and 28.42±2.3 in the surgery department. There were 29 females (29.9%) and 9 males (9.3%) in the dermatology group and 26 females (26.8%) and 33 males (34%) in the surgery group. The participants' departments, years of residency, and gender distribution are presented in Figure 1, and the distribution and mean scores of the answers are presented in Tables 1 and 2. There was no difference the mean age or years of residency between departments. There was a significant difference between the genders ($P = 0.002$), with males being more commonly represented in surgery and females in dermatology. The internal consistency of the scales (Cronbach α) was calculated as 0.93 for PI-WSUR, 0.92 for the PI-WSUR contamination and cleaning subscale, 0.96 for the first part of the CCS, 0.97 for the second part of the CCS, and 0.98 for the whole CCS. There was a significant correlation between CCS subscale scores and another variable ($r = 0.815$, $P < 0.001$). A positive correlation was observed between the PI-WSUR COWC subscale and the CCS ($r = 0.710$, $P < 0.001$).

The answers to the question "do you have education about contagious dermatologic diseases?" varied between departments ($P < 0.05$), with the answer "yes" being more frequently given by females in surgery and by men in dermatology. There is no difference between the answers given to the question "Have you ever researched contagious dermatologic diseases?".

There was no difference between the departments in the scores given to the scales, (PI-WSUR and CCS). In the gender subgroup analysis between departments, the total score of the PI-WSUR COWC subscale, the first part of the CCS, and the CCS total score differed ($P < 0.05$). This difference was observed, with females scoring higher in dermatology. Similarly, the PI-WSUR COWC subscale, CCS subscales,

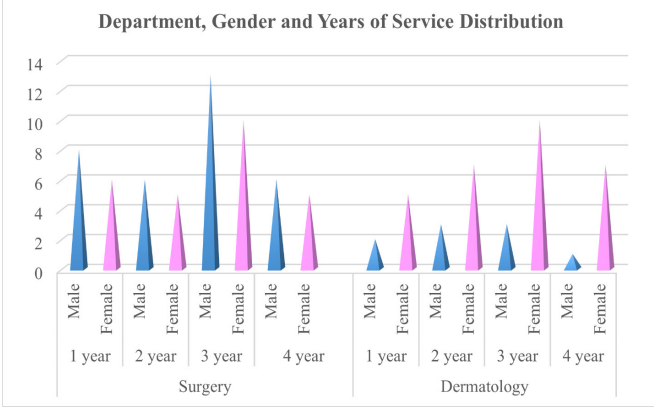

Figure 1. The distribution of unit, working year and gender

Table 1. Mean score of participants' answers to scales and survey questions

	Surgery	Dermatology
	Mean (min.-max.)	Mean (min.-max.)
PI-WSUR* (COWCS++)	13.07±8.95 (0-37)	15.84±9.86 (1-38)
PI-WSUR* (Total)	28.1±20.37 (0-96)	32.34±17.66 (6-88)
CCS+ (1. part)	663.56±319.82 (90-300)	784.74±320.34 (60-1200)
CCS+ (2. part)	641.02±356.01 (10-1300)	746.58±308.88 (160-1300)
CCS+ (total)	1304.58±650.29 (180-2600)	1531.32±587.1 (330-2450)
Senior influence	2.78±3.09 (0-10)	3.82±2.82 (0-10)
Hospital routine cleaning	3.49±2.71 (0-10)	4.29±1.96 (0-9)
Use of staff toilets	6.03±3.52 (0-10)	7.29±2.88 (0-10)
Fear of contamination outside the workplace	5.14±2.88 (0-10)	6.29±3.08 (1-10)
Confidence in protective equipment	6.15±2.15 (0-10)	6.76±2.03 (1-10)

*PI-WSUR: Padua Inventory-Washington State University Revision, ++COWC: contamination obsessions and washing compulsions subscale, +CCS: Contamination Cognitions Scale, Min.: Minimum, Max.: Maximum

Table 2. The distribution of answers

		Yes		No		Total	*P**
Education	Surgery	28 (47.46%)		31 (52.54%)		59 (100%)	**< 0.05**
	Dermatology	28 (73.68%)		10 (26.32%)		38 (100%)	
Research	Surgery	11 (18.64%)		48 (81.36%)		59 (%100)	-
	Dermatology	13 (34.21%)		25 (65.79%)		38 (%100)	
		Never	Rarely	Sometimes	Usually	Always	
Lay a napkin on the toilet seat	Surgery	4 (6.78%)	4 (6.78%)	7 (11.86%)	10 (16.95%)	34 (57.63%)	-
	Dermatology	2 (5.26%)	4 (10.53%)	4 (10.53%)	8 (21.05%)	20 (52.63%)	
Carry hand sanitizer	Surgery	16 (27.12%)	12 (20.34%)	14 (23.73%)	13 (22.03%)	4 (6.78%)	**< 0.05**
	Dermatology	6 (15.79%)	9 (23.68%)	2 (5.26%)	15 (39.47%)	6 (15.79%)	
Using hand sanitizer	Surgery	14 (23.73%)	14 (23.73%)	23 (38.98%)	5 (8.47%)	3 (5.08%)	**< 0.001**
	Dermatology	6 (15.79%)	6 (15.79%)	6 (15.79%)	14 (36.84%)	6 (15.79%)	
		Bare hand	With napkin	Usually not		Never	
Using a toilet brush	Surgery	15 (15.46%)	27 (27.84%)	10 (10.31%)		7 (7.22%)	-
	Dermatology	15 (15.46%)	18 (18.56%)	3 (3.09%)		2 (2.06%)	

**P*: *P* -value

and CCS total scores were higher in female dermatologists than in surgery residents ($P < 0.05$, $P = 0.007$, and $P < 0.05$, respectively). There were no differences between the male dermatologists and surgical residents.

In the other survey questions related to fear of contamination, a significant difference was observed in only three questions. The analyses for these questions were as follows: carrying hand sanitizers with you and using hand sanitizers out of the workplace were two of the three questions that yielded significant differences ($P < 0.05$ and $P < 0.001$, respectively). There were no differences between departments in carrying hand sanitizers. Those who report using hand sanitizers often outside the workplace are more likely to be in the dermatology department. In the analysis conducted within the interdepartmental gender subgroup, the use of hand sanitizers outside the workplace was higher among female dermatologists than among female surgeons ($P < 0.001$). Female dermatologists were more likely to carry and use hand sanitizers than were surgical residents ($P = 0.004$ and $P < 0.001$, respectively). There were no differences between the male dermatologists and surgical residents. The third difference observed was in the responses regarding the effect of seniors, professors, or other friends on the fear of contamination, where dermatologists received higher scores ($P < 0.05$). In the gender subgroup analysis, the scores of the female dermatologists were significantly higher than those of the surgery residents ($P < 0.05$). However, male dermatologists were not distinct in this analysis between groups or conditions.

The three questions that did not differ between the units but showed a difference in the subgroup comparison were about belief in the effectiveness of routine cleaning in the hospital, trust in protective equipment, and experiencing concerns about cleanliness and hygiene in the hospital. Female dermatologists gave higher scores than male surgeons in believing that routine cleaning in the hospital was effective and in trusting protective equipment ($P < 0.05$). Female dermatologists were more concerned about cleanliness and hygiene outside the workplace than surgeons ($P = 0.004$). Male dermatologists did not show any difference in their responses to these questions.

In the gender comparisons within each department, there was no difference in the surgical department. In the dermatology department, the PI-WSUR COWC subscale, and the subscales and total scores of CCS were higher for female dermatologists ($P < 0.05$). Female dermatologists were more concerned about cleanliness and hygiene outside the workplace than inside ($P = 0.003$).

Scores were grouped into high- and low-score categories: 24 individuals in the low-score group and 42 individuals in the high-score group for PI-WSUR COWC; 17 individuals in the low-score group and 54 individuals in the high-score group for CCS (Figure 2). Dermatologists were more common in

the high-scoring group on the CCS scale ($P < 0.05$). In the PI-WSUR COWC subscale, no significant differences were found between departments. There was no difference between genders in the analysis conducted within the departments themselves. In the interdepartmental analysis by gender, the rate of dermatologists was higher in the high score group compared to the low score group for females on both scales ($P < 0.05$); whereas for males, no difference was observed. The regression analysis for the high- and low-scoring group memberships of the participants is presented in Tables 3 and 4, respectively. When all variables were analyzed together in the PI-WSUR COWC subscale, the regression model demonstrated 84.8% accuracy ($P < 0.001$). The accuracy of the co-analysis of significant variables was 81.8% ($P < 0.001$). In these two analyses, the goodness-of-fit test result was not significant. In the final step of the backward stepwise likelihood ratio method, multivariate analysis of all variables yielded an accuracy of 81.8% ($P < 0.001$). The analysis with significant variables yielded results with an accuracy of 81.8% ($P < 0.001$). The goodness-of-fit test was also significant for both analyses ($P = 0.012$).

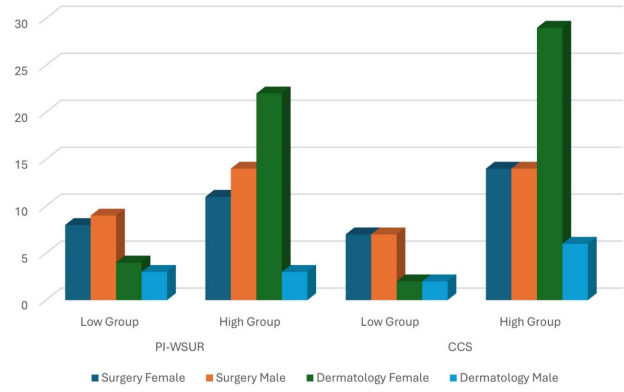

Figure 2. The distribution of participants according to gender, department and score groups (PI-WSUR: Padua Inventory-Washington State University Revision contamination obsessions and washing compulsions subscale, CCS: Contamination Cognitions Scale)

In the regression analysis of CCS, the multivariate analysis of all variables was found to be significant, achieving an accuracy of 85.9% ($P = 0.003$). The accuracy of the co-analysis of significant variables was 81.7% ($P = 0.002$). The goodness-of-fit analysis was not significant for these two analyses. The accuracy of the last model was 81.7% ($P < 0.001$), as determined

Table 3. Regression analysis of contamination scales (univariate and multivariate analysis)

PI-WSUR COWCS+	*P* -value	OR#	Confidence interval (95%)	
Univariate analysis			Lowest	Highest
Carry hand sanitizers*	0.005	6.35	1.73	23.26
Use hand sanitizers outside the workplace*	< 0.001	22.67	4.34	118.42
Fear of contamination outside the workplace	< 0.001	85.89	9.22	800.28
Multivariate analysis				
Use hand sanitizers outside the workplace*	0.030	107.50	1.57	7341.69
Multivariate analysis (significant variables)				
Use hand sanitizers outside the workplace*	0.036	26.82	1.2	577.8
Fear of contamination outside the workplace	0.012	26.523	2.078	338.554
CCS++				
Univariate analysis				
Age	0.026	4.67	1.20	18.11
Fear of contamination outside the workplace	< 0.001	77.37	6.88	870.56
Use hand sanitizers outside the workplace*	0.018	77.37	6.88	870.56
Multivariate analysis				
Age	0.025	0.48	0.256	0.911
Fear of contamination out of work place	0.02	167.24	2.28	12293.9
Carry hand sanitizers*	0.048	0.008	0	0.95
Multivariate analysis (significant variables)				
Fear of contamination outside the workplace	0.003	63.23	3.98	1004.7

*: Usually group, +PI-WSUR: Padua Inventory-Washington State University Revision Contamination Obsessions and Washing Compulsions Subscale, CCS++: Contamination Cognitions Scale, #OR: Odds ratio

Table 4. Regression analysis of contamination scales (multivariate backward stepwise likelihood ratio method)

PI-WSUR COWCS+	*P* -value	OR#	Confidence interval (95%)	
Backward stepwise likelihood ratio method (multivariate)			Lowest	Highest
Fear of contamination outside the workplace	0.012	26.15	2.07	329.8
Use hand sanitizers outside the workplace*	0.022	8.23	1.35	50.12
Backward stepwise likelihood ratio method (significant variables)				
Fear of contamination out of work place	0.012	26.52	2.08	338.6
Use hand sanitizers outside the workplace*	0.022	8.23	1.35	50.12
CCS++				
Backward stepwise likelihood ratio method (multivariate)				
Fear of contamination outside the workplace	<0.001	64.11	5.20	789.99
Backward stepwise likelihood ratio method (significant variables)				
Fear of contamination outside the workplace	<0.001	77.37	6.88	870.56

*: Usually group, +PI-WSUR COWCS: Padua Inventory-Washington State University Revision Contamination Obsessions and Washing Compulsions Subscale, CCS++: Contamination Cognitions Scale, #OR: Odds ratio

by backward-stepwise likelihood ratio method analysis of all variables. In the analysis of significant variables, the accuracy was 85.9% ($P < 0.001$). The goodness-of-fit was significant in both analyses ($P = 0.003$ and $P = 0.018$, respectively). The analysis revealed that experiencing the fear of contamination outside, similar to that experienced in the hospital, increased the probability of entering the high-score group on the fear of contamination scales. Additionally, carrying hand sanitizers and using them after touching something in public areas were also predictors of this outcome. On the other hand, age is a predictor that reduces the likelihood of entering the high-score group in some analyses.

Discussion

There is variation among the residents participating in the study in terms of their perceived level of education regarding contagious dermatological diseases. While dermatologists stated that they were educated in this regard, notably, female dermatologists believe they are not as well trained as their male counterparts. In surgery, women reported being more educated. The majority of the participants did not undertake any research related to contagious dermatological diseases. Among the participants researching this subject, women were more numerous in the dermatology unit, while men and women were similar in number in the surgical department.

Dermatologic disorders and sexually transmitted diseases cause stigmatization in patients.[12] Interestingly, in studies on infectious diseases, such as human immunodeficiency virus (HIV), hepatitis B (HBV), and hepatitis C (HCV), some physicians have negative attitudes towards patients. Excessive fear of contamination, personal prejudices, and a lack of education can hinder these ideas.[13-15] In a study evaluating the attitudes of medical school students towards HIV patients, negative attitudes were observed among students in both pre-clinical and post-clinical years. It was concluded that education was not effective enough to change these attitudes.[16] Another study revealed the negative attitudes of nursing students towards HIV patients and their fear of contamination, and it was reported that this situation decreased with education.[17] Considering that all participants received medical school training, and dermatologists have a better understanding of dermatological literature, the diversity of perceptions about education suggests that education may be insufficient to achieve its goal. In this regard, incorporating such training as part of in-service or even department-level education for residents may improve professional attitudes and reduce stress related to contamination fear.

Female dermatologists are more likely to carry and use hand sanitizers after touching something in public areas. The senior colleagues had a greater influence on their fear of contamination. In the analyses conducted within the departments, there was no difference in fear of contamination in surgery; however, in comparison, female dermatologists received higher scores. The fact that there was no difference in the fear of contamination scales between the units suggests that the presence of women in the surgical unit does not significantly affect the results and may also be attributed to the balancing effect of male dermatologists. Additionally, female dermatologists are more likely to experience concerns about hygiene outside the workplace than their male counterparts.

The number of individuals in the high-score group on both scales was high. Upon further analysis, individuals in the high-scoring group were more likely to be dermatologists,

particularly female dermatologists. In the regression analysis, carrying and using disinfectants, as well as experiencing similar fears outside the workplace, increased the probability of being in the high score group. Although department and gender are not defined as predictors of risk factors, being a woman and a dermatologist may mean experiencing more stress at work due to the high scores given by female dermatologists on the fear of contamination scales.

Studies have reported that obsessive-compulsive symptoms are more common among healthcare workers and women. They have higher levels of fear about dirt, germs, and viruses compared to other workers, and higher rates of compulsive handwashing compared to other workers due to the fear of contamination.[18] A study conducted in Italy found that healthcare workers on the front lines during the pandemic exhibited higher levels of obsessive-compulsive symptoms and experienced a more pronounced fear of contamination. These symptoms were observed more frequently in this group than in other healthcare workers, likely due to their higher risk of exposure to the infectious agent.[19] A study conducted in China reported that healthcare workers exhibited elevated levels of obsessive-compulsive symptoms both during and after the pandemic, with a pronounced fear of infection. The study also identified female gender as a risk factor in this context.[20] A systematic review and meta-analysis yielded similar results regarding the prevalence of obsessive-compulsive symptoms among healthcare workers; however, gender did not emerge as a significant risk factor. This finding suggests that male dermatologists who were relatively underrepresented in the studymay also be at risk, although this could not be demonstrated in this study. The authors also emphasized that this issue among healthcare professionals may negatively affect their mental health and lead to impact on healthcare.[21] Another study from Türkiye found that frontline healthcare workers during the COVID-19 pandemic exhibited higher levels of obsessive-compulsive symptoms compared to other healthcare professionals, which was attributed to more frequent contact with patients, increased use of protective equipment, and heightened fear of infection.[22] A study conducted in the United Kingdom identified fear of contamination as a factor that increases psychological stress and negatively affects healthcare workers' performance and job satisfaction. This fear also reduced their ability to tolerate uncertainty in high-risk environments. Furthermore, it was noted that such fear may lead to precautionary behaviors and deterioration in patient communication.[23]

In a study conducted among dermatologists regarding glove use and hygiene practices, it was found that they generally avoided shaking hands with patients before the examination, preferred to wear gloves during examinations, and reported wearing gloves when examining patients with HIV, HBV, or HCV, primarily to protect the patient. At the same time, the purpose of wearing gloves was to ensure the physician's self-protection, with 78% of physicians citing this reason. The habit of washing hands and using disinfectants is often present in those who wear gloves. Fear of contamination has been reported to be as high as 80%. Half of the physicians believed that wearing gloves did not disrupt the patient-physician relationship. The majority of these statements were made by younger and female dermatologists. However, it is not necessary to wear gloves when examining unbroken skin and when shaking hands.[24]

In another study examining the behavioral avoidance and hand hygiene practices of physicians in hospitals, physicians felt safer against contamination when both they and their colleagues provided adequate hand hygiene. After touching objects with a high probability of contamination (such as medical equipment, after using the toilet, or door handles in restrooms), they either used hand sanitizers or avoided further contact. Carrying hand sanitizers and disinfecting hands after touching telephone receivers were both reported less frequently than other preventive measures. The study highlights the influence of both environmental factors and personal perceptions on the fear of contamination and contamination-related behaviors.[25]

When compared with these findings, the study's results are consistent with the existing literature on fear of contamination. In the dermatology department, female dermatologists tend to place barriers between the patient and their environment, avoiding direct contact and relying more on protective equipment. In both departments, it is common to lay a napkin on the toilet seat while sitting, and to hold a toilet brush with a napkin. There is excessive discomfort regarding other personnel using staff toilets, reliance on protective equipment, and low confidence in routine cleaning in the hospital. The regression analysis findings indicate that carrying disinfectants and experiencing similar fears outside the workplace are factors that increase the likelihood of being in the group with a high fear of contamination. This reveals that personal perceptions contribute to fear of contamination.

Study Limitations

The limitations of the study are that it was not multicentered; more female dermatologists were involved, leading to underrepresentation of male dermatologists; all surgery departments were not included; there were insufficient participants for regression analysis; the answers given to

the study questions were based on self-reported data; it was performed on relatively healthy individuals; the evaluation scales focused on the fear of contamination but not on avoidance behavior. Another limitation of the present study is that the surveys were conducted online, which may have introduced certain biases such as social desirability bias. This potential influence should be taken into account when interpreting the findings, as participants might have responded in a way that they perceived to be more socially acceptable rather than reflecting their true opinions or behaviors.

Conclusion

In summary, based on the current literature and findings, dermatology residents tend to be more concerned about contamination, whereas female dermatologists appear to prioritize this concern more prominently. Education is insufficiently effective in alleviating this fear and avoidance behavior; there is even the perception that one is not educated about it. The fear of contamination in the dermatology department and the residents' behaviors based on this fear may have a negative impact on vulnerable dermatology patient populations, leading to stigmatization.

It may be helpful to create an environment that is safe for dermatologists, with developed hand hygiene facilities for both residents and patients in exam rooms, identify individuals who are predisposed to obsessive thoughts about contamination, and increase education on this subject. Furthermore, training should go beyond basic medical education, as our findings suggest that it does not sufficiently reduce the fear of contagion. Therefore, educational programs addressing commonly encountered concerns in clinical practice may help reduce the fear of contamination in professional settings. These concerns such as the duration of pathogen viability on inanimate surfaces, basic disinfection methods for such surfaces, the effectiveness of disinfectants used after contact, the probability of contracting an infectious disease following contact with contaminated surfaces, and the risk of transmission through bare-handed contact. Another important topic that could be included in such training programs is how physicians' avoidance behaviors and fear of contamination may negatively affect the physician-patient relationship, making patients feel uncomfortable or stigmatized.

Moreover, the question of why surgical residents, particularly female residents, express fewer concerns than do female dermatologists remains unanswered.

Ethics

Ethics Committee Approval: The study received approval from the Scientific Research Evaluation and Ethics Committee of Ankara Etlik City Hospital (approval number: AEŞH-BADEK-2024-044, date: 31.01.2024).

Informed Consent: Written informed consent was obtained from all participants prior to data collection.

Footnotes

Authorship Contributions

Surgical and Medical Practices: K.K., H.K., S.P.K., Concept: K.K., H.K., S.P.K., Design: K.K., H.K., S.P.K., Data Collection or Processing: K.K., H.K., S.P.K., Analysis or Interpretation: K.K., H.K., S.P.K., Literature Search: K.K., H.K., S.P.K., Writing: K.K., H.K., S.P.K.

Conflict of Interest: The authors declared that they have no conflict of interest.

