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# Comparison of Skin Findings on Both Sides of the Body in Patients with Hemiplegia and Hemiparesis

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## Abstract

**Aim:** It has been reported that some dermatological diseases have a different course on the hemiplegic/hemiparesis side of the body. We aimed to determine which skin diseases are common in hemiplegic/hemiparesis patients and whether there are differences between the skin findings on both sides.

**Materials and Methods:** Between March 2022-March 2023, 51 patients with a history of hemiplegia/hemiparesis longer than 6 months were evaluated. The patient group was based on data from the hemiplegic/hemiparesis side of the patients, and the control group was based on data from the healthy side. Demographic features of the patients and the characteristics of their neurological diseases were recorded. Dermatological findings of the healthy side and the hemiplegic/hemiparesis side of the patients were recorded separately and compared statistically with chi-square tests. A value of  $P < 0.05$  was considered significant.

**Results:** Of the total 51 patients, 23 (45.1%) were female and 28 (54.9%) were male with a mean age of  $65.00 \pm 11.38$  (41-85). Skin findings were detected in 46 (90.2%) patients; no dermatological pathology was detected in 5 (9.8%) patients. Xerosis and onychomycosis were detected most frequently and were located symmetrically. For all skin findings there was no statistically significant difference between the healthy side and hemiplegic/hemiparesis side of the body in the course and localisation of all skin findings ( $P > 0.05$ ).

**Conclusion:** Although we could not detect a significant difference between the healthy and hemiplegic/hemiparesis side of the body, hypotrichosis, cyanosis, and stasis dermatitis were found exclusively on the hemiplegic/hemiparesis side, while psoriasis lesions were more prominent on the intact side.

**Keywords:** Hemiplegic, hemiparesis, xerosis, psoriasis, hypotrichosis, cyanosis, stasis dermatitis

## INTRODUCTION

Hemiplegia is a neurological disorder characterized by a complete loss of muscle strength, and hemiparesis is a partial loss of muscle strength in one half of the body. Both conditions usually occur as a result of an acute hemorrhagic or ischemic cerebrovascular event.<sup>1</sup> Alterations in cutaneous blood flow and autonomic functions may also occur on the hemiplegic/

hemiparetic side of the body.<sup>2-4</sup> In addition, due to loss of motor function, difficulties with self-care may be observed. Inability to clean the skin adequately and moistness of the fold areas may cause hygienic problems. Besides these loss of sensation can also change the course of skin diseases. In fact, it has been observed that there are differences in the course of some skin diseases in patients with hemiplegia/hemiparesis.<sup>2-14</sup>

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In previous case reports, bullous pemphigoid, clubbing of fingers, scabies, some endogenous eczemas, and tinea versicolor lesions have been reported only on the hemiplegic/hemiparesic side or to be more prominent on that side.<sup>5,6,8,9,13,14</sup> In some case reports of patients with scleroderma and psoriasis, the lesions were reported on the healthy side.<sup>7,10</sup>

Since the research and case reports on this subject are limited in number, we conducted this study to evaluate which skin diseases are more common in hemiplegic/hemiparesic patients and whether there is a clinical difference between the hemiplegic/hemiparesic side and the intact side of the body. We aimed to achieve an early diagnosis and treatment opportunity, and to improve the quality of life for patients by determining the dermatological diseases that may occur in hemiplegic/hemiparesic patients.

## MATERIALS AND METHODS

Our research was planned and conducted by the Dermatology, Neurology, and Physical Therapy and Rehabilitation (PTR) clinics at Kocaeli University Faculty of Medicine (KOU-FM) and Kocaeli Derince Education and Research Hospital.

This research is a descriptive prospective study, and data collection started after approval was obtained from the Clinical Research Ethics Committee of Kocaeli University (approval number: 2022/05.03, date: 04.03.2022). A total of 51 hemiplegia/hemiparesis patients who were admitted to Neurology, PTR, and Dermatology outpatient clinics were included in the study. Between March 2022-2023, patients with a history of hemiplegia/hemiparesis for more than 6 months were included, and patients with neurological diseases with a duration of less than 6 months were excluded from the study. Demographic characteristics of the patients, comorbidities, characteristics of neurological diseases and dermatological findings were recorded on the patient examination forms. Detailed examinations, including microscopic examination and dermatoscopy, were performed if needed. Skin findings of the healthy side and the hemiplegic/hemiparesic side of the patients were recorded separately. The patient group was formed with the data obtained from the hemiplegic/hemiparesic body side, and the control group was formed with the data obtained from the healthy side of the same patients. Dermatological findings of the healthy side and the hemiplegic/hemiparesic side of the patients were compared statistically.

### Statistical analysis

Statistical evaluation was performed using the IBM SPSS 20.0 (IBM Corp., Armonk, NY, USA) package program. In order to determine the sample size of the study, the G\*Power

version 3.1.9.2 (Kiel University, Kiel, Germany) package program was used. In the power analysis, the values of “alpha = 0.05, Beta = 0.90, effect size = 0.65 “ were used, and accordingly, the number of patients was determined at least 51. Numerical variables were given as mean ± standard deviation and frequency (percentages). Fisher’s exact chi-square test, Yates’ chi-square test, and Monte Carlo chi-square test were used for categorical variables in order to evaluate the differences between the groups. A value of  $P < 0.05$  was considered statistically significant.

## RESULTS

The ages of the 51 patients, were between 41 and 85 (65.00 ±11.38). Twenty-three of our patients (45.1%) were women, 28 (54.9%) were men, and there was no statistically significant difference in distribution ( $P = 1$ ). Twenty-six (51.0%) patients had hemiparesis, 25 (49.0%) patients had hemiplegia, and the neurological deficit was on the right side in 26 (51.0%) patients and on the left side in 25 (49.0%) patients. The distributions were statistically similar ( $P = 1$ ). The duration of hemiplegia/hemiparesis was determined as 6 months-1 year in 22 (43.1%) patients, 1-2 years in 5 (9.8%) patients, and > 2 years in 24 (47.1%) patients. The cause of hemiplegia/hemiparesis was an ischemic event in 38 (74.5%) patients and a hemorrhagic event in 23 (25.5%) patients ( $P = 1$ ). Demographic features, characteristics of neurological deficit and comorbidities of patients are seen in Table 1.

According to the results of dermatological examination, there were no skin lesions in 5 (9.8%) patients. Onychomycosis and xerosis were detected most frequently in the whole group. Psoriasis vulgaris, pigmented purpuric dermatosis, stasis dermatitis, rosacea, scabies, oral candidiasis, anogenital warts, actinic keratosis and onychogryphosis were present in only 1 patient (1.9%). No dermatological pathology was detected in 5 patients (9.8%). Other dermatological findings according to the order of frequency are seen in Table 2.

The comparison of skin findings according to their localization on both sides of the body is seen in (Table 3). It was observed that the difference between the healthy side and the hemiplegic/hemiparetic side was not statistically significant ( $P > 0.05$ ). There was also no significant relationship between the duration of the disease and dermatological findings of the patients ( $P = 1$ ).

The distribution of skin findings on the hemiplegic/hemiparetic and healthy sides is seen in Table 4. Xerosis was located symmetrically in all patients, and onychomycosis was located symmetrically in 81.5% of them. Hypotrichosis, cyanosis, and stasis dermatitis were detected only on the hemiplegic/hemiparetic side of the patients. In most of the

contact dermatitis patients (75%), lesions were detected on the hemiplegic/hemiparesic side of the body. Psoriasis lesions were present on both sides, but were more prominent on one side. Erythema ab igne was seen in two patients. In 1 patient, it was seen only on the hemiplegic side of the body, but in the other patient, it was seen on both sides of the body but more prominent on the hemiplegic side.

**Table 1. Demographic features, characteristics of neurological damage and comorbidities of patients**

Number of patients (n)	51
Age (mean ± SD)	(41-85) 65.00±11.38 year
Female/male, n (%)	23 (45.1%)/28 (54.9%)
Neurological damage; hemiparesis/hemiplegia, n (%)	26 (51.0%)/25 (49.0%)
Damaged body side; right/lef, n (%)	26 (51.0%)/25 (49.0%)
Duration of neurological damage, n (%)	
6 month-1 year	22 (43.1%)
1-2 year	5 (9.8%)
> 2 year	24 (47.1%)
Cause of neurological damage, n (%)	
Ischemic event	28 (54.9%)
Hemorrhagic event	23 (45.1%)
Comorbidities, n (%)	
Hypertension	39 (76.5%)
Diabetes mellitus	17 (33.3%)
Coronary artery disease	11 (21.6%)
Rhythm disorders	8 (15.7%)
Hyperlipidemia	6 (11.8%)
Heart failure	2 (3.9%)
Hypothyroidism	2 (3.9%)
Chronic obstructive pulmonary disease	1 (2.0%)
No comorbidity	5 (9.8%)
SD: Standard deviation	

**Table 2. Skin findings of patients**

Skin findings	Number of patients n (%)
Onychomycosis	27 (52.9)
Xerosis	19 (37.2%)
Tinea pedis	5 (9.8%)
Hypotrichosis	5 (9.8%)
Seborrheic keratosis	5 (9.8%)
Lentigo	5 (9.8%)
Seborrheic dermatitis	4 (7.8%)
Contact dermatitis	4 (7.8%)
Cherry angioma	4 (7.8%)
Cyanosis	3 (5.8%)
Erythema intertrigo	3 (5.8%)
Erythema ab igne	2 (3.9%)

## DISCUSSION

As a result of the cerebrovascular hemorrhagic or ischemic events, changes in the motor, sensory, autonomic nervous system functions may occur on the hemiplegic/hemiparesic side of the body, and the alterations in neurological functions may change the clinical course of skin diseases.<sup>2,5-14</sup> In our study, there was no statistically significant difference between the healthy and hemiplegic/hemiparesic side of the body, but it was remarkable that some dermatological findings such as hypotrichosis, cyanosis, stasis dermatitis, were found to be located only on the hemiplegic/hemiparesic side and psoriasis lesions were more prominent on the healthy side.

In a previous study with hemiplegia/paraplegia patients, tinea pedis, onychomycosis, xerosis, and hypotrichosis of the lower extremities were reported as most commonly observed skin findings, and it was reported that the duration of neurological damage had no effect on the occurrence of these conditions. According to this study, limb edema was reported to be only on the hemiparesic side and other dermatological findings were reported as bilaterally located.<sup>11</sup> In another study, it was reported that endogenous eczema, such as nummular dermatitis, dyshidrotic dermatitis, Id reaction, and atopic dermatitis, were found on the neurologically damaged side.<sup>9</sup> Similarly, in a case

**Table 3. The comparison of skin findings according to their localization on both sides of the body**

Dermatological finding	Number of patients n (%)		P
	Hemiparesic/hemiplegic side	Intact side	
Onychomycosis	27 (52.9%)	23 (45.1%)	0.693
Xerosis	19 (37.3%)	19 (37.3%)	1
Tinea pedis	5 (9.8%)	4 (7.8%)	1
Hypotrichosis	5 (9.8%)	0	0.056
Seborrheic keratosis	5 (9.8%)	3 (5.9%)	0.715
Lentigo	5 (9.8%)	5 (9.8%)	1
Seborrheic dermatitis	4 (7.8%)	3 (5.9%)	1
Cherry angioma	4 (7.8%)	3 (5.9%)	1
Contact dermatitis	3 (5.9%)	1 (1.9%)	0.617
Erythema intertrigo	2 (3.9%)	3 (5.9%)	1
Cyanosis	3 (5.9%)	0	0.243
Erythema ab igne	2 (3.9%)	1 (1.9%)	1
Psoriasis vulgaris	1 (1.9%)	1 (1.9%)	1
Pigmented purpuric dermatosis	1 (1.9%)	1 (1.9%)	1
Stasis dermatitis	1 (1.9%)	0	1
Rosacea	1 (1.9%)	1 (1.9%)	1
Scabies	1 (1.9%)	1 (1.9%)	1
Anogenital wart	1 (1.9%)	1 (1.9%)	1
Actinic keratosis	1 (1.9%)	1 (1.9%)	1
Onychogryphosis	1 (1.9%)	1 (1.9%)	1

<b>Table 4. Localisation of skin findings</b>				
<b>Skin finding</b>	<b>Unilateral</b>		<b>Bilateral</b>	<b>Total</b>
	<b>Healthy side</b>	<b>Hemiplegic/hemiparesic side</b>		
Onychomycosis	1	3	22	27
Xerosis	0	0	19	19
Tinea pedis	0	1	4	5
Hypotrichosis	0	5	0	5
Seborrheic Keratosis	0	2	3	5
Lentigo	0	0	5	5
Seborrheic Dermatitis	0	1	3	4
Contact Dermatitis	1	3	0	4
Cherry angioma	1	0	3	4
Erythema intertrigo	1	0	2	3
Cyanosis	0	3	0	3
Erythema ab igne*	0	1	1	2
Oral candidiasis	0	0	1	1
Scabies	0	0	1	1
Anogenital verru	0	0	1	1
Rosacea	0	0	1	1
Stasis dermatitis	0	1	0	1
Actinic keratosis	0	0	1	1
Pigmented purpuric dermatosis	0	0	1	1
Onychogryphosis	0	0	1	1
Psoriasis*	0	0	1	1

\*Bilaterally located lesions are more prominent on the hemiplegic/hemiparesic side of the body

report, the bullous pemphigoid lesions of a hemiplegic patient were found to be more prominent on the hemiplegic side.<sup>5</sup> In addition, there was a case report describing a patient with severe motor-sensory loss where scabies lesions were located only on the hemiparetic side.<sup>8</sup> For seborrheic dermatitis, there were two studies but the results were contradictory. Thomas et al.<sup>12</sup> measured the sebum production in paraplegic patients and they reported that there was no difference. However, Burton et al.<sup>13</sup> had reported that, sebum production decreased on the neurologically damaged side of the body and they thought that it may be due to alterations in the sympathetic innervation. On the other hand, there was only one case report about psoriasis in the literature and the lesions were reported as located only on the healthy side of the body.<sup>10</sup> We also previously reported a case in which tinea versicolor lesions were located bilaterally but were more prominent on the hemiparesic side of the body.<sup>1</sup>

In our current research, onychomycosis was observed most frequently, and xerosis, tinea pedis, hypotrichosis followed it, respectively. We also observed that there was no relation between the duration of neurological deficit and the features of the dermatological findings. The main goal of our study was to compare the healthy side and the neurologically damaged side. When all the skin findings of our patients were evaluated, there was no significant difference between the two sides of the body. Oral candida, anogenital verrucae, rosacea, actinic keratosis, pigmented purpuric dermatosis, and onychogryphosis were present in only one patient, and all were located symmetrically. However, in our patients, hypotrichosis, cyanosis, and stasis dermatitis lesions were all located on the neurologically damaged side. We thought that this could be explained by decreased blood flow and immobilization.

On the other hand, our study found no statistically significant difference in the clinical course and localization of seborrheic dermatitis. This result is compatible with Thomas et al.<sup>12</sup>, but not compatible with Burton et al.<sup>13</sup>

For contact dermatitis, there were history of disinfectants and cologne usage in our patients. We thought that the localisation of contact dermatitis lesions is because of these chemicals and is not related to neurological damage.

In our study group, there was only one patient with psoriasis vulgaris. The patient presented with mild hemiparesis and slight loss of sensation on the hemiparesic side. His lesions were localized on both sides, but they were more prominent on the intact side. We thought that there were more lesions on the intact side because of the itching-induced Koebner phenomenon. On the other hand, there was only one case report about psoriasis in the literature. The lesions were reported as located only on the intact side of the body.<sup>1</sup> There was no sensation loss on either side of this patient, and there was friction due to the prosthesis on the hemiparetic side. Despite this, it has been reported that the lesions were seen on the healthy side and not on the hemiparesic side. So they thought that this may be due to other unexplained cortical factors.<sup>10</sup> So we also thought that Koebner phenomenon for psoriasis lesions may have an effect on the localization and amount of lesions, but these differences cannot be explained only by the Koebner phenomenon.

We detected scabies in only 1 patient, and in this hemiplegic patient, the lesions were symmetrically located. There was a case report of a patient with severe motor-sensory loss, indicating that scabies lesions were located only on the hemiparesic side.<sup>8</sup> For this case, Speight<sup>8</sup> thought that mechanical trauma such as itching reduces the parasite load, but since there is no itching sensation and exposure

to mechanical trauma in this patient, the parasite continues to increase on that side. They also reported that the patient was wearing gloves because the hand on the hemiparetic side was cold. So they thought that severe motor loss of the hemiparesic hand and gloves wearing may avoided the spread of the parasite to the opposite side by scratching.<sup>8</sup> Although our patient was hemiplegic, the lesion distribution was symmetrical and we thought that this was because scabies is an easily transmitted parasitic infection.

Erythema ab igne was observed in 1 patient only on the hemiparesic side and in 1 patient on both sides, but it was more prominent on the hemiparesic side. Erythema ab igne occurs as a result of hot contact and may be more prominent on the side where the heat application is more intense. So, we thought that decreased blood flow and motor function may lead to coldness of extremities, longer lasting hot application may lead to erythema ab igne lesions on the hemiplegic or hemiparetic side of the body. In addition, due to the loss of sensation, the patient may have kept the hot application for a long time because he could not feel the excess heat on the hemiplegic side.

