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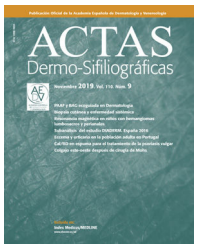

ORIGINAL ARTICLE

[Translated article] Epidemiological, Clinical, and Allergy Profile of Patients With Atopic Dermatitis and Hand Eczema: Evaluation of the Spanish Contact Dermatitis Registry (REIDAC)

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KEYWORDS
Atopic dermatitis;
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Sensitization;
Allergy;
Eczema

Abstract
Background: Hand eczema is common in patients with atopic dermatitis (AD), but few studies have described the characteristics of these patients in large, representative populations from different geographic regions and occupational settings.
Objective: To describe the epidemiological, clinical, and allergy profile of patients with hand eczema who underwent patch testing and compare patients with and without AD.
Methods: Analysis of data from the Spanish Contact Dermatitis Registry, a multicenter registry of patients who undergo patch testing in Spain.
Results: We included 1466 patients with hand eczema who were patch tested between January 2018 and June 2020. Those with AD were younger and had had symptoms for longer before testing. They were also more likely to have been exposed to occupational triggers (38% vs 53% for patients without AD). The only profession for which significant differences were found was hairdressing. The most common allergens were nickel sulfate, methylchloroisothiazolinone/methylisothiazolinone, cobalt chloride, potassium dichromate, fragrance mixes I and II, and formaldehyde. The most common diagnoses were allergic contact dermatitis (24% vs 31% in patients with and without AD, $P = .0224$) and irritant contact dermatitis (18% and 35% respectively, $P < .001$).
Conclusions: AD is common in patients with predominant hand eczema who undergo patch testing. Patients with hand eczema and AD have different clinical and epidemiological characteristics to hand eczema patients in general and their final diagnosis following patch testing is also different.

PALABRAS CLAVE
Dermatitis atópica;
Dermatitis de las manos;
Dermatitis de contacto;
Sensibilización;
Alergia;
Eccema

Perfil epidemiológico, clínico, y alérgico en pacientes con dermatitis atópica y dermatitis de las manos. Evaluación del Registro Español de Dermatitis de Contacto (REIDAC)

Resumen
Antecedentes: La dermatitis de las manos (DM) es frecuente en los pacientes con dermatitis atópica (DA). Pocos estudios describen las características de estos pacientes a partir de poblaciones amplias y representativas de ámbitos geográficos y laborales diferentes.
Objetivos: Describir el perfil epidemiológico, clínico y alérgico de los pacientes con DM a los que se realizan pruebas epicutáneas, comparando los pacientes con DA con los pacientes sin DA.
Métodos. El estudio se ha realizado a partir de los datos del REIDAC, un registro multicéntrico nacional de pacientes a los que se realizan pruebas epicutaneas.
Resultados: Se incluyeron 1466 pacientes parcheados por DM desde enero de 2018 hasta junio de 2020. Los pacientes con DA fueron más jóvenes y con una duración de los síntomas mayor. Los antecedentes ocupacionales como desencadenantes se registraron en menor medida que en los pacientes no atópicos (38 vs 53%). La única profesión en la que se encontraron diferencias significativas fue la peluquería. Los alérgenos más detectados fueron el sulfato de níquel, la metilcloroisotiazolinona/metilisotiazolinona, el cloruro de cobalto, el dicromato potásico, mezcla de fragancias I y II, y el formaldehido. Los diagnósticos más frecuentes fueron dermatitis alérgica de contacto (DAC); 24% en atópicos vs 31% en no atópicos ($P = 0{,}0224$) y el eccema de contacto irritativo; 18% atópicos vs 35% no atópicos ($P < 0{,}001$).

Conclusiones: La DA es frecuente en los pacientes parcheados con afectación predominante de las manos. Existen diferencias clínicas, epidemiológicas y de diagnóstico final de estos pacientes con respecto al conjunto de pacientes con DM.