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Supplementary Table 1. Survey questions	
1. Gender (female/male):	Female Male
2. Date of birth D/M/Y:	
3. Department:	Dermatology Surgery
4. When did you start your residency (D/M/Y):	
5. Have you ever had any diagnosis on psychiatric illnesses?	Yes No
6. Are you on medication about psychiatric problems?	Yes No
7. Do you have an education on contagious dermatologic diseases?	Yes No
8. Have you ever researched contagious dermatologic diseases?	Yes No
9. The following statements refer to thoughts and behaviors which may occur to everyone in everyday life. For each statement, choose the reply which best seems to fit you and the degree of disturbance which such thoughts or behaviors may create. Rate your replies as follows: 0= Not at all, 1= A little, 2= Quite a lot, 3= A lot, 4= Very much	
1. I feel my hands are dirty when I touch money	1 2 3 4
2. I think even slight contact with bodily secretions (perspiration, saliva, urine, etc.) may contaminate my clothes or somehow harm me	1 2 3 4
3. I find it difficult to touch an object when I know it has been touched by strangers or by certain people	1 2 3 4
4. I find it difficult to touch garbage or dirty things	1 2 3 4
5. I avoid using public toilets because I am afraid of disease and contamination	1 2 3 4
6. I avoid using public telephones because I am afraid of contagion and disease	1 2 3 4
7. I wash my hands more often and longer than necessary	1 2 3 4
8. I sometimes have to wash or clean myself simply because I think I may be dirty or ‘contaminated’	1 2 3 4
9. If I touch something I think is ‘contaminated’ I immediately have to wash or clean myself	1 2 3 4
10. If an animal touches me I feel dirty and immediately have to wash myself or change my clothing.	1 2 3 4
11. I feel obliged to follow a particular order in dressing, undressing and washing myself	1 2 3 4
12. Before going to sleep I have to do certain things in a certain order	1 2 3 4
13. Before going to bed I have to hang up or fold my clothes in a special way	1 2 3 4
14. I have to do things several times before I think they are properly done	1 2 3 4
15. I tend to keep on checking things more often than necessary	1 2 3 4
16. I check and re-check gas and water taps and light switches after turning them off	1 2 3 4
17. I return home to check doors, windows, drawers, etc. to make sure they are properly shut	1 2 3 4
18. I keep on checking forms, documents, cheques in detail to make sure I have filled them in correctly	1 2 3 4
19. I keep on going back to see that matches, cigarettes, etc. are properly extinguished.	1 2 3 4
20. When I handle money I count and recount it several times	1 2 3 4
21. I check letters carefully many times before posting them	1 2 3 4
22. Sometimes I am not sure I have done things which in fact I know I have done	1 2 3 4
23. When I read, I have the impression I have missed something important and must go back and re-read the passage at least two or three times	1 2 3 4
24. I imagine catastrophic consequences as a result of absentmindedness or minor errors which I make	1 2 3 4
25. I think or worry at length about having hurt someone without knowing it.	1 2 3 4
26. When I hear about a disaster, I think somehow it is my fault	1 2 3 4
27. I sometimes worry at length for no reason that I have hurt myself or have some disease	1 2 3 4
28. I get upset or worried at the sight of knives, daggers, and other pointed objects.	1 2 3 4
29. When I hear about suicide or crime, I am upset for a long time and find it difficult to stop thinking about it	1 2 3 4
30. I invent useless worries about germs and disease	1 2 3 4
31. When I look down from a bridge or a very high window, I feel an impulse to throw myself into space	1 2 3 4
32. When I see a train approaching, I sometimes think I could throw myself under it’s wheels	1 2 3 4
33. At certain moments, I am tempted to tear my clothes off in public	1 2 3 4
34. While driving I sometimes feel an impulse to drive the car into someone or something.	1 2 3 4
35. Seeing weapons excites me and makes me think violent thoughts	1 2 3 4
36. I sometimes feel the need to break or damage things for no reason	1 2 3 4
37. I sometimes have an impulse to steal other people’s belongings, even if they are of no use to me…	1 2 3 4
38. I am sometimes almost irresistibly tempted to steal something from the supermarket	1 2 3 4
39. I sometimes have an impulse to hurt defenseless children or animals.	1 2 3 4

10. Contamination Cognitions Scale

Instructions: Below is a list of objects. Please read the description of each object and try to imagine what would happen if you touched that object and were unable to wash your hands afterward. For each object listed, answer two questions:

(1) What is the likelihood that touching the object would result in your being contaminated? Answer using the following 0-100 scale:

0 10 20 30 40 50 60 70 80 90 100

not at all moderately likely extremely likely

(2) If you actually did become contaminated by touching the object, how bad would it be? Answer using the following 0-100 scale:

0 10 20 30 40 50 60 70 80 90 100

not at all moderately bad extremely bad

Object	Likelihood that touching object would cause contamination (0-100 scale)	If actually contaminated, how bad would it be? (0-100 scale)
Toilet handle in public restroom		
Toilet seat in public restroom		
Sink faucet in public restroom		
Public door handles		
Public workout equipment		
Public telephone receivers		
Stairway railings		
Elevator buttons		
Animals		
Raw meat		
Money		
Unwashed produce (e.g., fruits, vegetables)		
Foods that other people have touched		

12. Do your senior colleagues, professors' hygiene and/or avoidance behaviours at workplace affect your fear of contamination? (0-10) 0-not at all 10-completely

13. How much do you think of the effectiveness of routine hospital cleaning service? %0-100

14. Do you lay napkins on toilet seat in hospital restrooms? (Always Usually Sometimes Rarely Never)

15. How do you use the toilet brush in hospital restrooms?
a) I use it with my bare hand
b) I use it by holding it with a napkin
c) I do not use it most of the time
d) I never use it

16. How many points do you give about "I am not comfortable with the idea that other personnel use the staff toilet other than doctors in the hospital"? (0-10) 0-not at all 10-completely

17. How much do you feel fear of contamination out of the workplace? (%0-100) 0-not at all 100-completely

18. How much do you trust your protective equipment?
(%0-100) 0-not at all 100-completely

19. Do you carry hand sanitizer? (Always Usually Sometimes Rarely Never)

20. Do you use hand sanitizer out of the workplace?
(Always Usually Sometimes Rarely Never)

Original Article

YouTube Videos on Ingrown Toenails: Quality and Content

Cansu Altınöz Güney[1], Huriye Aybüke Koç[2], Güneş Gür Aksoy[3]
[1]Clinic of Dermatology and Venereology, Dinar State Hospital, Ayfonkarahisar, Türkiye
[2]Department of Dermatology and Venereology, Giresun University Faculty of Medicine, Giresun, Türkiye
[3]Clinic of Dermatology, Private Practice, Ankara, Türkiye

Abstract

Aim: Ingrown toenails affect quality of life, leading patients to seek information online, often on YouTube. This study aims to analyze narrator types, viewer engagement, content distribution, and video quality of YouTube videos on ingrown toenails.

Materials and Methods: On May 14, 2024, the first 100 YouTube videos related to "ingrown nail" and "onychocryptosis" were collected, excluding duplicates, non-English, irrelevant, or ads. The number of views, likes, comments, and narrators for non-informative videos (group A) were recorded. Informative videos (group B) were additionally coded across seven categories (symptoms, causes, prevention, foot soaks, podological, conservative, and surgical treatments), and evaluated for quality using DISCERN and global quality score.

Results: Non-informative videos attracted more views and engagement than educational ones. Most informative videos were created by podiatrists, doctors of podiatric medicine and surgery who specialize in the care of feet and ankles, and physicians, mainly focusing on surgical treatment, while nail technicians, professionals trained in cosmetic nail care and pedicure services, emphasized cosmetic and conservative approaches. Health websites more often covered symptoms, causes, and prevention than other topics. Videos from podiatrists achieved the highest quality scores, while dermatologists were notably absent.

Conclusion: Despite YouTube's lack of regulation, it is encouraging that ingrown nail videos are primarily created by doctors, providing information from symptoms to treatment options. However, content varies by narrator. Notably, less informative nail extraction and pedicure videos achieve higher viewer engagement. Podiatrist videos are of higher quality than those by nail technicians and physicians. Dermatologists can contribute by creating accurate, up-to-date videos to enhance public knowledge.

Keywords: Health education, information dissemination, ingrown, nails, social media

Introduction

Ingrown nail, medically termed onychocryptosis, occurs when the nail plate embeds into the nearby soft tissue, usually the lateral nail fold. It is a benign condition, but it can profoundly affect one's quality of life. The pain can be intense, hindering daily activities such as walking, running, and playing, as well as impacting work, choice of footwear, and even sleep.[1] Previous studies have reported a prevalence of 2.5% to 5% for ingrown toenail. In recent years, both the incidence and prevalence have risen, likely due to greater health awareness and possibly linked to lifestyle changes. It is suggested that increased physical activities contribute to these observed trends.[2] Ingrown nails can occur at any age, but they are most prevalent among teenagers and young adults, often affecting the hallux nails.[3]

Patients with ingrown nails often turn to various resources, particularly the Internet, to identify their condition and explore treatment options.[4] In the United States of America (USA), 74% of adults go online to seek health information. Many people use YouTube for medical advice, but concerns about the quality and accuracy of uncertified videos persist.[5]

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Adress for correspondence: Huriye Aybüke Koç, MD, Department of Dermatology and Venereology, Giresun University Faculty of Medicine, Giresun, Türkiye
Email: aybukecibelik@gmail.com
ORCID ID: 0000-0001-8665-3501

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Previous research has explored the reliability of advice on conditions like acne, rosacea, eczema, and alopecia areata.[6-9] Similar to ingrown hair removal and pimple popping videos, non-informative ingrown nail treatment videos are common on YouTube. These videos often garner significant views and engagement, with viewers expressing pleasure and satisfaction while watching.[10]

In this study, we aimed to analyze the distribution of content related to ingrown nail in videos, identify the creators of these videos, and evaluate their viewer engagement and quality.

Materials and Methods

Search Strategy

In this study, we searched for YouTube videos using the terms "ingrown nail" and "onychocryptosis" on May 14, 2024. The decision to restrict the YouTube video search to a single day was made to ensure methodological consistency and reproducibility. Because YouTube is a dynamic platform where results are continuously influenced by algorithms, user engagement, and trending topics, conducting all searches on one date minimizes temporal variability and reduces potential selection bias. Moreover, algorithmic personalization (e.g., location, previous viewing history) is a known methodological limitation in studies analyzing health-related YouTube content, as the algorithm can alter search results and recommendations according to user-specific factors. To minimize this influence, all searches were performed in a logged-out browser session on the same device, without prior watch history. The first 100 relevant videos from each search were selected for evaluation, as viewers typically don't go beyond this point. This approach is consistent with previous studies analyzing health-related YouTube content, where similar cut-offs have been applied. After applying exclusion criteria (duplicate; non-English; irrelevant; and advertisement videos), a total of 131 videos were included for analysis. This sample size was considered sufficient for descriptive analysis, as the median sample size in systematic reviews of YouTube health content has been reported to be approximately 94 videos.[11] The search results were saved in a playlist, and two independent researchers (CAG and HAK) analyzed the videos.

Ethical approval was not obtained for the study as access to the videos is legally available to the public.

Data Collection and Video Evaluation

Videos of podological or surgical procedures without narration were categorized as group A, with views, likes, and narrators recorded. Narrators were categorized into podiatrists (doctors of podiatric medicine and surgery who specialize in the care of feet and ankles), physicians, nail technicians (professionals trained in cosmetic nail care and pedicure services), patients, or health information websites. Group B, consisting of videos with informative content, was additionally assessed for content and quality scores (Figure 1).

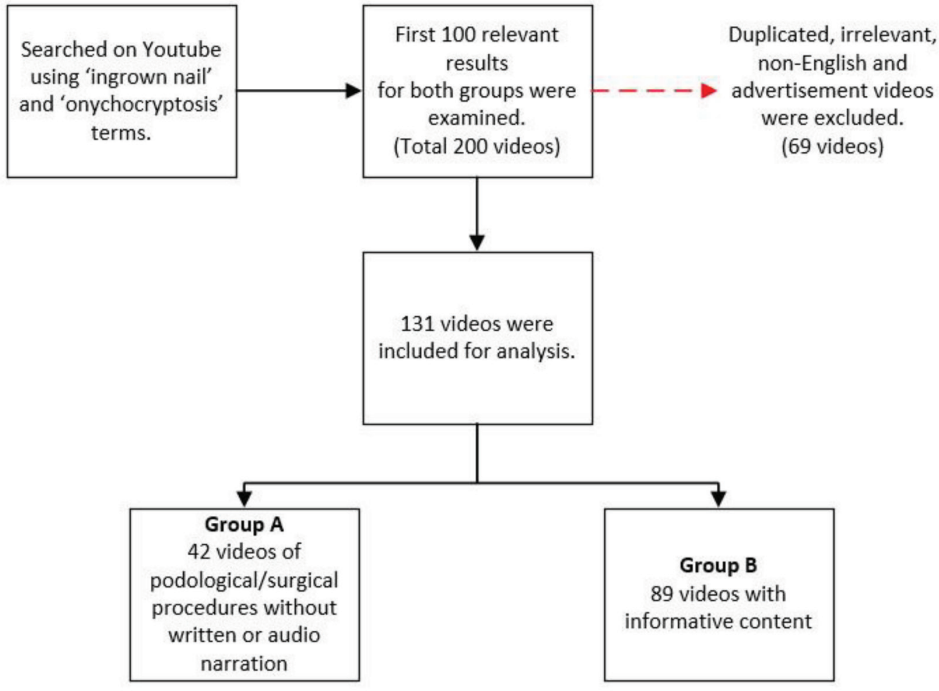

Figure 1. Flowchart depicting the process for identifying and selecting videos on YouTube

To analyze the content of the videos, seven coding categories were developed based on the literature[1,12-14] These categories included signs and symptoms, causes, general measures, soaking recommendations, podological approaches, conservative treatments, and surgical treatments. An additional category assessed whether professional help was recommended by nail technicians, health websites, and patients in the videos. Responses were coded as "yes" or "no" for the inclusion of each category, with specific treatment details also noted.

Viewer engagement was assessed using the engagement ratio, calculated as engagement ratio (%) = (likes + comments) × 100/views. DISCERN, a tool developed by Charnock et al.[15] includes 15 questions, each rated from 0 to 5, to objectively evaluate the quality of health information in videos. However, the original form can be time-consuming and resource-intensive, particularly when applied to large sets of short videos on platforms such as YouTube. For this reason, shortened and modified versions that retain the key quality criteria have been widely used in the literature.[16] A 5-point modified version of DISCERN was used in this study, focusing on clarity, reliability of sources, objectivity, availability of resources, and coverage of controversial topics.[17-19] The modified 5-point DISCERN scale maintains essential domains while allowing for a quicker, more practical, and consistent assessment. Additionally, we assessed the overall quality of the videos using the global quality score (GQS), a 5-point scale (1 = poor quality; 5 = excellent quality). This tool rates the videos' quality, flow, and the usefulness of the information to patients.

Statistical Analysis

Statistical analyses were conducted using MATLAB R2024a (MathWorks Inc., Natick, MA, USA). Descriptive statistical methods such as number, percentage, mean, standard deviation, minimum, and maximum values were used for data evaluation. The level of agreement between the two investigators on DISCERN and GQS values was calculated using intraclass correlation. Comparison between the two groups for ordinal variables and non-normally distributed continuous variables was performed using the Mann-Whitney U test. A P -value of less than 0.05 was considered statistically significant for all analyses.

Results

Out of the 131 videos in our study, 42 were non-informative, featuring procedures like nail trimming, filing, or nail avulsion surgeries, typically watched for their "satisfying" nature (group A). The remaining 89 videos were informative about ingrown nails (group B). Group A had significantly higher views, likes, and engagement ratios ($P < 0.001$). In both groups, podiatrists were the most frequent content creators, followed by nail technicians (Table 1). Among physicians, there were general surgeons, orthopedic surgeons, and general practitioners, but no dermatologists.

Among the 89 informative videos, the types of ingrown nails were as follows: two on retronychia, one on distal embedding, and the rest on lateral ingrowing. Table 2 provides a detailed analysis of video content by narrator.

The intraclass correlation coefficient was 0.78 for DISCERN and 0.85 for GQS, indicating good agreement between the two researchers. The detailed DISCERN and GQS scores for each video narrator type are presented in Table 3. According to the DISCERN, the highest average score was observed among podiatrists. Videos created by podiatrists were found to be of significantly higher quality than videos created by nail technicians ($P = 0.0137$). However, there was no statistically

Table 1. Characteristics of YouTube videos about ingrown nail

	Group A* (n = 42)	Group B** (n = 89)	Total (n = 131)
Video narrator (%)			
Podiatrist	30 (71.43%)	57 (64.04%)	87 (66.41%)
Nail technician	9 (21.43%)	12 (13.48%)	21 (16.03%)
Physician	1 (2.38%)	11 (12.36%)	12 (9.16%)
Health information website	2 (4.76%)	8 (8.99%)	10 (7.63%)
Patient	0	1 (1.12%)	1 (0.76%)
Video metrics (mean)		***P* value[b]**	
Total view counts	1.767.682	677.533	**< 0.001**
Like counts	45.154	6.247	**< 0.001**
Comment counts	523	246.2	0.096
Engagement ratio[a]	2.60	1.40	**< 0.001**

*Group A: Videos of podological or surgical procedures without written or audio narration
**Group B: Informative videos
[a]Engagement ratio = (likes + comments) / total views *100
[b]Mann-Whitney U test

Table 2. Analysis of the content of informative videos (n = 89)

Videos categorized by narrators	Mentions (n) - %
Total (n = 89)	• Sign and symptoms (32)-36% • Causes (31)-34.8% • General measures (17)-19.1% • Soaking (13)- 4.6% • Podological procedures (18)-20.2% • Conservative treatments (15)-16.9% • Surgical treatments (54)-60.7%
Podiatrists (n = 57)	• Sign and symptoms (20)-35% • Causes (18)-31.6% • General measures (11)-19.3% • Soaking (5)-8.8% • Podological procedures (9)-15.8% • Conservative treatments (5)-8.8% Cotton insertion (2) LED light-cured composite brace (2) Taping (1) • Surgical treatments (40)-70.2% Partial nail avulsion with chemical matricectomy (23)* Partial nail avulsion without matricectomy (6) Wedge resection (3) Total nail avulsion without matricectomy (3) Total nail avulsion with chemical matricectomy (1)
Nail technicians (n = 12)	• Sign and symptoms (3)-25% • Causes (2)-16.7% • General measures (1)-8.3% • Soaking (1)-8.3% • Encouragement for seeking professional help (4)-33.3% • Podological procedures (9)-75% • Conservative treatments (5)-41.7% Cotton insertion (2) Dental floss insertion (2) LED light-cured composite brace (1)
Physicians (n = 11)	• Sign and symptoms (4)-36.4% • Causes (5)-45.5% • General measures (2)-18.2% • Soaking (4)-36.4% • Conservative treatments (2)-18.2% Cotton insertion (1) Gutter method (1) • Surgical treatments (7)-63.6% Wedge resection (2) Partial nail avulsion with chemical matricectomy (1) Total nail avulsion with mechanical matricectomy (1)
Health information websites (n = 8)	• Sign and symptoms (5)-62.5% • Causes (6)-75% • General measures (3)-37.5% • Soaking (3)-37.5% • Encouragement for seeking professional help (4)-50% • Conservative treatments (3)-37.5% Conventional nail braces (2) Cotton insertion (1) Taping (1) • Surgical treatments (6)-75% Partial nail avulsion with chemical matricectomy (2)** Partial nail avulsion with matricectomy using electrocautery (1) Wedge resection (1)
Patient (n = 1)	• Encouragement for seeking professional help (1)-100% • Surgical treatments (1)-100%

Signs and symptoms: pain, redness, edema, discharge
Causes: hereditary factors, improper nail cutting, wearing unsuitable footwear, trauma
General Measures:cut toenails straight across, choose shoes with a comfortable toe box
Soaking the Affected Toe: in warm, soapy water or Epsom salt water
Podological procedures: nail plate trimming, filing, and angle correction
Conservative and surgical treatment: methods mentioned or demonstrated in the video
*Specified: 8 phenol, 4 NaOH
**Specified: 1 phenol

Table 3. DISCERN and GQS scores of informative videos by narrator type

Video narrator	DISCERN (Mean ± SD, range)	GQS (Mean ± SD, range)
Podiatrists (n = 57)	3.74±1.078 (0-5)	4.07±1.22 (1-5)
Nail technicians (n = 12)	2.67±1.43 (1-5)	2.92±1.24 (1-5)
Physicians (n = 11)	3.18±1.25 (2-5)	3.27±1.27 (2-5)
Health information websites (n = 8)	3.25±1.58 (0-5)	3.87±1.64 (1-5)
Patient (n = 1)	2 (2)	2 (2)

GQS: Global quality score, SD: Standard deviation

significant difference found between videos created by other narrators. Based on the GQS score, podiatrists had the highest average. Videos produced by podiatrists were significantly superior in quality to those created by nail technicians (P = 0.0035) and physicians (P = 0.042). However, no significant difference was observed in comparisons with other narrators. The single patient experience video was not included in the statistical comparison.

Discussion

Distal-lateral ingrown toenail is the most frequent presentation, and nearly all reviewed YouTube videos focused on this type. While it can occur at any age, it is particularly common among younger individuals.[13,20] Its pathogenesis is linked to nail shape and trimming habits, which predispose individuals to spicule formation and tissue penetration.[12,13] This triggers an inflammatory cascade that may advance from mild erythema and pain to infection, granulation tissue, and hypertrophy of the nail fold, as outlined in the three-stage classification system.[1]

Management of ingrown toenails remains controversial, with ongoing debates regarding both pathogenesis and optimal treatment strategies. The resulting uncertainty can contribute to inconsistent outcomes and dissatisfaction for patients and clinicians alike.[12,13] In parallel, the accessibility of online platforms has led many individuals to seek information and guidance on YouTube, now one of the most widely used sources of health-related content.[21] Our study evaluates these videos to better understand prevailing perspectives and approaches toward ingrown nail management in the digital sphere.

Although YouTube lacks effective screening mechanisms,[22] a substantial portion of ingrown nail content is uploaded by medical professionals. Interestingly, videos depicting nail avulsion or pedicures, often presented without educational value, tend to receive greater viewer engagement. This may reflect the broader popularity of visually stimulating procedures, comparable to the fascination with "pimple popping" content, which has even been linked to specific neural reward pathways.[10]

Our analysis shows that YouTube serves as a source of patient education on ingrown nails, though the accuracy and depth of information vary depending on the narrator. Health information websites emphasized symptoms and causes, physicians highlighted surgical interventions, and nail technicians focused on conservative approaches. A common misrepresentation observed in videos was the mislabeling of excessive granulation tissue as pyogenic granuloma.[12] Although conservative measures such as soaking, taping, cotton packing, gutter guards, and nail braces can be effective in early stages, they require consistent compliance. However, most videos provided only limited guidance on these techniques.[13] Nail avulsion refers to the surgical removal of part or all of the nail plate. Partial avulsion without matricectomy is discouraged for lateral ingrown toenails due to high recurrence. Total avulsion is also unsuitable as it may result in abnormal regrowth or anterior embedding.[13,23] Nonetheless, several YouTube videos were found to demonstrate these procedures. Wedge excision, which entails removal of the lateral nail plate, nail bed, and matrix, is effective for stages IIb and III when performed by experienced surgeons. However, incomplete resection may lead to recurrence, and in our analysis, this technique appeared in six videos.[1,24] Chemical cautery offers a less invasive alternative with high success rates. Phenol remains the most commonly used agent due to its antiseptic and analgesic properties, while sodium hydroxide provides comparable outcomes with faster healing.[1,12,13,25] Some videos referenced these agents, though many did not specify the cautery method. Electrocautery was rarely mentioned and is limited by the risk of periosteal injury and persistent pain.[13]

Videos by podiatrists had higher quality scores than others, reflecting their active contribution and expertise in nail disorders. Surprisingly, no dermatologist-produced videos appeared among the top 200, a finding consistent with prior literature that highlights the limited presence of dermatologists on YouTube. Instead, patient-generated content dominates, often lacking accuracy and reliability. Although professional videos generally receive fewer views and interactions, they tend to provide greater scientific accuracy and educational value.[26-28] In the context of nail diseases, the scarcity of dermatologist-produced content is a critical limitation, as dermatologists play a central role in the differential diagnosis

of nail disorders, identifying systemic associations, and recognizing malignant conditions. Inaccurate or misleading YouTube videos on nail diseases may contribute to misdiagnosis, unnecessary or harmful treatments, and delays in appropriate care. Enhancing the visibility of dermatologists and professional health organizations on platforms like YouTube could therefore help improve patient education on nail diseases, reduce misinformation, and support earlier recognition and management of serious conditions such as nail malignancies. Short, practical, and visually engaging content, ideally developed through multidisciplinary collaboration, may further increase public awareness and the dissemination of reliable information on nail health.

Study Limitations

This study has several limitations: it only included English videos, and the evaluation was done on a dynamic platform, where views and likes are subject to constant change. There is no consensus on the best method to evaluate healthcare-related videos; and, the assessment was subjective. Although two dermatologists independently performed the evaluation using validated tools, we acknowledge that including a broader range of evaluators might further strengthen reliability, which could be considered in future studies. Additionally, since patients weren't involved, it's unclear how well the audience understood the content. Despite these limitations, this is the first study to assess YouTube videos on ingrown nails.

Conclusion

Our findings indicate a notable variation in the content and quality of these publicly available videos. This study highlights the need for high-quality, up-to-date content on ingrown nails and its treatment, which may improve patient education, enhance doctor-patient communication, introduce innovative treatments, and support continuous professional development among medical practitioners.

Ethics

Ethics Committee Approval: Not applicable.

Informed Consent: Not applicable.

Footnotes

Authorship Contributions

Surgical and Medical Practices: C.A.G., G.G.A., Concept: C.A.G., Design: C.A.G., H.A.K., G.G.A., Data Collection or Processing: C.A.G., Analysis or Interpretation: C.A.G., H.A.K., G.G.A., Literature Search: C.A.G., H.A.K., Writing: C.A.G.

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Original Article

Interleukin-16 Serum Levels and Gene Polymorphism in Patients with Acne Vulgaris

Amany Mahmoud Yousef[1], Alaa Maree[1], Nermin Tayel[2], Omnia Mansour Mohammed[3], Basma Abd El Naby Mohamed[4]

[1]Department of Dermatology, Andrology and Sexually Transmitted Diseases, Menoufia University, Shebin El-Kom, Egypt
[2]Department of Molecular Diagnostics and Therapeutics, Genetic Engineering And Biotechnology Research Institute, Sadat City, Egypt
[3]Resident in Dermatology, Ministry of Health, Cairo, Egypt
[4]Department of Medical Biochemistry and Molecular Biology, Menoufia University, Shebin El-Kom, Egypt

Abstract

Aim: Interleukin-16 (IL-16), a cytokine that promotes inflammation, affects immune system cells in a variety of ways. The biological characteristics of IL-16, including its ability to activate CD4+ T-cell migration and proliferation, as well as stimulate the production of proinflammatory cytokines, suggest that it may be a key player in the pathophysiology of several illnesses associated with immunological disorders. The purpose of the study was to evaluate serum levels and gene polymorphism (rs4072111) of IL-16 in acne vulgaris (AV).