### Study Limitations

We believe that the number of patients in our study was insufficient. This was our major limitation. Our results were not statistically significant due to the limited number of patients within the subgroups having dermatological findings.

### CONCLUSION

We observed that onychomycosis, xerosis, tinea pedis, and hypotrichosis are common in hemiplegic/hemiparetic patients.

Most of the dermatological findings were located symmetrically, but hypotrichosis, cyanosis, and stasis dermatitis lesions were all located only on the neurologically damaged side.

In patients with hemiplegia/hemiparesis, skin diseases may show a different clinical course due to decreased blood flow, alterations in the autonomic nervous system, and changes in the motor-sensory functions.

For dermatological diseases, if not diagnosed and treated, there may be important complications. Dermatological findings such as stasis dermatitis, hypotrichosis and cyanosis are important because they can indicate circulatory disorders. Erythema ab igne can be precancerous; it should be diagnosed early; patients and their relatives should be educated about hot applications. It is also important to monitor immobile patients

for secondary fungal infections. So routine dermatological examination should be performed in patients with hemiplegia and hemiparesia to prevent the complications

The most important limitation of this study is the small number of cases. Therefore, we believe that there may be statistically significant differences if more patients are included in the study. Larger research should also be conducted for each dermatological finding specifically, especially, for stasis dermatitis, hypotrichosis, cyanosis, erythema ab igne, psoriasis vulgaris and seborrheic dermatitis, to describe their etiopathogenesis more clearly.

### Ethics

**Ethics Committee Approval:** This research is a descriptive prospective study, and data collection started after approval was obtained from the Clinical Research Ethics Committee of Kocaeli University (approval number: 2022/05.03, date: 04.03.2022).

**Informed Consent:** Patients were informed and patient consents were obtained.

### Footnotes

#### Authorship Contributions

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

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# Scabies on YouTube: The Quality, Accuracy, and Reliability of the Videos

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## Abstract

**Aim:** Scabies is a contagious skin disease characterized by itching and rashes, caused by a mite known as *Sarcoptes scabiei* var. hominis. Video sharing platforms like YouTube serve as valuable resources for individuals seeking to learn about diseases and their treatments. However, the quality of these videos can vary significantly. Videos that present misleading or incomplete information may misinform viewers and result in inappropriate treatments. Therefore, in the present study, we examined the quality and reliability of information in videos about scabies, which has seen a rise in prevalence in recent years, making it significant for both individual and public health.

**Materials and Methods:** A YouTube search was conducted in June 2024 using the keywords “scabies” and “scabies treatment.” A total of 105 videos were analyzed. Factors such as the source, availability, and duration of the videos, as well as the number of views, likes, dislikes, and comments, were recorded. The broadcasters were categorized as healthcare professionals (including medical doctors, dentists, and pharmacists), healthcare institutions (hospitals and universities), news channels (national TV networks), healthcare websites, and independent individuals. Modified DISCERN, Global Quality Scale (GQS), and the Journal of the American Medical Association (JAMA) scales were utilized to assess the quality, accuracy, and reliability of the videos. Overall intergroup data analyses were carried out.

**Results:** The comparison of the video sources revealed that videos published by independent individuals or institutions garnered more views compared to other sources ( $P < 0.05$ ). Videos published by independent individuals and institutions received significantly more likes, dislikes, and comments in comparison to the other sources ( $P < 0.05$ ). Health institutions and healthcare websites garnered fewer comments. There was no significant difference among the sources based on video length ( $P > 0.05$ ). The modified DISCERN, GQS, and JAMA scores of the videos uploaded by healthcare professionals were higher ( $P < 0.05$ ).

**Conclusion:** Although the quality of scabies content on YouTube varied, information from independent content providers was generally less reliable compared to professional sources, making it harder for individuals seeking health information to access accurate details and increasing the risk of misinformation. It is vital for both individual and public health that health professionals take a more active role on social media platforms like YouTube, and produce reliable, high-quality content.

**Keywords:** YouTube, social media, scabies, reliability, quality

## INTRODUCTION

Scabies is a contagious skin disease caused by a mite known as *Sarcoptes scabiei* var. hominis. The parasite burrows into the skin, resulting in severe itching and rashes. If left untreated, it can lead to various complications. Scabies is a

prevalent dermatological condition and public health concern that affects millions worldwide.<sup>1,2</sup>

Digital media is a common means of accessing healthcare information. Video sharing platforms such as YouTube are

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important resources for individuals who seek information about diseases and treatments.<sup>3</sup> However, the quality and accuracy of the content on these platforms could vary. Videos that contain misleading or incomplete information can misinform viewers and result in inaccurate treatments.<sup>4</sup> Analyzing the quality of information in these videos is critical for public health, improving access to accurate information, and reducing the impact of misleading information.<sup>3,4</sup>

Previous studies have reported that health videos on YouTube often include misleading, incomplete, or unscientific information, potentially leading to misconceptions and harmful self-care practices.<sup>3</sup> Therefore, it is crucial to assess the quality of videos published on diseases like scabies, as mismanagement could result in prolonged illness and increased contagion.

Thus, the present study aimed to analyze the information quality, accuracy, and reliability of videos published on YouTube about scabies as its prevalence has increased in recent years. The study also aimed to determine the potential effects of these videos on society and offer recommendations for health professionals and content producers.

## MATERIALS AND METHODS

On June 21, 2024, a YouTube search was conducted using the keywords “scabies” and “scabies treatment”. The “incognito” mode in Google Chrome (Google Inc., CA, USA) was utilized for browsing YouTube. The browsing history was deleted prior to the search to prevent previous online activities from impacting the search results. Advertising, music videos, videos without audio, videos in languages other than Turkish, and duplicate videos were excluded from the study. A total of 105 selected videos were reviewed by three experts in dermatology and venereal diseases, (N.G.G., Z.U., V.E.). The average scores of the three dermatologists who evaluated the videos were calculated. The source, age, and duration of the videos, as well as the number of views, likes, dislikes, and comments, were documented. The video sources were categorized as healthcare professionals (medical doctors, dentists, pharmacists), healthcare institutions (hospitals, universities), news channels (national TV channels), healthcare websites, and independent individuals.

The reliability of the videos was assessed using the modified DISCERN scale. The DISCERN score evaluates the accuracy and reliability of medical information presented in a video. For each item on the scale, the score ranges from 1 to 5, with a higher score indicating greater reliability.<sup>5</sup> The Global Quality Scale (GQS) and the Journal of the American Medical Association (JAMA) scales were utilized to assess video quality. The GQS is used to evaluate how positive the video content is for the general perception and audience. The GQS

is a five-point Likert-type scale that evaluates the overall educational quality of a video from the viewer’s perspective, and a higher score on the scale indicates better quality.<sup>6</sup> JAMA is a 4-point Likert scale that assesses quality based on authorship, ethics, citations, explanation, and validity criteria. The scale score reflects the medical accuracy and ethical transparency of the video (Table 1).<sup>7</sup>

Video popularity was calculated using a formula that included the video power index (VPI), “like rate”:  $[(\text{likes} \times 100)/(\text{likes} + \text{dislikes})]$ , and “view rate”: (daily views);  $VPI = [(\text{like rate} * \text{view rate})/100]$ .<sup>8</sup> YouTube has hidden the dislike count in 2022.<sup>9</sup> However, the dislike count was collected using other software.

## Statistical analysis

Descriptive statistics for qualitative study variables are presented as counts and percentages, while descriptive statistics for quantitative variables are displayed as means, standard deviations (SD), medians, and the 1<sup>st</sup> and 3<sup>rd</sup> quartiles. The normal distribution of the quantitative variables was assessed using the Shapiro-Wilk test. The Kruskal-Wallis test was employed to compare the means of more than two independent groups. The Dunn test was used as the post-hoc method for pairwise comparisons. Spearman correlation analysis was performed to assess the correlations between quantitative variables. A statistical significance level of 0.05 was established, and the analyses were conducted using SPSS (version 28) software.

## RESULTS

The study analyzed YouTube videos about scabies using various metrics. A total of 105 videos were examined, and their relationships with quality assessment criteria-such as video views, likes, and dislikes, comments, and video duration-were evaluated using DISCERN, GQS, JAMA, and VPI. Furthermore, videos were categorized into five groups based on their source: healthcare professionals (group 1), healthcare institutions (group 2), news channels (group 3), healthcare websites (group 4), and independent individuals or institutions (group 5).

### General Analysis of the Videos

**Views:** The average view count was 87166.23, and the SD of this figure was notably high (161920.388) (Table 2). The lowest 25% (Q1) had 2,346.50 views, the median was 652.00 views, and the 75% (Q3) was 015.00 views. The comparison of video sources showed that videos published by independent individuals or institutions received more views compared to others ( $P < 0.05$ ).

**Likes and dislikes:** The average number of likes was 835.37, and the median number of likes was 89.00. Videos published by independent individuals and institutions received significantly more likes compared to videos by other sources ( $P < 0.05$ ). The videos published by independent individuals or institutions also received significantly higher dislikes compared to others ( $P < 0.05$ ).

**Comments:** The average number of comments was 289.49, while the median number was 33.00. It was found that videos published by independent individuals or institutions garnered more comments ( $P < 0.05$ ). Posts from health institutions and websites received fewer comments.

**Video length:** The average duration of the videos was 7.22 minutes, and the median duration was 4.00 minutes. There is

no significant difference in the duration of the videos posted by different sources ( $P > 0.05$ ).

**Video Quality**

**DISCERN score:** The modified DISCERN score for the videos posted by healthcare professionals and organizations was significantly higher ( $P < 0.05$ ).

**GQS:** There were differences in GQS scores based on source, with videos posted by independent individuals receiving lower scores ( $P < 0.05$ ).

**JAMA score:** The JAMA scores of videos uploaded by healthcare professionals were higher ( $P < 0.05$ ) (Table 3).

Table 1. Description of the scores used in the assessment	
Description of the scores used in the assessment	
Modified DISCERN tool (1 point for every “yes,” 0 points for “no”)	
1. Is the aim of the video clear and understandable? 2. Are reliable sources of information used? (i.e., publication cited, speaker is rheumatologist). 3. Is the information presented balanced and unbiased? 4. Are additional sources of information listed for patient reference? 5. Are areas of controversy/uncertainty mentioned?	
GQS (select the appropriate one)	
1. Poor quality, poor flow of the video, most information missing, not useful for patients. 2. Generally poor quality, poor flow, some information given but many important topics missing, of very limited use to patients. 3. Moderate quality, suboptimal flow, some information is adequately discussed but other information inadequately discussed, somewhat useful for patients. 4. Good quality, good flow, most of the relevant information is listed, but some topics not covered, useful for patients. 5. Excellent quality and flow, very useful for patients.	
The JAMA criteria (each of the criteria was rated as 1 point)	
1. Authorship: Author and contributor credentials and their affiliations should be provided. 2. Attribution: References and resources for all content should be listed clearly, and all relevant copyright information noted. 3. Disclosure: Website “ownership” should be prominently and fully disclosed, as should any sponsorship, advertising, underwriting, commercial funding arrangements or support, or potential conflicts of interest. 4. Currency: Dates of uploaded content and subsequent updates should be provided	
GQS: Global Quality Scale, JAMA: The Journal of the American Medical Association	

Table 2. Basic data of analyzed videos					
	Mean	SD	Percentiles		
			Q1	Median	Q3
Days on Youtube	727.77	553.881	305.00	524.00	965.50
Number of views	87166.23	161920.388	2346.50	17652.00	93015.00
Number of like	835.37	2652.399	17.00	89.00	415.00
Number of dislike	30.09	74.316	0.00	0.00	8.50
Number of comment	289.49	564.461	1.00	33.00	292.00
Duration (minutes)	7.22	9.724	2.00	4.00	8.50
Modified DISCERN score	3.32	1.091	3.00	3.00	4.00
GQS score	3.27	1.043	3.00	3.00	4.00
JAMA score	1.59	0.698	1.00	1.00	2.00
VPI score	132.57836	223.508542	4.23250	33.60500	137.42750
Like rate	97.8483	3.32390	96.7250	100.0000	100.0000
Viewing rate	136.57802	229.696973	4.23250	33.60500	146.54000
GQS: Global Quality Scale, JAMA: The Journal of the American Medical Association, VPI: Video power index, SD: Standard deviation					



<b>Table 3. Comparison of video metrics, popularity, reliability and quality scores by video sources</b>				
	<b>Video sources*</b>	<b>Mean</b>	<b>SD</b>	<b>P</b>
Days on YouTube	1	755.00	497.968	0.319
	2	648.82	570.639	
	3	765.09	553.060	
	4	558.06	439.236	
	5	913.53	738.133	
Number of views	1	99718.52	174390.269	0.002
	2	57537.71	149923.679	
	3	95802.73	117861.566	
	4	23524.89	57911.212	
	5	160180.20	251838.643	
Number of like	1	919.48	1646.832	0.010
	2	256.06	814.740	
	3	468.41	724.361	
	4	247.72	638.816	
	5	2572.67	6202.797	
Number of dislike	1	35.69	74.943	0.012
	2	16.29	63.090	
	3	16.86	28.451	
	4	7.89	22.082	
	5	80.93	133.741	
Number of comment	1	369.59	593.258	< 0.001
	2	97.94	358.551	
	3	267.45	325.115	
	4	66.22	176.263	
	5	651.93	982.486	
Duration (minutes)	1	6.34	6.096	0.212
	2	4.94	5.285	
	3	5.14	3.427	
	4	12.06	18.901	
	5	8.73	8.396	
Modified DISCERN score	1	4.10	0.724	< 0.001
	2	3.29	0.849	
	3	3.23	0.922	
	4	3.41	0.870	
	5	1.87	0.915	
GQS score	1	3.93	0.799	< 0.001
	2	3.18	0.728	
	3	3.32	0.894	
	4	3.29	1.105	
	5	2.00	0.756	
JAMA score	1	2.14	0.639	< 0.001
	2	1.29	0.470	
	3	1.55	0.739	
	4	1.47	0.624	
	5	1.07	0.258	
VPI score	1	142.00259	232.113110	0.009
	2	83.39882	149.613497	
	3	160.48455	231.979953	
	4	89.58365	230.006815	
	5	177.89327	264.487520	
Like rate	1	97.9576	3.46012	0.030
	2	98.7082	2.64170	
	3	97.0964	3.69457	
	4	98.8359	2.31412	
	5	96.6460	3.88171	
Viewing rate	1	146.43345	239.646270	0.008
	2	86.07647	156.247841	
	3	164.57227	236.596469	
	4	92.44659	237.964387	
	5	183.71667	269.022424	

\*Healthcare professionals: 1, healthcare organizations: 2, news channel: 3, health-related websites: 4, independent users: 5, GQS: Global Quality Scale, JAMA: The Journal of the American Medical Association, VPI: Video power index, SD: Standard deviation

### Video Popularity Based on the Source

**VPI:** The popularity index of videos published by independent individuals and institutions was higher compared to other sources ( $P < 0.05$ ).

**Likes and views:** The mean like count was 97.8483, while the mean view count was 136.57802. Videos posted by independent individuals or institutions, received more views compared to other sources ( $P < 0.05$ ).

### Analysis of the Videos Based on the Source

**Healthcare workers (group 1):** Videos posted by this group were generally high quality, but they were viewed and liked less, however, their DISCERN, GQS, and JAMA scores were the highest.

**Healthcare institutions (group 2):** Videos shared by healthcare institutions had high quality, but they lagged behind those uploaded by independent individuals in terms of audience engagement and interaction (likes, comments).

**News channels (group 3):** Videos posted by news channels received more views compared to group 4, and had higher engagement than group 2. Interactions were greater than those of the other groups, but lower than those of group 5. The DISCERN and GQS scores were not as high as those of videos posted by healthcare workers and institutions.

**Healthcare websites (group 4):** Videos shared by this group had moderate quality and low engagement rates.

**Independent individuals/institutions (group 5):** Videos posted by this group had the highest number of views, but their quality scores were the lowest. Content created by independent individuals generally received more views and likes; however, it lacked medical accuracy.

The correlations between the video parameters are presented in Table 4.

