Original Article

Contact Sensitization in Atopic Dermatitis Patients with Refractory Dermatitis

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Abstract

Aim: Allergic contact dermatitis (ACD) may accompany atopic dermatitis (AD) more frequently than previously recognized. This study aimed to identify concomitant contact sensitization and common allergens in patients with refractory AD.

Materials and Methods: In this prospective single-center study (September 2022–February 2024), 62 AD patients with treatment-resistant or atypically distributed lesions suggestive of contact dermatitis underwent patch testing using the European baseline series. Patch test reactions were evaluated on days 2 and 4 according to International Contact Dermatitis Research Group criteria; reactions graded as + or higher were considered positive. Results were compared with those of 306 non-AD patients who underwent patch testing for suspected ACD during the same period.

Results: The positivity rate for at least one allergen in AD patients was 62.9%, which was significantly higher than that observed in non-AD patients (40.2%). Nickel sulfate was the most frequently identified allergen.

Conclusion: These findings suggest that patients with AD may have increased susceptibility to contact sensitization, and patch testing in recalcitrant cases may help identify potential triggering allergens.

Keywords: Atopic dermatitis, contact sensitization, patch tests

Introduction

Atopic dermatitis (AD) is a chronic, relapsing inflammatory disease of the skin that is frequently accompanied by other atopic conditions, including asthma, food allergy, and allergic rhinoconjunctivitis. The relationship between AD and the risk of contact sensitization remains controversial.[1] Early studies suggested a reduced prevalence of contact allergy in AD patients, possibly related to distinct immunological mechanisms.[1] However, impaired epidermal barrier function and prolonged or repeated exposure to topical treatments in AD may facilitate increased percutaneous penetration of irritants and allergens, thereby enhancing the risk of contact sensitization.[2] Clinically, distinguishing AD from concomitant allergic reactions, particularly allergic contact dermatitis (ACD), can be challenging, and both conditions may coexist in the same patient.[1] In this context, patch testing represents a valuable diagnostic tool, especially in AD patients with treatment-resistant disease, atypical lesion distribution, or clinical features suggestive of superimposed contact allergy.[2,3] Accordingly, current recommendations support patch testing in selected AD patients who present with these characteristics. Beyond reporting patch-test positivity rates, the present study aims to clarify the clinical utility of patch testing in AD patients who present with refractory, atypically distributed lesions and to compare their contact-sensitization profiles with those of non-AD patients.

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Materials and Methods

A prospective study was conducted at our tertiary referral center between September 1, 2022, and February 29, 2024. The study included AD patients who were suspected of having concomitant ACD. AD was diagnosed according to the Hanifin–Rajka criteria, based on a detailed medical history and a current physical examination. Patients were eligible for inclusion if they presented with treatment-resistant lesions—defined as those that failed to resolve despite adequate topical therapy, or that recurred shortly after treatment discontinuation—or clinical features suggestive of contact dermatitis, including hand eczema, periorbital dermatitis, dermatitis with atypical distribution, adolescent- or adult-onset AD, and nummular dermatitis. Patients younger than eight years of age, pregnant women, individuals receiving active immunosuppressive therapy, patients with ultraviolet exposure within the preceding month, those who had applied topical treatments to the test area within one week prior to testing, and patients with active lesions involving the test area were excluded from the study. Disease severity was assessed using the scoring atopic dermatitis (SCORAD) index.[4] Patients were categorized into two groups according to age: pediatric (< 18 years) and adult (≥ 18 years). All participants underwent patch testing using the 2019 European baseline series, consisting of 30 allergens (chemotechnique diagnostics). Patch tests were applied to the upper back using IQ Ultra™ Chambers and were left in place for 48 hours. Patch test readings were performed on day 2 (D2) and day 4 (D4) by a single physician, following the routine protocol of our clinic and in accordance with the criteria of the International Contact Dermatitis Research Group.[4] Dynamic patch-test evaluation was applied: crescendo and plateau reactions were interpreted as positive, whereas decrescendo reactions were considered irritant and excluded from analysis. Due to limitations related to the study design and patient accessibility, day 7 (D7) readings were not routinely performed. Reactions graded as "+" or higher on D4 were considered positive. During the same period, consecutive patients suspected of ACD who did not have a diagnosis of AD were included as non-AD patients, serving as the control group.