Materials and Methods: Forty AV cases and forty controls who were matched for age and sex participated in this cross-sectional study. To assess the severity of acne, the Global Acne Grading System was utilized; serum IL-16 was evaluated using ELISA; and real-time polymerase chain reaction was used to evaluate *IL-16 (rs 4072111)* gene polymorphism.

Results: IL-16 serum levels were considerably greater in acne cases than in controls, according to this study. Additionally, severe cases had a much higher level of IL-16 than mild and moderate cases. Concerning *IL-16* gene polymorphism (rs 4072111), CC genotypes were substantially more in cases than in controls, and significantly enhanced the risk of the occurrence of acne *(P* = 0.025). Compared to variant T, the presence of allele C raises the risk of acne (*P* -value = 0.035).

Conclusion: Compared to the T allele, the presence of the allele C raised the possibility of developing acne.

Keywords: Acne, gene polymorphism, interleukin-16, rs4072111

Introduction

Acne vulgaris (AV), a chronic inflammatory skin disorder of the pilosebaceous follicles, affects people worldwide. It ranks eighth among skin conditions, affecting about 9% of the world's population.[1] The distinct clinical picture of AV can be either inflammatory (papules, pustules, nodules, and cysts) or non-inflammatory (closed/white and open/black comedones), causing skin discoloration and scarring and requiring continuous, long-term care. Lesions are seen on the chest, upper back, face, and neck.[2]

Acne can be attributed to the interaction of several genes and environmental variables, or it might be impacted by polygenic inheritance. Many genes have been studied in acne patients.[3]

Inflammation is a key factor in the pathophysiology of AV. Adaptive and innate immune systems work together to trigger the immune response during inflammation. Proinflammatory cytokines, including interleukin-16 (IL-6), TGF-β, and IL-1β, are produced by antigen-presenting cells resident in the skin, sebocytes, and keratinocytes in response to changes in the follicular microenvironment. Macrophages generate

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Adress for correspondence: Amany Mahmoud Yousef, MD, Department of Dermatology, Andrology and Sexually Transmitted Diseases, Menoufia University, Shebin El-Kom, Egypt
Email: doc.amanyyoussef@gmail.com
ORCID ID: 0009-0003-1607-3634

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proinflammatory cytokines and phagocytose oxidized lipids. The first cells to produce IL-17 were mast cells (MCs), which were followed by innate lymphoid cells and Th cells. Multiple T helper 17- and Th1-derived cytokines are expressed, and the adaptive Th-mediated response is crucial in the early stages of acne.[4]

IL-16 (a multifunctional cytokine) was initially described in 1982. According to the early findings for triggering the chemotaxis of CD4+ T-cells, the factor was initially referred to as lymphocyte chemoattractant factor. Since then, evidence has shown that IL-16 can attract and stimulate a wide variety of other cells expressing the CD4 molecule, such as dendritic cells, eosinophils, and MCs.[5]

Because of its association with CD4+ T-cells and pleiotropic effects on immune system cells, IL-16 may be involved in the pathogenesis of acne. This study is the first to be published in the literature on the role of IL-16 in this illness.[6,7]

The purpose of this study was to evaluate serum levels of IL-16 and its gene polymorphism (rs4072111) in AV and its correlation with acne severity.

Materials and Methods

This cross-sectional case-control study was conducted on patients with varying degrees of AV who visited the dermatology, andrology, and sexually transmitted diseases clinic between March 2024 and August 2024, and on a community-based control group of sex- and age-matched healthy volunteers without prior AV in their medical history.

Sample Size Justification

The sample was determined based on all patients attending the dermatology outpatient clinic in our institution during the defined 6-month period. Therefore, an a priori sample size calculation was not performed since the study aimed to include the maximum available number of AV patients during that timeframe.

Ethical Consideration

Before sample collection, this study was approved by the Menoufia University Faculty of Medicine Research Ethics Committee (approval number: DERMA/2, date: 3/2024) and all participants provided written informed consent.

Exclusion criteria:

1. Patient with any other cutaneous disorders.

2. Patients with any systemic or cutaneous immune-mediated skin diseases.

3. Patients who have used any kind of topical acne therapy over the last month.

4. Patients using any systemic treatment for acne in the previous 3 months.

Every patient was subjected to:

1. Complete medical history, including name, age, sex, acne onset, course (stationary or progressive), duration, and family history.

2. Comprehensive general examination.

3. Thorough dermatological examination to identify the site of AV (shoulders, back, and/or face) and the kind of lesions which may be non-inflammatory (comedones) or inflammatory (papule, pustule, or nodule), and the Global Acne Grading System (GAGS), which depend on the location and the quantity of lesions that were categorized into mild (1-8), moderate (19-30), severe (31-39), and extremely severe (> 39) categories, assesses the severity of acne.[8]

Laboratory Assessment

Blood Sampling

Venipuncture was used to collect seven milliliters (mL) of venous blood under strict aseptic conditions. The blood was processed as follows: For measuring complete blood count, DNA extraction, and genotyping of *IL-16* gene (rs4072111), 2 mL was collected in EDTA tubes. 3 mL was collected into a plain tube and underwent centrifugation for ten minutes at 4000 rpm. The serum was kept cold at -80 °C until additional investigations were carried out.

DNA Extraction Step

The DNA was extracted from whole blood using the GeneJET Genomic DNA Purification Kit (Thermo Scientific, Lithuania; cat. #K0721). Using the Nanophotometer N-60 (Implen, Germany), DNA concentration, quality, and purity were evaluated. The assessment of the purity of DNA-extracted samples by spectrophotometry involves detecting other contaminants and absorbance from 230 nm to 320 nm. DNA will have a A260/A280 ratio of 1.7 to 2.0, indicating good quality.

Real-time PCR Step

***IL-16* gene polymorphism detection:** Single-nucleotide polymorphism (SNP) of the *IL-16* gene (rs4072111) was assessed by the real-time polymerase chain reaction (PCR) technique using a TaqMan probe. The primers, Master Mix II (2x), and probes were supplied by Thermo Fisher Scientific. The probe sequences were marked with [VIC/FAM] fluorescent dyes. The sequences of specific primers were:

IL-16 Gene (rs4072111)

Forward primer: 5'-CACTGTGATCCCGGTCCAGTC-3',Reverseprimer: 5'-GCTCAGGTTCACAGAGTGTTTC CATA-3', and the sequence of the probe was TGCAG TAGG GAATGGTTTGCTTGG[T/C]CTGAGTACAGCA GTGTTGGTGTGTG. Add 12.5 µL of the master mix to 1.25 µL of the genotyping assay of primer/probe mix and 6.25 µL of DNase-free water for each sample. Use 5 microliters of genomic DNA extract, and for the negative control reaction, use 5 microliters of DNase-free water. The cycling conditions were 4 minutes of initial denaturation at 94 °C, 40 cycles of denaturation at 94 °C for 30 seconds, primer annealing and extension at 60 °C for 40 seconds, and the final extension at 72 °C for 3 minutes. The Real-Time PCR Instrument, Applied Biosystems® 7500, with software version 2.0, was used to complete the data analysis.

Human IL-16 ELISA kit: Assayed by Elabscience®

Statistical Analysis

IBM SPSS software version 20.0 was utilized to analyze the data statistically (Armonk, NY: IBM Corp, released 2011). Percentages and numbers were used to summarize categorical data. Using the Shapiro-Wilk test, normality was evaluated for continuous data. Quantitative data were described using the following metrics: mean, standard deviation (SD), median, range (minimum and maximum), and interquartile range. The tests used were: for categorical data, the chi-square test was used to compare groups. For quantitative data that are normally distributed, the Student's t-test is used to compare the two groups under study. For quantitative variables that are not normally distributed, the Mann-Whitney test is used to compare the two groups under study. The equilibrium of the Hardy-Weinberg equation was determined by examining the population of the sample under study.

A *P* -value of less than 0.05 was deemed statistically significant.

Results

Forty AV patients and forty controls who were matched for age and sex participated in this cross-sectional case-control study.

The age of cases ranged from 14 to 35 years, with 20.80±5.82 as the mean ± SD value. Thirteen (32.5%) were female, and 27 (67.5%) were male. The control subjects' ages varied from 15 to 39 years, and their mean ± SD value was 22.47±6.95; (80%) of the controls were men, and 8 (20%) were women. Age and gender did not significantly differ between the cases and controls.

Concerning clinical data, the age of disease onset varied from 12 to 32 years, with 15.83±3.71 years (mean ± SD). The course of the disease was stationary in 20 (50%) cases and progressive in 20 (50%) cases. The mean ± SD value for the disease duration is 4.43±4.21, with a range of 1 to 17 years. Nineteen patients (47.5%) had a positive family history, whereas twenty-one patients (52.5%) had a negative one Table 1.

The acne was detected in the face in 26 (65%) of patients, in the back in 6 (15%), and in the face and back in 8 (20%) of patients Table 1.

As for acne severity, 18 (45%) of the cases were mild, 14 (35%) were moderate, and 8 (20%) were severe; the acne score ranged from 6 to 36, with a mean ± SD value of 20.18±8.69. Of the cases, 26 (65%) had inflammatory acne, 6 (15%) had comedonal acne, and 8 (20%) had both inflammatory and comedonal acne: Table 1.

Given that the average serum level of IL-16 was higher in patients (mean ± SD 17.22±13.10) than in controls (mean ± SD 7.90±7.56), there was a significant difference between the two groups ($P = 0.001$) Table 2.

Concerning the relation between serum concentrations of IL-16 and various clinical parameters within the AVgroup, there was a noteworthy correlation found between the acne severity and IL-16 serum levels, with severe cases exhibiting markedly higher values in comparison to mild and moderate cases ($P = 0.005$), Table 3. Furthermore, IL-16 levels were positively correlated with GAGS scores, as shown in Figure 1.

Regarding the *IL-16 rs4072111* gene, the genotype TT was absent in both cases and controls, while the control group had a noticeably higher prevalence of the TC genotype (30%) when compared with the AV group (10%), with a statistically significant $P = 0.025$. Similarly, the C allele was predominant in both groups but was more frequent in the acne group (95% vs. 85%), with a *P* -value of 0.035, as shown in Table 4. No statistically significant relationship was detected between rs4072111 genotypes, or allele, and different parameters in the AV group.

Discussion

AV is a persistent cutaneous inflammation of the upper pilosebaceous unit, and is among the most prevalent skin conditions with a complicated etiology. A crucial element in the pathophysiology of AV is inflammation. The immune system's innate and adaptive components work in tandem to elicit immunological reactions during the inflammatory phase of acne.[4]

IL-16 belongs to a class of cytokines known as chronic inflammatory cytokines, which also includes TNFα and β, Eotaxin, and IL-1, IL-6, IL-8, IL-11 and IL-17. These cytokines mediate either tissue-specific or systemic inflammation.[9]

Contrary to the majority of other precursor molecules, it has been discovered that both IL-16's mature and pro-molecule forms are biologically active.[10] The precursor protein's N-terminal domain (pro-IL-6) translocates into lymphocytes' nuclei and acts as a transcriptional repressor with cell cycle-regulating properties, while the cytoplasmic C-terminal domain of mature IL-16, which is secreted from the cell, binds to CD4 and can serve as a growth factor, chemoattractant, and differentiation factor on a range of hematopoietic cell types that are implicated in an inflammatory response.[10]

The pro-inflammatory cytokine IL-16 is produced and secreted by CD8+ cells, including MCs, eosinophils, peripheral lymphocytes, and epithelial cells, in response to mitogen or antigen activation. The CD4 molecule, found on macrophages, monocytes, T-cells, and dendritic cells, is the primary receptor for IL-16.[5]

IL-16 has been thoroughly outlined in numerous studies as an immunomodulatory cytokine that aids in the regulation of CD4+ cell activation and recruitment at inflammatory locations, including atopic dermatitis (AD)[11], pemphigoid[12], systemic lupus erythematosus (SLE)[13], cutaneous T-cell lymphomas.[14] However, no data exist about the association between AV and IL-16.

A total of 40 patients with different types of AV and 40 community-based healthy participants, matched in age and sex, participated in the current investigation as a control group.

The outcome of this investigation showed that the IL-16 serum levels of acne cases and controls differed significantly, with acne cases having greater levels. the fact that IL-16 was produced and secreted by T-cells, MCs, eosinophils, monocytes, fibroblasts, dendritic cells, and epithelial cells may account for the elevated blood level of IL-6 in AV patients.[5]

Table 1. Clinical data of cases under the study (n = 40)

	n	%
Age of onset (years)		
Minimum-maximum	12.00-32.00	
Mean ± SD	15.83±3.71	
Median (IQR)	15.00 (13.00-17.00)	
Course		
Stationary	20	50.00
Progressive	20	50.00
Duration in years		
Minimum-maximum	1.00-17.00	
Mean ± SD	4.43±4.21	
Median (IQR)	2.50 (2.0-6.0)	
Family history		
No	19	47.5
Yes	21	52.5
Site		
Face	26	65.0
Back	6	15.0
Face and back	8	20.0
Type of acne		
Inflammatory	26	65.0
Comedonal	6	15.0
Both	8	20.0
Severity		
Mild	18	45.0
Moderate	14	35.0
Severe	8	20.0
GAGS score		
Minimum-maximum	6.00-36.00	
Mean ± SD	20.18±8.69	
Median (IQR)	19.50 (11.50-28.0)	

IQR: Interquartile range, SD: Standard deviation, GAGS: Global Acne Grading System

Table 2. Comparison of interleukin 16 serum levels among acne cases and controls

	Acne vulgaris (n = 40)	Control (n = 40)	U	*P*
IL16 serum levels by ELISA				
Min.-max.	2.14-66.63	1.93-26.76	320.00*	< 0.001*
Mean ± SD	17.22±13.10	7.90±7.56		
Median (IQR)	16.50 (9.33-20.98)	4.56 (9.33-20.98)		

P: *P* -value for comparing between groups
*: Statistically significant at $P \leq 0.05$
IQR: Interquartile range, SD: Standard deviation, U: Mann Whitney test, Min.: Minimum, Max.: Maximum

Each of these cells contributes to the pathophysiology of acne. IL-16 can increase the synthesis of many cytokines that promote inflammation by mononuclear cells, including IL-1β, tumor necrosis factor-alpha (TNF-α), and IL-6.[15] These cytokines have an important role in acne pathogenesis.

IL-1β promotes keratinocyte proliferation, which leads to clogging of the follicular opening and microcomedone development.[16]

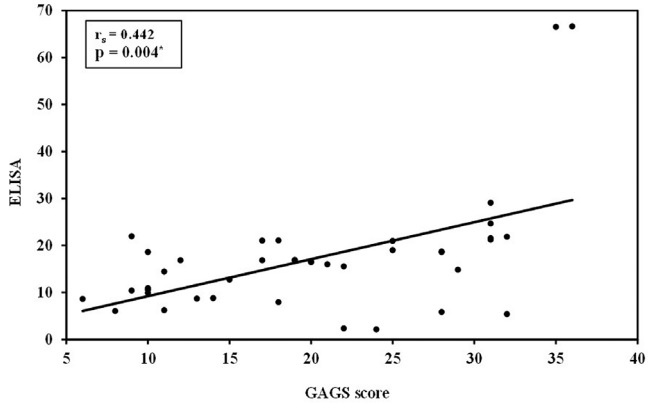

Figure 1. Correlation between IL-16's serum levels by ELISA and GAGS score in acne vulgaris group (n = 40)
IL: Interleukin, GAGS: Global Acne Grading System

The study of Triatmakusuma et al.[17], demonstrated a positive correlation between serum IL-6 levels and the severity of AV. IL-6's role in acne is illustrated by its ability to facilitate the production of various cytokines, proteases, and free radicals. IL-6, induces T-cell differentiation, B-cell maturation, and immunoglobulin production.

IL-16 promotes Th2 and Th17 cytokine production.[18] IL-17 is a crucial cytokine that aids in the pathophysiology of AV. IL-17 can target keratinocytes, endothelial cells, monocytes, and fibroblasts to produce pro-inflammatory mediators and recruit neutrophil infiltration. Th17 cell activation is also influenced by the elevated expression of pro-inflammatory cytokines IL-1β, IL-6, and TNF-α, which are induced by IL-16.[19]

Thus, IL-16 may contribute to the pathophysiology of acne.

Additionally, our results demonstrated that serum IL-16 levels increased in proportion to the severity of AV, with a statistically significant difference between moderate and severe cases and between mild and severe ones.

Similar to our results, AD patients showed elevated serum levels of IL-16 in association with the disease severity (as determined by SCORAD score)[11], The SLE disease activity index score showed a correlation between IL-16 and SLE

Table 3. Relation between serum levels of IL-16 and different clinical parameters in acne vulgaris group (n = 40)

	n	Serum levels of IL-16 by ELISA		Test of significance	*P*
		Mean ± SD	Median (minimum-maximum)		
Gender					
Male	27	19.38±14.75	16.85 (5.40-66.63)	U = 127.500	0.168
Female	13	12.71±7.32	10.48 (2.14-24.64)		
Site					
Face	26	19.31±15.43	17.57 (2.34-66.63)	H = 2.618	0.270
Back	6	11.46±6.11	13.57 (2.14-16.92)		
Face and back	8	14.73±5.23	15.83 (7.92-21.22)		
Course					
Stationary	20	20.69±17.04	17.66 (2.34-66.63)	U = 149.500	0.174
Progressive	20	13.74±6.04	15.63 (2.14-21.83)		
Type of acne					
Inflammatory	26	19.22±15.37	16.59 (2.14-66.63)	H = 1.140	0.566
Comedonal	6	13.67±5.39	13.62 (7.92-21.22)		
Both	8	13.38±6.97	12.62 (5.40-21.83)		
Severity (GAGS grade)					
Mild	18	12.85±5.28	10.69 (6.03-21.93)	H = 10.590*	0.005*
Moderate	14	14.32±6.16	16.50 (2.14-20.94)		
Severe	8	32.10±22.33	23.24 (5.40-66.63)		
Family history					
No	19	14.35±5.47	15.54 (6.03-24.64)	U = 173.500	0.486
Yes	21	19.81±17.11	16.75 (2.14-66.63)		

P: *P* -value for the relation between ELISA and different clinical parameters
SD: Standard deviation, U: Mann-Whitney test, H: Kruskal-Wallis test, GAGS: Global Acne Grading System, IL: Interleukin
*: Statistically significant

Table 4. Comparing the IL-16 genotypes of patients and controls

	Acne vulgaris (n = 40)		Control (n = 40)			
	No.	%	No.	%	χ^2	*P*
Genotypes						
TT	0	0.0	0	0.0	5.0*	0.025*
TC	4	10.0	12	30.0		
CC	36	90.0	28	70.0		
$^{HW}p_0$	0.739		0.264			
Allele						
T	4	5.0	12	15.0	4.444*	0.035*
C	76	95.0	68	85.0		

χ^2: Chi-square test
$^{HW}p_0$: *P* value for χ^2 for goodness of fit for Hardy-Weinberg equilibrium (HWE) (If $P < 0.05$-not consistent with HWE)
P: P -value for comparison between the two studied groups
*: Statistically significant
IL: Interleukin

activity.[20] Furthermore, Richmond et al.[14] showed that IL-16 closely matches the Sézary syndrome disease stage.

Considering the important roles recognized for cytokines in the process that regulates the immune response, potential alterations in cytokine expression or genes may have traceable consequences on a person's vulnerability to inflammation. Numerous studies have demonstrated that genetic changes can either increase or decrease the likelihood of developing acne.[3]

The human genome's chromosome 15q26.3 contains the gene that codes for the cytokine IL-16, which has eight exons and spans about 17 kb. The SNP rs4072111 is located at position 434 of the longer isomorph's second PDZ domain. The IL-16 protein exists in two different forms, known as isoforms 1 and 2: leukocyte IL-16 and neuronal IL-16, respectively.[21]

The coding and regulatory regions of the *IL-16* gene contain polymorphisms that may affect gene transcription and result in individual differences in IL-16 production.[22]

Numerous autoimmune, neurological, viral, inflammatory, and cardiovascular disorders have been linked to functional polymorphisms in the *IL-16* gene.[23]

To our knowledge, this research is the first to look at the possible impact of *IL16* gene variants (rs4072111) in AV patients.[3]

The results of our study demonstrated that the frequency of the genotype (CC) was substantially greater in patients than in controls and significantly enhanced the risk of acne occurrence. additionally, compared to variant T, the presence of allele C raises the risk of acne.

Polymorphisms in the *IL-16* gene could be connected to a higher risk of developing inflammatory and autoimmune disorders, according to several studies. According to Xue et al.[13], the T allele of rs4072111 was commonly found in patients with SLE, suggesting a genetic link between polymorphisms in the *IL-16* gene and SLE vulnerability. Furthermore, Chen and Chen[24] found that the risk of peri-implantitis in the Chinese population was linked to the CT genotype of the *IL-16* gene, rs4072111 SNP.

More rs4072111 CT genotype carriers were found in those with periodontitis than in the healthy control group, according to a study conducted in the Brazilian population.[25]

Glas et al.[26] observed a relationship between Crohn's disease and the IL-16-295 SNP. Furthermore, IL16 polymorphisms may be involved in the pathogenesis of alopecia areata (AA) or the manifestation of AA symptoms in the Korean population, according to Lew et al.[27] likewise, Reich et al.[28] demonstrated that individuals with polysensitized allergic contact dermatitis had a much higher prevalence of the IL-16-295 CC genotype in contrast to healthy controls. Given that inflammation has a key role in acne pathogenesis, this could account for our findings.

In contrast to our findings, some researchers discovered a non-significant correlation between a variation in the *IL-16* gene and certain allergy disorders, such as atopy or asthma.[29]

Additionally, our research's findings contradicted those published by Purzycka-Bohdan et al.[30], who did not notice variations in psoriasis genotype and allele frequencies of patients for the -295 T/C *IL-16* gene polymorphism. This difference may result from variations in the ethnic backgrounds of the populations under study, as well as variations in the SNPs within the *IL-16* gene that were investigated in these illnesses.

Since IL-16 may be linked to the pathophysiology of acne, an inflammatory disease, blocking its effects with monoclonal antibodies would likely be a suitable treatment for cases of AV. This is because blocking IL-16 may attenuate inflammatory responses, reduce recruitment of target cells to the inflammatory sites, and decrease the secretion of pro-inflammatory cytokines.

Additionally, the increased IL-16 levels in proportion to AV severity suggest that IL-16 may be used as a marker for acne severity.

Study Limitations

This study has some limitations. First, the small sample size may limit the statistical power and generalizability of the findings. Second, as this is a single-center study conducted on

Egyptian patients, the results may not be representative of other populations or ethnic groups. Finally, other environmental and clinical factors that may contribute to acne pathogenesis were not evaluated in the present study. Therefore, further large-scale, multicenter studies are needed to validate and expand our findings.

Conclusion

Our study's results indicate a strong correlation between AV and the *IL-16* gene polymorphism (rs4072111), with AV patients more likely to have the CC genotype and C allele than healthy controls. Furthermore, AV patients had considerably higher IL-16 levels, which were also related to the severity of the condition, suggesting that this cytokine may play a role in the pathophysiology of acne. These findings demonstrate the immunological and genetic components of AV and imply that IL-16 could be a useful biomarker for the severity and susceptibility of the condition.

Ethics

Ethics Committee Approval: This study was approved by the Menoufia University Faculty of Medicine Research Ethics Committee (approval number: DERMA/2, date: 3/2024).

Informed Consent: Written informed consent was obtained from all participants.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.M.Y., A.M., N.T., O.M.M., B.A.E.N.M., Concept: A.M.Y., A.M., N.T., O.M.M., B.A.E.N.M., Design: A.M.Y., A.M., N.T., O.M.M., B.A.E.N.M., Data Collection or Processing: A.M.Y., A.M., N.T., O.M.M., B.A.E.N.M., Analysis or Interpretation: A.M.Y., A.M., N.T., O.M.M., B.A.E.N.M., Literature Search: A.M.Y., A.M., N.T., O.M.M., B.A.E.N.M., Writing: A.M.Y., A.M., N.T., O.M.M., B.A.E.N.M.