**Table 4. Correlation analysis of video metrics**

		Number of views	Number of like	Number of dislike	Number of comment	Duration (minutes)	DISCERN score	GQS score	JAMA score	VPI score	Like rate	Viewing rate
Days on Youtube	r	0.405	0.314	0.436	0.340	0.036	-0.040	-0.083	-0.078	0.050	-0.492	0.055
	P	< 0.001	0.001	< 0.001	< 0.001	0.718	0.695	0.411	0.440	0.622	< 0.001	0.590
Number of views	r	1.000	0.916	0.805	0.816	0.304	-0.120	-0.133	0.068	0.911	-0.682	0.913
	P		< 0.001	< 0.001	< 0.001	0.002	0.234	0.187	0.502	< 0.001	< 0.001	< 0.001
Number of like	r	0.916	1.000	0.831	0.835	0.470	-0.065	-0.075	0.078	0.863	-0.709	0.864
	P	< 0.001		< 0.001	< 0.001	< 0.001	0.521	0.460	0.441	< 0.001	< 0.001	< 0.001
Number of dislike	r	0.805	0.831	1.000	0.792	0.347	-0.165	-0.160	-0.088	0.681	-0.940	0.687
	P	< 0.001	< 0.001		< 0.001	< 0.001	0.100	0.113	0.384	< 0.001	< 0.001	< 0.001
Number of comment	r	0.816	0.835	0.792	1.000	0.413	-0.063	-0.037	0.112	0.743	-0.687	0.745
	P	< 0.001	< 0.001	< 0.001		< 0.001	0.534	0.717	0.266	< 0.001	< 0.001	< 0.001
Duration (minutes)	r	0.304	0.470	0.347	0.413	1.000	0.071	0.077	0.054	0.361	-0.266	0.363
	P	0.002	< 0.001	< 0.001	< 0.001		0.481	0.446	0.593	< 0.001	0.007	< 0.001
DISCERN score	r	-0.120	-0.065	-0.165	-0.063	0.071	1.000	0.837	0.601	-0.088	0.192	-0.088
	P	0.234	0.521	0.100	0.534	0.481		< 0.001	< 0.001	0.383	0.055	0.383
GQS score	r	-0.133	-0.075	-0.160	-0.037	0.077	0.837	1.000	0.602	-0.082	0.173	-0.080
	P	0.187	0.460	0.113	0.717	0.446	< 0.001		< 0.001	0.420	0.084	0.427
JAMA score	r	0.068	0.078	-0.088	0.112	0.054	0.601	0.602	1.000	0.106	0.160	0.105
	P	0.502	0.441	0.384	0.266	0.593	< 0.001	< 0.001		0.295	0.112	0.298
VPI score	r	0.911	0.863	0.681	0.743	0.361	-0.088	-0.082	0.106	1.000	-0.529	1.000
	P	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.383	0.420	0.295		< 0.001	< 0.001
Like rate	r	-0.682	-0.709	-0.940	-0.687	-0.266	0.192	0.173	0.160	-0.529	1.000	-0.537
	P	< 0.001	< 0.001	< 0.001	< 0.001	0.007	0.055	0.084	0.112	< 0.001		< 0.001
Viewing rate	r	0.913	0.864	0.687	0.745	0.363	-0.088	-0.080	0.105	1.000	-0.537	1.000
	P	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.383	0.427	0.298	< 0.001	< 0.001	

GQS: Global Quality Scale, JAMA: The Journal of the American Medical Association, VPI: Video power index

## DISCUSSION

Scabies is a dermatological disease whose incidence has significantly increased since 2018, becoming a social concern.<sup>1,2</sup> YouTube is a platform where people from all walks of life can upload videos containing health information.<sup>3</sup> The information regarding YouTube videos on scabies was not previously investigated. This study is the first to analyze the quality of scabies videos on YouTube. Our findings indicate that the quality of these videos varies and that the content is inadequate and not produced by reliable health sources.

The videos posted by healthcare professionals and professional organizations received higher DISCERN and GQS scores, indicating that these sources could provide reliable information. However, the number of views and likes for these videos was lower compared to the content created by independent individuals or organizations, suggesting that the public generally preferred popular but low-quality content. A study analyzing YouTube videos on acne found that videos posted by healthcare professionals were of higher quality but less popular, similar to our findings.<sup>10</sup> A survey of vitiligo indicated that the content shared by healthcare professionals was of higher quality but received fewer views.<sup>11</sup> Another study reported that videos on urticaria uploaded by physicians were of higher quality, more reliable, and more beneficial than videos uploaded by non-physicians. In contrast, the videos posted by non-physicians were more popular and viewed more.<sup>12</sup> Content produced by independent individuals and social media figures is not as reliable as information provided by professional sources, yet it reaches a wider audience, increasing the risk of spreading false or inadequate knowledge. Although the video quality is lower than that of professionals, the public shows a strong interest in these videos, highlighting a serious issue in digital health literacy. It could be argued that the public needs better guidance on accessing reliable information sources.

Similar findings have been reported in studies on non-dermatological diseases. Syed-Abdul et al.<sup>13</sup> reported that the most popular videos on YouTube were posted by non-professionals and that these videos typically lacked scientific accuracy. In a study examining bladder cancer videos on YouTube, Loeb et al.<sup>14</sup> found that content produced by professional sources had lower viewing rates but provided high-quality information. Similarly, our study found that videos posted by independent individuals and social media influencers garnered more views and interactions compared to those shared by professional sources, indicating that the public generally preferred popular yet scientifically inaccurate content.

Our findings emphasized the need for health professionals and organizations to create videos that capture the public's attention while providing accurate, reliable information. High activity levels on popular platforms like YouTube could be crucial for enhancing health literacy and preventing the spread of misinformation. Strategies should be developed to boost views and engagement rates of content produced by health professionals. These strategies should involve clickbait titles and descriptions, visually and aurally appealing videos, and concise, understandable, and thus more accessible content. It is also advisable for health authorities to implement verification mechanisms to curb the spread of misinformation on these platforms. Syed-Abdul et al.<sup>13</sup> argued that misinformation on YouTube was a significant issue and recommended that health organizations take a more active role on this platform.

## Study Limitations

The current study has certain limitations. It only examined videos published on YouTube, without exploring other social media platforms or websites. Second, the video analysis was conducted using subjective evaluation tools, (DISCERN, GQS, JAMA) based on the ratings of different reviewers. Only videos in the Turkish language were included in the analysis. Lastly, the videos considered in this study may be altered or removed over time; therefore, the findings reflect the current status on the platform and should be generalized with caution.

## CONCLUSION

The quality of content about scabies on YouTube varies significantly, and information from independent content creators is often less reliable compared to that posted by professional sources. This can challenge individuals seeking health information and increase the risk of misinformation. It is vital for both individual and public health, that healthcare professionals take a more active role in social media platforms like YouTube and produce reliable, high-quality content.

## Ethics

**Ethics Committee Approval:** Not applicable.

**Informed Consent:** Not applicable.

## Footnotes

### Authorship Contributions

Concept: N.G.G., Z.U., V.E., Design: N.G.G., Z.U., V.E., Ö.P., S.Ö., Data Collection or Processing: N.G.G., V.E., Ö.P., S.Ö.,

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# Psoriasis Frequency in Antalya/Türkiye; An Approach to Assess the Psoriasis Occurrence Among Patient Relatives/Companions

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## Abstract

**Aim:** Methodological variations, geographical factors, and ethnic differences contribute to the wide variability in the prevalence of psoriasis. There are limited studies on the prevalence of psoriasis in Türkiye, and no similar study has been conducted in our region. This study aimed to assess the frequency of psoriasis in Antalya.

**Materials and Methods:** This single-center, descriptive study included healthy adult volunteers over 18 years old accompanying patients at internal medicine outpatient clinics in Akdeniz University, Antalya, Türkiye. We aimed to recruit 1000 participants for this study by utilizing the quota sampling method.

**Results:** Of the 1075 participants, 980 (age range, 18-83; mean  $\pm$  standard deviation, 45.90 $\pm$ 14.00) agreed to participate in the study. Among the 27 suspected cases, 19 were confirmed to be psoriasis (12 females and 7 males). There were 9 new cases diagnosed. Psoriasis prevalence was 1.93 per 100 [confidence interval (1.2-2.9)]. Plaque psoriasis was present in the majority (94.7%) of diagnosed patients. The smoking rate was 42.1%. The body surface area was  $\leq$  10% in all patients. 94.7% of patients had the Psoriasis Area Severity Index values  $\leq$  10. 44.4% had a family history of psoriasis. Disease severity was lower than that in our center's previous registry survey.

**Conclusion:** The frequency observed in our study was found to be higher than that reported in both Turkish studies and global studies. Diagnosed patients had mild psoriasis. Quota sampling is appropriate for estimating rare dermatological conditions in patients' relatives or companions. This screening approach allows for the cost-effective collection of data in a shorter period, with a reduced workforce.

**Keywords:** Psoriasis, prevalence, cross-sectional survey

## INTRODUCTION

Psoriasis is an immune-mediated, inflammatory skin disease affecting a significant proportion of the population. It typically presents as discrete, erythematous, pruritic plaques covered in silvery scales, giving the disease its name. The disease has a chronic course, with recurrent attacks. Both men and women are equally affected by the disease.<sup>1</sup> The age at which the disease onset occurs increases during two distinct periods. The first increase occurs between the ages of

20 and 30. The second and smaller increase occurs between the ages of 50 and 60.<sup>2,3</sup> The precise etiology of the disease remains uncertain. However, genetic predisposition has a significant impact on the development of the disease. The disease likely begins with the activation of the immune system in response to various environmental stimuli, particularly in individuals with a genetic predisposition.

The prevalence of psoriasis in Europe and America is estimated to be around 2-3%. Conversely, African and Asian countries report a lower prevalence rate of 0.5 to 1%.<sup>4</sup> Two

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studies have been conducted to examine the prevalence of psoriasis in Türkiye. Both studies were carried out in the northern region of Türkiye. The study conducted in Trabzon province and its districts found that the prevalence of psoriasis was 1.1% [95% confidence interval (CI) 0.9-1.3].<sup>5</sup> Another study conducted in Mudurnu district, Bolu province reported a psoriasis prevalence rate of 0.5%.<sup>6</sup> The region of Antalya, located in southern Türkiye, has not been the subject of a previous prevalence study on psoriasis.

This study aimed to establish the frequency of psoriasis in Antalya, Türkiye. The results of the investigation are intended to address the existing knowledge gap concerning the psoriasis frequency in Türkiye and to provide a foundation for more comprehensive approaches to the early diagnosis and treatment of patients. To achieve this objective, the quota sampling screening method was employed in the present study to ascertain the prevalence of rare dermatological diseases in the relatives or companions of the patients. This methodology was previously validated in a study conducted at our clinic on the prevalence of hidradenitis suppurativa.<sup>7</sup>

## MATERIALS AND METHODS

This descriptive study was conducted between May and October 2023 at Akdeniz University in Antalya, Türkiye, among healthy adult volunteers over the age of 18 who were accompanying patients attending internal medicine outpatient clinics. The departments of dermatology, rheumatology, and the outpatient clinics of physical therapy and rehabilitation were excluded from the study to avoid the potential for significant bias. Participants who were under the age of 18, pregnant, or unable to provide consent (e.g., due to unconsciousness or psychiatric condition) were excluded from the study. We set out to reach 1000 participants in this study by employing the quota sampling method. Approval was granted by the Clinical Research Ethics Committee of Akdeniz University Faculty of Medicine (approval number: KAEK-138, date: 08.02.2023). A digital data collection form was used to data anonymously.

Data collection was conducted by trainee doctors (DS and SOI). After verbal consent was obtained, the researchers explained the purpose of the study to the potential participants and administered the questionnaire. An experienced dermatologist (EA) examined participants with suspected or previously diagnosed psoriasis during the screening phase to confirm the diagnosis. Data on the characteristics of patients diagnosed with psoriasis, including demographics and clinical factors, were recorded.

SPSS v23.0 was used for statistical analysis. Mean and standard deviation (SD) were used for continuous variables, and percentages were used for frequency distributions. The

chi-square test was used to compare categorical variables;  $P < 0.05$  was considered significant.

## RESULTS

A total of 1,075 individuals were invited to participate in the study. Nine hundred eighty (mean age  $\pm$  SD, 45.90  $\pm$  14.00) agreed to participate (Table 1). Among the 27 participants initially suspected of having psoriasis, a total of 19 individuals (12 women and 7 men) were ultimately diagnosed with the condition. There were nine cases determined to be first-time diagnoses. The study verified the diagnoses of ten participants who had previously been diagnosed with psoriasis. A dermatologist diagnosed all except for 2 of the 10 patients. One of them was diagnosed by a family physician and the other by a rheumatologist. The estimated frequency of psoriasis in the study participants was 1.93 [95% CI (1.2-2.9)] (Table 2). The frequency of psoriasis was calculated as 2.0% among women and 1.8% among men. The proportion of individuals with a family history of psoriasis was significantly higher in the group diagnosed with psoriasis (44.4%) compared to the group without psoriasis (16.8%) ( $P = 0.002$ ).

**Table 1. Demographic features of study participants**

Variable	Participants	Psoriasis group
	980	19
<b>n</b>		
<b>Sex (%)</b>		
Male	370 (38.7)	7 (36.8)
Female	601 (61.3)	12 (63.2)
<b>Age, median</b>	45.9	44.5
<b>Body mass index (%)</b>		
Normal (18.5-24.9)	354 (36.1)	11 (57.9)
Overweight (25-29.9)	367 (37.5)	4 (21.1)
Obese (30-39.9)	236 (24.0)	4 (21.1)
Morbidly obese (> 40)	23 (2.4)	

**Table 2. Clinical characteristics of patients diagnosed with psoriasis**

Clinical features	Data
<b>Mean age (<math>\pm</math> SD)</b>	44.53 $\pm$ 11.64
<b>Number of diagnosed psoriasis cases</b>	19 (12 females, 7 males)
<b>Prevalence of psoriasis (overall)</b>	1.93% (95% CI: 1.2-2.9)
<b>Prevalence of psoriasis (females)</b>	2.0% (12)
<b>Prevalence of psoriasis (males)</b>	1.8% (7)
<b>Family history of psoriasis</b>	44.4% (8)
<b>Most common type of psoriasis</b>	Plaque psoriasis (94.7%)
<b>Patients with multiple comorbidities</b>	47.4% (9)
<b>Patients with BMI above normal</b>	42.2% (8)
<b>BSA, mean</b>	1.6
<b>PASI score, mean</b>	2.1

BMI: Body mass index, BSA: Body surface area, SD: Standard Deviation, CI: Confidence interval, PASI: Psoriasis Area and Severity Index

The majority of the patients (94.7%) had plaque psoriasis, the most prevalent type of the disease. 47.4% of these had multiple comorbidities and 42.2% had a body mass index above normal. The active smoking rate among diagnosed patients was 42.1%.

The calculation of body surface area (BSA) and Psoriasis Area and Severity Index (PASI) scores was performed for every patient diagnosed with psoriasis. None of the diagnosed patients had BSA values higher than 10%. In addition, the PASI values of 94.7% of patients were  $\leq 10$ . In the study, the mean PASI and BSA values of patients diagnosed with psoriasis were 2.1 and 1.6, respectively.

## DISCUSSION

Our findings indicate that 1.93% of adults in the Antalya region have clinically confirmed psoriasis. The diagnosed patients in the study experienced a milder form of psoriasis. The frequency of psoriasis was higher (44.4%) among first- and second-degree relatives.

The frequency of psoriasis in a sample group of 980 individuals was found to be higher than that reported in previous studies conducted in Türkiye and many other countries worldwide. Two studies examined psoriasis prevalence in Türkiye. Serdaroğlu et al.<sup>6</sup> conducted the first study in Mudurnu district, of Bolu province, involving 8502 participants from all age groups. Psoriasis prevalence was 0.5% in this study. Smokers and alcohol users had a higher prevalence than non-users. In Trabzon province, Yaylı et al.<sup>5</sup> reported a 1.1% prevalence of psoriasis in adults. In a sample of 7,885 adults, women had a disease prevalence of 1.2%, while men had 1%.<sup>5</sup> Serdaroğlu et al.<sup>6</sup> found a lower prevalence than our study, possibly because of they included of all age groups and less frequent observation of the disease in pediatric patients. The reason for the higher frequency (1.1% versus 1.93%) we obtained compared to Yaylı et al.<sup>5</sup> study<sup>6</sup> could be linked to disparities in sample sizes, geographical variations, and methodological differences.

Serdaroğlu et al.<sup>6</sup> noted higher rates of smoking and alcohol consumption in individuals with psoriasis. In our study, the smoking rate among psoriasis patients was 42.1%. Smoking stimulates the production of interleukin-1beta (IL-1 $\beta$ ) and increases pro-inflammatory cytokine production, including Tumor Necrosis Factor-alpha, IL-1, IL-6, and IL-12. These cytokines significantly influence the pathogenesis of psoriasis. Our study's results are in line with the literature.<sup>8-10</sup>

Yaylı et al.<sup>5</sup> study, revealed that 18.3% of psoriasis patients had a family history, which increased the disease risk by eight times. Individuals diagnosed with psoriasis in our study had a

significantly higher proportion of family history of psoriasis (44.4%) compared to those without psoriasis (16.6%). The prevalence rate supports previous studies in highlighting the importance of family history in psoriasis development.

Our study, unlike the two previous ones in Türkiye, also assessed the clinical characteristics of the patients. All diagnosed patients had a BSA  $\leq 10\%$  and 94.7% had PASI values  $\leq 10$ . Mean PASI and BSA values of 2.1 and 1.6, respectively, indicate mild psoriasis in most patients. We analyzed data from 142 patients in our psoriasis outpatient clinic and found that plaque psoriasis was the most common type, accounting for 92.2% of cases. The age range of the participants was 18 to 69 years, with a mean  $\pm$  SD of 40.10 $\pm$ 12.90. The patients' mean PASI and BSA scores were 3.6 and 5.6, respectively. Out of a total of 142 patients, the percentage of patients with PASI and BSA  $> 10$  scores was 3.5% and 14%, respectively. The values were much higher than those in the prevalence study ( $P < 0.05$ ). This may be because patients with more severe disease sought treatment at specialized healthcare facilities.