Statistical Analysis

Statistical analyses were performed using SPSS software version 25.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as number and percentage. The normality of the distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Comparisons between two groups were performed using Student's t-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. Categorical variables were compared using the chi-square test. A P-value < 0.05 was considered statistically significant.

Ethics Committee Approval

Ethical approval was obtained from the Karadeniz Technical University Institutional Ethics Committee (protocol number: 2022/119, date: June 30, 2022; approval number: 24237859-435). Written informed consent was obtained from all participants.

Results

Patch testing was performed on 62 AD patients aged 9–83 years [19 males (30.6%) and 43 females (69.4%); mean age, 31.19 ± 17.97 years]. According to the SCORAD index, 51 patients (82.3%) had mild disease and 11 patients (17.7%) had moderate disease (Table 1). The indications for patch testing in AD patients were: hand eczema (n = 19, 31%); periorbital dermatitis (n = 13, 21%); dermatitis with atypical distribution suggestive of contact dermatitis (n = 10, 16%); dermatitis resistant to standard treatments (n = 9, 14%); adolescent- or adult-onset AD (n = 6, 10%); and nummular dermatitis (n = 5, 8%). At least one positive patch test reaction was observed in 39 AD patients (62.9%). Positivity was detected in 26 of 43 females (60.5%) and 13 of 19 males (68.4%); there was no statistically significant difference between the sexes (P = 0.55). Among patients with positive reactions, 20 (51.3%)

Table 1. Sociodemographic characteristics and comorbidities of atopic dermatitis patients

Age (y), mean (SD)	31.19 (± 17.97)
Gender, n (%)	
Male	19 (30.6%)
Female	43 (69.4%)
Body mass index	24.01 (± 5.30)
SCORAD severity, n (%)	
Mild	51 (82.3%)
Moderate	11 (17.7%)
Treatment history, n (%)	
Topical agents only	39 (62.9%)
Systemic agents combined with topical	23 (37.1%)
Average disease duration (years)	10.89 (± 10.44)
Average number of exacerbations (per year)	5.19 (± 3.75)
Concomitant atopic comorbidity, n (%)	
Allergic rhinitis	18 (29%)
Allergic rhinoconjunctivitis	8 (12.9%)
Asthma	13 (21%)

Data are presented as mean ± standard deviation (SD) for continuous variables and as number (n) and percentage (%) for categorical variables. SCORAD: Scoring atopic dermatitis

reacted to a single allergen, while 19 (48.7%) reacted to two or more allergens, yielding a total of 65 positive reactions. The dynamic pattern analysis of patch test reactions is summarized in Table 2. Patch test positivity was observed in 32 of 51 (62.7%) patients with mild AD and 7 of 11 (63.6%) patients with moderate AD. No statistically significant difference in positivity rates was observed between the two groups (P = 1.000). Patients with severe AD could not be included in the study. The most frequently identified allergens in AD patients were nickel sulfate (n = 19, 30.6%), potassium dichromate (n = 7, 11.3%), fragrance mix I (n = 5, 8.1%), chloromethylisothiazolinone/methylisothiazolinone (n = 5, 8.1%), and textile dyes (n = 4, 6.5%). Of the 62 AD patients, 17 (27.4%) were pediatric patients and 45 (72.6%) were adult patients. At least one patch-test reaction was detected in five of 17 pediatric patients, most commonly nickel sulfate (n = 2; 11.8%). Among adults, 34 of 45 patients had positive reactions; nickel sulfate was again the most frequent allergen (n = 17, 37.8%). Nickel sulfate positivity was significantly higher in adults than children (P = 0.047). Positivity for potassium dichromate was higher in adults (n = 6, 13.3%) than in children (n = 1, 5.9%); however, this difference did not reach statistical significance (P = 0.662) (Table 3).