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Original Article

Hair Transplantation in Women: A Retrospective Study of Surgical Outcomes and Patient Satisfaction Using FUT and FUE Techniques

Ekrem Civas[1], Ümit Akpınar[1], Yıldız Hayran[2], Berna Aksoy[3], Neslihan Müge Fişek İzci[4], Hasan Mete Aksoy[1]

[1]Private Clinic, Ankara, Türkiye
[2]Clinic of Dermatology and Venereology, Ankara Bilkent City Hospital, Ankara, Türkiye
[3]Department of Dermatology, Biruni University Faculty of Medicine, İstanbul, Türkiye
[4]Department of Dermatology, Bahçeşehir University Faculty of Medicine, İstanbul, Türkiye

Abstract

Aim: Female pattern hair loss (FPHL) is the leading cause of alopecia in women, often resulting in psychological distress. In advanced stages, hair transplantation is the only effective restorative option. This study evaluated outcomes of follicular unit transplantation (FUT) and follicular unit extraction (FUE) in women.

Materials and Methods: FPHL is the leading cause of alopecia in women, often resulting in psychological distress. In advanced stages, hair transplantation is the only effective restorative option. This study evaluated outcomes of FUT and FUE in women.

Results: The mean age was 37 years. Indications included FPHL (46.8%) and hairline restoration (32.3%). FUT was performed in 28 patients (45.2%) and FUE in 34 (54.8%). The median graft count was 1,700. Three-hair grafts were more frequent in younger patients with good donor quality and in FUE cases. No major complications occurred. Median closure rate was 99%. Overall, 67.7% reported high satisfaction. Higher satisfaction correlated with better donor density and quality, thicker/wavier hair, and greater graft numbers. Logistic regression showed hairline indication [odds ratio (OR) 4.94, $P = 0.029$] and curly/wavy hair (OR 5.82, $P = 0.015$) as independent predictors.

Conclusion: Both FUT and FUE are safe and effective in women. FUE offers broader indications and higher satisfaction. Careful patient selection, donor evaluation, and realistic expectations remain essential for optimal outcomes.

Keywords: Alopecia, female, hair transplantation, hair surgery, women

Introduction

Hair plays a central role in women's beauty, sexuality, and, above all, femininity. Many women report that having healthy, attractive hair is essential for their overall well-being. Conversely, when their hair does not look good, women may experience anxiety, feel less attractive, and develop low self-esteem. The importance of hair is underscored by findings, showing that 40% of women report difficulties in maintaining their marriages, and 63% report that their careers are negatively affected by hair loss.[1] These observations highlight the necessity of developing, testing, and evaluating all available options for the treatment of alopecia in women.

Epidemiological studies have shown that approximately 12% of women in their 30s and nearly 40% of women in their seventh decade experience hair loss.[2] Causes of alopecia in women include scarring alopecias (primary and secondary) and non-scarring forms such as female pattern hair loss (FPHL), telogen effluvium, anagen effluvium, and alopecia

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Adress for correspondence: Ümit Akpınar, MD, Private Clinic, Ankara, Türkiye
Email: drumitakpinar@gmail.com
ORCID ID: 0000-0002-5816-760X

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areata.[3] Among these, FPHL is the most common cause and is characterized by progressive thinning and decreased density from the hairline toward the vertex.[1-3]

The diagnostic work-up of female hair loss is rigorous and includes a thorough medical and family history, hair pull test, trichogram, trichoscopy, laboratory investigations, and, in cases where scarring alopecia is suspected, scalp biopsy.[4] No single classification system is sufficient for categorizing FPHL in women. In clinical practice, the Ludwig, Hamilton, and Olsen classifications are commonly employed.[5]

Treatment options for female hair loss (particularly FPHL) include topical and systemic medications, interventional approaches, and hair transplantation.[2,4,5] While medical therapies may help normalize hair distribution in the early stages of FPHL, outcomes in advanced disease remain unsatisfactory, even when progression is halted. In late-stage cases, particularly Ludwig stage II and III, hair transplantation becomes the only effective means of restoring lost hair and improving aesthetic appearance.[4,5]

The body of literature evaluating the efficacy of follicular unit transplantation (FUT) and follicular unit extraction (FUE) in women is steadily growing.[5-7] In this manuscript, we aimed to investigate the efficacy, safety, and patient satisfaction associated with FUT and FUE in female hair transplantation through a retrospective analysis. To aid in the practical understanding of these techniques, we provide a concise comparison in Table 1, highlighting their respective advantages and limitations. This summary is intended to guide dermatologists and clinicians who may be less familiar with surgical hair restoration in women.

Materials and Methods

Study Design and Setting

The study protocol was approved by the Bahçeşehir University Ethics Committee (approval number: 2024-04/10, date: 13.05.2025).

The study was conducted in accordance with the latest version of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to surgery, and additional verbal consent was obtained when patients were contacted by phone for the satisfaction survey.

Female patients who underwent hair transplantation at a private clinic in Ankara, Türkiye, between 2005 and 2023, were included in the study through a retrospective chart review. Demographic and clinical characteristics, surgical method, donor area and graft details, presence of complications, follow-up duration, and closure rates were extracted from patient records.

Subsequently, patients were contacted by telephone and their satisfaction with the procedure was assessed using a 5-point Likert scale (1 = not satisfied at all, 2 = not satisfied, 3 = neutral, 4 = satisfied, 5 = very satisfied). For analysis, patient satisfaction was categorized into two groups: low satisfaction (Likert 1-3) and high satisfaction (Likert 4-5).

Surgical Procedures

Patient Selection

The study included female patients diagnosed with FPHL/AGA who sought to improve the appearance of their hairline, undergo eyebrow transplantation, or correct visible secondary alopecic scars. Eligible patients were those with realistic expectations, adequate donor capacity to meet the anticipated outcomes, and no medical contraindications for surgery.

Diagnosis was established through clinical examination, family history, dermoscopy, and laboratory investigations. Prior to surgery, details of the FUT and FUE techniques were explained to all patients, potential complications were discussed, and written informed consent was obtained.

Donor Evaluation

Follicular unit and hair density were measured using a hair densitometer. Additional donor characteristics-including hair

Table 1. Comparison of FUT and FUE techniques in female hair transplantation

Feature	FUT	FUE
Donor harvesting	Linear strip excision	Individual FU excision
Scar	Linear scar	Multiple dot-like scars
Need for shaving	No	Yes (regional/complete)
Recovery	Suture removal, longer healing	Faster healing, no sutures
Main advantage	Large graft numbers in one session	No linear scar, versatile indications
Main limitation	Linear scar	Need for shaving, risk of donor thinning

FUT: Follicular unit transplantation, FUE: Follicular unit extraction

shaft thickness, hair color, skin color, and hair texture (straight or wavy)-were also assessed. These donor parameters were evaluated in conjunction with the size of the alopecic area and the patient's expectations to determine surgical eligibility and planning.

Preoperative Considerations

In all patients, the hairline zone and the front half of the mid scalp were planned as a priority. The decision for the haircut was made together with the patient, considering the availability of donor hair and grafts needed.

Surgical Technique

At the Private clinic all female patients underwent FUT between 1999 and 2009. From 2009 to 2014, FUE was performed in patients who declined FUT. Since 2014, patients have been allowed to choose their preferred method following a detailed discussion of both techniques. The final decision regarding the transplantation method was primarily based on patient preference. To illustrate this decision-making process, Table 2 summarizes the key patient-related factors influencing the choice between FUT and FUE.

For the FUE technique, classic, serrated, and trumpet punches (1 mm in diameter, 4 mm in depth) were used. All punches were operated with a micromotor-assisted rotary handpiece. During the first 100 graft extractions, punch angulation relative to the skin, motor rotation speed, applied pressure, and depth of insertion were carefully optimized.

Postoperative Care

All patients received first-generation cephalosporins for one week postoperatively, along with topical antibiotic ointment applied to the donor site. Patients were also advised to use 2% minoxidil spray twice daily for at least six months following surgery. In women with FPHL, continued medical therapy was recommended to slow or halt progression of existing hair loss, often for an indefinite period.[8]

Follow-Up

At follow-up visits, the presence of complications, donor area closure rate, and patient satisfaction with the procedure were systematically evaluated.

Survey Outcomes

The primary outcomes of this study were the evaluation of the efficacy, safety, and patient satisfaction associated with FUT and FUE in female hair transplantation. The secondary outcome was to identify factors influencing patient satisfaction with both procedures.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS for Windows, Version 22.0; SPSS, Inc., Chicago, USA). Descriptive statistics were presented as number (n) and percentage (%) for categorical variables, mean (standard deviation) for normally distributed continuous variables, and median (interquartile range) for non-normally distributed continuous variables. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test, whereas continuous variables were compared using Student's t-test or the Mann-Whitney U test, as appropriate.

A significance level of $P < 0.05$ was considered statistically significant for all comparisons. Patient characteristics were compared according to satisfaction status. Variables with P -values < 0.15 in univariate analyses were included in a multivariate logistic regression model to identify independent predictors of satisfaction. Model adequacy was evaluated using the Hosmer-Lemeshow goodness-of-fit test.

Results

General Characteristics of the Patients

A total of 62 women were included in the study, with a mean age of 37 years (Table 3). The most common indications for hair transplantation were FPHL (46.8%) and correction of the

Table 2. Patient considerations in choosing between FUT and FUE

Patient factor	FUT	FUE
Desire to avoid linear scar	✗	✓
Willingness to shave donor	✓ (not required)	✗ (shaving required)
Need for maximum grafts in one session	✓	✗ (limited by density)
Preference for faster recovery	✗ (suture removal, longer healing)	✓ (no sutures, quicker healing)
Suitable for eyebrow or scar transplantation	Less common	✓

FUT: Follicular unit transplantation, FUE: Follicular unit extraction

hairline (32.3%) (Table 4). General patient characteristics are summarized in Tables 3 and 4.

Most patients had straight, medium-thickness, black hair. The median Ludwig stage was II, and donor quality and density were classified as medium in the majority of cases. Regional shaving was the preferred method in most women (91.9%). In all patients, the donor area was the parietal-occipital region.

The median total number of transplanted grafts was 1,700, with the majority of grafts containing three hair shafts (median 900 grafts of type III). Grafts containing three hairs were more frequently obtained in younger patients with medium or high donor quality ($P = 0.003$) and donor density ($P = 0.016$).

No complications were observed. The median follow-up period was 20 months. The median donor area closure rate was 99%, with closure of 100% achieved in 50% of patients, 99-90% in 24.2%, 89-50% in 21%, and < 50% in 4.8%. The median satisfaction score was 4 on the Likert scale (satisfied). Overall, 21% of patients reported being very satisfied, 46.8% satisfied, 27.4% undecided, and 4.8% dissatisfied with the procedure.

Table 3. General characteristics of patients [mean ± SD and median (min.-max.)]

	Mean ± SD	Median (min.-max.)
Age	37.11±9.92	34.5 (24-67)
Weight	64.35±9.87	65 (48-92)
Height	167.69±5.34	168 (155-185)
Body mass index	22.88±3.33	22.4 (17.24-35.94)
Ludwig hair loss degree	1.72±0.65	2 (1-3)
Total number of grafts	1651.03±720.45	1700 (200-3200)
I	327.62±130	300 (35-700)
II	602.38±314.49	600 (100-1500)
III	895.48±363.84	900 (345-1700)
Total hair shafts	3739.37±1888.11	3700 (300-7300)
Control period (months)	19.39±9.42	20 (4-40)
Closure % rate	86.9±19.72	99 (25-100)
Satisfaction	3.84±0.81	4 (2-5)

SD: Standard deviation, Min.: Minimum, Max.: Maximum

Table 4. General characteristics of patients (n, %)

Category	Variable	n	%
Indication	Hairline	20	32.3
	Ludwig	29	46.8
	Eyebrow	9	14.5
	Scar	4	6.5
Fitzpatrick skin type	2	9	14.5
	3	25	40.3
	4	25	40.3
	5	1	1.6
	6	2	3.2
Natural hair color	Blonde	1	1.6
	Red	1	1.6
	Auburn	10	16.1
	Gray	1	1.6
	Brown	19	30.6
	Black	30	48.4
Hair thickness	Thin	22	35.5
	Medium	39	62.9
	Thick	1	1.6
Hairstyle	Straight	40	64.5

Table 4. Continued

Category	Variable	n	%
	Wavy	17	27.4
	Curly	5	8.1
Donor area	Parietal-occipital	62	100.0
Hair shaving method	Intermittent	1	1.6
	Regional	57	91.9
	Complete	4	6.5
Donor FU density	Sparse	12	19.4
	Medium	39	62.9
	Intense	11	17.7
Donor quality	Poor	12	19.4
	Medium	34	54.8
	Good	16	25.8
Method	FUT	28	45.2
	FUE	34	54.8
Complication	None	62	100.0

FUT: Follicular unit transplantation, FUE: Follicular unit extraction

Surgical Methods Used

Among the 62 patients, 28 (45.2%) underwent FUT between 2005 and 2016, and 34 (54.8%) underwent FUE between 2011 and 2023. Patient characteristics according to surgical technique are summarized in Table 5.

FUT, as the earlier adopted transplantation method, was performed mainly for FPHL and hairline restoration, whereas FUE was additionally applied for eyebrow and scar transplantation ($P = 0.004$). Donor quality and density were significantly higher in the FUE group ($P < 0.05$). Grafts containing three hairs were more frequently obtained in patients treated with FUE ($P < 0.001$). The follow-up period was significantly longer in FUT patients ($P = 0.001$).

Overall, patients who underwent FUE reported significantly higher satisfaction compared with those who underwent FUT ($P = 0.028$).

Factors Affecting Patient Satisfaction

As described in the methods section, patients were classified into two groups according to satisfaction with hair transplantation: low satisfaction (n = 20, 32.3%) and high satisfaction (n = 42, 67.7%). Factors associated with patient satisfaction are summarized in Table 6.

Higher satisfaction was observed in patients with greater donor density ($P = 0.042$, r = 0.26), better donor quality ($P = 0.038$, r = 0.26), and higher graft numbers ($P = 0.037$, r = 0.27). These findings were consistent with both retrospective data and our clinical experience. A negative correlation was identified between follow-up duration and satisfaction, with higher satisfaction reported by patients assessed at an earlier follow-up ($P = 0.013$, r = -0.31). Satisfaction tended to be higher in patients who underwent FUE compared with FUT, although this difference did not reach statistical significance (Table 6).

According to multivariate logistic regression analysis (Table 7), patients who underwent hair transplantation for hairline restoration were 4.94 times more likely to belong to the high-satisfaction group compared to those treated for other indications [$P = 0.029$, 95% confidence interval (CI): 1.17-20.79]. Similarly, individuals with curly or wavy hair had a 5.82-fold higher likelihood of being in the high-satisfaction group compared with those with straight hair ($P = 0.015$, 95% CI: 1.41-24.15).

Discussion

We report on 62 women who underwent FUT or FUE hair transplantation at our private clinic between 2005 and 2023. In the earlier years, FUT was primarily performed for FPHL and hairline restoration, whereas in later years, FUE was also utilized for eyebrow and scar transplantation. Grafts containing three hairs were more frequently obtained in younger patients with medium-to-good donor quality and density, as well as in those treated with FUE. Donor quality and density were significantly higher among patients who underwent FUE, and consequently, these patients reported greater satisfaction with their procedures.

Satisfaction was also higher among patients treated for hairline restoration and in those with thicker, wavier hair, higher donor density, better donor quality, and a greater number of grafts transplanted.

Tablet 5. Characteristics of patients who underwent FUT and FUE

Characteristics	FUT	FUE	*P*
Age, mean (SD)	36.14 (8.3)	37.9 (11.2)	0.48
Weight, mean (SD)	66.8 (10.2)	62.3 (9.3)	0.074
Height, mean (SD)	166.9 (4.7)	168.3 (5.8)	0.31
BMI, mean (SD)	24.03 (3.9)	21.9 (2.9)	0.012
Indication, n (%) Hairline Ludwig Eyebrow Scar	 8 (28.6) 19 (67.9) 0 1 (3.6)	 12 (35.3) 10 (29.4) 9 (26.5) 3 (8.8)	**0.004**
Ludwig hair loss degree, n (%) 1 2 3	 8 (42.1) 8 (42.1) 3 (15.8)	 3 (30) 7 (70) 0	0.24
Fitzpatrick skin type 2 3 4 5 6	 3 (10.7) 11 (39.3) 14 (50) 0 0	 6 (17.6) 14 (41.2) 11 (32.4) 1 (2.9) 2 (5.9)	0.38
Hair color, n (%) Blonde Red Auburn Gray Brown Black	 0 0 4 (14.3) 0 15 (53.6) 9 (32.1)	 1 (2.9) 1 (2.9) 6 (17.6) 1 (2.9) 4 (11.8) 21 (61.8)	**0.015**
Hair thickness, n (%) Thin Medium Thick	 14 (50) 14 (50) 0	 8 (23.5) 25 (73.5) 1 (1.6)	0.074
Hair style, n (%) Straight Wavy Curly	 19 (67.9) 9 (32.1) 0	 21 (61.8) 8 (23.5) 5 (14.7)	0.099
Hair shaving method, n (%) Intermittent Regional Complete	 0 28 (100) 0	 1 29 4	0.11
Donor FU density, n (%) Sparse Medium Intense	 9 (32.1) 17 (60.7) 2 (7.1)	 3 (8.8) 22 (64.7) 9 (26.5)	**0.023**
Donor quality, n (%) Bad Medium Good	 9 (32.1) 16 (57.1) 3 (10.7)	 3 (8.8) 18 (52.9) 13 (38.2)	0.012
Total graft count, median (IQR)	1575 (1385-2075)	1800 (500-2400)	0.74
1	300 (250-387.5)	300 (200-437.5)	0.86
2	600 (500-800)	550 (150-800)	0.094
3	700 (500-900)	1200 (700-1400)	< 0.001
Total hair shaft count	3615 (3062-4950)	4555 (650-5600)	0.82
Follow-up period, month, median (IQR)	24 (18.5-28.5)	12 (8.75-24)	0.001
Patient satisfaction, n (%) Very satisfied Satisfied Undecided Not satisfied	 3 (10.7) 13 (46.4) 9 (32.1) 3 (10.7)	 10 (29.4) 16 (47.1) 8 (23.5) 0	0.028

FUT: Follicular unit transplantation, FUE: Follicular unit extraction, SD: Standard deviation, IQR: Interquartile range

Table 6. Factors affecting patient satisfaction

Characteristics	Low satisfaction (not satisfied and undecided)	High satisfaction (satisfied and very satisfied)	*P*
Age, mean (SD)	39.7 (8.9)	35.8 (10.2)	0.16
Weight, mean (SD)	66 (11.2)	63.6 (9.2)	0.37
Height, mean (SD)	167.9 (4.5)	167.6 (5.8)	0.84
BMI, mean (SD)	23.4 (4.1)	22.6 (2.9)	0.37
Indication, n (%) Hairline Others (Ludwig, eyebrow, scar)	 3 (15) 17 (85)	 17 (40.5) 25 (59.5)	0.045
Ludwig hair loss degree, n (%) 1 2 3	 4 (33.3) 7 (58.3) 1 (8.3)	 7 (41.2) 8 (47.1) 2 (11.8)	0.83
Fitzpatrick skin type 2 3 4 5 6	 2 (10) 10 (50) 8 (40) 0 0	 7 (16.7) 15 (35.7) 17 (40.5) 1 (2.4) 2 (4.8)	0.64
Hair color, n (%) Blonde Red Auburn Gray Brown Black	 1 (5) 0 2 (10) 0 9 (45) 8 (40)	 0 1 (2.4) 8 (19) 1 (2.4) 10 (23.8) 22 (52.4)	0.29
Hair thickness, n (%) Thin Medium Thick	 11 (55) 9 (45) 0	 11 (26.2) 30 (71.4) 1 (2.4)	0.024
Hair style, n (%) Straight Wavy/curly	 17 (85) 3 (15)	 23 (54.8) 19 (44.2)	0.020
Hair shaving method, n (%) Intermittent Regional Complete	 0 20 (100) 0	 1 (2.4) 37 (88.1) 4 (9.5)	0.27
Donor FU density, n (%) Sparse Medium Intense	 6 (30) 13 (65) 1 (5)	 6 (14.3) 26 (61.9) 10 (23.8)	0.038
Donor quality, n (%) Bad Medium Good	 7 (35) 11 (55) 2 (10)	 5 (11.9) 23 (54.8) 14 (33.3)	0.011
Method, n (%) FUT FUE	 12 (60) 8 (40)	 16 (38.1) 26 (61.9)	0.11

FUT: Follicular unit transplantation, FUE: Follicular unit extraction, FU: Follicular unit, SD: Standard deviation

Table 7. Multivariate logistic regression analysis evaluating patient satisfaction

	OR	95% CI	*P* value
Indications			
Others (Ludwig, eyebrow, scar)	1		
Hair line	4.94	1.17-20.79	0.029
Hair style			
Straight	1		
Wavy/curly	5.82	1.41-24.15	0.015

OR: Odds ratio, CI: Confidence interval

This may be explained by the ability to achieve denser FU placement and to transplant a greater proportion of three-hair grafts when donor quality and density are favorable and using the FUE method.

These findings, while consistent with our clinical experience, should be interpreted with caution. The associations identified have not yet been validated in larger comparative studies, and further prospective research is needed to confirm these observations and establish causality.

As follow-up duration increased, patient satisfaction tended to decrease, which may be because earlier patients had undergone FUT. Approximately 15% of all hair transplant surgery patients are female.[9] Satisfactory results can be achieved in appropriately selected cases, and hair transplantation continues to be the only effective method to restore lost hair for significant female alopecia.

Diagnosis of female hair loss is more complex than the diagnosis of hair loss in men. Distinguishing FPHL from telogen effluvium and alopecia areata incognita is often challenging. Fortunately, trichoscopy has made this differentiation more straightforward in recent years. Surgeons performing hair transplantation in women-especially those who are not dermatologists-should be trained and experienced in trichoscopy. Patients presenting with a receding hairline, a wide forehead, or concerns about a masculinized appearance are generally straightforward candidates for transplantation.

Selecting the right patient is a crucial step in hair transplantation. Realistic expectations are an essential prerequisite; if anticipated surgical outcomes do not align with patient expectations, it may be more appropriate not to proceed with the procedure. Even technically successful results may be perceived as unsatisfactory if expectations are unrealistic.

According to our clinical experience, the following female patients were considered suitable candidates for hair transplantation:

1. Those willing to accept an average cosmetic outcome that can realistically be achieved given the donor-recipient area balance, and who maintain realistic expectations.
2. Patients with Ludwig stage II-III FPHL and high donor density.
3. Patients with a high hairline and average-to-high donor density.
4. Patients with visible secondary scarring alopecia.
5. Patients with primary scarring alopecia in a stable phase.
6. Patients with traction alopecia and sufficient donor supply.

Conversely, the following groups were considered unsuitable candidates for hair transplantation:

1. Patients with diffuse unpatterned alopecia or diffuse alopecia.
2. Patients with insufficient donor supply.
3. Patients with telogen effluvium.
4. Patients with active primary scarring alopecia.
5. Patients with unrealistic expectations.

The suitability of female patients for hair transplantation primarily depends on donor characteristics, which represent the most critical stage of the procedure. In our clinical practice, we have observed considerable variation in donor hair quality among female patients. Based on these observations, we have proposed a donor classification system, which is presented in the Supplementary Appendix. As this classification is derived from clinical experience and has not yet been formally validated, future multicenter and methodology-focused studies are needed to assess its reproducibility and clinical utility.

Patients with moderate to high donor density are suitable candidates for both FPHL and hairline correction. In contrast, patients with low donor density may be suitable only for limited procedures, such as correction of frontal or frontotemporal recession, modest hairline lowering, or localized scarring alopecia.

One of the main limitations of the FUE technique in female patients is the need to shave the donor area to a length of approximately 1 mm. This conclusion is primarily based on

our practical surgical experience, as supporting evidence in the literature remains scarce. Although long-hair punches have been introduced in recent years, they are not yet adequate to yield a sufficient number of grafts for large sessions and are more appropriate for covering small areas.

The decision regarding haircut length should be made in collaboration with the patient, taking into account lifestyle, occupation, and timing of return to work. From the surgeon's perspective, the simplest approach to facilitate graft harvesting and implantation is complete scalp shaving, as in male patients. When this option was explained, a small number of patients preferred full shaving. For women who routinely cover their hair with a hijab or bonnet, shaving was not a major concern. Importantly, patients should be informed that complete shaving can increase the number of harvestable grafts.

In patients with sparse parietal hair or those wishing to avoid social detection of hair transplantation, shaving was limited to the occipital region if sufficient grafts could be harvested. The least noticeable haircut was achieved by leaving hair between shaved strips, provided that the patient's safe donor width was adequate. Avoiding partial shaving in the parietal regions, unlike in men, may lead to excessive thinning of a narrow area in order to obtain the desired graft numbers. Patients should be informed that hair shaft diameter in the donor region may subsequently decrease. Additionally, there is a risk of scar coalescence and postoperative telogen effluvium.