Psoriasis prevalence varies in different parts of the world. Geographical, genetic, and environmental factors may play a role in the observed results. Methodological differences, such as study design, sample sizes, or data collection methods, may also contribute to variations in psoriasis prevalence studies. Parisi et al.<sup>4</sup> meta-analysis showed psoriasis prevalence globally, varies from 0.11% to 1.58%. The region, including Australia and New Zealand, had the highest average prevalence (1.58%). Psoriasis prevalence in Western Europe was 1.52%. Australia had the highest prevalence (1.88%) and Taiwan had the lowest (0.05%). Our study revealed a 1.93% frequency of psoriasis in the Antalya population. This value is higher than the averages reported in both Turkish and global prevalence studies.

Türkiye has both public and private health services. The system is funded by a 5% surtax on employers. The public sector covers around 75.2% of health expenses. No referral is needed for patients to be admitted to any health facility, including primary, secondary, or tertiary, even on the same day. In comparison to other countries, tertiary health facilities provide care for patients with a diverse range of diseases, regardless of the severity. The structure of the Turkish health system allows to some extent, for the extrapolation of epidemiological data from tertiary healthcare facilities to the population at certain rates.

## Study Limitations

Our study had some limitations. The participants were older compared to the Trabzon population-based study. Additionally,

there was a higher proportion of women in our study. This could be because women are more likely to accompany their spouses or children to the hospital. Selection bias may be another limitation of this study design.

## CONCLUSION

Our study demonstrates the efficacy of the quota sampling screening method as a reliable tool for estimating the frequency of rare dermatological diseases in the relatives or companions of patients. This method, successfully employed in a previous study on hidradenitis suppurativa prevalence at our clinic, offers significant advantages. It provides a more cost-effective and time-efficient approach to data collection, requiring fewer staff members. Given the high cost and logistical challenges of conducting population-based prevalence surveys, the quota sampling method presents a viable alternative for future research.

## Ethics

**Ethics Committee Approval:** Approval was granted by the Clinical Research Ethics Committee of Akdeniz University Faculty of Medicine (approval number: KAEK-138, date: 08.02.2023).

**Informed Consent:** After verbal consent was obtained, the researchers explained the purpose of the study to the potential participants and administered the questionnaire.

## Footnotes

### Authorship Contributions

Concept: E.A., M.E., Design: E.A., M.E., Data Collection or Processing: G.A.Ö., D.S., S.Ö.I., Analysis or Interpretation: E.A., M.E., C.V., G.A.Ö., Literature Search: E.A., M.E., C.V., G.A.Ö., Writing: E.A., M.E., C.V.

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

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# Paraoxonase Enzyme Activity and Determination of Phenotypic Polymorphism in Patients with Acne Vulgaris

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## Abstract

**Aim:** This study aims to compare serum paraoxonase 1 (PON1) activity between patients diagnosed with acne vulgaris (AV) and a healthy control group, and to determine the PON1 phenotype.

**Materials and Methods:** The study sample consists of 50 patients with moderate to severe AV who presented to the Clinic of Dermatology at Balıkesir University Faculty of Medicine. Additionally, healthy volunteers (n = 52) with similar age and gender characteristics to the patient group were included as the control group. The diagnosis of AV was made using the Global Acne Grading System. The serum PON1 activities in both AV patients and healthy volunteers were measured by spectrophotometric methods, and statistical comparisons were made among the groups. Furthermore, the PON1 phenotypic polymorphism was determined.

**Results:** In our study, serum PON1 activity levels were found to be significantly lower in AV patients (36,149±14,536) compared to the control group (48,173±18,753) ( $P = 0.001$ ). The distribution of PON1 phenotypes demonstrated a trimodal pattern. In the patient group, the QQ phenotype was observed in 48%, odds ratio in 24%, and risk ratio in 28%. In the control group, these rates were 5.8%, 44.2%, and 50%, respectively.

**Conclusion:** The notably reduced activity of the antioxidant enzyme PON1 in patients with AV, as compared to the control group, indicates that oxidative stress could be a significant factor in its etiopathogenesis.

**Keywords:** Acne vulgaris, paraoxonase, paraoxonase phenotypic polymorphism

## INTRODUCTION

Acne vulgaris (AV) is a condition characterized by prolonged inflammation of the pilosebaceous follicles, predominantly found on the face, back, and torso. AV is a common condition, affecting approximately 80% of adolescents and young adults.<sup>1</sup> Although the exact etiopathogenesis of acne remains unclear, four main factors are widely recognized: sebaceous gland hyperplasia with elevated sebum production,

hyperkeratinization of the pilosebaceous ducts, abnormal colonization primarily by *Cutibacterium acnes* (*C. acnes*), and inflammation.<sup>2</sup> Many researchers have examined the role of oxidative stress in the development of AV, investigating the connections between inflammation, oxidative stress, and acne pathogenesis. Although the roles of oxidative and antioxidative system parameters in acne pathogenesis are not definitively established, these parameters have been widely examined in various studies.<sup>3-5</sup>

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The link between acne and oxidative stress is often attributed to *C. acnes* colonization. *C. acnes* is thought to initiate inflammation by producing low-molecular-weight chemotactic factors and triggering neutrophil chemotaxis. Some researchers have suggested that AV is a disease related to oxidative stress, primarily driven by increased sebum production.<sup>6,7</sup>

Paraoxonase 1 (PON1), a calcium-dependent ester hydrolase, has recently gained attention for its antioxidant properties. Serum PON1 is found in plasma associated with high-density lipoproteins (HDL), playing a critical role in preventing the oxidation of plasma lipoproteins. PON1 enzyme activity can vary significantly due to polymorphism, and many clinical studies have explored the relationship between PON1 enzyme activity and various diseases.<sup>8-11</sup>

This study aims to investigate the role of oxidative stress in AV pathogenesis by assessing PON1 enzyme activity and identifying the phenotypic polymorphism of this enzyme in acne patients.

## MATERIALS AND METHODS

### Study Groups

Our study included 50 patients diagnosed with moderate to severe AV according to the Global Acne Grading System, who presented to the Clinic of Dermatology at Balıkesir University Faculty of Medicine between November 18, 2014, and May 18, 2015. These patients, aged between 18 and 40, provided informed consent. A control group of 52 healthy individuals with similar age and gender characteristics, presenting to the dermatology clinic for non-acne-related issues, was also included. Exclusion criteria included individuals who had received systemic or topical acne treatment in the past three months, had systemic diseases that could influence PON1 activity, were on systemic medications, had smoking, alcohol, or substance dependence, engaged in regular exercise beyond daily activities, and pregnant women. The study received ethical approval from the Ethics Committee of Balıkesir University Faculty of Medicine (approval number: 2014/94, date: 17.11.2014) for the study titled "Measurement of Paraoxonase Enzyme Activity and Determination of P/Q192 Polymorphism in AV Patients." This research was also funded by the Balıkesir University Scientific Research Projects Unit under project number 2015/135.

### Blood Samples

Blood samples collected from the patient and control groups were left to sit for 30 minutes, then centrifuged at 4000 rpm for 10 minutes. The separated sera were stored at -20 °C.

### Enzyme Activity Measurement

PON enzyme activity was measured using a spectrophotometric method. For the activity measurement, 0.05 mL of serum sample (enzyme source) was added to a previously prepared 1 mL buffer solution (100 mM Tris-base, pH 8.0) along with substrate (2 mM paraoxon) and coenzyme (2 mM CaCl<sub>2</sub>). The absorbance change at a wavelength of 412 nm was recorded over one minute at 37 °C. This method determined the rate of enzymatic conversion of paraoxon to p-Nitrophenol. The procedure was repeated with a control sample lacking the enzyme, and the difference between the two readings was calculated as enzyme activity. One unit of PON activity was defined as the amount of p-Nitrophenol formed per minute, in nanomoles.

### Determination of Q and R-Types

For the activity measurement, 0.05 mL of serum sample was rapidly added to a 1 mL pre-prepared buffer (100 mM Tris-base, pH 10.5) and substrate (1 mM paraoxon) solution. The baseline activity value at 412 nm was recorded over one minute at 37 °C. To measure salt-stimulated activity, 1 M NaCl was added as a coenzyme to the same solutions, and the salt-stimulated activity value was recorded. This method assessed the enzymatic conversion rate of paraoxon to p-Nitrophenol. The procedure was repeated with a control sample lacking the enzyme, and the difference between the two values was calculated as enzyme activity. PON activity was defined as the amount of p-Nitrophenol produced per minute, measured in micromoles (μmol). After measuring the basal and salt-stimulated activities of PON, the following formula was used for phenotype determination (Figure 1).<sup>12</sup>

### Hydrolysis of Paraoxon

When high-activity PON enzyme is stimulated by 1 M NaCl, the low-activity form is inhibited, resulting in a trimodal distribution in this analysis. Values up to 60% represent homozygous Q (A), values between 60% and 200% correspond to QR (AB), and values above 200% indicate homozygous R (B) individuals.

$$\frac{\text{Paraoxonase activity in the presence of 1 M NaCl} - \text{Basal paraoxonase activity}}{\text{Basal paraoxonase activity}} \times 100$$

**Figure 1.** Percentage of Paraoxonase Activity Induced by NaCl

## Biochemical Parameters

Serum levels of PON1, total cholesterol (TC), HDL, low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and triglycerides (TG) were analyzed in both the patient and control groups, and their intergroup differences were compared. Additionally, the correlation between PON1 activity and TG, HDL, LDL, and TC levels was examined within each group.

## Statistical analysis

Statistical analysis of the study findings was performed using the SPSS 21.0 software package. Pearson's chi-square test was applied to compare categorical parameters. A t-test was used for comparing parameters between two groups. For comparisons involving more than two groups, the One-Way ANOVA test was used, followed by the Bonferroni test to identify which groups contributed to the observed differences. Pearson correlation analysis was conducted to examine relationships between parameters. The results were analyzed at a 95% confidence level, with statistical significance set at  $P < 0.05$ .

## RESULTS

The study included 50 patients aged 18-33, with an average age of  $21.7 \pm 2.96$  years. The control group consisted of 52 individuals aged 18-27, with an average age of  $22.5 \pm 2.53$  years. Among the patients, 29 (58.0%) were female and 21 (42.0%) were male, while in the control group, 32 (61.5%) were female and 20 (38.5%) were male. There were no significant differences in age or gender between the groups ( $P = 0.128$ ,  $P = 0.435$ ).

Levels of serum PON1, TC, HDL, LDL, VLDL, and TG were assessed in both the patient and control groups, and the differences between the groups were analyzed. No statistically significant differences were found between the two groups for TC, TG, HDL, or LDL levels ( $P > 0.05$ ). However, PON1 activity was significantly lower in the patient group ( $36,149 \pm 14,536$ ) compared to the control group ( $48,173 \pm 18,753$ ) ( $P = 0.001$ ;  $P < 0.05$ ). Statistical comparison of PON1 activity indicated that it was markedly lower in AV patients compared to the control group (Table 1).

When the correlation between PON1 activity and TG, HDL, LDL, and TC levels was analyzed in both the patient and control groups, no significant relationship was found between PON1 activity and these parameters ( $P > 0.05$ ) (Table 2).

## Phenotypic Distribution

After measuring basal and salt-stimulated PON1 activities in both the patient and control groups, phenotypic distributions were determined as described in the materials and methods section. The phenotypic polymorphism of PON1 showed a trimodal distribution: QQ, QR, and RR. The effects of polymorphism on PON1 activity, as well as TG, TC, HDL, and LDL levels, were evaluated. A significant difference in phenotype distribution was observed between the groups ( $X^2 = 23,360$ ;  $P = 0.001$ ;  $P < 0.05$ ). In the patient group, 24 individuals (48.0%) had the QQ phenotype, 12 (24.0%) had the QR phenotype, and 14 (28.0%) had the RR phenotype. In the control group, 3 individuals (5.8%) had the QQ phenotype, 23 (44.2%) had the QR phenotype, and 26 (50.0%) had the RR phenotype (Table 3).

The effects of QQ, QR, and RR phenotypes on PON1 activity, as well as TG, TC, HDL, and LDL levels, were evaluated in both the patient and control groups. In the patient group, the QQ, QR, and RR phenotypes had a statistically significant effect on PON1 activity ( $P = 0.003$ ;  $P < 0.05$ ). PON1 activity levels in individuals with the RR phenotype ( $46,556 \pm 9,400$ ) were higher than those with the QQ phenotype ( $30,342 \pm 15,650$ ).

Similarly, in the control group, the impact of QQ, QR, and RR phenotypes on PON activity was significant ( $P = 0.003$ ,  $P < 0.05$ ). Individuals with the RR phenotype in the control group had higher PON activity levels ( $55,560 \pm 21,103$ ) compared to those with the QR phenotype ( $41,808 \pm 12,887$ ).

## DISCUSSION

Recent research suggests that inflammation and immune responses may be among the most crucial factors in acne pathogenesis. However, there is still no consensus on what triggers this inflammatory process.<sup>13,14</sup>

**Table 1. Comparison of TC, TG, HDL, LDL, and PON1 activity between groups**

	Patient (n = 50)	Control (n = 52)	t	P
TC (mg/dL)	159,740±28,722	165,100±28,383	-0.947	0.346
TG (mg/dL)	69,820±22,370	78,020±36,872	-1,351	0.176
HDL (mg/dL)	55,840±12,151	55,289±11,053	0.240	0.811
LDL (mg/dL)	89,340±23,407	93,800±23,515	-0.960	0.340
PON1 activity	36,149±14,536	48,173±18,753	-3,609	<b>0.001</b>

TC: Total cholesterol, TG: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, PON1: Paraoxonase 1

**Table 2. Effect of PON1 activity on TC, TG, HDL, and LDL levels in patients and control group**

	Patient		Control	
	r	p	r	P
TC	-0.035	0.810	0.082	0.565
TG	-0.221	0.123	0.139	0.326
HDL	0.107	0.459	0.049	0.731
LDL	-0.046	0.749	0.057	0.690

PON1: Paraoxonase 1, TC: Total cholesterol, TG: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

**Table 3. Phenotypic distribution among different groups**

		Patient		Control		P
		n	%	n	%	
Phenotype	QQ	24	48.0%	3	5.8%	X <sup>2</sup> =23,360 P = 0.001
	QR	12	24.0%	23	44.2%	
	RR	14	28.0%	26	50.0%	

Studies highlighting oxidative stress in acne pathogenesis have examined the relationship between inflammation, oxidative stress, and acne, with growing evidence suggesting that oxidative stress may play a significant role in the development of AV.<sup>4,6,15</sup>

The association between acne and oxidative stress is often linked to the colonization of *C. acnes* bacteria on the skin. *C. acnes* produces several low-molecular-weight chemotactic factors that initiate inflammation and attract neutrophils to the area. In addition, it secretes various enzymes, including protease, lecithinase, hyaluronidase, and neuraminidase.<sup>16</sup>

These enzymes, produced by *C. acnes* and neutrophils, can damage the follicle wall. As a result of this damage, follicular contents leak into the dermis, creating a foreign body reaction that intensifies inflammation. Activated neutrophils release proteolytic enzymes and reactive oxygen species (ROS), further exacerbating tissue damage and deepening the inflammatory response. This tissue damage is often described as autoxidative injury.<sup>16</sup>

Some researchers also propose that AV is a disease driven by oxidative stress, with increased sebum production playing a key role. The rise in sebum production, along with changes in its composition, contributes to sustained inflammation through irritation and damage to the follicular wall by enzymes and ROS released from neutrophils.<sup>3,4,6,15</sup>

Many studies investigating oxidative stress in AV pathogenesis have identified significant differences in oxidative stress parameters between acne patients and healthy controls.<sup>3</sup>

PON1, a calcium-dependent ester hydrolase, is one of the enzymes associated with HDL and is the first among these enzymes with well-studied structural characteristics. One of PON1's primary functions is hydrolyze organophosphate

neurotoxins, aromatic carboxylic acid esters, and insecticides, which is considered its initial physiological role.<sup>17</sup>

In recent years, PON1 activity has been evaluated as a marker of oxidative stress in several dermatological diseases which involve oxidative stress in their etiology, including alopecia areata, recurrent aphthous stomatitis, rosacea, androgenetic alopecia (AGA), and psoriasis.<sup>10,18-21</sup>

In 2015, Takci et al.<sup>21</sup> compared serum PON1 activity and lipid hydroperoxide levels in 39 patients with rosacea and 40 healthy controls. Their study found that serum PON1 activity was lower, while serum lipid hydroperoxide levels were significantly higher in rosacea patients compared to controls. Based on these findings, the authors suggested that reduced PON1 levels may indicate a role of oxidative stress in the etiology of rosacea.<sup>21</sup>

In a study conducted by Bilgili et al.<sup>22</sup> with 39 alopecia areata patients and 39 healthy controls, serum PON1 activity was reported to be lower in the patient group. The same research team also examined serum PON1 levels in 31 patients with recurrent aphthous stomatitis and 31 healthy controls, finding that PON1 activity was significantly reduced in the patient group. These findings suggest that oxidative stress may play a role in the etiology of these diseases.<sup>22</sup>

Tantawy et al.<sup>10</sup> conducted a study to explore the potential role of ROS in the pathogenesis of AGA by assessing serum PON1 levels in AGA patients and examining their association with disease severity. Their findings indicated that serum PON1 levels were significantly reduced in AGA patients compared to the control group, with a notable decline in PON1 levels correlating with increased severity of AGA ( $P < 0.001$ ). These results suggest that PON1 may serve as a sensitive and specific biomarker for AGA and could be useful as a predictive indicator for this condition in healthy individuals.<sup>10</sup>

In a similar context, Oszukowska et al.<sup>20</sup> investigated the atherogenic potential in psoriasis by analyzing both antioxidant and pro-oxidant factors, including PON-1,  $\alpha$ -tocopherol, uric acid, and homocysteine, comparing these parameters between psoriasis patients and a healthy control group. Their research revealed that PON-1 activity in psoriasis patients was significantly lower than in healthy subjects ( $P < 0.001$ ).<sup>20</sup>

In our study, we investigated PON1 enzyme activity and phenotypic polymorphism in serum samples from 50 AV patients and 52 controls with similar age and gender distributions. We observed that the serum PON1 activity levels in AV patients ( $36,149 \pm 14,536$ ) were significantly lower compared with the levels in the control group ( $48,173 \pm 18,753$ ).