Table 2. Dynamic pattern analysis of the patch test reactions in 62 atopic dermatitis patients

No.	Patch test allergen	Positive reactions in atopic dermatitis patients n	Crescendo % (n)	Plateau % (n)	Decrescendo n
1	Potassium dichromate	7	71 (5)	29 (2)	2
2	p-Phenylenediamine	3	33 (1)	67 (2)	0
3	Thiuram mix	1	0 (0)	100 (1)	0
4	Neomycin sulfate	1	100 (1)	0 (0)	0
5	Cobalt chloride	3	67 (2)	33 (1)	3
6	Caine mix	0	0 (0)	0 (0)	1
7	Nickel sulfate	19	63 (12)	37 (7)	0
8	2-Hydroxyethyl methacrylate	1	100 (1)	0 (0)	0
9	Colophonium	1	0 (0)	100 (1)	1
10	Paraben mix	0	0 (0)	0 (0)	0
11	N-Isopropyl-N'-phenyl-p-phenylenediamine	1	0 (0)	100 (1)	1
12	Lanolin	1	0 (0)	100 (1)	0
13	Mercapto mix	0	0 (0)	0 (0)	0
14	Epoxy resin	1	100 (1)	0 (0)	1
15	Myroxylon pereirae	2	100 (2)	0 (0)	1
16	4-tert-Butylphenol formaldehyde resin	1	100 (1)	0 (0)	1
17	Mercaptobenzothiazole	0	0 (0)	0 (0)	0
18	Formaldehyde	1	100 (1)	0 (0)	0
19	Fragrance mix I	5	40 (2)	60 (3)	0
20	Sesquiterpene lactone mix	0	0 (0)	0 (0)	0
21	Quaternium-15	1	0 (0)	100 (1)	2
22	Propolis	1	0 (0)	100 (1)	3
23	Methylchloroisothiazolinone and methylisothiazolinone	5	60 (3)	40 (2)	0
24	Budesonide	0	0 (0)	0 (0)	0
25	Tixocortol pivalate	1	100 (1)	0 (0)	0
26	Methyldibromo glutaronitrile	1	100 (1)	0 (0)	4
27	Fragrance mix II	2	50 (1)	50 (1)	1
28	Hydroxylisohexyl 3-cyclohexenecarboxaldehyde	1	100 (1)	0 (0)	1
29	Methylisothiazolinone	1	100 (1)	0 (0)	1
30	Textile dye mix	4	50 (2)	50 (2)	4

Dynamic pattern analysis was performed in atopic dermatitis patients on days 2 and 4. Reaction patterns were categorized as crescendo or plateau. Reactions showing a decrescendo pattern that did not reach a positive reaction grade were considered irritant reactions and were not included as positive reactions. Initial irritant reactions were excluded from the analysis. Data are presented as numbers (n) and percentages (%). The value n represents only the patients with at least one positive reaction to the relevant allergen, not the total number of patients tested

Patch testing was also performed in 306 non-AD patients [122 males (39.9%) and 184 females (60.1%); mean age 33.47 ± 15.58 years]. No significant differences were observed between AD and non-AD groups with respect to age (P = 0.390) or sex distribution (P = 0.225). At least one positive patch test reaction was detected in 123 non-AD patients (40.2%). The overall positivity rate was significantly higher among AD patients than among non-AD patients (62.9% vs. 40.2%; P = 0.001). Nickel sulfate was the only allergen showing a statistically significant difference between the two groups (P = 0.016) (Table 4). Non-AD and AD patients were generally comparable with respect to demographic characteristics.

Patch testing for hand eczema was performed in 201 of 306 non-AD patients and 19 of 62 AD patients. At least one positive reaction was identified in 82 non-AD patients (40.8%) and in 16 AD patients (84.2%), indicating a statistically significant difference between the groups (P < 0.001). In non-AD patients with hand eczema, the most frequent allergens were nickel sulfate (n = 36, 17.9%) and potassium dichromate (n = 10, 5%). Similarly, nickel sulfate (n = 9, 47.4%) and potassium dichromate (n = 4, 21.1%) were the most common allergens among AD patients with hand eczema. Both allergens were significantly more frequent in AD patients than in non-AD patients (P = 0.005 and P = 0.023, respectively) (Table 5).