Punches with a standard diameter of 1.0 mm were used with a micromotor. For eyebrow and sideburn transplantation in women, punches smaller than 1.0 mm are preferable. As hair follicle depth in women is shorter than in men, an incision depth of 2-3 mm is generally sufficient to facilitate graft extraction with forceps. For this reason, 4 mm punches were routinely used in our patients, as longer punches may be more difficult to control.

In Ludwig stage II-III patients, dense placement of grafts along the hairline and midscalp provides sufficient coverage, allowing residual sparseness to be concealed by longer hairstyles. Extending transplantation to the vertex in women does not typically provide additional cosmetic benefit. This recommendation is derived from our clinical experience and may not be universally applicable. Closing the transition zone with one- and two-hair FUs, reinforcing the frontal tuft with two- to three-hair FUs, and then advancing grafts posteriorly into the midscalp (and further if indicated by baldness pattern) indirectly creates the appearance of greater density.[10]

Among the specific complications of FUE in women are postoperative donor telogen effluvium, typically resolving within 3-4 months, and cicatricial alopecic patches resulting from coalescence of punch scars when excessive extractions are performed. Limiting excision to approximately 20-25% of the donor area in the first session can minimize these risks.

For women with Ludwig stage II FPHL or hairline correction, approximately 2,000 FUs are required for satisfactory results, which can be achieved in patients with medium to high donor density. Greater numbers of study participants are necessary for Ludwig stage III patients. However, partial haircutting with the FUE method imposes limitations, and when combined with excision restrictions of 1 cm^2 in the donor area, alternative approaches are required. In suitable candidates with medium-to-good donor characteristics, hybrid surgery can be considered. These sessions may be performed on the same day or sequentially; in the latter case, FUT may be performed first, followed by FUE six months later.[11]

Study Limitations

This study has several limitations. First, its retrospective and single-center design restricts the generalizability of the findings. Second, the relatively small sample size (n = 62) may not fully reflect the heterogeneity of female hair loss presentations and surgical outcomes. Third, subjective measures such as patient satisfaction may be influenced by recall bias, given the variability in follow-up durations. Finally, the absence of a control or comparison group limits the ability to directly assess the superiority of one technique over another. Future prospective, multicenter studies with larger sample sizes and standardized follow-up protocols are warranted to validate the proposed donor classification and strengthen the surgical recommendations presented.

Conclusion

Hair transplantation represents a valuable treatment option for carefully selected female patients with alopecia, particularly those with FPHL, high hairlines, or scarring alopecia. In this retrospective study of 62 women, both FUT and FUE proved to be effective and safe techniques. Higher satisfaction was observed among patients with favorable donor quality and density, thicker and wavier hair, and larger numbers of transplanted grafts.

FUE offered greater versatility in indications-such as eyebrow and scar transplantation-and was associated with higher satisfaction rates compared with FUT. Ultimately, careful patient selection, thorough donor evaluation, and the establishment of realistic expectations remain essential determinants of optimal outcomes in female hair transplantation.

Ethics

Ethics Committee Approval: The study protocol was approved by the Bahçeşehir University Ethics Committee (approval number: 2024-04/10, date: 13.05.2025).

Informed Consent: Written informed consent was obtained from all participants prior to surgery, and additional verbal consent was obtained when patients were contacted by phone for the satisfaction survey.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.C., Ü.A., Concept: E.C., Ü.A., Y.H., B.A., Design: E.C., Ü.A., Y.H., B.A., Data Collection or Processing: E.C., Ü.A., Y.H., B.A., N.M.F.İ., H.M.A., Analysis or Interpretation: E.C., Ü.A., Y.H., B.A., N.M.F.İ., H.M.A., Literature Search: Y.H., B.A., N.M.F.İ., Writing: E.C., Ü.A., Y.H., B.A., H.M.A.

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SUPPLEMENTARY 1. Donor classification in females

Good donor	Moderate donor	Bad donor
• > 60 FU in 1 mm^2 • FUs mostly having 2-3 hairs	• 40-50 FU in 1 mm^2 • FUs mostly having 2-3 hairs	• < 40 FU in 1 mm^2 • FUs mostly having 1-2 hairs

FU: Follicular unit

Original Article

Comparative Evaluation of Oral Baricitinib and Tofacitinib in Alopecia Areata: A Retrospective Cohort Study Based on SALT Scores

Merve Küçükşahin, Erhan Ayhan

Department of Dermatology, Dicle University Faculty of Medicine, Diyarbakır, Türkiye

Abstract

Aim: Alopecia areata (AA) is an autoimmune, non-scarring hair loss disorder in which interferon-γ/interleukin-15 signaling amplifies inflammation via the Janus kinase (JAK)/STAT pathway, providing a mechanistic rationale for oral JAK inhibition. To assess the real-world effectiveness and safety of oral baricitinib and tofacitinib in AA and to examine clinical and lifestyle predictors of treatment response.

Materials and Methods: We retrospectively reviewed 65 patients (age 7-55 years) with AA/AT/AU who received tofacitinib or baricitinib at a tertiary dermatology clinic (Dicle University, Türkiye) between 15 August 2021 and 29 March 2024. Disease severity was assessed by the Severity of Alopecia Tool (SALT). The primary outcome was the change in SALT from pre- to post-treatment. Responses were categorized into no (0-24.9%), partial (25-49.9%), good (50-74.9%), or excellent (75-100%) reduction. Analyses were used paired t-tests, one-way ANOVA, with Bonferroni post-hoc tests, Pearson correlations, and χ^2/Fisher's exact tests (two-tailed, $P \leq 0.05$). Ethics approval was obtained, and procedures conformed to the Declaration of Helsinki.

Results: Cohort characteristics included AU 63.1%, AT 10.8%, AA 23.1%; severe SALT (50-100) in 86.2%. Overall SALT decreased from 91.15±18.76 to 49.08±38.20 ($P = 0.001$). In subgroup analyses, SALT fell from 96.80±7.61 to 43.40±40.63 when using tofacitinib ($P = 0.020$) and from 86.09±23.04 to 45.71±35.55 when using baricitinib ($P < 0.001$). Response distributions were as follows: tofacitinib-50.0% no, 6.0% partial, 6.0% good, 38.0% excellent; baricitinib-23.1% no, 20.5% partial, 10.3% good, 46.1% excellent. Between-drug SALT differences were not significant (ANOVA F = 1.66, $P = 0.198$). Tofacitinib duration correlated with greater improvement (r = 0.415, $P = 0.001$) and was longer in excellent responders compared to non-responders (23.08±17.95 vs. 6.28±5.19 months, $P = 0.005$); no duration-response correlation was observed with baricitinib ($P = 0.671$).

Conclusion: In a severe, predominantly AU cohort, oral JAK inhibitors produced clinically meaningful SALT reductions with acceptable safety. Effectiveness appeared comparable between agents, while longer tofacitinib exposure was associated with greater benefit, whereas baricitinib achieved substantial responses over shorter intervals. Prospective studies should clarify the roles of treatment duration, clinical phenotype, and lifestyle/metabolic factors in optimizing outcomes.

Keywords: Alopecia areata, janus kinase inhibitors, treatment

Introduction

Alopecia areata (AA) is an autoimmune disease of the scalp and body hair that does not leave scars and exhibits polygenic and multifactorial characteristics.[1] The clinical presentation varies depending on the pattern of involvement and prevalence. The most common form presents as well-defined patches on the scalp, while more severe cases may progress to extensive forms such as alopecia totalis and alopecia universalis. Clinical subtypes of AA include patchy, ophiasis, sisaipho, reticular, diffuse, and incognita forms.[2-5]

The etiopathogenesis of AA is not fully understood, but it is thought to be related to genetic predisposition, environmental

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Adress for correspondence: Erhan Ayhan, Assoc. Prof., MD, Department of Dermatology, Dicle University Faculty of Medicine, Diyarbakır, Türkiye
Email: magnetar21@hotmail.com
ORCID ID: 0000-0003-1416-2636

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triggers, and loss of tolerance of the immune system against the hair follicle.[6] The secretion of IFN-γ by CD8+ NKG2D+ cytotoxic T-cells increases interleukin (IL)-15 production and creates a cycle that triggers inflammation via Janus kinase (JAK)/STAT pathways.[7-9] This process facilitates the transition to a dystrophic anagen phase in hair follicles, with peribulbar lymphocyte infiltration.[10]

While the severity and extent of AA are assessed using the SALT score, the patient's age and disease extent are decisive in treatment selection.[10,11] Although there are many topical and systemic treatment options, their efficacy is limited, especially in resistant cases, due to high relapse rates and side effects. Oral JAKis (JAKi), developed in recent years, are promising alternatives for patients requiring systemic treatment.[12]

This study aims to evaluate disease severity in AA patients treated with oral JAKi and to analyze prognostic and sociodemographic factors affecting treatment response.

Materials and Methods

Between August 15, 2021, and March 29, 2024, we retrospectively reviewed 65 patients aged 7-55 years who presented to the outpatient clinic of Dicle University Faculty of Medicine with diagnoses of AA, alopecia totalis, or alopecia universalis, and were treated with oral JAKis. The study protocol was approved unanimously by the Dicle University Faculty of Medicine Ethics Committee (approval number: 300, date: 17.04.2024), and all procedures complied with the principles of the World Medical Association Declaration of Helsinki.

We collected patients' sociodemographic data, clinical characteristics, prognostic factors of AA, previous treatments, SALT scores, the JAKis used, and adverse events. Treatment response to JAKis was assessed by changes in SALT score. Based on the percentage reduction in SALT from pre-treatment to post-treatment, responses were categorized into four groups: no response (0-24.9%), partial response (25-49.9%), good response (50-74.9%), and excellent response (75-100%).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics v21. Continuous variables are presented as mean ± standard deviation, and categorical variables as frequency and percentage (%). Normality of distributions was evaluated. For normally distributed paired measurements (pre- vs. post-treatment), the paired t-test was used. Differences in continuous variables among groups were analyzed with one-way ANOVA followed by Bonferroni post-hoc tests. The Pearson correlation coefficient was used to assess the direction and strength of associations between normally distributed continuous variables. For categorical comparisons, the chi-square (χ^2) test and Fisher's exact test were applied. All hypotheses were two-tailed, and $P \leq 0.05$ was considered statistically significant.

Results

The majority of participants (61.5%) were male, with an average age of 26.12±10.59 years. The age distribution ranged from 7 to 56 years, with a median age of 24. The majority of the sample was in the adult age group (81.5%), and in terms of marital status, the proportion of single individuals was prominent (64.6%). When body mass index levels were examined, more than half of the participants were classified as normal (46.2%) or overweight (33.8%). A high response rate was achieved in the group of non-smokers and non-drinkers using tofacitinib and baricitinib. A high response rate was observed in the group of normal weight individuals using tofacitinib and baricitinib. Tables 1 and 2 show the factors affecting the treatment of tofacitinib and baricitinib.

The demographic characteristics of the patients are shown in Table 3. However, no significant difference was observed in these relationships among all groups.

In this study, the most common comorbidity accompanying AA was thyroid disorders (5 patients). Thyroid disorders were followed by diabetes mellitus, depression, atopic dermatitis, Hepatitis-B carrier status, or chronicity. Cardiac pathologies observed in patients included MVP and patent foramen ovale. In the gastrointestinal system, ulcerative colitis, GER, and gastric ulcer were observed. There was diversity in dermatological conditions, such as oral lichen planus, urticaria, vitiligo, and atopic dermatitis, observed. Anxiety and depression were identified as psychosocial disorders in patients.

When evaluating the clinical characteristics of AA patients, alopecia universalis was observed in 63.1% of cases, AA in 23.1%, and alopecia totalis in 10.8%. Among the patterns of hair loss, patchy hair loss was the most common (84.6%), while ophiasis was detected in 32.3% of cases. Among the areas of involvement, hair loss was present in all patients (100%), followed by eyebrow and eyelash involvement (89.2%), body hair (70.8%), and nail involvement (43.1%). Among nail abnormalities, the most common involvement pattern was trachyonychia (29.2%), while longitudinal ridging and leukonychia were observed at similar rates. In terms of clinical severity, 86.2% of participants showed severe involvement-

Table 1. Sociodemographic comparison of tofacitinib treatment response

Variable	Non-response	Partial	Good	Very good	*P* -value
Age					
Adult	77.8%	50.0%	100%	75.0%	0.700
Child	22.2%	50.0%	0%	25.0%	
Gender					
Female	44.4%	50.0%	50.0%	50.0%	0.991
Male	55.6%	50.0%	50.0%	50.0%	
Education					
Primary	5.6%	50.0%	50.0%	25.0%	
Middle	11.1%	0%	0%	8.3%	0.522
High school	66.7%	50.0%	50.0%	33.3%	
University	16.7%	0%	0%	33.3%	
Marital status					
Single	77.8%	50.0%	50.0%	75.0%	0.725
Married	22.2%	50.0%	50.0%	25.0%	
Smoking					
No	83.3%	50.0%	50.0%	91.7%	0.307
Yes	16.7%	50.0%	50.0%	8.3%	
Alcohol					
No	94.4%	100.0%	100%	100.0%	0.822
Yes	5.6%	0%	0%	0%	
BMI					
Underweight	11.1%	50.0%	0%	8.3&	
Normal	55.6%	50.0%	0%	33.3%	0.469
Overweight	27.8%	0%	100%	50.0%	
Obese	5.6%	0%	0%	8.3%	

BMI: Body mass index

SALT score 50-100. Moderate involvement (SALT score 20-49.9) was observed in 12.3%, and mild involvement (SALT score 0-19.9) in 1.5%.

As shown in Table 2, the most common treatment method in AA patients, is topical corticosteroids, which all participants used. In addition, the most frequently preferred topical agents were anthralin (49.2%), minoxidil (43.1%), and calcineurin inhibitors (29.2%). Intralesional corticosteroid application was used in 64.6% of cases. Among systemic treatments, cyclosporine was prominent (75.4%), while other immunosuppressive agents were used less frequently (e.g., methotrexate 6.2%; azathioprine 1.5%). SADBE was used as immunotherapy in 18.5% of cases, while defensipron was used to a limited extent. Phototherapy preference was concentrated on the PUVA at 40%. The use of supplements was relatively low, with iron and zinc supplementation reported in 10.8% of cases. PRP applications were limited to 4.6% (Table 4). In this study, the JAKis most commonly used in patients diagnosed with AA were found to be tofacitinib (52.3%) and baricitinib (60%). Tofacitinib was generally administered at a dose of 5 mg twice daily (97%), while baricitinib was standardized at 4 mg once daily (100%). The average treatment duration for tofacitinib was 7.55±13.32 months, with a median of 3 months (a range 0-72 months). This duration was shorter for baricitinib, with an average of 3.68±4.43 months, a median of 3 months, and a range of 0-18 months. When treatment efficacy was assessed using the SALT score, the very good response rate (75-100% reduction) was 46.1% in the baricitinib group and 38% in the tofacitinib group. The non-response rate (less than 25% reduction) post-tofacitinib treatment was 50%, while this rate was 23.1% in the baricitinib group. The mean SALT score before JAK inhibitor treatment was 91.15±18.76 in all patients, while a decrease to 49.08±38.20 was observed after treatment (Table 5).

As shown in Table 6, no significant relationship was found between disease duration and treatment response in either JAK inhibitor group. In the tofacitinib group, disease duration ranged from 95 to 103 months depending on response levels ($P = 0.985$), while in the baricitinib group, this value ranged from 76 to 90 months, ($P = 0.988$). These findings indicate that disease duration has a limited effect in determining treatment response. However, a significant difference was observed in terms of treatment duration. A statistically significant relationship was found between treatment duration and response level in patients using tofacitinib ($P = 0.005$).

Table 2. Sociodemographic characteristics and baricitinib treatment response

Characteristic	Non-response	Partial response	Good response	Very good response	*P* -value
Age group					
Adult	100.0%	87.5%	75.0%	77.8%	0.497
Child	0.0%	12.5%	25.0%	22.2%	
Gender					
Female	37.5%	12.5%	50.0%	27.8%	0.530
Male	62.5%	87.5%	50.0%	72.2%	
Education level					
Primary	0.0%	12.5%	50.0%	5.6%	
Middle	12.5%	12.5%	25.0%	0.0%	0.067
High school	37.5%	37.5%	25.0%	72.2%	
University	50.0%	37.5%	0.0%	22.2%	
Marital status					
Single	75.0%	62.5%	75.0%	50.0%	0.593
Married	25.0%	37.5%	25.0%	50.0%	
Smoking history					
No	75.0%	25.0%	75.0%	61.1%	0.167
Yes	25.0%	75.0%	25.0%	28.9%	
Alcohol history					
No	100.0%	100.0%	100.0%	94.4%	0.767
Yes	0.0%	0.0%	0.0%	5.6%	
BMI category					
Underweight	0.0%	12.5%	25.0%	5.6%	
Normal	62.5%	50.0%	50.0%	50.0%	0.436
Overweight	37.5%	12.5%	0.0%	28.9%	
Obese	0.0%	25.0%	25.0%	5.6%	

BMI: Body mass index

Tablo 3. Demographic characteristics of participants (n = 65)

Variable	Statistic/category	n (%)
Gender	Female/male	25 (38.5%)/40 (61.5%)
Age	Mean ± SD/median (min.-max.)	26.12±10.59/24 (7-56)
Age group	Adult/child	53 (81.5%)/12 (18.5%)
Marital status	Single/married	42 (64.6%)/23 (35.4%)
Body mass index	Mean ± SD/median (min.-max.)	26.43±4.64/24.50 (11-37)
Smoking	Yes/no	20 (30.8%)/45 (69.2%)
Alcohol use	Yes/no	2 (3.1%)/63 (96.9%)

SD: Standard deviation, Min.: Minimum, Max.: Maximum

The duration of use was significantly longer in patients who responded very well (23 months), while it was only 6 months on average in those who did not respond. This suggests that tofacitinib treatment is more effective when used in the long-term.

In the baricitinib group, no significant difference was found between treatment duration and response (P = 0.671). Regardless of response levels, the duration of use ranged from approximately 4 to 6 months, while the "very good response" rate remained quite high (46.1%). This indicates baricitinib's potential to achieve maximum effect in a shorter time.

In this study, the relationship between the SALT score and the duration of JAK inhibitor use was evaluated using Pearson correlation analysis. A moderate positive and statistically significant relationship was found between the duration of tofacitinib use and the SALT score (r = 0.415; P = 0.001). This finding indicates that clinical efficacy increases with longer duration of tofacitinib use. No significant relationship was found between duration of baricitinib use and SALT score (r = 0.097; P = 0.443), suggesting that response to baricitinib treatment may be independent of duration.

Table 4. Treatments used in patients with alopecia areata

Treatment type	Treatment modality	n	%
Topical treatments	Topical corticosteroids	65	100.0
	Vitamin D analogs	4	6.2
	Topical retinoids	16	24.6
	Topical calcineurin inhibitors	19	29.2
	Topical minoxidil	28	43.1
	Topical anthralin	32	49.2
	Topical tar preparations	18	27.7
	Topical methoxsalen	6	9.2
	Topical prostaglandin analogs	11	16.9
	Intralesional corticosteroids	42	64.6
Systemic treatments	Methotrexate	4	6.2
	Cyclosporine	49	75.4
	Systemic corticosteroids	19	29.2
	Sulfasalazine	5	7.7
	Azathioprine	1	1.5
Immunotherapy	SADBE	12	18.5
	Diphencyprone	2	3.1
Phototherapy	PUVA therapy	26	40.0
Supplemental therapies	Iron	7	10.8
	Magnesium	2	3.1
	Zinc	7	10.8
	Biotin	3	4.6
	Vitamin D	2	3.1
Other procedures	PRP application	3	4.6

Additionally, a negative correlation was observed between the duration of use of tofacitinib and baricitinib (r = -0.384; P = 0.002), which may reflect differences in treatment preference and patient groups.

The change in SALT score was compared according to the JAK inhibitor used. According to the results of the one-way ANOVA test, no statistically significant difference was found among the groups using tofacitinib, baricitinib, or both drugs together (F = 1.66; P = 0.198). The highest mean SALT score was observed in the tofacitinib group (49.56±39.23), followed by baricitinib (35.37±32.28) and the combination therapy group (28.50±28.96). These findings indicate that, although both treatment options are effective, the differences in mean scores are not statistically significant).

In all patients, the SALT score decreased from 91.15±18.76 to 49.08±38.20 after JAK inhibitor treatment. In tofacitinib users, it decreased from 96.80±7.61 to 43.40±40.63 (P = 0.020), and in baricitinib users, it decreased from 86.09±23.04 to 45.71±35.55 (P < 0.001) (Table 7).

Discussion

JAK proteins regulate numerous physiological and immunological processes by transmitting signals from cell surface receptors to the nucleus.[13] The role of the JAK-STAT pathway in the pathogenesis of AA has been demonstrated through the release of interferon-gamma, which increases

Table 5. JAK inhibitor comparison table (tofacitinib vs. baricitinib)

Parameter	Tofacitinib	Baricitinib
Usage frequency	52.3% (n = 34)	60% (n = 39)
Average treatment duration (months)	7.55±13.32 (median: 3, range: 0-72)	3.68±4.43 (median: 3, range: 0-18)
Dosage	5 mg BID (97%) 2.5 mg BID (3%)	4 mg QD (100%)
Treatment response-SALT score reduction		
No response (< 25%)	50%	23.1%
Partial response (25-50%)	6%	20.5%
Good response (50-75%)	6%	10.3%
Excellent response (75-100%)	38%	46.1%

JAK: Janus kinase, SALT: Severity of Alopecia Tool

Table 6. Treatment response comparison by duration and drug use

Parameter	No response	Partial response	Good response	Excellent response	P -value (tofa)	P -value (bari)
Disease duration (months)	Tofa: 103.33±67.40	Tofa: 96±16.97	Tofa: 96±67.80	Tofa: 95±51.54	0.985	
	Bari: 87±53.57	Bari: 76.5±77.22	Bari: 90.75±63.98	Bari: 83.33±81.43		0.988
Drug use duration (months)	Tofa: 6.28±5.19	Tofa: 6±2.83	Tofa: 10±0.00	Tofa: 23.08±17.95	**0.005**	
	Bari: 4.25±1.48	Bari: 6.25±5.25	Bari: 6±2.44	Bari: 6.56±5.06		0.671

Table 7. Change in SALT score before and after JAK inhibitor use

Patient group	SALT score (before JAKi)	SALT score (after JAKi)	*P* -value
All patients	91.15±18.76	49.08±38.20	0.001
Tofacitinib users	96.80±7.61	43.40±40.63	0.020
Baricitinib users	86.09±23.04	45.71±35.55	< 0.001

JAK: Janus kinase, SALT: Severity of Alopecia Tool

IL-15 production in hair follicles. This mechanism contributes to the maintenance of the disease by triggering the inflammatory process. Therefore, JAKis are potential therapeutic agents that support the regrowth of hair follicles.[7-9]

Systematic reviews and meta-analyses on the efficacy of JAKis in the treatment of AA have generally reported positive results.[14,15] The high success rates of SALT50 with agents such as tofacitinib and ruxolitinib indicate that these treatments are promising in terms of clinical response.[16,17] Baricitinib, in particular, was the first JAK inhibitor to be approved for AA treatment after demonstrating superiority over placebo in phase 3 trials.[1] However, differences in study designs, heterogeneity of patient populations, and limited follow-up periods limit the generalizability of the results.

In our study, treatment with JAKis resulted in a significant reduction in SALT scores. The mean SALT score before treatment was 91.15±18.76, while after treatment this value decreased to 49.08±38.20. Scores decreased from 96.8 to 43.4 in patients using tofacitinib and from 86.09 to 45.71 in those using baricitinib. The decrease in SALT scores after treatment with both agents was statistically significant ($P < 0.05$). These data clearly demonstrate the clinical efficacy of JAKis. However, no significant difference was found between the tofacitinib and baricitinib groups in terms of the change in SALT score ($P = 0.07$). This suggests that both drugs may have similar levels of efficacy.