PON1 enzyme activity varies significantly due to polymorphisms. Although its exact physiological role in the body is not entirely understood, many clinical studies have explored the relationship between PON1 activity and various diseases. Additionally, some studies have examined whether there is a link between PON1 polymorphism and specific diseases.<sup>11,23,24</sup>

The second part of our research focused on determining the PON1 phenotype in AV patients, an area that has not been extensively studied. In the patient group, the QQ phenotype was observed at 48%, QR at 24%, and RR at 28%, while in the control group, these frequencies were 5.8%, 44.2%, and 50%, respectively.

Our results show a higher prevalence of the QQ allele and a lower frequency of the RR allele in the AV group compared to the control group. The elevated rate of the QQ allele, associated with lower enzyme activity, is one of the most notable findings of our study.

The primary rationale for selecting PON1 as a focus in this study was the lack of prior investigation into its relationship with AV. Previous studies have established that PON1 activity is associated with inflammatory and oxidative stress-related diseases.<sup>10,19,21,25</sup> In this context, we hypothesized that exploring the potential effects of PON1 on AV could provide novel insights and enhance the originality of our research. Furthermore, establishing a link between PON1 activity and AV may suggest that this enzyme could serve as a potential biomarker, aiding in the assessment of disease severity or the monitoring of treatment efficacy.

### Study Limitations

Among the limitations of our study is the relatively small sample size. To better elucidate the relationship between AV and PON enzyme activity, studies with a larger and more

diverse population are needed. Additionally, the limited geographic and genetic diversity of the patient and control groups restricts the generalizability of the results. Furthermore, the cross-sectional design of our study prevents drawing definitive conclusions about the causal relationship regarding changes in PON1 activity. We believe that these limitations should be considered in more comprehensive, future studies.

## CONCLUSION

This study investigated PON1 activity and determined its phenotypic polymorphism in AV cases, which had not been previously explored. PON1 activity levels in the patient group ( $36,149 \pm 14,536$ ) were found to be significantly lower than the control group ( $48,173 \pm 18,753$ ) ( $P < 0.05$ ). The finding of reduced activity of PON1, an enzyme with antioxidant properties, in acne patients suggests that oxidative stress may play a role in the etiology of AV.

The second part of our study revealed that the high prevalence of the low-activity QQ allele in the acne group is one of the most striking results. We believe that our study is significant because it is the first to investigate the PON1 phenotype in patients with AV. Based on our findings, we propose that individuals with the low-activity QQ allele may have increased susceptibility to acne development due to oxidative stress.

### Ethics

**Ethics Committee Approval:** This study was approved by Balıkesir University Faculty of Medicine Ethical Committee (approval number: 2014/94, date: 03.11.2021).

**Informed Consent:** It was obtained.

### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: İ.C., Ç.B., N.G., S.Ö., A.K., Concept: İ.C., Ç.B., N.G., S.Ö., A.K., Design: İ.C., Ç.B., N.G., S.Ö., A.K., Data Collection or Processing: İ.C., Ç.B., N.G., S.Ö., A.K., Analysis or Interpretation: İ.C., Ç.B., N.G., S.Ö., A.K., Literature Search: İ.C., Ç.B., N.G., S.Ö., A.K., Writing: İ.C., Ç.B., N.G., S.Ö., A.K.

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# Hypotrichosis and Juvenile Macular Dystrophy-First Homozygous Family Case from Türkiye

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## Abstract

Hypotrichosis with juvenile macular dystrophy (HMJD) is a rare autosomal recessive disease that leads to blindness in the first thirty years of life. It is characterized by hypotrichosis and progressive macular degeneration. Approximately fifty cases of this very rare entity have been reported. HMJD is associated with mutations in the *CDH3* gene. This article presents the case of a 4-year-old child who visited the dermatology clinic with hypotrichosis and underwent genetic screening due to clinical suspicion. His father, who was initially diagnosed with retinitis pigmentosa, was later identified as having HMJD. In both cases, the homozygous c.830del variant in the *CDH3* gene was detected. Considering eye involvement, revealed bilateral pigmentary changes at the fovea and loss of the outer retinal layers. In the second case, marked pigmentary changes in the posterior pole bilateral photoreceptor layer irregularity and retinal pigment epithelium atrophy, and a full-thickness macular hole on the right eye and foveal atrophy on the left eye were found. This is the first report of homozygous Turkish father-daughter cases with HMJD. Our discoveries offer deeper insights into *CDH3*-associated HMJD, providing valuable knowledge that could enhance the expertise of both dermatologists and ophthalmologists.

**Keywords:** *CDH3* mutation, genetics, homozygous, hypotrichosis, macular dystrophy

## INTRODUCTION

Hypotrichosis with juvenile macular dystrophy (HJMD) is a rare autosomal recessive disorder causing hypotrichosis and progressive macular degeneration, leading to blindness within the first thirty years of life.<sup>1</sup>

HJMD is associated with mutations in the *CDH3* gene, leading to abnormal expression of P-cadherin.<sup>2</sup> Approximately fifty cases of HJMD have been reported in the literature, which is included in the orphan diseases category (ORPHA:1573).<sup>3</sup> We present a case of a 4-year-old girl with clinically and genetically confirmed HJMD, born as a result of a consanguineous marriage, along with the case of her father, who received the same diagnosis following clinical suspicion.

This is the first reported case of a homozygous Turkish father-daughter case with HJMD, which highlights the importance of considering genetic screening in patients upon suspicion. Moreover, the presence of a macular hole in the father's case, which has not been previously described in HJMD, expands the spectrum of ocular manifestations associated with this disorder. Additionally, the absence of body hair in the father may reveal a broader spectrum of the disease. These findings contribute to the existing literature by providing novel insights into the phenotypic variability of *CDH3*-related diseases.

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## CASE 1

A 4-year-old girl presented to our dermatology outpatient clinic with a complaint of thin and sparse hair. Her medical history revealed that she had a congenital heart defect and had recently experienced mild vision loss. It was discovered that the patient was born to consanguineous parents.

Thin, short, and sparse hair was detected in the dermatological examination of her scalp with reduced density compared to normal. The patient exhibited a diffuse woolly hair appearance on her scalp (Figure 1). The hair pull-test was negative. Eyebrows, eyelashes, and body hair appeared normal. Upon dermatological examination of other body regions, including teeth, skin, nails, mucosae, and extremities, there were no abnormal findings. Trichoscopy of the scalp revealed short and thin vellus hairs (Figure 2).



**Figure 1.** The 4-year-old girl, the index case, had fine, short, and low-density hair on the scalp



**Figure 2.** Short and thin vellus-type hairs on trichoscopy

There were no abnormalities in the patient's biochemical values. The patient had no growth retardation.

Due to complaints related to vision, she was referred to the ophthalmology department. During her examination, the best-corrected visual acuity was evaluated as 0.7 logMAR in both eyes, without relative afferent pupillary defect. The patient had no pupillary or anterior segment abnormalities, and extraocular movements were normal. Intraocular pressure was measured as 18 mmHg in the right eye and 19 mmHg in the left eye. Dilated fundus examination revealed bilateral pigmentary changes at the fovea (Figures 3a, b). Optical coherence tomography (OCT) of the patient showed loss of the outer retinal layers (Figures 4a, b).

The clinical findings and complaints of the patient raised suspicion for the diagnosis of HJMD, and the patient was referred to the medical genetics department. All exons

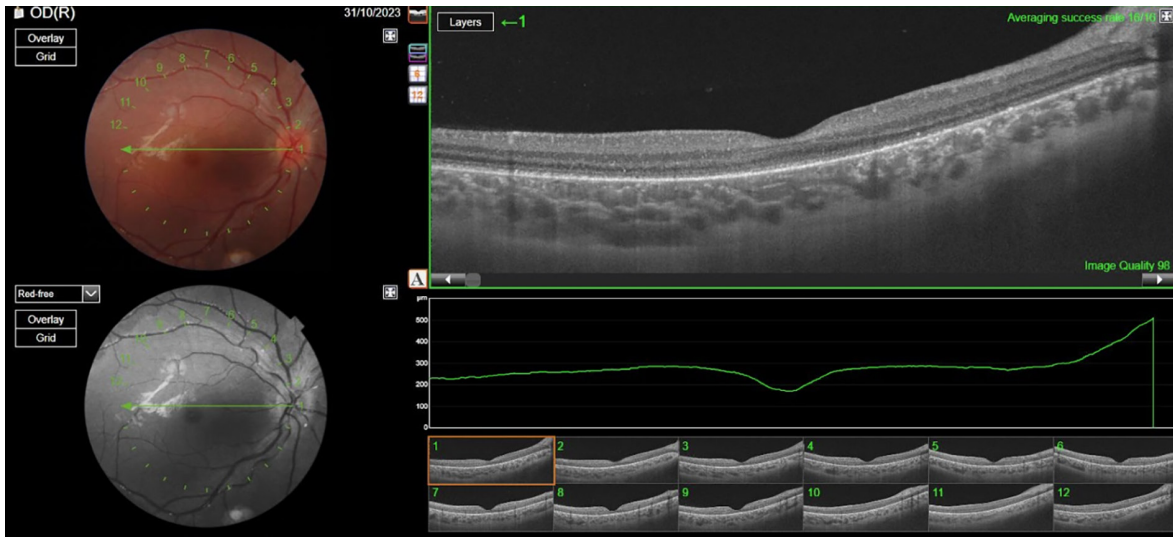


**Figure 3a.** Color fundus photograph of the patient's right eye

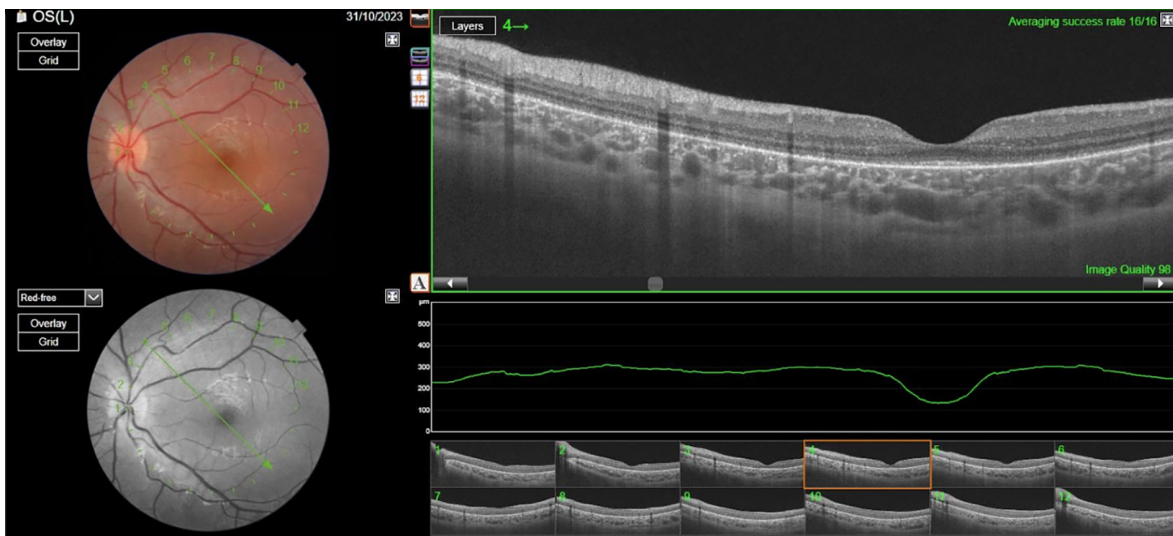


**Figure 3b.** Color fundus photograph of the patient's left eye





**Figure 4a.** Optical coherence tomography (OCT) image of the patient's right eye



**Figure 4b.** Optical coherence tomography (OCT) image of the patient's left eye

of genes and exon-intron junction regions, using library products prepared with the twist clinical exome sequencing (CES) kit from DNA samples isolated from peripheral blood, were amplified by polymerase chain reaction, followed by next-generation DNA sequencing analysis on the MGI DNBSEQ-G400 instrument.

As a result of CES, the homozygous c.830del(p.Gly277AlafsTer20) variant in the *CDH3*(*NM\_001793.6*) gene was detected and this variant has been previously described in the literature. It has been reported as pathogenic in ClinVar on five occasions (RCV001851938). The variant has not been observed in population frequency studies. According to in silico assessment tools, it is damaging. Based on the available information, this variant is classified as pathogenic according to the American College of Medical Genetics and Genomics guidelines (PVS1, PM2, PM3, PP5).<sup>4</sup>

Our clinical suspicion in the patient was confirmed by genetic analysis, and the patient's family was referred for genetic counseling. The absence of other anomalies besides hypotrichosis and retinal dystrophy excluded ectodermal dysplasia, ectrodactyly, and macular dystrophy, collectively known as Ectodermal dysplasia-ectrodactyly-macular dystrophy syndrome. No clinical pathology was detected in the patient's two siblings and mother. Nevertheless, the patient's siblings and mother were sent for genetic analysis and the details are provided under the second case.

With written consent from the parents and verbal consent from the patient, two scalp biopsies were performed, and no specific findings were present in histopathology.

## CASE 2

When the father brought his daughter for a second examination, similar hair findings were noticed in him as well.

The 45-year-old male patient also had thin and sparse hair. Additionally, he described thinning of his body hair. He also complained of vision loss and stated that he had been diagnosed with “retinitis pigmentosa”.

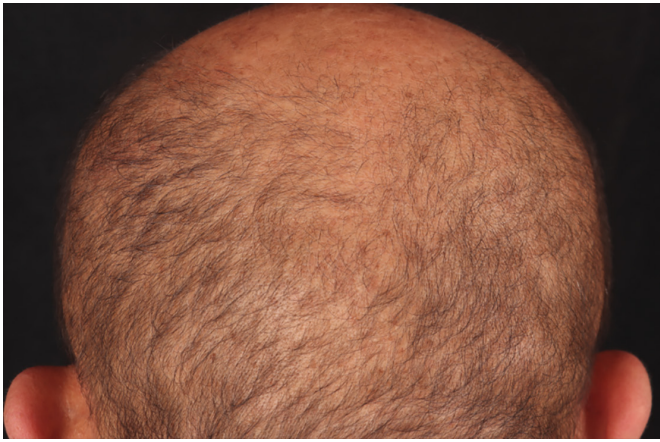
During the dermatological examination, the patient had thin, short, and sparsely distributed hair, with reduced density compared to normal (Figure 5). The density of eyebrows, beard, and eyelashes was normal; however, there was decreased hair density on the upper and lower extremities, indicating hypotrichosis (Figure 6). Vellus-type hair with thin, short, and low density was observed on trichoscopy over actinic damage on the scalp (Figure 7). Hair pull-test was negative. On both extensor surfaces of the knees, annular erythematous and infiltrated plaques covered with silver-colored scales, with diameters of 3\*3 and 4\*3 cm, were observed and evaluated

as psoriasis (Figure 8). Examination of the teeth, nails and mucous membranes was normal.

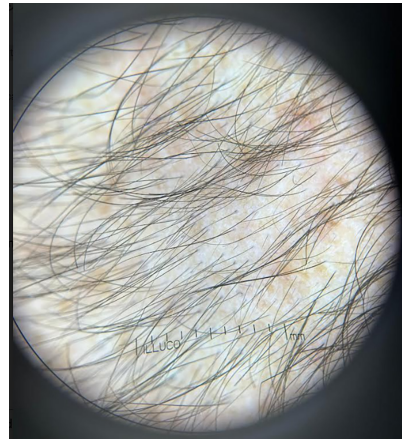
There were no abnormalities in the patient’s laboratory values, cardiac, and other systemic examinations.

He was referred to the ophthalmology department, and his best-corrected visual acuity was 0.8 logMAR in the right eye and 1.7 logMAR in the left eye. Intraocular pressure was 14 mm Hg in the right eye and 12 mm Hg in the left eye, as measured with a Goldmann applanation tonometer. Biomicroscopic examination revealed no anterior segment pathology. Fundus examination showed marked pigmentary changes in the posterior pole (Figures 9a, b). In OCT, bilateral photoreceptor layer irregularity and retinal pigment epithelium atrophy, full-thickness macular hole on the right eye (Figure 10a), and foveal atrophy on the left eye (Figure 10b) were detected.