Table 3. Positivity rates of the two most frequent allergens in patch testing among adult and pediatric AD patients

	Nickel sulfate		Potassium dichromate	
	Number of positive reactions/total number of tests (n/nT, %)	***P*-value**	**Number of positive reactions/total number of tests (n/nT, %)**	***P*-value**
Pediatric group	n = 2/17 (11.8%)	**0.047**	n = 1/17 (5.9%)	0.662
Adult group	n = 17/45 (37.8%)		n = 6/45 (13.3%)	

Comparisons between adult and pediatric AD patients were performed using Fisher's exact test. Data are presented as the number of positive reactions per the total number of tests (n/nT) and as percentages (%). A P-value of < 0.05 was considered statistically significant. AD: Atopic dermatitis

Table 4. European baseline series and patch test positivity rates in AD and non-AD patients

No.	Patch test allergen	Conc. (%)	Positive reactions in AD patients n (% of tested)	Positive reactions in non-AD patients n (% of tested)	*P*-value
1	Potassium dichromate	0.5	7 (11.3%)	13 (4.2%)	0.057
2	p-Phenylenediamine	1.0	3 (4.8%)	7 (2.3%)	0.382
3	Thiuram mix	1.0	1 (1.6%)	8 (2.6%)	1.000
4	Neomycin sulfate	20.0	1 (1.6%)	5 (1.6%)	1.000
5	Cobalt chloride	1.0	3 (4.8 %)	12 (3.9%)	0.725
6	Caine mix	10.0	0 (0.0%)	2 (0.7%)	1.000
7	Nickel sulfate	5.0	19 (30.6%)	53 (17.3%)	**0.016**
8	2-Hydroxyethyl methacrylate	2.0	1 (1.6%)	2 (0.7%)	0.426
9	Colophonium	20.0	1 (1.6%)	5 (1.6%)	1.000
10	Paraben mix	16.0	0 (0.0%)	3 (1.0%)	1.000
11	N-Isopropyl-N'-phenyl-p-phenylenediamine	0.1	1 (1.6%)	1 (0.3%)	0.309
12	Lanolin	30.0	1 (1.6%)	2 (0.7%)	0.426
13	Mercapto mix	2.0	0 (0.0%)	5 (1.6%)	0.594
14	Epoxy resin	1.0	1 (1.6%)	2 (0.7%)	0.426
15	Myroxylon pereirae	25.0	2 (3.2%)	5 (1.6%)	0.335
16	4-tert-Butylphenol formaldehyde resin	1.0	1 (1.6%)	2 (0.7%)	0.426
17	Mercaptobenzothiazole	2.0	0 (0.0%)	4 (1.3%)	1.000
18	Formaldehyde	2.0 aq.	1 (1.6%)	2 (0.7%)	0.426
19	Fragrance mix I	8.0	5 (8.1%)	12 (3.9%)	0.180
20	Sesquiterpene lactone mix	0.1	0 (0.0%)	2 (0.7%)	1.000
21	Quaternium-15	1.0	1 (1.6%)	2 (0.7%)	0.426
22	Propolis	10.0	1 (1.6%)	6 (2.0%)	1.000
23	Methylchloroisothiazolinone and methylisothiazolinone	0.02 aq.	5 (8.1%)	9 (2.9%)	0.068

Table 4. Continued

No.	Patch test allergen	Conc. (%)	Positive reactions in AD patients n (% of tested)	Positive reactions in non-AD patients n (% of tested)	*P*-value
24	Budesonide	0.01	0 (0.0%)	0 (0.0%)	N/A
25	Tixocortol pivalate	0.1	1 (1.6%)	0 (0.0%)	0.168
26	Methyldibromo glutaronitrile	0.5	1 (1.6%)	4 (1.3%)	1.000
27	Fragrance mix II	14.0	2 (3.2%)	9 (2.9%)	1.000
28	Hydroxylisohexyl 3-cyclohexenecarboxaldehyde	5.0	1 (1.6%)	1 (0.3%)	0.309
29	Methylisothiazolinone	0.2 aq.	1 (1.6%)	7 (2.3%)	1.000
30	Textile dye mix	6.6	4 (6.5%)	12 (3.9%)	0.324