In the literature, treatment duration and dose are highlighted as key factors affecting response tofacitinib therapy.[18] Meta-analyses in pediatric patients have also reported longer treatment duration in responders.[19] In our study, the mean duration of use in patients who responded well to tofacitinib was 23.08±17.95 months, which was significantly longer than in non-responders ($P = 0.005$). Furthermore, a positive and moderately significant correlation was found between the SALT score and the duration of tofacitinib treatment ($r = 0.415$, $P = 0.001$). In baricitinib treatment, no significant difference was found in the duration of use between response categories ($P = 0.671$), and no relationship was observed between the change in SALT score (SALT) and duration of use ($r = 0.097$, $P = 0.443$). This may be attributed to the use of baricitinib for shorter and more homogeneous periods. Our findings suggest that treatment duration may be a decisive factor in clinical response, particularly for tofacitinib.

In our study, treatment response was higher in individuals who did not smoke, did not consume alcohol, and had no positive family history. Several epidemiological studies have found that smoking increases the risk of AA. Current smokers showed a higher risk of AA incidence compared to non-smokers, with a risk ratio of 1.88. The duration and volume of tobacco use are also associated with AA risk. A history of smoking for more than 10 years constitutes an increased risk for an aortic aneurysm (AA).[20] Smoking activates various cytokines and inflammatory pathways by increasing CD4+ Th1, TH4, and Th17.[21-23] Alcohol consumption can activate immunological mechanisms.[20] Mild ethanol intoxication impairs the ACTH and cortisol secretion response to intravenous CRH administration. This suggests that alcohol consumption may impair AA development.[24] Furthermore, obesity increases the risk of AA (odds ratio: 1.15).[25] However, the detailed mechanism of obesity-related AA remains unclear.[26] In our study, although it was observed that alcohol and tobacco consumption increased the risk of AA and negatively affected the response to treatment, the results were not statistically significant.

Findings in the literature suggesting that JAKis may be more effective in common disease forms such as AU and AT, are supported by our study.[27] This may be because AU or AT patients have more inflammation and that JAKi treatment suppresses excessive inflammation better. In particular, the treatment response was found to be statistically significant in individuals with common diseases using tofacitinib ($P < 0.001$).

A meta-analysis found that the JAK treatment response was more effective in women.[27] When treatment response was evaluated by sex in this study, response rates in the tofacitinib group were equal in women and men, while in the baricitinib group, the very good response rate was higher in men. However, this difference was not clinically significant. Treatment response is higher in adults than in children, but these results should be interpreted with caution due to the small number of children.

No significant relationship was found between disease duration and treatment response. This can be explained by factors such as the active phase of the disease and the individual immune response profile. Similarly, the literature reports that AA duration does not determine JAKi treatment response.[7,28]

Study Limitations

The results of our study were mostly related to adults. The relapse rates in JAKi treatment could not be evaluated. In order to calculate the effective relapse rate, patients needed to have discontinued JAKi treatment for at least 3 months. A longer period was needed to observe serious JAKi side effects in patients. The duration of baricitinib use in our patients was shorter.

Conclusion

JAKis are effective, and safe agents in the treatment of AA, and the duration of treatment may be decisive for the clinical response, especially for tofacitinib. Baricitinib, on the other hand, can provide similar responses in a shorter period. Considering that the response to treatment is shaped by individual, immunological, and lifestyle factors, it is important to clarify these relationships with larger sample sizes and longer-term studies.

Ethics

Ethics Committee Approval: The study protocol was approved unanimously by the Dicle University Faculty of Medicine Ethics Committee (approval number: 300, date: 17.04.2024), and all procedures complied with the principles of the World Medical Association Declaration of Helsinki.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.K., E.A., Concept: M.K., E.A., Design: M.K., E.A., Data Collection or Processing: M.K., E.A., Analysis or Interpretation: M.K., E.A., Literature Search: M.K., Writing: M.K., E.A.

Conflict of Interest: The authors declared that they have no conflict of interest.

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Original Article

Evaluation of the Accuracy, Reliability, Quality, and Readability of Artificial Intelligence Chatbots-Generated Responses to Acne-Related Questions

Ecem Bostan[1], Mahmut Talha Uçar[2], Elif Dönmez[3]

[1]Department of Dermatology and Venereology, Ankara Medipol University Faculty of Medicine, Ankara, Türkiye
[2]Department of Public Health, University of Health Sciences Hamidiye Faculty of Medicine, İstanbul, Türkiye
[3]Department of Oncology Nursing, University of Health Sciences Hamidiye Faculty of Nursing, İstanbul, Türkiye

Abstract

Aim: Since artificial intelligence (AI) has entered our lives, it has been widely used in daily medical practice to determine accurate diagnoses, predict prognosis, and inform about various treatment modalities. Acne vulgaris is one of the most frequently encountered skin problems in dermatology. Patients with acne can consult AI. The aim of the present study was to evaluate the accuracy, reliability, quality, and readability of AI-generated responses to frequently asked acne-related questions.

Materials and Methods: To evaluate the accuracy, reliability, quality, and readability of AI-generated responses to acne-related queries, a multi-domain assessment approach involving four validated tools [modified DISCERN, Global Quality Scale (GQS), Flesch Reading Ease score (FRES), and 5-point Likert scale] was used.

Results: Among the three generative AI chatbots, DeepSeek achieved the highest mean FRES, followed by ChatGPT-4.0 and ChatGPT-4.5. For modified DISCERN scores, ChatGPT-4.5 achieved the highest mean score, followed by ChatGPT-4.0 and DeepSeek, indicating superior information quality in ChatGPT-4.5 responses. The mean FRES was highest for DeepSeek among the three generative AI chatbots, whereas ChatGPT-4.5 had the highest mean modified DISCERN score. This suggests that ChatGPT-4.5 responses have higher informational quality. In terms of accuracy, ChatGPT-4.5 again achieved the highest mean score. ChatGPT-4.5 scored the highest GQS, slightly above ChatGPT-4.0, with DeepSeek scoring the lowest.

Conclusion: These results highlight that ChatGPT-4.5 generally provided more accurate, higher-quality responses, whereas DeepSeek offered superior readability according to the Flesch Reading Ease metric.

Keywords: Acne vulgaris, artificial intelligence, patient education as topic

Introduction

Generative artificial intelligence (AI) models such as ChatGPT, Gemini, and DeepSeek are now widely used in our daily lives to gather information on various subjects. Generative AI can learn from substantial amounts of data and generate new content such as text, images, music, and video.[1] Therefore, chatbots have emerged as popular and preferred tools for patients to seek medical advice and counseling before consulting a physician.

Patients with restricted access to medical care may utilize chatbots for frequently encountered dermatologic conditions such as acne, atopic dermatitis, psoriasis, and rosacea. A recent study that investigated the accuracy and sufficiency of ChatGPT, Google Bard, and Bing in answering questions about

Adress for correspondence: Ecem Bostan, Assoc. Prof., MD, Department of Dermatology and Venereology, Ankara Medipol University Faculty of Medicine, Ankara, Türkiye
Email: bostanecem@gmail.com
ORCID ID: 0000-0002-8296-4836

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common dermatological disorders showed that ChatGPT's responses to these questions were the most accurate and the most convenient.[2] The same study also found that ChatGPT and BingAI exhibited superior diagnostic performance, and these conversational chatbots emphasized the importance of consulting a physician for their medical conditions.[2] Image-based AI algorithms were developed to assess acne severity and identify acne morphologies; they successfully classified patients with acne.[3]

Widespread use of chatbots to gather medical information about different health conditions may give rise to significant ethical problems when false or inconvenient medical knowledge, especially about treatment modalities, is transferred to users. Therefore, the establishment of generative AI tools that can provide accurate, reliable, and readable responses to users, especially regarding medical problems, is of considerable importance.

In the present study, the accuracy, reliability, quality, and readability of AI-generated responses to the most commonly asked acne vulgaris-related questions were evaluated.

Materials and Methods

The reliability, quality, readability, and accuracy of AI-generated responses to acne-related queries (Table 1) were evaluated using a comprehensive, multi-domain assessment framework comprising four validated instruments.

Table 1. Acne-related questions retrieved from Quora and asked to ChatGPT-3.5, ChatGPT-4, and DeepSeek

	Questions
1	How can I deal with acne?
2	How can I get rid of pimples and scars?
3	How will a dermatologist help with my acne problem?
4	How well does accutane work for acne?
5	How do I deal with my adult acne?
6	Do milk and dairy products cause acne? Why?
7	Does laser treatment really get rid of acne scars permanently?
8	What is the best effective way to get rid of pimples due to hormonal imbalance?
9	How can you prevent breakouts?
10	What are the best creams to remove acne scars?
11	Why do antibiotics cause acne?
12	What is the best skincare routine for acne?
13	What is the best treatment for acne scars?
14	Does sunlight help with acne? Why?
15	What does tretinoin do for acne?
16	What is the most recommended face wash to get rid of acne?
17	Does acne eventually go away without treatment?
18	Can acne scars and redness be removed with natural remedies?
19	Why do pimples (acne) form?
20	Will my acne scars go away?

To collect representative patient questions, the keyword "acne" was searched on the Quora platform, one of the most active patient-driven discussion forums where individuals openly share their dermatological concerns in everyday language. This platform was preferred because its publicly available user-generated content reflects natural phrasing and real-world health literacy, providing an authentic basis for evaluating chatbot performance in patient communication contexts.

Analytics regarding response volume, user engagement, and upvotes were used to rank 670 questions by popularity. After the exclusion of irrelevant or inappropriate entries (n = 8), 662 questions remained. Among these, the 40 most frequently discussed were reviewed collaboratively by a board-certified dermatologist and a public health researcher. Through this multidisciplinary evaluation, twenty clinically relevant and commonly asked questions were identified for inclusion in the analysis (Figure 1).

AI-generated responses to these questions were independently obtained from ChatGPT-4.0, ChatGPT-4.5, and DeepSeek. Both the dermatologist and the public health researcher subsequently assessed each response. The dermatologist focused on the medical accuracy and clinical relevance of the information provided, while the public health researcher evaluated the reliability, quality, and readability of the texts from a health-communication perspective. The primary outcome of the study was the overall accuracy and reliability of AI-generated responses, as measured by the mDISCERN, GQS, and accuracy assessment tools. The secondary outcomes included readability [Flesch Reading Ease scores (FRES)] and inter-rater reliability [Cronbach's alpha and intraclass correlation coefficients (ICC)].

All responses were generated between 21 April and 5 May 2024, representing a time-specific snapshot of chatbot performance. Ethical approval was not required because the study utilized publicly accessible online data without involving human participants, patient records, or identifiable personal information. Accordingly, the study meets institutional criteria for exemption from human-subjects ethics review.

Reliability Assessment (Modified DISCERN)

The reliability of each response was assessed by the dermatologist using the modified DISCERN instrument[4] (Supplementary File 1), which comprises eight items that evaluate the clarity of aims, achievement of objectives, relevance, citation of sources, timing of publication, balance and impartiality, provision of supplementary resources, and

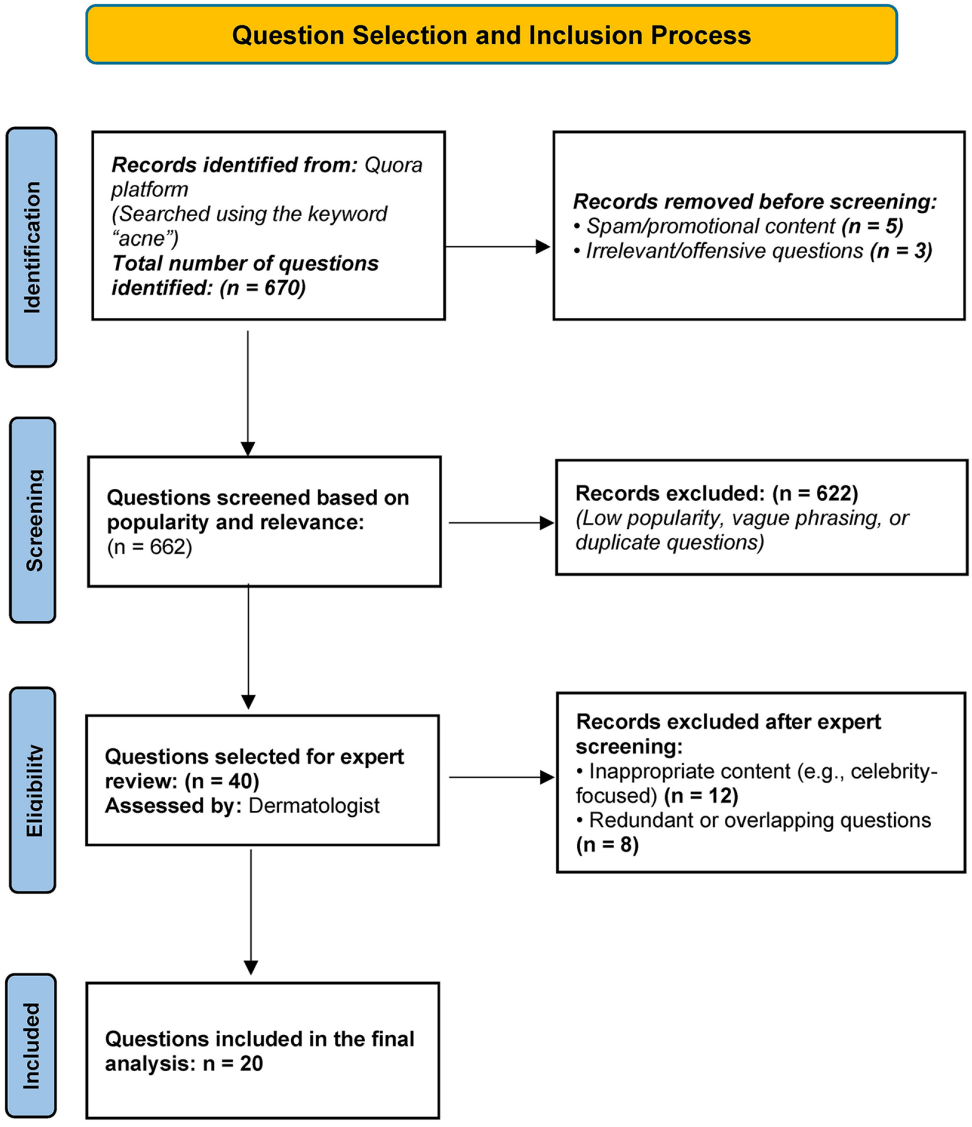

Figure 1. PRISMA-based flow diagram showing the identification, screening, eligibility assessment, and inclusion of acne-related questions collected

acknowledgement of uncertainty. Each item was rated on a 5-point Likert scale (1 = low, 5 = high), with total scores ranging from 8 to 40.[4] Higher scores indicate greater reliability and information integrity.

Quality Assessment (Global Quality Scale)

Overall quality was also rated by the dermatologist using the Global Quality Scale (GQS)[5] (Supplementary File 2), a validated 5-point instrument designed to assess the coherence, comprehensiveness, and patient-centered utility of online health information. A score of 1 reflected poor quality and minimal usefulness, whereas a score of 5 indicated excellent content flow and substantial patient benefit.[5]

Readability Assessment (Flesch Reading Ease Score)

Readability was assessed by a public health researcher using the FRES, which evaluates the ease of comprehension based on average sentence length and the average number of syllables per word. Scores range from 0 to 100, with higher scores indicating easier readability. The FRES for each response was calculated using a standardized online tool (https://readabilityformulas.com),[6] and interpreted according to established classification thresholds: very easy (90-100), easy (80-89), fairly easy (70-79), standard (60-69), fairly difficult (50-59), difficult (30-49), and very difficult (0-29).[6]

Accuracy Assessment

The accuracy of each AI-generated response was evaluated using a five-point Likert scale adapted from previous studies

assessing the quality of medical information generated by large language models.[7-9] This method has been widely adopted in the recent literature to assess the factual accuracy and clinical consistency of AI-generated health content.[7-9] Scores ranged from 1 to 5, where:

1 – indicated completely incorrect or misleading information;

2 – represented mostly incorrect content with minor correct elements;

3 – reflected a balance of correct and incorrect information;

4 – denoted mostly correct information with minor inaccuracies or omissions;

5 – indicated completely accurate information consistent with current dermatological guidelines and evidence-based practice.

Each response was independently rated by two evaluators with clinical expertise in dermatology and public health. Discrepancies in scoring were resolved through discussion and consensus.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (Version 29.0). Descriptive statistics were presented as mean ± standard deviation. The Kruskal-Wallis test was used to compare the three AI models (ChatGPT-4.0, ChatGPT-4.5, and DeepSeek) across four evaluation domains: reliability (mDISCERN), quality (GQS), readability (FRES), and accuracy. Where significant differences were found, pairwise comparisons were conducted using the Mann-Whitney U test with Bonferroni correction. Effect sizes were calculated using eta-squared (η^2) for Kruskal-Wallis analyses and rank-biserial correlation (r) for pairwise Mann-Whitney U tests to quantify the magnitude of differences. Statistical significance was set at $P < 0.05$.

Results

Among the chatbot models, DeepSeek had the highest mean FRES (44.50±14.16), followed by ChatGPT-4.0 (42.40±11.39) and ChatGPT-4.5 (23.70±9.27). This suggests that DeepSeek and ChatGPT-4.0 produced responses that were more readable than those of ChatGPT-4.5. Regarding modified DISCERN scores, ChatGPT-4.5 had the highest mean (30.75±3.40), followed by ChatGPT-4.0 (28.55±2.93) and DeepSeek (25.40±3.36). This suggests that ChatGPT-4.5 responses were of a higher quality. In terms of GQS, ChatGPT-4.5 scored highest (4.15±0.81), slightly above ChatGPT-4.0 (4.10±0.71); DeepSeek had the lowest score (3.70±0.73). When accuracy was evaluated, ChatGPT-4.5 showed the highest mean accuracy (4.25±0.55), followed by ChatGPT-4.0 (4.05±0.51), and DeepSeek (3.95±0.51). This indicates relatively consistent accuracy across the models. The summary of mDISCERN, GQS, and readability scores is shown in Table 2, whereas the radar plots of responses generated by ChatGPT4.0, ChatGPT4.5, and DeepSeek for reliability, quality, readability, and accuracy across 20 acne-related questions are depicted in Figure 2.

A Kruskal-Wallis test was conducted to compare the performance of ChatGPT-4.0, ChatGPT-4.5, and DeepSeek across four evaluation metrics: GQS, mDISCERN, FRES, and accuracy assessment.

Global Quality Score

No statistically significant difference was found among the three models in terms of GQS [χ^2 (2) = 4.746, P = 0.093]. However, ChatGPT-4.5 had the highest mean rank (34.58), followed by ChatGPT-4.0 (32.80) and DeepSeek (24.13).

Modified DISCERN Score

A significant difference was observed among the models [χ^2 (2) = 19.961, $P < 0.001$]. ChatGPT-4.5 showed the highest mean rank (42.33), followed by ChatGPT-4.0 (31.38); DeepSeek had the lowest (17.80), indicating that its information quality scores were significantly lower.

Flesch Reading Ease Score

The difference among the models was statistically significant [χ^2 (2) = 24.703, $P < 0.001$]. DeepSeek achieved the highest readability rank (39.63), closely followed by ChatGPT-4.0 (37.15), while ChatGPT-4.5 ranked lowest (14.73), suggesting that ChatGPT-4.5 responses were more difficult to read.

Table 2. The summary of mDISCERN, GQS, and Readability scores

Model*	mDISCERN (mean ± SD)	GQS (mean ± SD)	Flesch Reading Ease score (mean ± SD)
ChatGPT-4.0	28.55±2.93	4.25±0.44	41.8±11.67
ChatGPT-4.5	30.7±3.28	4.25±0.44	39.4±15.82
DeepSeek	25.05±4.77	3.75±0.85	45.55±10.87

*Effect sizes (η^2): mDISCERN = 0.32, FRES = 0.38, GQS = 0.03, Accuracy = 0.01
GQS: Global Quality Scale, FRES: Flesch Reading Ease score, SD: Standard deviation

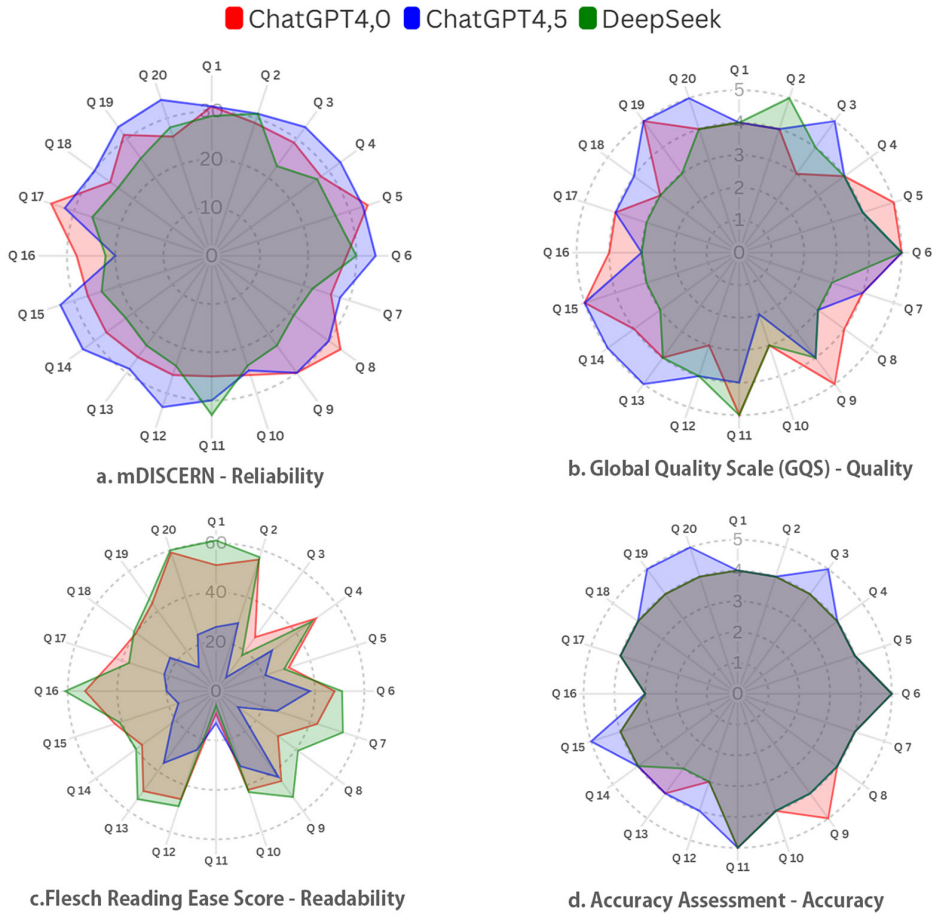

Figure 2. Radar plots of chatbot responses for reliability, quality, readability and accuracy across 20 acne-related questions

Accuracy Assessment

The models did not differ significantly in terms of accuracy [χ^2 (2) = 3.361, P = 0.186]. ChatGPT-4.5 ranked highest (34.88), followed by ChatGPT-4.0 (29.60) and DeepSeek (27.03).

Post-hoc Comparisons for mDISCERN

Pairwise comparisons using the Mann-Whitney U test with Bonferroni correction (adjusted α = 0.0167) revealed significant differences among the three chatbot models.

ChatGPT-4.5 vs. ChatGPT-4.0: ChatGPT-4.5 yielded significantly higher mDISCERN scores than ChatGPT-4.0 (U = 109.5; Z = -2.47; P = 0.014).

Although this value was statistically significant at the conventional 0.05 level, it narrowly missed significance following Bonferroni correction.

ChatGPT-4.0 vs. DeepSeek: ChatGPT-4.0 demonstrated significantly higher scores than DeepSeek (U = 92.0, Z = -2.94, P = 0.003); this difference remained significant after correction.

In the comparison between ChatGPT-4.5 and DeepSeek, A marked difference was observed in favour of ChatGPT-4.5, which substantially outperformed DeepSeek (U = 54.0; Z = –3.97; P < 0.001), even after adjustment for multiple comparisons.

These findings support the superior information quality of ChatGPT-4.5, particularly in comparison to DeepSeek.

Post-hoc Comparisons for Readability

Pairwise comparisons based on the FRES revealed significant differences between models, as determined by Mann-Whitney U tests with Bonferroni adjustment (α = 0.0167):

ChatGPT-4.0 vs. ChatGPT-4.5:

ChatGPT-4.0 generated significantly more readable responses than ChatGPT-4.5 (U = 38.5, Z = -4.37, P < 0.001).

ChatGPT-4.0 vs. DeepSeek:

No statistically significant difference in readability was observed between ChatGPT-4.0 and DeepSeek (U = 171.5, Z = -0.77, P = 0.440).