A decrease in visual acuity and bilateral irregularities in the retinal pigment epithelium were observed. Based on these



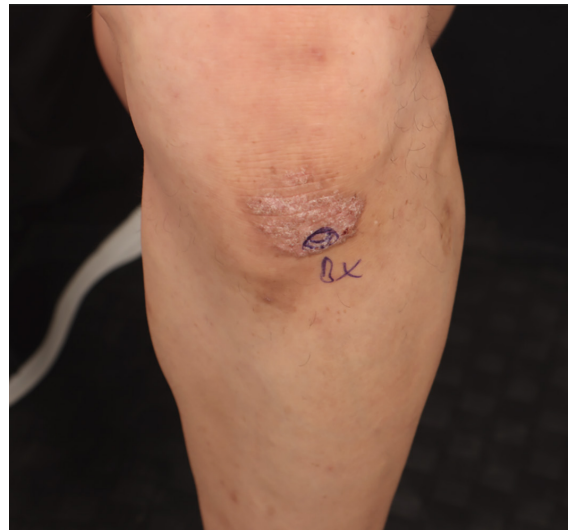
**Figure 5.** Fine, short, and low-density hair of the father



**Figure 7.** Vellus-type hair with thin, short, and low density observed on trichoscopy over actinic damage on the scalp



**Figure 6.** Hypotrichosis in the upper and lower extremities



**Figure 8.** Reduction in hair, and psoriatic plaque on the patient’s left leg

findings, the patient was referred to the genetics department for genetic studies with a suspicion of HJMD. As a result of the known mutation analysis performed by Sanger sequencing, the c.830del (p.Gly277AlafsTer20) variant in the CDH3 was also detected as homozygous. Thus, the patient was also diagnosed with HJMD.

Subsequent Sanger segregation studies for the same variant of the unaffected children of the father and the mother of the index case (above-mentioned 4-year-old girl) revealed that both the unaffected children and the mother were heterozygous carriers of the variant (Figure 11).

The patient consented, and biopsies from the scalp and a psoriatic plaque revealed findings consistent with psoriasis, with no specific results from scalp samples.

## DISCUSSION

HJMD is a rare autosomal recessive disease first described in 1935, which can result in blindness between the ages of 20

and 40.<sup>5</sup> Nearly all patients have had short, sparse hair since birth and progressive macular degeneration. The condition typically affects the hair and does not affect other body hair, however, it can sometimes affect the eyebrows and eyelashes as well.<sup>6</sup> The thinning of body hair observed in our second patient suggests that this condition may affect body hair. Due to clinical suspicion, in the examination conducted on the father of our index patient, the absence of body hair emerges as a significant finding. Unlike what is known, body hair may also be affected, suggesting that this issue may need further investigation.

This disease is associated with mutations in the *CDH3* gene, which encodes P-cadherin expressed in the retinal pigment epithelium and hair follicles.<sup>7</sup>

The retinal component of this syndrome has been re-evaluated, revealing earlier ocular involvement than previously suggested in its previous description as “juvenile”. Contemporary investigations have demonstrated a wider retinal impact extending beyond macular involvement.<sup>8</sup>

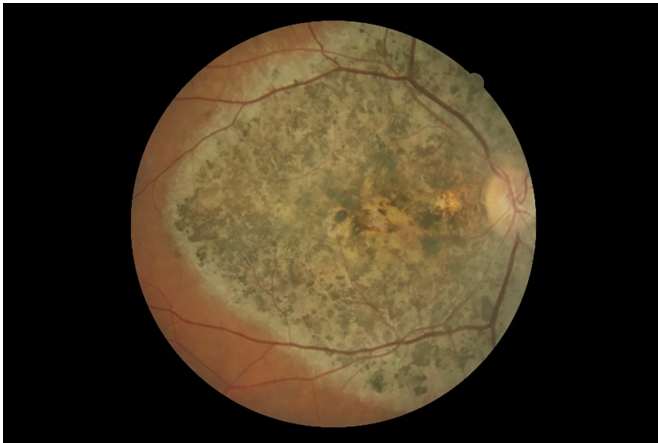


Figure 9a. The eye color fundus photography of the patient's right eye

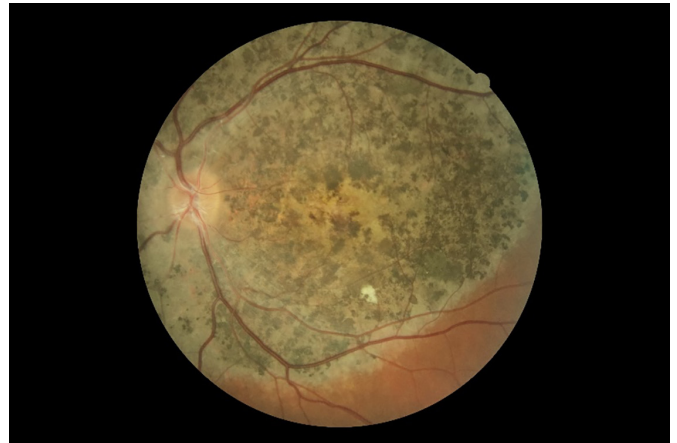


Figure 9b. The eye color fundus photography of the patient's left eye

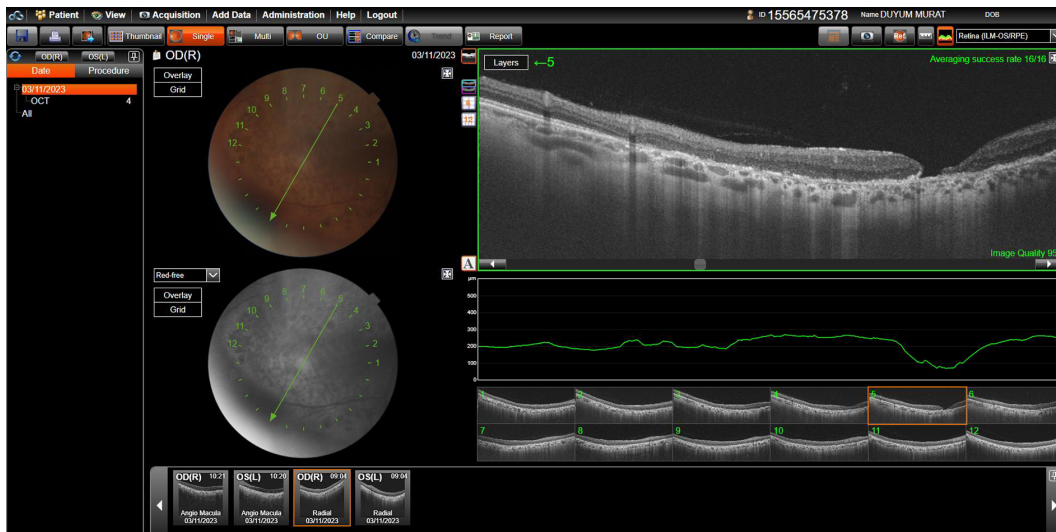


Figure 10a. The patient's right eye optical coherence tomography (OCT) image

In the two cases presented, fundus photography revealed various alterations in the retinal pigment epithelium, notably, accentuating the axial reflex. Both cases exhibited a circular pigmented area indicative of chorioretinal atrophy upon color fundus examination. Conversely, in case 2, OCT showed backscattering phenomena alongside diverse changes in the retinal pigment epithelium and photoreceptor layer. To the best of our knowledge, this marks the initial observation of a macular hole within the diagnosis of HJMD, shedding new light on the syndrome's ocular manifestations.

The diagnosis of the girl, which is very rare and based on clinical suspicion, was made alongside that of her father. The father was previously misdiagnosed with "retinitis pigmentosa" due to decreased vision. To the best of our knowledge, this is the first reported father-daughter case of HJMD from Türkiye, thereby contributing novel data to the existing literature.

HJMD currently lacks a definitive treatment. In cases where hypotrichosis raises suspicion and screenings reveal ocular findings inconsistent with typical macular degeneration, thorough systemic evaluation is crucial. Such patients may exhibit sparse scalp hair alongside an underlying genetic disorder. Effective diagnosis and prognosis of conditions like HJMD require close collaboration between dermatologists, ophthalmologists, and medical geneticists. Regular follow-up is essential to monitor and manage the likelihood of the condition progressively deteriorating over time.

HJMD, a very rare disorder with approximately fifty reported cases in the literature, is characterized by hypotrichosis and progressive macular degeneration and leads to blindness within the first thirty years of life. In daily practice, differentiating diagnoses for patients with hair disorders, such as hair loss, and conducting genetic analysis when necessary are crucial for diagnosing genetic diseases associated with

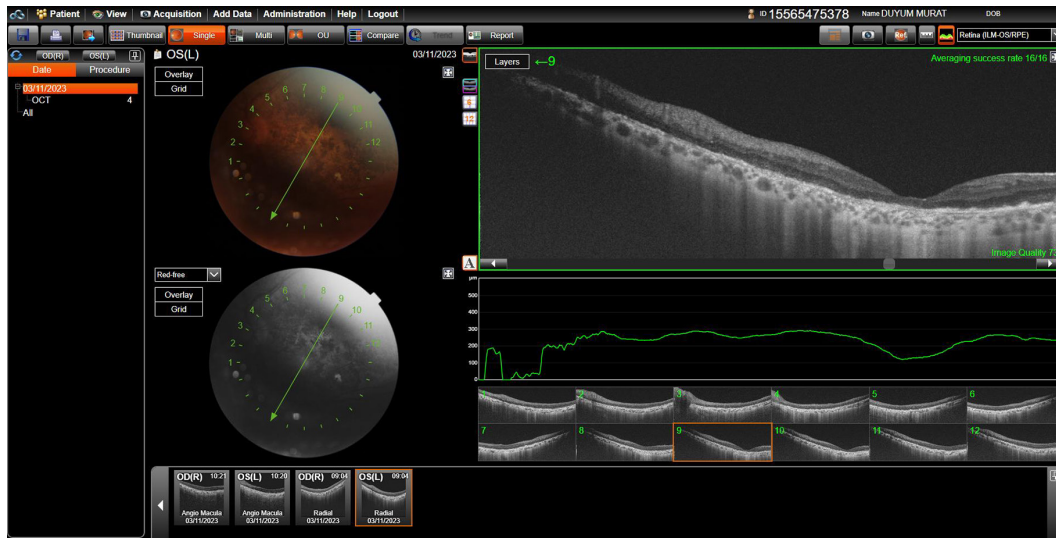


Figure 10b. The patient's left eye optical coherence tomography (OCT) image

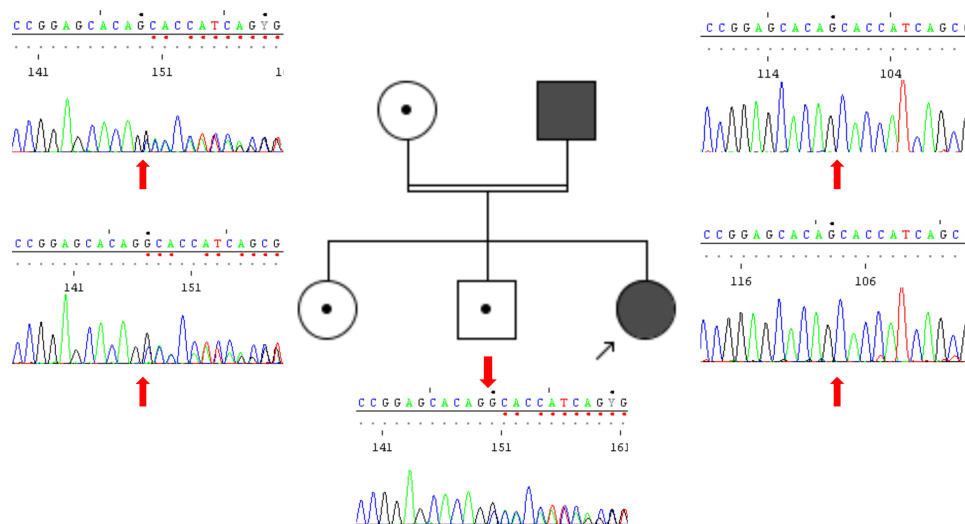


Figure 11. Pedigree of the family and Sanger sequencing images of the proband, affected father, mother and the healthy siblings

hair abnormalities. As in this case, although there is no definitive treatment for these diseases, providing genetic counseling for affected individuals and their families to guide future reproductive decisions as well as monitoring patients for potential effects are important. In our index case, the father, who brought the patient for examination, also exhibited hair-related findings and described having an “eye disorder,” leading to a diagnosis through genetic testing. Additionally, while HJMD typically causes hypotrichosis on the scalp, it rarely affects the eyebrows, eyelashes, or body hair, and involvement is generally not expected. However, the presence of reduced body hair in the father is a significant finding. Furthermore, the coexistence of psoriasis in the father suggests that additional clinical features may be present within the spectrum of this disease. Moreover, the identification of a macular hole in the father adds a novel ocular manifestation to the disease spectrum, broadening the current understanding of CDH3-related disorders. This paper is significant because it contributes to the literature with the first reported father-daughter HJMD case from Türkiye.

## Ethics

**Ethics Committee Approval:** Ethics Committee approval was obtained from the İstanbul Kent University Ethics (approval number: E-10420511-051-34424, date: 02.07.2024).

**Informed Consent:** Written consent for publication of the cases including the photographs was obtained.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: N.C., Concept: N.C., Design: N.C., Data Collection or Processing: N.C., A.G., M.K.,

E.M.K., E.Ç., H.İ.Y., Analysis or Interpretation: N.C., A.G., M.K., Literature Search: N.C., A.G., M.K., Z.T, Writing: N.C., A.G., M.K., Z.T.

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

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# Slime-Associated Contact Dermatitis with Active Inflammatory Border Sign Mimicking Tinea Manuum

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## Abstract

Slime has become increasingly popular among children in recent years, leading to a rise in cases of hand dermatitis. In this report, we present two cases of hand dermatitis linked to slime exposure. Both cases featured the “active border sign” associated with mechanical trauma and sensitivity to isothiazolinones. Patch testing revealed positive reactions to methylisothiazolinone/methylchloroisothiazolinone, and symptoms improved after allergen avoidance. These cases highlight the importance of recognizing slime-induced dermatitis for effective diagnosis and management.

**Keywords:** Contact dermatitis, allergic contact dermatitis, methylisothiazolinone, patch test, tinea manuum

## INTRODUCTION

In recent years, playing with slime has gained immense popularity among children, which has coincided with a notable increase in cases of hand dermatitis. The weak skin barrier in children makes them more susceptible to this condition, especially when exposed to allergens found in slime.<sup>1</sup> Sensitization to various allergens, notably isothiazolinones, is prevalent, particularly in homemade slime formulations. Accurate diagnosis through patch testing is crucial for identifying the causative allergen and preventing recurrent episodes.<sup>2</sup> We present two cases of hand dermatitis related to slime exposure, including the “active border sign” associated with mechanical trauma, and isothiazolinone sensitization.

## CASE REPORT

A 9-year-old girl presented with hand dermatitis localized to the palms that started a year ago. When questioned about her history of slime contact, she stated that she had prepared slime at home 1 year ago. Despite discontinuation of slime contact, her symptoms persisted. Clinical examination revealed erythematous plaques with vesicles and vesicle residue on the palmar surfaces of both hands (Figure 1a). A mycologic examination was conducted due to the presence of the active border, and the result was negative. The second patient, an 8-year-old girl, presented with an 8-month history of hand dermatitis. She reported involvement in homemade slime preparation using liquid soap, dishwashing detergent, and unspecified additives prior to the onset of symptoms.

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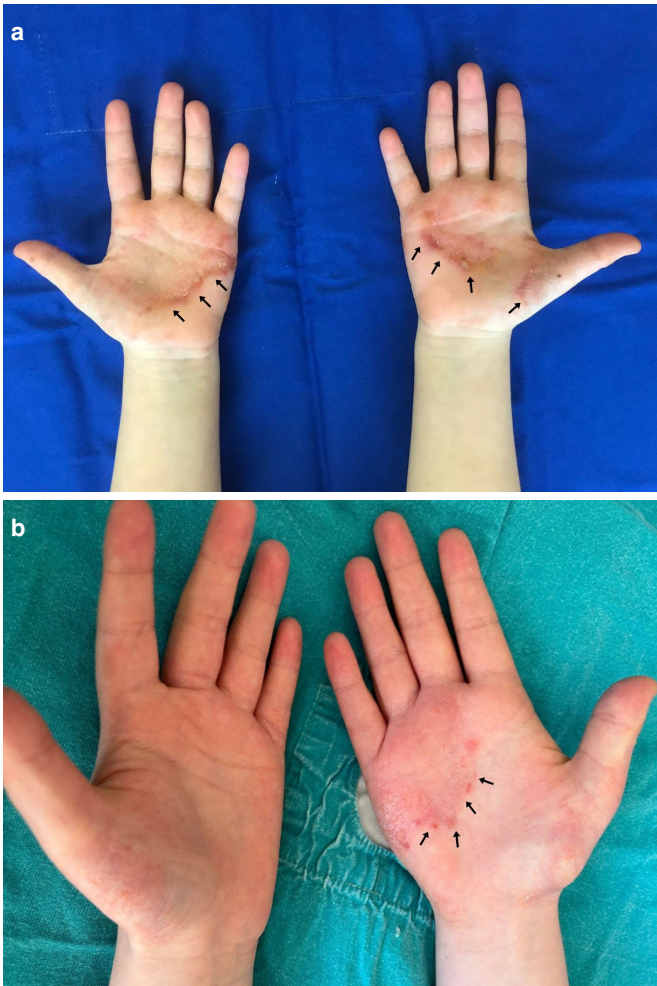
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Clinical examination revealed an erythematous plaque with an active border and residual vesicular debris on the right palm, showing partial regression (Figure 1b). Both patients underwent patch testing with the European Baseline Series, utilizing IQ Ultra Chambers from Chemotechnique Diagnostics (Vellinge, Sweden). Positive reactions (++) to the methylisothiazolinone/methylchloroisothiazolinone (MI/MCI) 0.02% aqueous solution were observed at 48 and 72 hours in both cases (Figure 2a,b). Patients were advised to avoid products containing isothiazolinones. Over the subsequent one-year follow-up period, no recurrence of symptoms was noted. Informed consent for publication was obtained from the patient's family.