The substances are listed according to their order in the series. The vehicle was petrolatum unless otherwise indicated. Comparisons of patch test positivity rates between patients with and without AD were performed using Fisher's exact test. Data are presented as the number and percentage of patients with positive reactions. A *P*-value < 0.05 was considered statistically significant, and such values were indicated in bold. N/A: Not applicable, Conc.: Concentration, AD: Atopic dermatitis

Table 5. Comparison of the four most frequent allergens between AD and non-AD patients with hand eczema

	AD patients	Non-AD patients	*P*-value
	Number of positive reactions/total number of tests (n/nT, %)	Number of positive reactions/total number of tests (n/nT, %)	
Nickel sulfate	9/19 (47.4%)	36/201 (17.9%)	**0.005**
Potassium dichromate	4/19 (21.1%)	10/201 (5%)	**0.023**
Fragrance mix I	2/19 (10.5%)	7/201 (3.5%)	0.177
Textile dye mix	2/19 (10.5%)	7/201 (3.5%)	0.177

Comparisons between groups were performed using the chi-square test or Fisher's exact test, as appropriate. A *P*-value such values were indicated in bold was considered statistically significant. AD: Atopic dermatitis

Discussion

Our findings indicate that contact allergy represents an important comorbidity in AD patients, supporting the use of patch testing in this population. While some studies[5-7] have focused exclusively on pediatric AD patients, others[8-11] have included patients across all age groups. Although ACD can develop at any age, it is more frequently observed in adults.[12] Patch testing is performed less frequently in pediatric patients,[13] possibly due to the higher prevalence of AD during childhood and the clinical difficulty in distinguishing AD from ACD.[14] The predominance of adult patients in our cohort may be explained by these factors. ACD is generally more common among females in the general population. Although AD is slightly more prevalent in males during childhood, it becomes more common in females after puberty.[15] Previous studies have shown that most patients referred for patch testing, regardless of AD status, are female.[5,8-11,16,17] A similar sex distribution was observed in our study. Consistent with the findings of Ibekwe et al.,[4] we did not observe a significant association between sex and contact sensitization. However, some studies[5] have reported higher positivity rates in females. This difference may be explained by the higher frequency of patch test referrals among female patients.

The predominance of patients with mild disease in our study may be explained by the general indication for patch testing in patients with localized lesions. The absence of severe cases may be related to difficulties in achieving drug-free intervals required for patch testing, the need for symptom control, and the frequent use of active immunosuppressive therapy in this patient group. Although direct comparisons are limited by different disease-severity scoring systems in the literature, some studies have included patients with severe AD.[4-6]

Within the limits of our study population, AD severity (restricted to mild and moderate disease) was not associated with patch test positivity ($P = 1.000$). While some studies[4,5,17] have reported similar findings, others[6] have demonstrated higher positivity rates with increasing disease severity. These discrepancies may be related to differences in study populations, allergen series, and methodological approaches.

Higher rates of positive patch test reactions are expected among selected patient populations than in the general population. In our study, patch-test positivity was significantly higher among patients with AD than among those without AD. However, the literature reports inconsistent findings. Peng et al.[9] reported positivity rates of 78.4% in AD patients and

66.8% in non-AD patients; Malajian and Belsito[11] reported 71.7% and 64.5%, respectively. Large retrospective studies have also demonstrated a higher prevalence of contact allergy among patients with AD.[7,8,18] Conversely, some studies[10,19] have reported lower sensitization rates in AD patients, whereas others[20] have demonstrated similar prevalence rates of contact allergy between AD and non-AD patients. The relatively high positivity rate observed in our cohort may be related to the inclusion of patients with treatment-resistant or recurrent disease and possible exposure to multiple allergens. The use of the European baseline series, which includes a broad range of allergens, as well as the relatively higher mean age of our study population—which may increase cumulative allergen exposure—may also have contributed to these findings.