ChatGPT-4.5 vs. DeepSeek:

DeepSeek responses were significantly more readable than those of ChatGPT-4.5 (U = 46.0; Z = -4.17; $P < 0.001$).

Collectively, these findings highlight the relatively poor readability of ChatGPT-4.5 responses compared to both ChatGPT-4.0 and DeepSeek, with DeepSeek showing the highest readability overall.

For GQS, the internal consistency was poor, with a Cronbach's alpha of 0.388. The single-measure ICC was 0.106 [95% confidence interval (CI): -0.052 to 0.353], indicating low reliability between evaluators. The average-measure ICC was 0.262 (95% CI: -0.175 to 0.621), and the results were not statistically significant ($P = 0.097$). Regarding mDISCERN, the internal consistency was moderate (Cronbach's alpha = 0.542). The single-measure ICC was 0.264 (95% CI: 0.013-0.554) and the average-measure ICC was 0.518 (95% CI: 0.038-0.788), suggesting a fair level of agreement. These results were statistically significant ($P = 0.020$). The FRESs showed high internal consistency (Cronbach's alpha = 0.865). The single-measure ICC was 0.353 (95% CI: 0.004-0.674) and the average-measure ICC was 0.620 (95% CI: 0.012-0.861); both estimates were statistically significant ($P < 0.001$), indicating good inter-rater reliability. For accuracy assessment, the inter-rater reliability was high. Cronbach's alpha was 0.843, indicating excellent internal consistency across evaluators. The single-measure ICC was 0.602 (95% CI, 0.348-0.800), and the average-measure ICC was 0.819 (95% CI, 0.616-0.923), both were statistically significant ($P < 0.001$). These results confirm a strong absolute agreement between the models in terms of response accuracy. The summary of reliability metrics is shown in Table 3.

Discussion

Findings of this study indicate that ChatGPT-4.5 generally provided more accurate, higher-quality responses to acne-related queries, while DeepSeek provided superior readability as measured by the Flesch Reading Ease metric. To our knowledge, the present study is the first investigation to evaluate and compare three generative AI tools. We believe that the preliminary findings of our study will stimulate further investigations into the accuracy, reliability, quality, and readability of conversational AI-generated responses to questions about general skin problems.

As generative AI tools are now being increasingly used in our daily lives for purposes such as gathering information about various subjects, creating images, video, or text, or simply chatting, patients might find it easier to consult generative AI tools about their health problems. When prompt face-to-face dermatologic care is difficult to access, conversational AI programs that can compile information from large, complex datasets may be a satisfactory alternative.[10] Several studies have been conducted recently to evaluate the accuracy, credibility, and comprehensiveness of the information generated by conversational AI programs.[10-13] In a recent study by Gawey et al.,[12] the readability of ChatGPT-retrieved responses to the most frequently-asked questions about hidradenitis suppurativa (HS) were compared with the readability of the information provided by HS Foundation, HS Patient Guide and HS related websites. In this study, ChatGPT's responses were found to have a higher mean readability grade compared with other HS-related sources, even though FRES was significantly lower for ChatGPT than for other HS-related sources.[12] These findings underline the fact that the higher reading level of ChatGPT may impair the users' perception. Although comprehensibility is essential for readers to understand the information presented by AI tools, it is not the only criterion for appraising data generated by generative AI programs. Another study by Kamminga et al.[11] which compared the responses of large language models (ChatGPT-3.5, ChatGPT-4 and Gemini) and Dutch patient information resources (PIRs) to melanoma-related questions in terms of medical accuracy, readability, completeness and personalization and reproducibility, showed that ChatGPT-related answers had the highest accuracy whereas Gemini-generated responses were the best in readability, completeness and personalization. The same study also revealed that the best-performing large language models surpassed gold-standard PIRs on personalization and completeness, but not on accuracy and readability.[11] These results suggest that even though large language models demonstrated promising results,

Table 3. The summary of reliability metrics

Evaluation criteria	Cronbach's alpha	Single ICC*	CI** (single ICC)	Avg ICC	CI (Avg ICC)	*P*
GQS	0.388	0.106	-0.052-0.353	0.262	-0.17-0.621	0.097
mDISCERN	0.542	0.264	0.013-0.554	0.518	0.038-0.788	0.02
Flesch Reading Ease	0.865	0.353	0.004-0.674	0.62	0.012-0.861	< 0.001
Accuracy assessment	0.843	0.602	0.348-0.800	0.819	0.616-0.923	< 0.001

*ICC indicates intraclass correlation coefficient
**CI indicates confidence interval
GQS: Global Quality Scale

fortification and surveillance of accuracy and reproducibility are still needed.[11] In our study, among the three generative AI models, ChatGPT-4.5-derived responses had the highest quality and correctness, according to investigators' assessment, whereas DeepSeek was the easiest to read. This outcome underscores that different large language models have varying strengths and weaknesses. There appears to be a need for the standardization, personalization, and consolidation of large language models.

Recently, an investigation by Boostani et al.[13] evaluated the performance of GPT-4o and Gemini Flash 2.0 in diagnosing acne and rosacea-related clinical photographs. The outcomes of this study showed that GPT-4o demonstrated higher accuracy than Gemini in diagnosing rosacea and acne, but subtyping performance was markedly lower.[13] The considerably diagnostic accuracy (93%) of GPT-4o for acne and rosacea emphasizes the potential and competence of large language models in diagnosing skin diseases.[13] Furthermore, the performance of different ChatGPT versions in the dermatology specialty examination was assessed.[14-16] In one of these studies,[16] GPT-4 was found to obtain an overall accuracy of 75% on 250 randomly chosen dermatology board-style questions whereas in another investigation,[15] ChatGPT-4 performed better with an overall accuracy of 90% when compared to the performance (63%) of ChatGPT-3.5. Even though we did not investigate the performance of generative AI tools on the dermatology specialty examination, we also found that ChatGPT-4.5 ranked highest (34.88), followed by ChatGPT-4.0 (29.60), and DeepSeek (27.03) when the accuracy of the answers to acne vulgaris-related questions was assessed. Collectively, these results suggest that AI might become an essential adjunct for improving dermatology education and facilitating patient care and communication in the coming years.[17] Patients might find it easier to consult AI about the causes, prognoses and treatment options for different health problems, since gaining access to timely in-person medical care is not always feasible. However, ethical conflicts that may arise from the use of AI chatbots as the primary source of consultation for various health problems remain to be elucidated.

In addition to satisfying users' various skin-related problems and assisting with the dermatology speciality examination, AI has also gained prominence in cosmetic dermatology.[18-20] In a clinical study by Cazzaniga et al.,[21] artificial neural network models were used to estimate the clinical response to excimer laser therapy in vitiligo patients. Furthermore, the use of robot-assisted hair removal laser systems has been proven to be efficacious and safe.[22,23] An inception-based convolutional neural network has also been used to detect facial wrinkles and aid in deciding whether the forehead region needs filler injections; this model demonstrated an accuracy of 85.3%.[24] These studies once again highlight that integrating AI into aesthetic dermatology will most likely provide a more standardized and personalized approach to treatment for cosmetic interventions. AI seems to be a promising, complementary tool that enables the unification of the physician's ingenuity with the use of large amounts of evidence-based data.

This study has several notable strengths. First, it represents one of the earliest comparative analyses of generative AI chatbots—specifically ChatGPT-4.0, ChatGPT-4.5, and DeepSeek—in the context of acne vulgaris, a frequently encountered dermatological condition. The study's novelty and focused scope provide valuable insights into the evolving role of AI in patient education and dermatologic self-care. Second, the methodological rigor of the study is underscored by the use of four validated tools—modified DISCERN, GQS, FRES, and a 5-point Likert scale—offering a multidimensional evaluation of AI-generated content in terms of reliability, quality, readability, and accuracy. The inclusion of both a board-certified academic dermatologist and a public health researcher as independent evaluators further strengthens the validity and clinical relevance of the findings. Additionally, appropriate statistical analyses, including Kruskal-Wallis tests and Bonferroni-corrected post-hoc comparisons, were conducted to ensure the robustness of inter-model comparisons. These features collectively enhance the reliability and applicability of the study's results.

Study Limitations

Several limitations of the present study must also be acknowledged. The scope of the study was limited to acne vulgaris; therefore, the findings may not be generalizable to other dermatologic or systemic medical conditions. Furthermore, chatbot responses were retrieved and evaluated at a single point in time, representing a snapshot of model performance. Because generative AI tools are frequently updated, their future outputs may differ from those analyzed in this study. Although validated instruments were employed and inter-rater reliability statistics were used to mitigate this bias, some degree of subjectivity in evaluators' scoring cannot be entirely excluded. Additionally, the study focused exclusively on English-language content and relied on questions sourced from a single online platform (Quora), which may introduce language- and platform-related biases and limit the cross-cultural applicability of the findings. Despite these limitations, the study provides an important foundation for future research and contributes to the growing discourse on the integration of AI in dermatologic education and patient care.

Conclusion

With the ongoing involvement of AI in our daily lives, there is growing interest in incorporating AI into medicine. AI is now widely used in dermatology, facilitating the diagnosis of various skin diseases and providing detailed information on prognosis and treatment options. Our study also showed that generative AI programmes appear to be effective in answering acne-related questions and building bridges between patients and physicians, although there seems to be a need to strengthen several parameters (reliability, accuracy, and readability) across generative AI tools.

Ethics

Ethics Committee Approval: Not applicable.

Informed Consent: Not applicable.

Footnotes

Authorship Contributions

Concept: M.T.U., E.D., Design: M.T.U., E.D., Data Collection or Processing: E.B., M.T.U., E.D., Analysis or Interpretation: E.B., M.T.U., Literature Search: E.B., Writing: E.B., M.T.U., E.D.

Conflict of Interest: The authors declared that they have no conflict of interest.

Financial Disclosure: The authors declared that this study received no financial support.

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Supplementary File 1. mDISCERN criteria scoring
mDISCERN criteria total score (8-40 points)
1. Are the aims clear? 1-5 point
2. Does it achieve its aims? 1-5 point
3. Is it relevant? 1-5 point
4. Is it clear what sources of information were used to compile the publication (other than the author or producer)? 1-5 point
5. Is it clear when the information used or reported in the publication was produced? 1-5 point
6. Is it balanced and unbiased? 1-5 point
7. Does it provide details of additional sources of support and information? 1-5 point
8. Does it refer to areas of uncertainty? 1-5 point

Supplementary File 2. Global Quality index scoring	
Global Quality index scoring	**Score**
Poor quality, poor flow of the site, most information missing, not at all useful for patients	**1**
Generally poor quality and poor flow, some information listed but many important topics missing, of very limited use to patients	**2**
Moderate quality, suboptimal flow, some important information is adequately discussed but others poorly discussed, somewhat useful for patients	**3**
Good quality and generally good flow, most of the relevant information is listed, but some topics not covered, useful for patients	**4**
Excellent quality and excellent flow, very useful for patients	**5**

Case Report

Dupilumab in The Reactive Perforating Collagenosis Management in a Patient with Multimorbidity: A Case Report

Yusuf Can Edek[1], Mehmet Gülengül[1], Samed Şahin[1], Betül Öğüt[2], Esra Adışen[1]
[1]Department of Dermatology, Gazi University Faculty of Medicine, Ankara, Türkiye
[2]Department of Pathology, Gazi University Faculty of Medicine, Ankara, Türkiye

Abstract

Acquired perforating dermatoses (APD) are a group of diseases characterized by transepidermal excretion of dermal connective tissue materials and characterized by itchy skin lesions. Reactive perforating collagenosis (RPC) is the type of APD in which transepidermal collagen fiber elimination is detected. The number of cases in which dupilumab has been successfully used in the treatment of RPC is increasing in the literature. There are case reports showing the safe and effective use of dupilumab in RPC patients with comorbidities such as chronic kidney disease, Wilson disease, coronary artery disease, cerebrovascular disease, and hepatocellular cancer. In this case report, we present a female RPC patient with multimorbidity who had complete treatment response with dupilumab.

Keywords: Acquired perforating dermatoses, dupilumab, reactive perforating collagenosis

Introduction

Acquired perforating dermatoses (APD) are a group of diseases characterized by transepidermal excretion of dermal connective tissue materials, with itchy skin lesions. Reactive perforating collagenosis (RPC) is a type of APD in which transepidermal collagen fiber elimination is detected. The disease may be accompanied by many comorbidities such as diabetes mellitus, chronic kidney disease, malignancy, and endocrine diseases.[1,2]

In this case report, we present a female RPC patient with multimorbidity who had complete treatment response to dupilumab.

Case Report

A 79-year-old female patient presented to our dermatology outpatient clinic with pruritic lesions. In the anamnesis taken from the patient, it was learned that her complaints had been going on for two years. During this process, she received various topical treatments (topical steroid, topical calcineurin inhibitor), systemic treatments (oral antihistamines, steroid, doxycycline, colchicine), and phototherapy [narrowband-UVB (NB-UVB), two times weekly, 49.8 J/cm^2 cumulative dose] for her pruritus, and her symptoms persisted despite treatment. The patient described that her itching was severe [Visual Analogue Scale (VAS): 8] and that it greatly reduced her quality of life [Dermatological Quality of Life Index (DLQI): 15]. Her prior medical records showed hypertension, coronary artery disease, hyperlipidemia, gastritis. The medications of the patient included amlodipine, *nebivolol, furosemide,* pitavastatin, and lansoprazol. The patient had no history of atopy, infection, or trauma.

Dermatological examination showed widespread erythematous keratotic papules, nodules, and excoriations on the trunk and extremities (Figures 1a-c). Histopathological

Adress for correspondence: Yusuf Can Edek, MD,
Department of Dermatology, Gazi University Faculty of Medicine, Ankara, Türkiye
Email: yusuf-can-35@hotmail.com
ORCID ID: 0000-0002-3877-8681

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examination of a punch biopsy taken from a papule on the trunk showed epidermal ulceration and basophilic inflammatory debris. Transepidermal elimination of collagen fibers was detected in the epidermis with Elastin Van Gieson stain, (Figure 2). Considering the patient's clinical examination and histopathological evaluation together, the patient was diagnosed with RPC. It was decided to initiate dupilumab treatment in the patient who had multiple comorbidities and was resistant to many treatment agents. The patient received an initial subcutaneous dose of 600 mg of dupilumab, followed by 300 mg every two weeks. In the first month follow-up, it was observed that the itching had decreased significantly, her quality of life had improved, and lesions had regressed. At the third month follow-up, the patient continues her treatment without any active complaints (VAS:0, DLQI:1) or side effects (Figures 1b-d and 3).

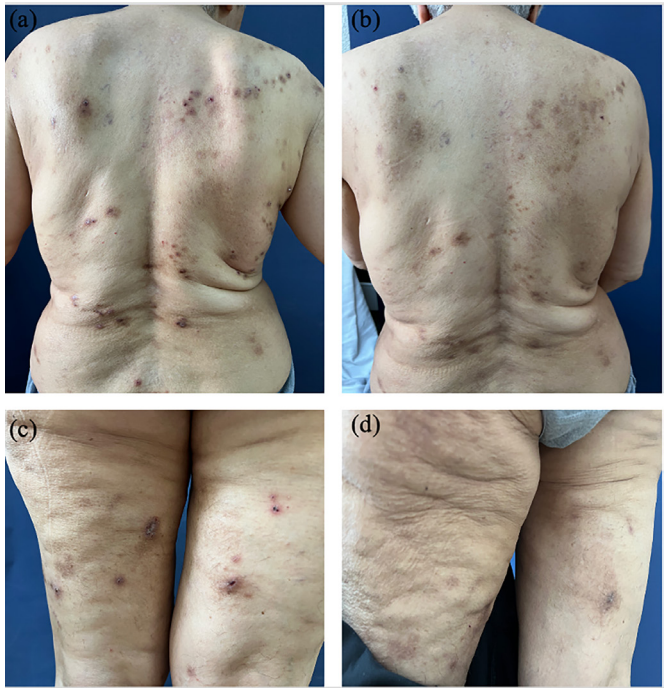

Figure 1. Diffuse erythematous keratotic papules and nodules on the patient's trunk (a), and lower extremities (c), regressed appearance of the patient's lesions with post-inflammatory hyperpigmentation in the third month of the treatment (b),(d)

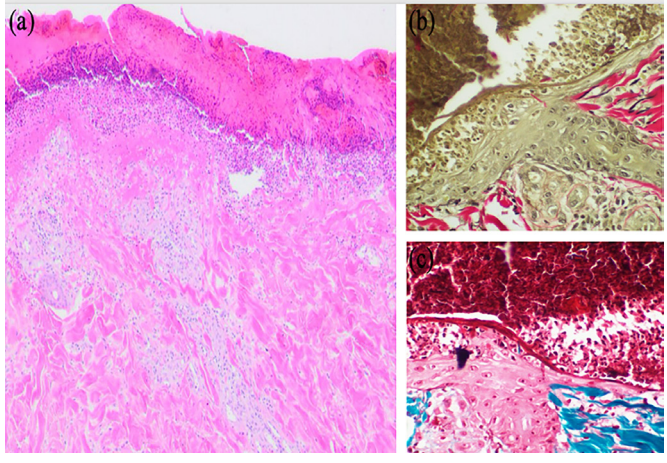

Figure 2. Histopathological examination, epidermal ulceration and basophilic inflammatory debris (a) (H&E, x40), transepidermal elimination of collagen fibers (b), (c) (Elastin Van Gieson, Masson trichrome, x200, x20)
H&E: Hematoxylin and eosin

Discussion

The primary goal of RPC treatment should be to prevent itching, and moisturizers, topical steroids, and systemic antihistamines can be used for this purpose. Keratolytic agents, phototherapy, methotrexate, and allopurinol are among the therapeutic agents that can be prescribed in the management of RPC. Although various topical and systemic agents can be used in the treatment of RPC, it can sometimes be challenging.[1,2] While many treatment agents were used in our patient, her complaints remained resistant to treatment. In cases resistant to treatments, the use of tofacitinib, baricitinib, and dupilumab has been reported recently.[3-5]

Dupilumab is a monoclonal antibody that reduces interleukin (IL)-4 and IL-13 levels by binding to the IL-4 receptor. Liu et al.[5] found increased IL-4 and IL-13 expression in RPC tissues in their study, and they stated that type-2 inflammation plays a role in RPC pathogenesis and that dupilumab may be an effective treatment agent. The number of cases in which dupilumab has been successfully used in the treatment of RPC is increasing in the literature.[5-9] There are case reports showing the safe and effective use of dupilumab in RPC patients with comorbidities such as chronic kidney disease, Wilson disease, coronary artery disease, cerebrovascular disease, and hepatocellular cancer.[5-8] Gil-Lianes et al.[9] applied dupilumab and NB-UVB therapy in a patient resistant to oral antihistamines, topical, systemic steroids, phototherapy, and cyclosporine in the management of atopic dermatitis and PRC. In our case, due to lack of response to multiple treatment agents, dupilumab was administered, and a full treatment response was achieved.

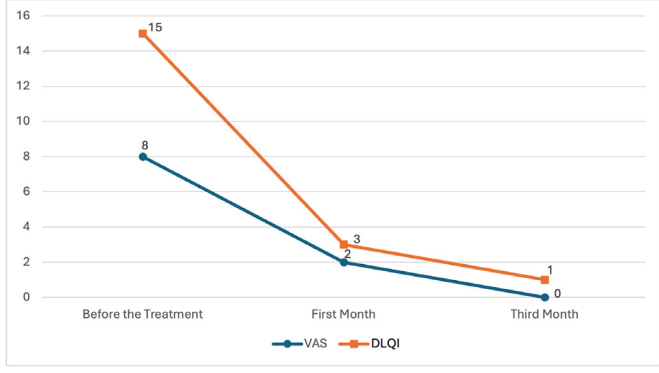

Figure 3. Change in patient's VAS and DLQI scores over time with treatment
VAS: Visual Analogue Scale, DLQI: Dermatology life quality index

Conclusion

With this case report, we would like to emphasize that dupilumab is an effective and safe treatment in the management of RPC, even in patients with multimorbidity.

Footnote

Informed Consent: Informed consent was obtained from the patient.

Authorship Contributions

Surgical and Medical Practices: Y.C.E., M.G., S.Ş., B.Ö., E.A., Concept: Y.C.E., M.G., S.Ş., B.Ö., E.A., Design: Y.C.E., M.G., S.Ş., B.Ö., E.A., Data Collection or Processing: Y.C.E., M.G., S.Ş., B.Ö., E.A., Analysis or Interpretation: Y.C.E., M.G., S.Ş., B.Ö., E.A., Literature Search: Y.C.E., M.G., S.Ş., B.Ö., E.A., Writing: Y.C.E., M.G., S.Ş., B.Ö., E.A.

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Case Report

Eruptive Milia within the Red Tattoo Pigment: A Case Report with Dermoscopic Features and Literature

Fatmanur Hacınecipoğlu, Bengü Çevirgen Cemil, Fatma Korkmaz, Selda Pelin Kartal
Clinic of Dermatology, University of Health Sciences Türkiye, Ankara Etlik City Hospital, Ankara, Türkiye

Abstract

Eruptive milia within tattoos are rare and usually self limited, yet they can mimic tattoo related inflammatory reactions that require aggressive treatment. We report a 21 year old man with tiny white papules confined to the red ink portions of a recent tattoo; dermoscopy showed multiple, millimetric, bright-white round clods, without a specific vascular component; with a smooth surface and no scale over a homogeneous red background supporting a diagnosis of milia. Recognizing this benign entity and distinguishing it from red pigment reactions such as lichenoid, granulomatous/sarcoidal, or pseudolymphomatous changes helps avoid unnecessary treatments (e.g., corticosteroids, excision or laser therapy).

Keywords: Eruptive, milia, tattoo, red pigment

Introduction

Tattoo-related dermatoses include allergic (eczematous), granulomatous, lichenoid, photosensitive, pseudolymphomatous, and infectious reactions, collectively affecting approximately 2% of tattooed individuals.[1] Eruptive milia within tattoos are a rare complication; only a few cases have been reported, and a recent review identified eight instances of tattoo-associated milia.[2] Milia in tattoos are thought to result from follicular occlusion or epidermal injury caused by ink injection, possibly accentuated by hypersensitivity to pigment components.[2,3] Red ink (cinnabar) is most frequently implicated in tattoo-related reactions, and lichenoid responses to red pigment have occasionally included secondary milia.[4] Herein, we describe a rare case of eruptive milia arising in a red-ink tattoo, highlighting its dermoscopic features and summarizing previously reported cases to help clinicians in distinguishing this benign entity from red pigment-related inflammatory reactions.

Case Report

A healthy 21-year-old man presented with asymptomatic white papules confined to the red-ink portions of a newly applied forearm tattoo; the papules appeared one month after its completion. The patient used only dexpanthenol cream for aftercare. Clinical examination of his right forearm revealed multiple millimetric, white, dome-shaped papules scattered across the red-pigmented areas, sparing the surrounding skin (Figure 1). Dermoscopy showed multiple, millimetric, bright-white, round clods with a smooth surface and no scale, set on a homogeneous red background and lacking a specific vascular component (Figure 2). Based on these clinical and dermoscopic findings, a diagnosis of eruptive milia within the tattoo was made. Topical therapy with 0.025% tretinoin cream was initiated nightly. The patient was scheduled for a three-month follow-up; however, he was lost to follow-up, and the treatment outcome could not be assessed.