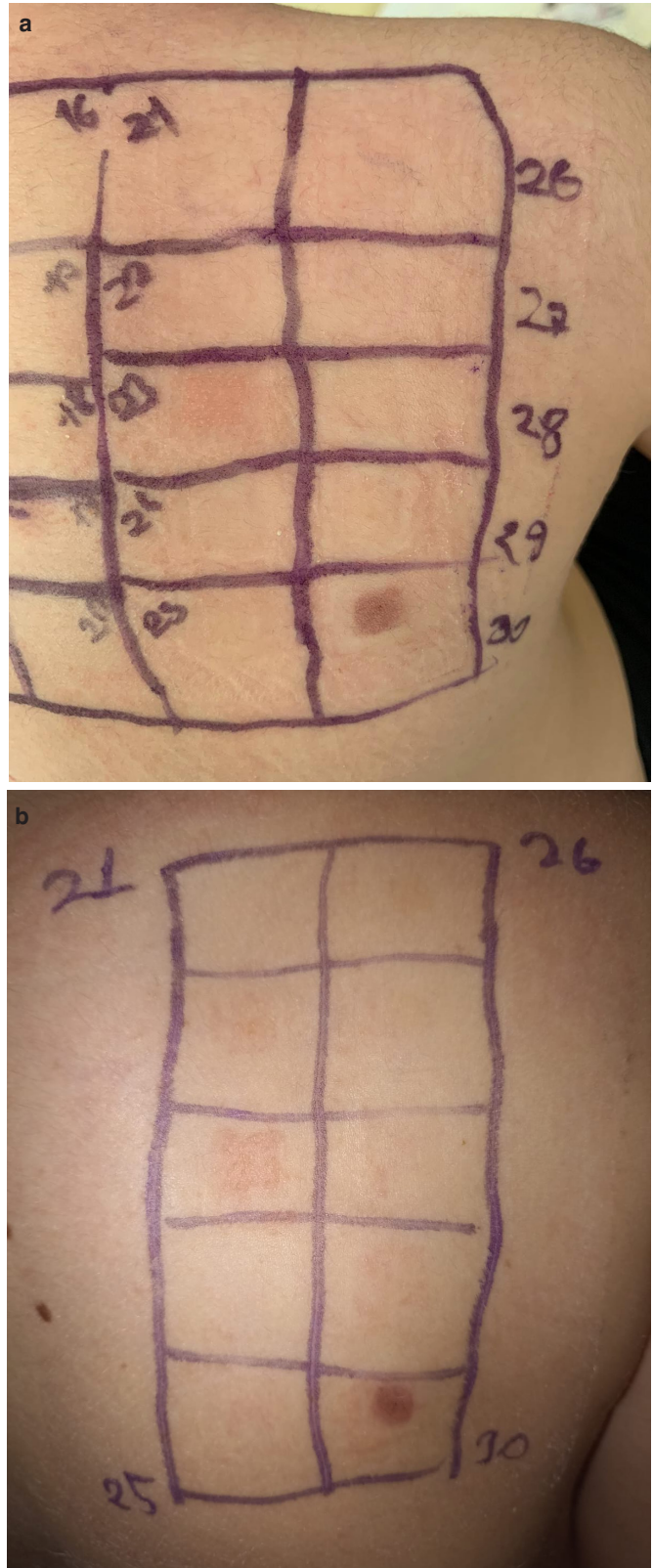
## DISCUSSION

Slime is often made from liquid soap, glue, detergent, borax, and food coloring. MI/MCI is a preservative found in many cleaning products and cosmetics, including slime.<sup>1</sup> In addition to MI/MCI, other allergens such as parabens and fragrances in slime ingredients can also cause hypersensitivity reactions.



**Figure 1.** (a,b) The active inflammatory border is indicated by arrows on the palms of both patients

Children exposed to homemade or industrial slime may develop eczematized plaques with vesicular remnants on their palms, raising suspicion of isothiazolinone sensitivity.



**Figure 2.** (a,b) Patch test results at 72 hours showed a 2+ reaction to methylisothiazolinone/methylchloroisothiazolinone

Patch testing in our study confirmed this sensitivity.<sup>2</sup> Since isothiazolinones are common in hygiene and household products, it is important to identify them to prevent future occurrences.<sup>3</sup> In our cases, avoiding contact with these allergens led to significant improvement without recurrence. In both cases, the mechanical trauma from repeatedly sticking and pulling slime off the skin contributed to irritant contact dermatitis, especially on the palmar surfaces of the hands. This “active border sign” has been observed in reported cases and may be confused with tinea manuum.<sup>1-3</sup> We postulate that this clinical finding is related to the repetitive mechanical damage caused by slime adhering to the palm during play, along with the irritating effects of the substances in the slime. This study is notable for identifying both allergic and irritant contact dermatitis in patients exposed to slime and recognizing the “active border sign,” which indicates mechanical trauma. These cases, by considering both allergic and irritant components, may provide insights into the understanding, diagnosis, and management of slime-induced dermatitis.

In conclusion, while slime is a common and seemingly harmless activity among children, its potential to cause hand dermatitis, both irritant and allergic, should not be overlooked. Early identification through patch testing and educating parents on avoiding specific allergens can improve clinical outcomes, as shown in our cases.

## Ethics

**Informed Consent:** Informed consent for publication was obtained from the patient’s family.

## Footnotes

### Authorship Contributions

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# Photoprevention with Oral *Polypodium leucotomos* Extract and Treatment with Medium-Depth Chemical Peeling in Xeroderma Pigmentosum: A Case Report

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## Abstract

Early diagnosis of xeroderma pigmentosum (XP) is mandatory to establish adequate sun protection, and regular examinations to detect and treat the premalignant and malignant overgrowths as early as possible. Aqueous extract from the leaves of *Polypodium leucotomos* (PLE) attracts attention due to its photopreventive and anticarcinogenic properties; however, more experience is needed in patients with XP. Chemical peelings help to rejuvenate the photodamaged and cancer-prone skin. However, data about their use in patients with XP is scarce. Herein, we discuss our experience with oral PLE extract and medium-depth peeling in a 34-year-old female patient with XP and the treatment outcomes.

**Keywords:** Actinic keratosis, chemexfoliation, xeroderma pigmentosum, polypodium

## INTRODUCTION

Xeroderma pigmentosum (XP) is an autosomal recessively inherited disorder characterized by increased susceptibility to photosensitivity and skin cancer formation due to defects in nucleotide excision repair genes that repair ultraviolet-damaged DNA.<sup>1</sup> The prevalence of XP is about 1/1000000 in the United States of America; however, it is higher in populations with more frequent parental consanguinity.<sup>2</sup>

Patients with XP experience various premalignant and malignant skin tumors and pigmentary changes, including multiple freckles, lentigines, actinic keratosis, melanoma, non-melanoma skin cancers, and sunburns from an early age. In addition, patients are at risk of ultraviolet-related ocular injury, progressive neurological degeneration, and worsening of skin disorders over time.<sup>1</sup>

Currently, there is no curative treatment for XP. Early diagnosis of XP is mandatory to establish adequate sun protection and regular examinations to detect and treat premalignant and malignant overgrowths as early as possible. Managing ultraviolet-damaged skin, actinic keratosis, field cancerization, dyspigmentation, and poikilodermatous changes is mandatory to prevent skin cancer. Chemoprevention and treatment with oral retinoids, topical imiquimod, and topical 5-fluorouracil, as well as physical modalities including various skin resurfacing options, (e.g., dermabrasion, chemical peelings, carbon dioxide or erbium-YAG laser), are frequently performed for XP patients.<sup>1</sup> However, even if the most appropriate and effective treatment is applied, the need to comply with the treatment and come for regular follow-up visits throughout the lifespan may be challenging for XP patients.

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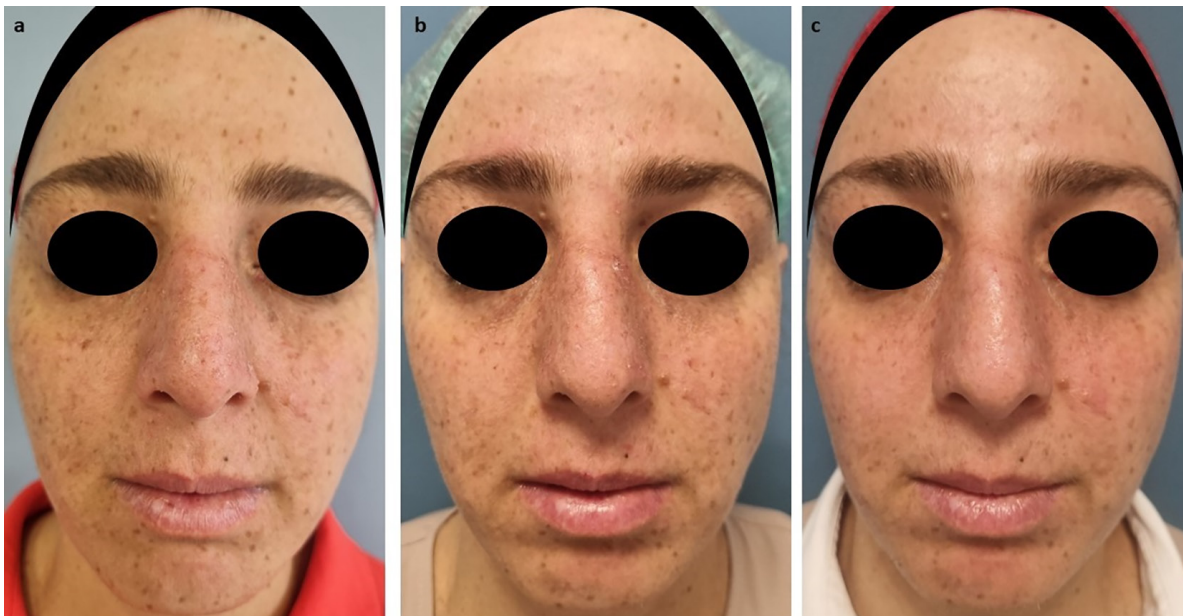
## CASE REPORT

A 34-year-old woman with known XP since the age of 6 presented to the outpatient clinic with recurrent crusted lesions and brown spots on her face. She had a homozygous p.Ala656Val missense mutation in the *ERCC2* gene. She had no ocular or neurological findings and reported frequent sunburns, particularly during the summer months of childhood. The patient's parents had a third-degree consanguineous marriage, and two out of her three siblings had the same disease. During childhood, the patient only used moisturizer and sunscreen irregularly. Due to health insurance issues, she could not attend regular check-ups, use the recommended treatments, or be checked for internal malignancies, which may be associated with the *ERCC2* mutation. She did not have any malignant skin tumors and had a history of actinic keratosis. On dermatological examination, erythematous, scaly papules were present on the dorsum of the nose and bilateral malar regions, along with widespread lentiginosities and generalized freckling on the face (Figures 1a, 2a, 3a).

Since the patient was not adherent to previously prescribed topical fluorouracil cream, due to local side effects such as irritation, erythema, and burning sensation, 3% diclofenac gel was recommended for use on the whole face. The patient regularly took 240 mg/d oral *Polypodium leucotomos* (PLE) (Heliocaps capsules with Fernblock®) for 6 months, from May 2024 to October 2024; however, she had not been diligent in using topical treatment and sunscreen, she did not accept additional interventions for actinic keratosis. During 6 months of follow-up, the patient preferred regular oral PLE since its

use provided almost no sunburns and discomfort compared to the summer days in the previous year when engaged in outdoor activities. The actinic keratosis area and severity index score changed from 1.8 to 2.0 after 6 months, and no malignant tumors nor additional clinically relevant actinic keratosis were detected (Figures 1b, 2b, 3b).

For a better and rapid clearance of pre-existing lesions, the patient accepted to have a medium-depth chemical peeling with a solution containing 15% trichloroacetic acid (TCA) and 3% phenol (Easy TCA Pain Control®, Skintech PharmaGroup, Spain). A 2.7 mL solution was applied to the whole face in 3 layers in small circular movements using cotton buds. The deep dermal application was applied to the hyperkeratotic areas of actinic keratosis. When a uniform white frosting with an erythematous background appeared as a marker of medium-depth peeling, a post-peel cream with antioxidant and moisturizing properties was applied to the skin. After about 2 weeks of rough desquamation, actinic keratosis was cleared, and remarkable clearance of small, light brown mottled pigmentations, freckles, and small lentiginosities was observed (Figures 1c, 2c, 3c). There were no side effects such as postinflammatory hypo/hyperpigmentation, scarring, or postpeel erythema. Twice daily use of topical diclofenac gel was recommended 2 weeks after the peeling session. She was warned about the importance of regular follow-ups and sun protection. Although the patient was called for monthly follow-ups, she did not come due to socioeconomic problems. The patient in this manuscript has given written informed consent to the publication of their case details and clinical photographs.



**Figure 1.** Frontal view of the patient, (a) Before oral PLE supplement and 3% diclofenac gel; (b) After 6 months; (c) Total clearance of actinic keratosis after single session of medium-depth peeling with 15% TCA + 3% phenol solution  
PLE: *Polypodium leucotomos*, TCA: *Trichloroacetic acid*

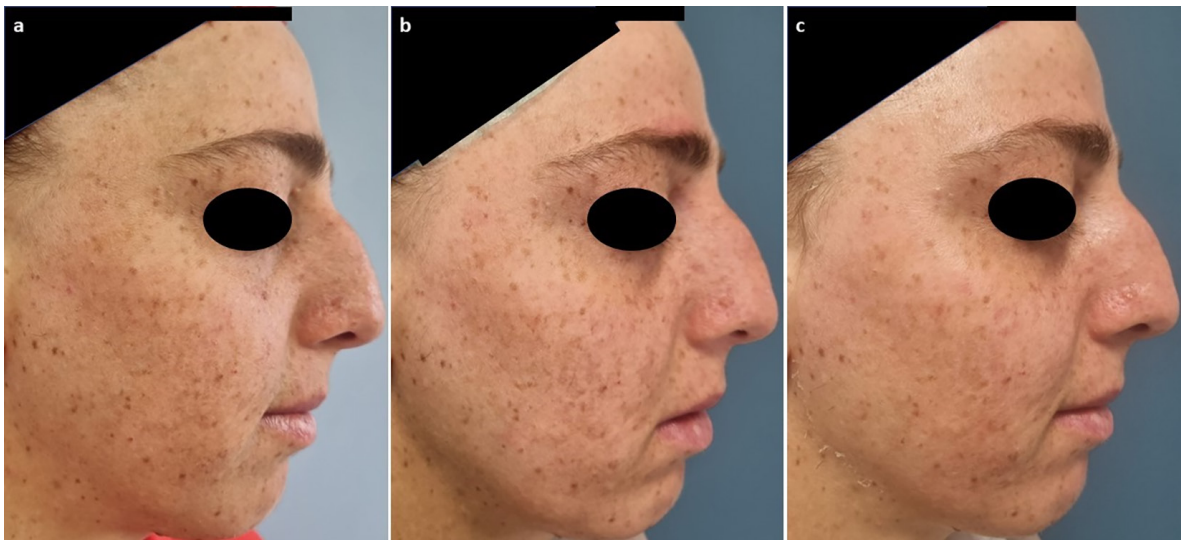
## DISCUSSION

Aqueous extract from the leaves of PLE attracts attention due to its photopreventive and anticarcinogenic properties. Research in the last decades has shown that PLE inhibits reactive oxygen species, prevents DNA mutations, and repairs photodamaged DNA products such as cyclopyrimidine dimers when exposed to the ultraviolet to infrared radiation spectrum.<sup>3</sup> PLE was administered to XP patients based on these observations, and promising outcomes were achieved. A prospective study showed that 11 of 18 (61%) patients with XP who were put on oral supplements and topical SPF50+

sunscreen containing PLE did not develop new lesions over 12 months.<sup>4</sup> Treatment of actinic keratosis and field cancerization needs proper management to remove clinical and subclinical damages and overgrowths and appropriate monitoring to reduce the risk of actinic keratosis. Among various targeted and field-directed therapies, oral supplements of PLE are recommended as part of strict photoprevention strategies, especially in patients engaging in outdoor activities.<sup>5</sup> The significant decrease observed in the recurrence of actinic keratosis at 6 months after two sessions of photodynamic therapy combined with PLE supplementation is remarkable for managing field cancerization as a combination therapy.<sup>6</sup>



**Figure 2.** Left profile of the patient, (a) before oral PLE supplement and 3% diclofenac gel; (b) after 6 months; (c) total clearance of actinic keratosis after single session of medium-depth peeling with 15% TCA + 3% phenol solution  
 PLE: *Polypodium leucotomos*, TCA: *Trichloroacetic acid*



**Figure 3.** Right profile of the patient, (a) before oral PLE supplement and 3% diclofenac gel; (b) after 6 months; (c) total clearance of actinic keratosis after single session of medium-depth peeling with 15% TCA + 3% phenol solution  
 PLE: *Polypodium leucotomos*, TCA: *Trichloroacetic acid*

In our case, oral PLE provided remarkable photoprotection and comfort in summer. Furthermore, using it as an adjuvant treatment with topical 3% diclofenac gel seems to help prevent new premalignant tumors, although this gel is less effective compared to topical fluorouracil cream.