Numerous studies have evaluated contact sensitization or ACD in pediatric patients with or without AD. Due to heterogeneity in study populations, age groups, methodologies, and patch test series, the reported findings vary considerably. Nevertheless, the overall trend suggests higher patch test positivity rates among children with AD. The most frequently reported allergens include metals—particularly nickel sulfate—as well as fragrances and preservatives.[4-7,14] In our study, the contact sensitization rate among pediatric AD patients was 29.4%, and the allergen profile was consistent with previous reports. However, the relatively small sample size and the inclusion of patients with treatment-resistant disease may limit the generalizability of our findings.

Comparison of patch test results in AD patients with suspected ACD is challenging due to heterogeneity in sample size, demographic characteristics, disease severity, diagnostic criteria, allergen series, and methodological approaches. Several studies have reported common allergens in patients with AD: Peng et al.[9] identified nickel sulfate (33.3%), cobalt chloride (19.6%), and methylisothiazolinone (22.5%) as the most frequent allergens, whereas Choi et al.[10] reported nickel sulfate (26.4%), cobalt chloride (24.5%), and potassium dichromate (9.4%). A Japanese study identified nickel and topical medications as common allergens in treatment-resistant AD.[21] Trimeche et al.[17] reported textile dyes (24.7%), nickel (20.2%), cobalt (12.7%), and chloromethylisothiazolinone/methylisothiazolinone (8.5%) as prevalent allergens. In another study involving 48 patients with treatment-resistant AD, the most frequent allergens were bichromate (27%), nickel (27%), wool alcohol (24%), and cocamidopropyl betaine (24%).[22] The impaired skin barrier in AD facilitates allergen penetration. This process may be further exacerbated by filaggrin mutations, which reduce the skin's chelating capacity and may increase susceptibility to metal sensitization.[23] Nickel represents a notable exception among contact allergens, as sensitization rates may be comparable in AD and non-AD patients or even higher among AD patients.[2] This has been attributed to a relatively Th17-skewed immune response, characterized by attenuated Th1 activity, in AD patients exposed to nickel.[2] Consistent with previous literature and our findings, metals—particularly nickel—remain the most frequently identified allergens, which likely reflects widespread daily exposure.

Frequent topical exposure represents another important risk factor for contact sensitization in these patients.[20] Fragrances, formaldehyde-releasing preservatives, and topical antibiotics are well-recognized sensitizers.[23] In the general population, fragrance sensitization rates range from 0.7% to 2.6%,[24] whereas higher rates have been reported in selected patient populations. Among patients referred for suspected ACD, the North American Contact Dermatitis Group reported fragrance allergy rates (including fragrance mix I, fragrance mix II, and balsam of Peru) ranging from 5.3% to 11.3%.[25] In our study, sensitization rates were 8.1% for fragrance mix I and 3.2% for both fragrance mix II and balsam of Peru. These rates were higher than those reported in the general population but lower than those observed in selected patient cohorts. Increased use by AD patients of personal care products, cleaning agents, and herbal topical preparations containing fragrances —often due to impaired skin barrier function—may contribute to greater exposure. Conversely, some patients who are aware of fragrance sensitivity may preferentially use fragrance-free products, which could partially explain the lower rates compared with selected populations.

Although patients with AD are considered at increased risk of Group A corticosteroid allergy,[26] only one patient (1.6%) in our study demonstrated a positive reaction to tixocortol-21-pivalate; no reactions to budesonide were observed. Previous studies have reported significantly higher rates of budesonide sensitization in AD patients compared with non-AD patients.[10] However, some studies have reported lower rates of budesonide sensitization among AD patients, possibly reflecting differences in patterns of topical treatment exposure.[20] The relatively low sensitization rate observed in our study may be related to the absence of an extended corticosteroid series, the possibility of missed late reactions due to final readings performed on day 4, and the local preference for prescribing corticosteroids from Groups C and D for treatment-resistant patients. These findings highlight the importance of performing more comprehensive corticosteroid testing, including late patch test readings,[27] to improve the detection of corticosteroid sensitization in AD.