Adress for correspondence: Fatmanur Hacınecipoğlu, MD, Clinic of Dermatology, University of Health Sciences Türkiye, Ankara Etlik City Hospital, Ankara, Türkiye
Email: fatmanurhno@gmail.com
ORCID ID: 0000-0002-1027-9549

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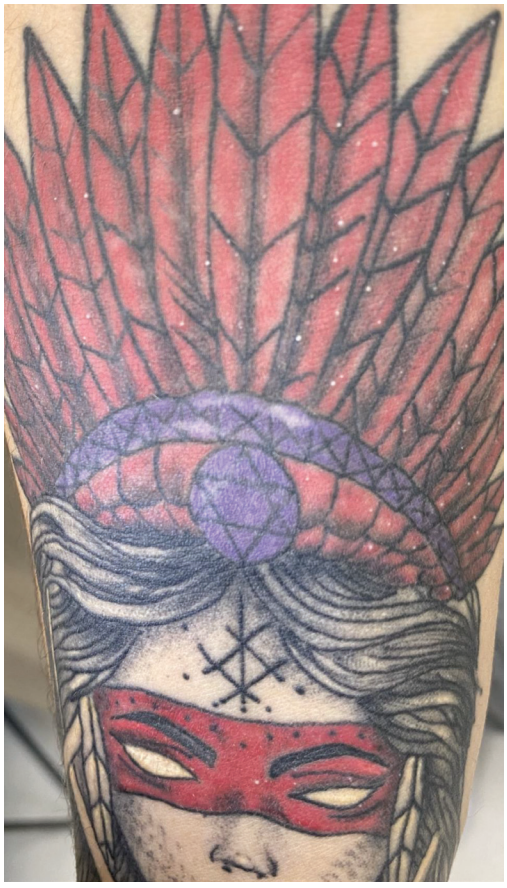

Figure 1. Numerous milimetric white, dome-shaped papules were scattered across the red pigmented areas of the tattoo, sparing the surrounding skin on the right forearm

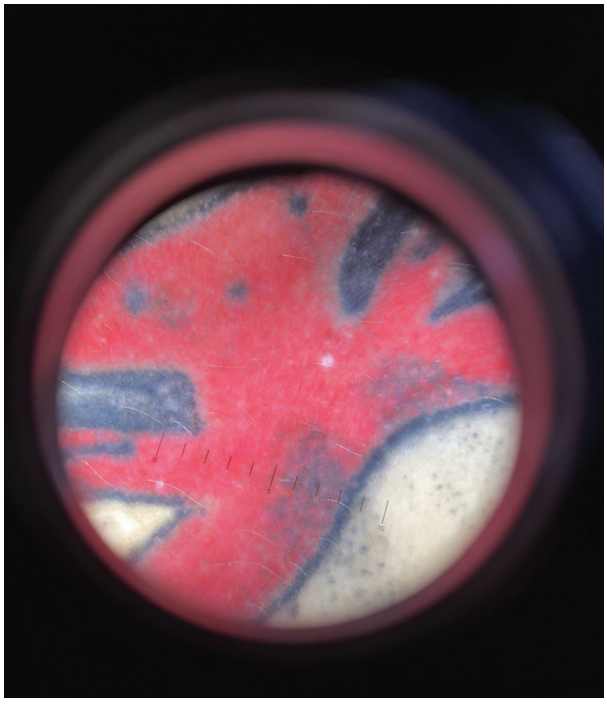

Figure 2. On dermoscopy (polarized, 10x): multiple, millimetric, bright-white round clods, without a specific vascular component; with a smooth surface and no scale over a homogeneous red background

Discussion

Eruptive milia that develop within tattoos are uncommon, yet increasingly recognized in the dermatologic literature.[2,3] Lesions typically emerge within weeks to a few months after tattooing and may occur with various pigments, though red ink is most often implicated. Red pigments, frequently containing metals or azo dyes (e.g., mercury, cadmium, ferric hydrate), are well known to provoke immunologic reactions such as lichenoid, granulomatous, or pseudolymphomatous processes, whereas black carbon-based inks are largely inert.[5]

Only eight cases of tattoo-related eruptive milia have been reported to date, commonly involving red or other bright pigments such as yellow or green.[2,3] Details of these cases, including patient demographics, pigment color, onset time, treatment, and outcome are summarized in Table 1.[2,3,6-9] Reported lesions were either limited to specific color areas or distributed throughout multicolored tattoos while sparing adjacent normal skin.

The pathogenesis remains incompletely understood but appears multifactorial, primarily related to mechanical trauma and adnexal injury. Repetitive needle penetration induces an acute, aseptic inflammatory reaction that can damage the follicular infundibulum or eccrine ducts, predisposing to secondary cyst formation.[2,3] Histopathologic findings from a previously reported lichenoid tattoo reaction with eruptive milia demonstrated partial destruction of adnexal structures, supporting this proposed mechanism.[6] Post-tattoo care measures, such as occlusive ointment massage, may promote keratin retention within micro-wounds and follicular ostia, contributing to milia formation.[3] Other secondary causes of milia, including burns, dermabrasion, and ablative laser procedures, reinforce the role of epidermal trauma and abnormal keratinization.[2] Although hypersensitivity to pigment components, especially red dyes, may induce localized inflammation, current evidence favors trauma-induced adnexal disruption and keratin accumulation as the main pathogenic mechanism.[2]

While the diagnosis of milia is generally clinical, differentiation from other post-tattoo papular eruptions, such as granulomatous, pseudoepitheliomatous, pseudolymphomatous, or lichenoid reactions, is crucial. Dermoscopy showing tiny bright-white round clods on a smooth, non-scaly surface without a vascular component supports the diagnosis and helps avoid unnecessary biopsies. Nevertheless, the dermoscopic patterns of tattoo-associated reactions have been described only in a few case reports, and systematic data remain limited. Granulomatous reactions typically display brownish-gray structureless areas with white scale, crystalline structures, and branching or irregular vessels.[10] Pseudoepitheliomatous

Table 1. Characteristics of published cases of eruptive milia associated with tattoos

Author (year)	Age/sex	Pigment color	Onset time after tattoo	Treatment	Outcome/notes
Lucke et al.,[6]	36, male	Red (milia associated with lichenoid reaction)	-	N/A	N/A
Koh et al.,[7]	24, male	Multiple colors	1 month	Urea 10% + salicylic acid 2%	Mild improvement
Miller et al.,[8]	28, male	Red and yellow	3 months	None	Near-complete spontaneous resolution at 6 months
Ross et al.,[3]	19, female	Multiple colors	1 month	Urea 40% + tretinoin 0.1%	Resolved by 2 months
Uraga et al.,[9]	26, female	Red, blue	5 months	Not stated	Not stated
Kluger,[2]	32, male	Red, black, green	2.5 months	Topical tretinoin	Outcome not reported
Kluger,[2]	N/A, female	Grey	N/A	N/A	N/A
Kluger,[2]	N/A, male	Black	N/A	N/A	N/A
Present case	21, male	Red	1 month	Topical tretinoin	Patient lost to follow-up

N/A: Not available

hyperplasia exhibits two distinct dermoscopic zones: a central keratotic area with white scale, pink-white structureless regions, comedo-like openings, white circles, red globules, hemorrhage, and hairpin or irregular vessels, surrounded by a peripheral gray-to-bluish-white zone.[11] Tattoo-associated pseudolymphoma demonstrates a homogeneous violaceous to violet-pink background with ill-defined borders and occasional white-yellow perifollicular halos.[12] In lichenoid tattoo reactions, dermoscopy reveals diffuse white scaling, pink-white structureless areas, comedo-like openings keratotic plugs, shiny white lines, rosettes, and linear or irregular vessels, but not the blue-white or gray-white areas and Wickham's striae seen in idiopathic lichen planus.[13]

Although biopsy was not performed in our patient, previously reported cases describe small keratin-filled cysts lined by stratified squamous epithelium, containing concentrically laminated keratin. Tattoo pigment granules are commonly seen extracellularly in the dermis and within dermal macrophages, while spongiosis and inflammation are absent, confirming a benign, non-inflammatory process.[3]

Eruptive milia are benign, primarily of cosmetic concern, and may resolve spontaneously without treatment.[8] In published cases, topical keratolytics (urea) softened the stratum corneum and released keratin plugs, whereas topical retinoids enhanced epidermal turnover and prevented new cyst formation.[3] The treatments used, and their outcomes are summarized in Table 1.[2,3,6-9] These conservative approaches are typically curative, and manual extraction or laser therapy is reserved for resistant cases. In our patient, topical tretinoin was prescribed; however, he was lost to follow-up, and treatment response could not be documented.

Conclusion

Eruptive milia within tattoos are rare, benign, and self-limited lesions that may mimic inflammatory or granulomatous tattoo reactions. Recognition of their clinical and dermoscopic features prevents misdiagnosis and unnecessary interventions. Awareness of this entity, particularly in red-ink tattoos, helps clinicians distinguish it from immune-mediated tattoo complications. Although follow-up was unavailable in our case, prior reports indicate good response to topical keratolytics or retinoids, underlining the effectiveness of conservative management.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of clinical details and images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.Ç.C., F.K., Concept: F.H., S.P.K., Design: F.H., S.P.K., Data Collection or Processing: B.Ç.C., F.K., Analysis or Interpretation: F.H., B.Ç.C., F.K., S.P.K., Literature Search: F.H., Writing: F.H., B.Ç.C., F.K., S.P.K.

Conflict of Interest: The authors declared that they have no conflict of interest.

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Coexistence of Two Rare Complications in a Hidradenitis Suppurativa Patient: Amyloidosis and Osteomyelitis

Yusuf Can Edek, Samed Şahin, Esra Adışen
Department of Dermatology, Gazi University Faculty of Medicine, Ankara, Türkiye

Dear Editor,

Herein, we present a male patient with hidradenitis suppurativa (HS) who has amyloidosis and osteomyelitis, two rare complications of HS.

A 54-year-old male patient with HS was evaluated in our clinic due to an increase in the severity of his symptoms. In the anamnesis taken from the patient, it was learned that his complaints included recurrent painful discharge and swelling in intertriginous areas for 20 years. During this time, the patient received systemic antibiotics, isotretinoin, and underwent surgery on his lesions. The patient, who was followed up for Hurley stage III HS, had a history of previously diagnosed gastrointestinal (four years) and renal amyloidosis and was receiving hemodialysis (five years). The patient was started on adalimumab three years ago due to its effectiveness in the treatment of HS and amyloidosis.

In the dermatologic examination of the patient, draining tunnels were observed in the inguinal area and gluteal region (Figure 1). The patient's laboratory tests revealed elevated acute-phase reactants (C-reactive protein: 103 mg/L, erythrocyte sedimentation rate: 110 mm/hr). Upon the patient's description of severe pain and difficulty in movement in the lumbosacral region, a lumbosacral magnetic resonance imaging (MRI) was performed. When osteomyelitis and abscess structures were detected on MRI (Figure 2), adalimumab was discontinued, and ertapenem antibiotherapy (6 weeks) was prescribed. The patient's adalimumab treatment was restarted after a regression was detected in his clinical complaints, laboratory tests, and MRI, and he continues this treatment.

Secondary systemic amyloidosis is caused by deposition of a distinctive non-immunoglobulin protein called amyloid A (AA), as a systemic complication of severe chronic inflammatory diseases, such as HS. Various pro-inflammatory cytokines, such as interleukin (IL)-1 and IL-6, have been reported to play a common role in the pathogenesis of HS and amyloidosis. Prolonged and severe HS can elevate serum AA levels, which may lead to amyloidosis. In cases of proteinuria and persistent diarrhea in HS patients, it is crucial to screen for amyloidosis. TNF-α inhibitors stand out as the preferred agents in the treatment of HS patients who have amyloidosis.[1-3] HS cases with renal and gastrointestinal amyloidosis involvement have been reported in the literature.[2,3] Our case had both renal and gastrointestinal amyloidosis, and adalimumab was used in the treatment.

Osteomyelitis, one of the rare complications of HS, can develop because of trauma, hematogenous spread, or contiguous spread. MRI is an important imaging method in the evaluation of gluteal and inguinal HS lesions and in the detection of complications. Although osteomyelitis is known as one of the complications of HS, it has been rarely reported in the literature. Similar to our case, Mathew et al.[4] detected osteomyelitis in two patients with Hurley stage III. Additionally, Blaizot et al.[5] reported three HS patients with bacterial osteomyelitis of the sacrum and coccyx. HS patients who have significant acute-phase reactants elevation and severe pain should be monitored for osteomyelitis.

This case highlights the possibility of coexisting amyloidosis and osteomyelitis, rare complications of HS, and emphasizes the importance of recognizing these complications.

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Address for correspondence: Yusuf Can Edek, MD, Department of Dermatology, Gazi University Faculty of Medicine, Ankara, Türkiye
Email: yusuf-can-35@hotmail.com
ORCID ID: 0000-0002-3877-8681

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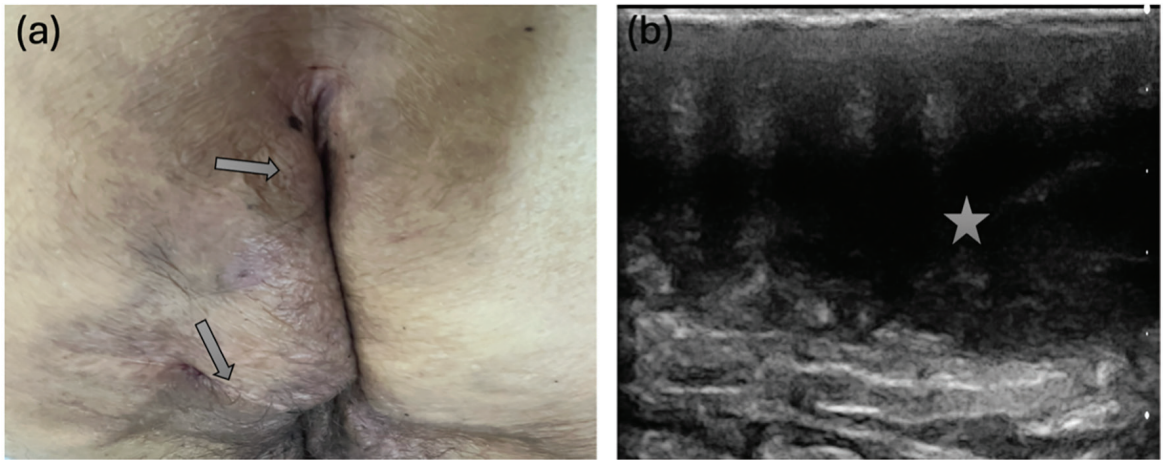

Figure 1. (a) Draining tunnels in the glutea (arrow), (b) ultrasonographic image sinus tract (star) in the glutea

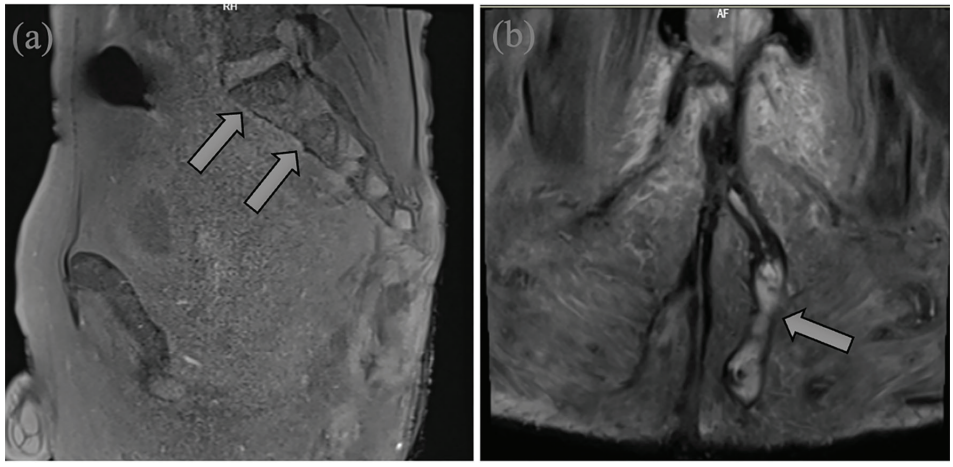

Figure 2. Magnetic resonance imaging (a) concomitant osteomyelitis in the sacral vertebrae (arrow), (b) complicated perianal fistula (arrow) starting from the anal canal and extending superiorly along the presacral area, opening to the skin at the level of the gluteal sulcus, containing abscess formations
AF: Atrial fibrillation, RH: Rhesus

Ethics

Informed Consent: The patient in this manuscript have given written informed consent to the publication of his case details.

Authorship Contributions

Surgical and Medical Practices: Y.C.E., S.Ş., E.A., Concept: Y.C.E., S.Ş., E.A., Design: Y.C.E., S.Ş., E.A., Data Collection or Processing: Y.C.E., S.Ş., E.A., Analysis or Interpretation: Y.C.E., S.Ş., E.A., Literature Search: Y.C.E., S.Ş., E.A., Writing: Y.C.E., S.Ş., E.A.

Conflict of Interest: The authors declared that they have no conflict of interest.

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Subcutaneous Emphysema Induced by Intralesional Cryotherapy

Zeynep Karaca Ural
Department of Dermatology, Atatürk University Faculty of Medicine, Erzurum, Türkiye

Dear Editor,

Subcutaneous emphysema (SE) is a rare complication characterized by the accumulation of air within the subcutaneous tissue.[1] It is most commonly associated with visceral trauma and infections.[2] However, it may also occur rarely following dermatologic procedures, particularly after hydrogen peroxide irrigation, punch biopsies, or cryotherapy.[3] In this letter, we present a case of extensive SE that developed after intralesional cryotherapy (ILC) to treat an auricular keloid and subsequently spread into deep fascial planes.

A 35-year-old otherwise healthy woman presented with a 1-cm nodular lesion on the posterior aspect of the right lobulus auriculae that developed two years after an ear-piercing procedure (Figure 1a). The histopathological findings were consistent with keloid. The patient had undergone surgical excision and intralesional steroid injections. Because of recurrence, combination therapy consisting of ILC followed by intralesional steroid injection was initiated. During the third session, intralesional steroid was first administered, followed by ILC using an open-ended needle attached to a metallic cryoprobe shaft. Before the procedure, a needle was inserted through the nodule, with its tip left protruding externally; however, following cryotherapy, the needle was removed from the lesion before the device was disconnected.

Five minutes after the procedure, the patient developed marked facial edema, uvular deviation to the right, dyspnea, and crepitus on palpation of the mandibular and postauricular regions (Figure 1b). Computed tomography of the maxilla and thorax revealed widespread SE extending from the postauricular region to the supraclavicular region and radiating into the parapharyngeal, submandibular, and mediastinal spaces (Figure 2). The patient was followed up, and the emphysema regressed spontaneously within 3-5 days. However, exertional symptoms persisted for 1-2 months before complete resolution.

While SE has occasionally been reported after spray or contact cryotherapy, its development following ILC remains exceedingly rare, with only a few cases documented in the literature.[1-3] In our case, the presence of multiple prior ILCs, the use of an open-ended needle, or the possibility that the needle tip had shifted toward the lesion during the procedure may have created a pathway allowing nitrogen gas to leak into the subcutaneous tissue. Previous reports have also emphasized that disruptions in skin integrity may serve as one-way valves for pressurized gas, facilitating the development of SE.[2,3]

The case reported by Falay Gür et al.[1] was the first to describe SE following ILC, with the complication attributed to the use of an open-ended needle and the lack of a safety system. Martínez-Coronado et al.[3] reported that spray cryotherapy, when applied after intralesional injections, increased the risk of SE, particularly in elderly patients, in those with damaged skin barriers or atrophic skin, or in areas with a thin dermis. In such settings, the use of a cotton-tipped applicator is recommended to minimize the risk.[2,3]

Specialized cryoprobe systems, such as CryoShape, which are designed with a closed distal tip and a double-lumen structure, may reduce tissue trauma and prevent gas leakage. In contrast, open-ended needle systems may increase the risk of SE, particularly when a needle is connected to the cryotherapy device before insertion into the lesion or disconnected only after needle removal.[1] In most cases of SE reported in

Adress for correspondence: Zeynep Karaca Ural, Asst. Prof., MD, Department of Dermatology, Atatürk University Faculty of Medicine, Erzurum, Türkiye
Email: zeynepkaraca.zk90@gmail.com
ORCID ID: 0000-0002-3333-7027

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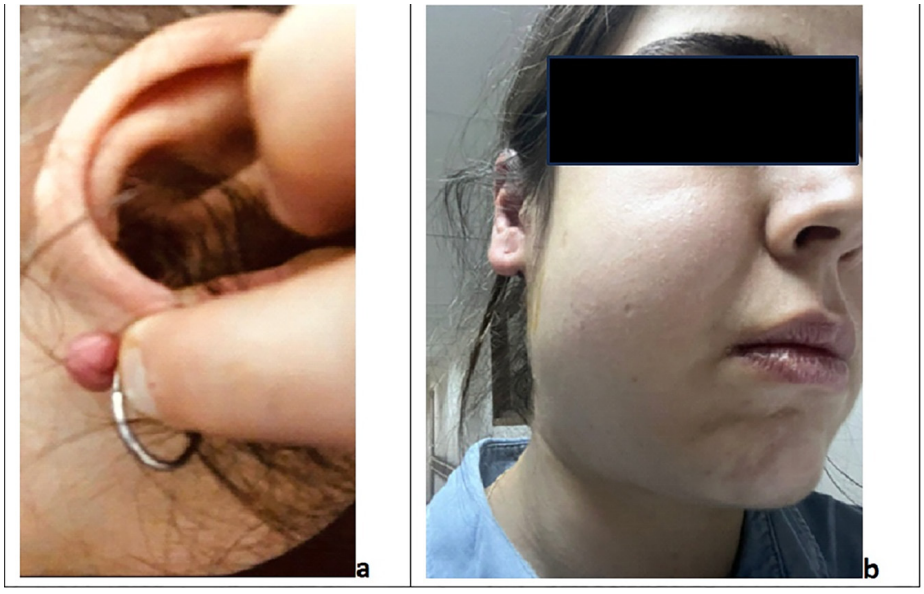

Figure 1. (a) Nodular lesion located on the posterior aspect of the auricle before the procedure; (b) post-procedural edema observed in the mandibular region

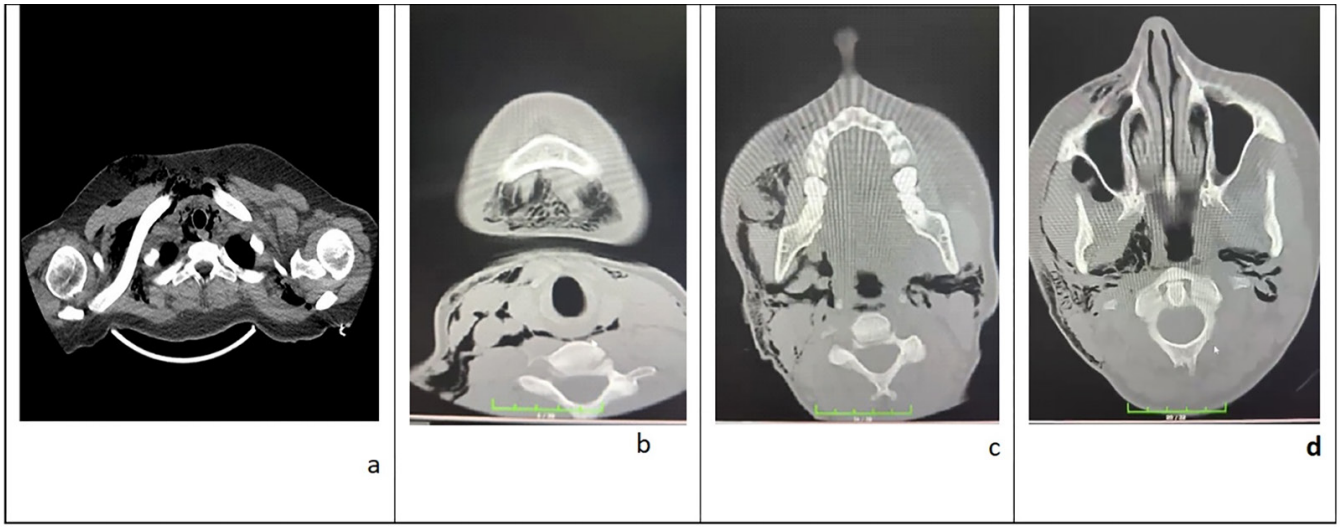

Figure 2. Computed tomography images showing (a,b) air densities extending from the mediastinal area into the subcutaneous tissues between the cervical muscle layers, including the retropharyngeal, submandibular, and sublingual spaces, as well as along the upper posterior and anterior thoracic walls and the posterior mediastinum; (c,d) subcutaneous emphysema more prominently involving the right side of the neck, extending into the bilateral parapharyngeal, masticator, and parotid spaces, the right temporal fossa, posterior cervical triangle, and nasopharyngeal spaces, surrounding the adjacent vascular structures

the literature, the condition resolved spontaneously with supportive care, and no additional treatment was required.[3,4] Similarly, in our patient, facial swelling and crepitus subsided rapidly. However, unlike previously reported cases, our patient-who was followed jointly with the thoracic surgery department-experienced exertional dyspnea that persisted for up to two months. We believe this prolonged symptom may have been related to the extensive spread of SE, including mediastinal involvement. The complaint also resolved spontaneously during the follow-up period.

This case underscores the importance of appropriate technique and equipment selection during ILC. To minimize the risk of SE, clinicians should prefer closed-system cryoprobes, avoid open-ended needles, and exercise particular caution in anatomically vulnerable areas or in previously treated lesions.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of clinical details and images.

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