The treatment of severely photodamaged and cancer-prone skin of patients with XP using resurfacing modalities, including dermabrasion and chemical peelings, has resulted in significant control of new growths of premalignant and malignant tumors within months to years.<sup>7</sup> Full-face medium-depth peels with 35-40% TCA and deep peels with 35% phenol have been reported as effective for the treatment and prevention of new tumors.<sup>7,8</sup> As observed in our patient, a low concentration of phenol (3%) combined with 15% TCA was sufficient to penetrate the dermis when applied in subsequent coats. Deep phenol peels require experience and close monitoring of patients due to potential cardiotoxic effects. Therefore, deep peeling applications using high concentrations of phenol may be an appropriate approach to reserve for patients with medium-depth peeling who have a low treatment success rate. A medium-depth peel with the proper technique may remove the non-clinically detectable subtle lesions and prophylactically clear the photodamaged skin. The procedure is more straightforward, cheaper, and better tolerated than dermabrasion techniques. Furthermore, the combination with other topical agents is reasonable due to their effects on facilitating drug transport.

Oral *Polypodium leucotomos* extract is a promising adjuvant treatment for the control of field cancerization, especially for patients prone to photocarcinogenesis and potentially non-compliant with treatments such as XP. Since treatments for actinic keratosis and field cancerization may take significantly longer and require compliance, chemical peelings may serve as a relatively shorter and better-tolerated management option, which can be combined with topical agents when needed.

## Acknowledgements

We thank Cantabria Labs for providing oral PLE supplements (Heliocaps capsules with Fernblock®), and we appreciate SkinTech PharmaGroup and Estetik Dermal, for delivering the chemical peeling products for the patient's treatment free of charge.

## Ethics

**Informed Consent:** The patient in this manuscript has given written informed consent to the publication of their case details and clinical photographs.

## Footnotes

### Authorship Contributions

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# Refractory Epidermolysis Bullosa Pruriginosa with Rapid Clinical Response to Upadacitinib Treatment

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## Abstract

Epidermolysis bullosa pruriginosa (EBP) is a rare subtype of dystrophic EB. Topical corticosteroids, tacrolimus, oral thalidomide, and immunosuppressants are among the treatment options that can be given, but there is no consistently effective treatment. Some case reports have shown positive results in treatment with omalizumab, dupilumab, and Janus kinase inhibitors. We present a 37-year-old female EBP patient who had not responded to multiple previous treatments (systemic steroids, hydroxychloroquine, dapsone, omalizumab, and cyclosporine) but achieved a rapid clinical response to upadacitinib treatment. We are sharing our case to encourage the consideration of upadacitinib as an alternative treatment for refractory EBP cases.

**Keywords:** Epidermolysis bullosa pruriginosa, JAK inhibitors, upadacitinib

## INTRODUCTION

Epidermolysis bullosa pruriginosa (EBP) is a rare subtype of dystrophic EB (DEB), a group of autosomal dominant or recessive genodermatoses caused by mutations in the *COL7A1* gene.<sup>1</sup> There is no definitive cure, but topical corticosteroids, tacrolimus, oral thalidomide, and immunosuppressants are among the treatment options that can be given to EBP cases.<sup>1</sup>

Mutations in the *COL7A1* gene result in deficient or dysfunctional collagen VII, which leads to dysfunction of the anchoring fibrils beneath the basal lamina.<sup>2</sup> In addition to the features of DEB, such as vesiculobullous lesions and nail dystrophy, EBP also presents with intensely pruritic, nodular, prurigo-like lichenified lesions.

We present a rapid clinical response to upadacitinib therapy in a patient with EBP who had previously tried treatments without response.

## CASE REPORT

Our 37-year-old female patient presented to our dermatology clinic with complaints of rash and itching that had persisted for 1.5 years. She had previously undergone five different biopsies at external centers, none of which could provide a definitive diagnosis. The genetic test diagnosed EBP due to the Col7a1 mutation. She had no known skin disease or other chronic disease. The patient has 3 living healthy children after one miscarriage. Her children do not exhibit any signs of EB. There isn't known history of skin, autoimmune, or hereditary disease in the patient's first-degree relatives, except for rheumatoid arthritis (RA) in the mother.

Dermatological examination revealed vesiculobullous lesions on the back, predominantly in the sacral and bilateral lumbar regions; along the bilateral upper extremities, predominantly on the extensor face; concentrated in the bilateral pretibial areas; along the entire crus and thighs, thoracic and abdominal regions; and on the scalp. These bullous lesions had opened, resulting in widespread eroded lesions with an erythematous

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base and crusting in some areas. These lesions collectively formed foci of bleeding and infection. In addition, there were scattered milia all over the body (Figure 1). The skin lesions were accompanied by severe pruritus. There was a complaint of stricture in the proximal oesophagus due to EBP involvement.

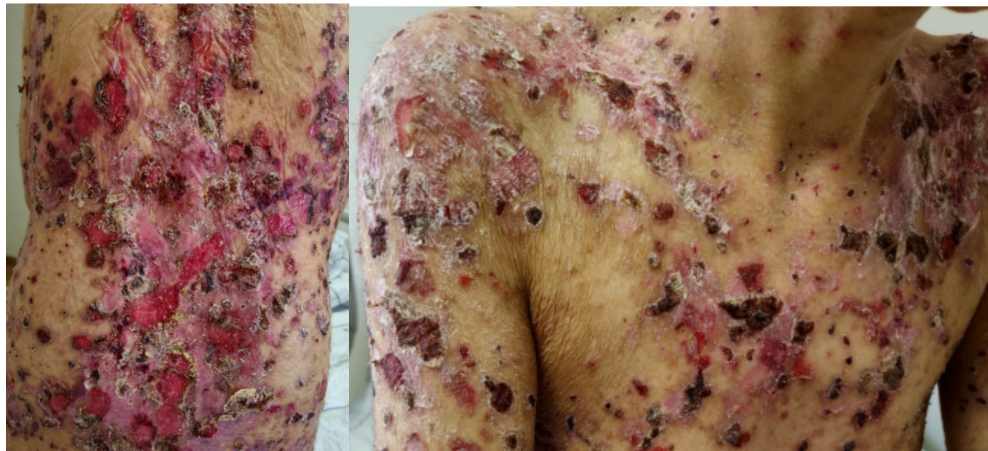
The patient was given systemic steroids, hydroxychloroquine, dapsone, omalizumab, and cyclosporine treatments in other clinics, but no treatment elicited a response.

When she applied to our service, the patient had not received any systemic treatment for 15 days, and her laboratory tests were as follows: hemoglobin: 6.3, erythrocyte sedimentation rate: 111 (reference range 0-25), and C-reactive protein: 147 (reference range 0-5). During his hospitalization, his numerical rating scale (NRS) score was ten, and pruritus control was attempted with a combination of antihistamines. After one month of symptomatic treatment, including intravenous antibiotics, systemic antihistamines, topical steroids, epithelializers, there was no improvement in pruritus and new lesions continued to appear.

The 40 kg patient was started on upadacitinib at a dose of 15 mg/day. On the second day of treatment, pruritus decreased. On the 10<sup>th</sup> day, the patient's NRS score was 2. No new lesions were observed, and existing lesions regressed rapidly (Figure 2).

## DISCUSSION

EBP is a rare subtype of DEB, characterized by hallmark DEB features, including vesiculobullous lesions and nail dystrophy. Additionally, hypertrophic, lichenified, and pruritic plaques or nodules, which typically emerge during adolescence but may be present at birth, are frequently observed. Over time, these lesions can lead to purplish linear scarring and milia formation.<sup>3</sup> Our patient presented with nail dystrophy and vesiculobullous lesions on an erythematous base, which were predominantly distributed in trauma-prone regions, such as the sacral area and extensor surfaces of the extremities. These lesions were associated with crusting and erosion, and their chronicity or healing resulted in the development of papules, plaques, scarring, and milia. The disease involved nearly 75% of the patient's body surface, sparing only the face and palmar



**Figure 1.** Skin lesions at the time of patient's admission to our service



**Figure 2.** Skin lesions on day 10 of the patient's upadacitinib therapy

regions. Mucosal involvement was also noted with a proximal esophageal stricture.

The diagnosis of EBP relies on a combination of clinical features, histopathological findings, and genetic testing. Characteristic trauma-induced lesions, family history, and molecular analysis are key diagnostic pillars.<sup>3</sup> In this case, no family history of similar symptoms was reported, and the patient's complaints had begun 1.5 years before presentation. During this period, six skin biopsies were performed, which revealed findings consistent with DEB, including subepidermal cleavage, fibrin deposition, milia, hyperkeratosis, vascular proliferation, and perivascular lymphohistiocytic infiltration. However, a definitive diagnosis could not be established until genetic testing identified a pathogenic mutation in the *COL7A1* gene, confirming the diagnosis of EBP.<sup>4</sup>

The exact pathogenesis of pruritus in EBP remains unclear, and our treatment goals are to eliminate pruritus and prevent new lesions. Recently, EBP has been shown to have a Th2 cell-driven immune response, resulting in elevated serum levels of interleukin (IL)-4, IL-5, IL-13, and IgE.<sup>5</sup> Furthermore, some case reports have demonstrated favourable responses to omalizumab<sup>6</sup> and dupilumab<sup>2</sup> in EBP patients, supporting this notion regarding the underlying pathogenesis of pruritus in EBP. Our patient had previously received omalizumab treatment at an outside centre, which initially reduced pruritus but did not provide long-term success.

Janus kinases (JAKs) are intracellular enzymes that play a role in the signalling of cytokines and growth factors in various cellular processes such as inflammatory response, haematopoiesis, and immune system function. The JAK family of enzymes modulates gene expression and cellular function by phosphorylating signal transducers and activators of transcription. The JAK family consists of four members (JAK1, JAK2, JAK3 and TYK2). Upadacitinib is a selective and reversible JAK inhibitor. It inhibits JAK1 or JAK1/JAK3 signalling via cytokine receptors that involve JAK2. JAK1 inhibition blocks multiple signalling pathways, contributing to symptoms such as skin lesions and pruritus in atopic dermatitis.<sup>7</sup> Two previous cases of EBP have been reported with good treatment outcomes using JAK inhibitors, baricitinib (a JAK1/2 inhibitor)<sup>1</sup> and tofacitinib (a JAK1/3 inhibitor).<sup>8</sup> Upadacitinib, which is indicated for the treatment of RA, psoriatic arthritis, ankylosing spondylitis, atopic dermatitis, and ulcerative colitis<sup>7</sup>, has been successfully used off-label in two EBP cases reported in the literature.<sup>2,7</sup> In one case, Kim et al.<sup>5</sup> reported in August 2022 that a significant reduction in pruritus and new lesions wasn't reported after ten weeks of upadacitinib use.

Our patient's clinical response to upadacitinib was much faster, similar to the duration of effect seen in atopic dermatitis, which is also rapid. By the 10<sup>th</sup> day, the patient's pruritus had nearly entirely resolved. New lesions were not observed, and existing lesions regressed rapidly.

Furthermore, the patient's rapid response highlights the importance of addressing the psychosocial burden associated with EBP. Chronic pruritus and erosive lesions significantly impair quality of life, leading to sleep disturbances, anxiety, and depression.<sup>9</sup> The prompt alleviation of symptoms improved the patient's physical condition and positively impacted her mental well-being, as noted during follow-up visits.

In conclusion, our case highlights the potential role of upadacitinib as a novel and effective treatment for refractory EBP. This therapeutic approach addresses both the inflammatory and pruritic components of the disease, offering a promising alternative for patients who fail to respond to conventional therapies. We are sharing our case to encourage the consideration of upadacitinib as an alternative treatment option for refractory EBP cases.

## Ethics

**Informed Consent:** The authors certify that they have obtained all appropriate patient consent forms. In the forms, the patient has given his/her/their consent for his/her/their images and other clinical information to be reported in the journal.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: Z.U., Z.A., Concept: Z.U., Design: Z.K.U., Data Collection or Processing: Z.A., Literature Search: Z.U., Z.A., Writing: Z.A., Z.K.U.

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# A Conventional Method for Treating Psoriatic Erythroderma in the Age of Biological Therapies: Modified Wet Wrap Therapy with Oat Bath

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## Dear Editor,

Erythroderma is a serious and potentially life-threatening condition characterised by generalized erythema and scaling covering at least 75-90% of the skin. Here we report on a successful treatment approach for psoriatic erythroderma that involved combining modified wet wrap therapy with oat baths. This novel method proved to have minimal side effects and led to a rapid response, which is particularly noteworthy considering the patient's age and comorbidities.<sup>1</sup>

A 70-year-old man with a known history of hyperthyroidism and previous prostate cancer diagnosis was admitted to our clinic. He complained of erythema all over his body, along with scaling, chills, and weakness (Figure 1a). After a thorough review of the patient's medical history, a complete clinical examination, and a histopathological analysis, the patient was admitted to the clinic with a confirmed diagnosis of psoriatic erythroderma. Given the patient's advanced age and overall health condition, a wet dressing treatment was initiated following an oat bath, with the objective of achieving a rapid improvement. Methotrexate 15 mg/week was initiated as a systemic treatment for the disease and to maintain remission.

An oat bath was prepared by adding approximately 80 grams of ground oat flour to 120 liters of water. The oat bath was applied to the patient for 15-20 minutes. Afterward, 25 grams of clobetasol propionate was applied to the anterior surface of the body. Subsequently, the anterior surface of the body was covered with large cloths moistened with warm water

and then overlaid with a blanket. Following a two-hour application period, a similar procedure was repeated on the posterior surface of the trunk (Figure 1b, c). The treatment was administered for a total of four consecutive days. The patient's complaints of erythema, scaling, chills, and laboratory values improved significantly by the end of the four-day treatment period (Figure 1d, e).

In our clinic, we successfully employed an oat bath and modified wet wrap treatment in a case of psoriatic erythroderma, which we developed based on our previous experiences. Wet wrap therapy has been classically described as a salvage treatment option for atopic dermatitis.<sup>2</sup> Its ability to successfully treat patients with psoriasis has been shown over time.<sup>3</sup> Similar to our approach, there is only one study in the literature that has explored the use of wet wrap treatment in patients with psoriatic erythroderma.<sup>3</sup> The Table 1 summarises the classic wet wrap treatment for atopic dermatitis and psoriatic erythroderma.<sup>2,3</sup> Our methodology differs from the studies on atopic dermatitis and psoriasis in two important ways. First, we have modified the wet wrap treatment. Second, we have combined it with oat baths. With the oat bath, we aimed to enhance the effect of topical corticosteroid treatment by increasing its absorption and to benefit from the anti-inflammatory, antioxidant, moisturising, cleansing and soothing effects of oats.<sup>4</sup> Consequently, while the literature indicates longer application times for the wet wrap treatment, our preference is a 2-hour application.

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Figure 1. Images of the patient before (a), during (b, c) and after (d,e) Wet Wrap Therapy-Oat Baths

Table 1. Wet Wrap Therapy Methods in the literature			
Study/indication	Bathing	Wet wrapping	Application frequency/duration
Devillers and Oranje <sup>2</sup> /atopic dermatitis	5-10 minutes with warm water before application	Diluted fluticasone propionate 0.05% is used. The first layer is a bandage soaked in warm water and the second layer is a dry bandage. The dressings are remoistened every 2-3 hours.	1 time a day, for 3-24 hours. Maximum 3-4 consecutive days in total.
Navrotski et al. <sup>3</sup> /erythrodermic psoriasis	-	After applying medium-high strength corticosteroid (betamethasone dipropionate 0.05% or clobetasol dipropionate 0.05%) to all affected surfaces, first layer is formed with a warm moist cotton cloth and second layer with a dry cotton cloth. The patient is wrapped with a blanket to minimise heat loss.	2-4 times a day for 1 hour. In total 2-5 times a week.
Our study	Oat bath 15-20 minutes	After applying clobetasol dipropionate 0.05% cream to all affected areas, first layer is formed with a warm damp cotton cloth and second layer with a dry cotton cloth. The patient is wrapped in a blanket to minimise heat loss.	1 time a day for 2 hours. 4 consecutive days in total.

Patients with psoriatic erythroderma should begin systemic treatment promptly to achieve long-term disease control.<sup>3</sup> Once the modified wet dressing treatment was completed, we commenced methotrexate therapy at 15 mg per week. The patient was followed up for 3 months, and no additional flare-ups were observed during the monthly examinations.

In conclusion, the oat bath and modified wet dressing treatment, used for the first time in our clinic with Antalya approach, may be preferred as an alternative to systemic treatment and as a salvage treatment, especially in elderly psoriatic erythroderma patients with comorbidities. Further similar observations on this topic will provide more objective information on the efficacy of this new method.

### Footnotes

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

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