Among the tested allergens, only nickel sulfate showed a statistically significant difference in positivity between AD and non-AD patients in our study. Malajian and Belsito[11] reported higher positivity rates for nickel sulfate, cobalt chloride, potassium dichromate, and fragrance mix I in AD patients; these differences were statistically significant for

all allergens except fragrance mix I. Similarly, Peng et al.[9] found significantly higher positivity rates for nickel sulfate and cobalt chloride in AD patients. The frequent detection of metal allergens—particularly nickel sulfate—in AD patients is consistent with previous literature. However, Qian et al.[8] reported a higher prevalence of ACD related to cosmetics, topical medications, and dyes in AD patients, and observed an inverse association with metal allergens. Furthermore, a large-scale review[28] reported lower nickel sensitization rates in AD patients than in non-AD patients and found no positive correlation between AD and nickel sensitization. Similarly, a study conducted in Singapore reported that nickel was the most frequent allergen in both AD and non-AD patients, with no statistically significant difference in sensitization rates between the two groups.[20] These discrepancies may be explained by differences in study methodologies, patient populations, and allergen series used.

In our study, positivity to nickel sulfate was significantly higher in adult AD patients than in pediatric AD patients, likely reflecting greater cumulative exposure. Although only a limited number of studies have directly compared these age groups, Boonstra et al.[22] similarly reported higher rates of nickel sensitization in adult patients.

The lack of additional clinically meaningful information derived from dynamic patch test evaluation in AD patients should be considered a strength of the study, as it helps define the practical limits of this approach beyond standard readings.

To the best of our knowledge, studies specifically addressing allergen profiles and patch test positivity in patients with hand eczema and a history of AD remain limited. Most available studies have focused on patch-test results in patients with hand eczema, regardless of AD status. In our study, patch test positivity in AD patients presenting with hand eczema (84.2%) was markedly higher than in the overall AD population (62.9%) and in non-AD patients with hand eczema (40.8%). These findings suggest increased susceptibility to contact sensitization in this subgroup. A recent large multicenter study conducted in a Chinese population also demonstrated that AD in patients with hand eczema was associated with altered contact sensitization patterns, further supporting the clinical importance of evaluating contact allergy in this subgroup.[29] Previous studies have also reported high sensitization rates in patients with hand eczema.[30] Nickel sulfate, which was frequently detected in our study and in previous reports, remains a major allergen across age groups.

Study Limitations

Conducting the study in a tertiary referral center limited long-term follow-up, thereby preventing assessment of clinical compliance, confirmation of ACD diagnosis, and evaluation of rates of clinical relevance. However, patients were advised to avoid allergens that yielded positive test results and were clinically relevant based on their clinical history. The absence of D7 readings, due to study design and logistical constraints—particularly as many patients were referred from remote areas—may have resulted in missed delayed-type hypersensitivity reactions, especially to corticosteroids. Additional limitations include the relatively small sample size and single-center design, which may limit generalizability. However, because our center is a tertiary referral center that receives complex, treatment-resistant cases from surrounding provinces, our cohort provides clinically meaningful data for this patient subgroup. Furthermore, the use of a single allergen panel for patch testing may not fully capture sensitization to less common allergens. Although non-AD patients were matched for age and sex, complete matching for all potential confounding variables was not feasible, which may have affected the strength of intergroup comparisons.

Conclusion

Our findings indicate that contact sensitization rates are higher in AD patients than in the general population. Patch testing appears to be particularly valuable for identifying contact sensitization, particularly to metal allergens, in patients with treatment-resistant or recurrent disease. The low rate of corticosteroid sensitization observed in this study warrants further investigation using an expanded patch test series. Larger-scale prospective studies are required to optimize the management of AD and to further elucidate the relationship between contact sensitization and ACD.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Karadeniz Technical University Institutional Ethics Committee (protocol number: 2022/119, date: June 30, 2022; approval number: 24237859-435).

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

Footnotes

Authorship Contributions

Concept: L.B.S., A.F., İ.E.A., D.A.A., Design: L.B.S., A.F., İ.E.A., D.A.A., Data Collection or Processing: A.O.M., Analysis or Interpretation: L.B.S., A.F., İ.E.A., D.A.A., Literature Search: A.O.M., L.B.S., Writing: A.O.M., L.B.S.

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