Introduction

Atopic dermatitis (AD) is the most common chronic inflammatory skin disease, affecting 15%–20% of children and 1%–3% of adults.[1] Hand eczema (HE) is one of the most characteristic—yet nonspecific—manifestations of adult AD. A history of AD is one of the main risk factors for HE. Nevertheless, HE is also frequent in the general population, and we might expect it to affect up to 20% of adults during their lifetime; in fact, up to 10% report compatible symptoms within the previous 12 months.[2,3] A recent systematic review and meta-analysis revealed that a previous history of AD was associated with an increased prevalence of DM compared with baseline, 1 year, and the patient's lifetime.[4] As for pathogenesis, some experimental studies have shown that increased transepidermal water loss in patients with atopy leads to greater penetration and absorption of irritants and allergens than in patients with healthy skin.[5,6] AD has been identified as a risk factor for HE in patients aged <30 years,[7] although its influence decreases with age.[8,9]

Few studies have compared the clinical characteristics of atopic HE patients with those of nonatopic HE patients. In particular, data for large, representative populations from different geographical and occupational settings should be sought.

The objective of this study was to compare the epidemiological, clinical, and allergy profile of patients with AD and HE who undergo patch testing with that of nonatopic HE patients.

Material and Methods

The study was based on data from the Spanish Contact Dermatitis Registry (Registro Español de Dermatitis de Contacto [REIDAC]), a prospective Spanish multicenter registry (https://dermatitis.contacto.aedv.es/), for the period January 2018 to June 2020. We recorded data for all patients who underwent patch testing for HE and compared those with and without AD.

REIDAC is a centralized registry developed by the Spanish Contact Dermatitis and Skin Allergy Research Group (Grupo Español de Investigación en Dermatitis de Contacto y Alergia Cutánea [GEIDAC]), together with the Research Department of the Healthy Skin Foundation (Fundación Piel Sana) and the Spanish Academy of Dermatology and Venereology (Academia Española de Dermatología y Venereología [AEDV]), which brings together the main contact dermatitis departments in Spain. The epidemiological, clinical, and allergy-related variables of patients who underwent patch testing at the participating centers were recorded in the registry. The methodology and data collection have been described elsewhere.[10] In this study, we recorded sex, age, other sites affected, association with occupational factors, occupation, and duration of symptoms. The patient was considered to fulfill the criteria for AD if he/she had ever been diagnosed with AD or fulfilled the criteria at the time of consultation for predominantly flexural eczema, together with other atopy-related data. Patients with only minor criteria of AD such as hyperlinear palms, keratosis pilaris, xerosis, or chronic cheilitis were not included in this diagnosis.[11] The tests were performed according to the recommendations of the European Society of Contact Dermatitis.[12] In REIDAC, the allergy workup is performed using the Spanish standard series and complementary series at the clinician's discretion.[13] This study only took into account data from the GEIDAC standard series. Only patients with lesions affecting the hands as the main site were considered to have HE, although patients with areas other than the hands affected (secondary involvement) could also be included. The main causal factor of a picture of HE (allergic dermatitis, irritant dermatitis, or AD) was based on clinical criteria. Quantitative variables were analyzed using the *t* test; qualitative variables were analyzed using the χ^2 test. The statistical analysis was performed using Stata Statistical Software: Release 16 (Stata Corp. 2015).

Results

We included 1466 patients who had undergone patch testing for HE. Of these, 326 (22%) had a history of AD. The MOAHLFA index for the group as a whole was as follows: male, 32%; occupational, 49%; atopy, 22%; hand, 100%; leg, 3%; face, 5%; age >40, 62%.

Of the 1466 patients included, 996 were women (68% [72% of those with atopy] and 470 were men (32% [28% of those with atopy]) ($P = .0931$).

Table 1 shows the epidemiological characteristics of patients with HE.

Patients with AD were younger, had a longer mean duration of symptoms before the patch tests. The occupational history was less commonly considered the trigger than in nonatopic patients (38% vs. 53%).

By age, AD was more common in students (OR, 4.29 [2.69–6.86]) and less common in retirees (OR, 0.49 [0.27–0.84]).

The occupational history of patients who underwent patch testing is shown in Table 2. Most patients with HE and AD (81%) were actively employed, although occupational triggers were not as important as in the nonatopic patients. By profession, the only one for which differences between the groups was found was hairdressing, where patients with HE were mainly nonatopic (85%) ($P = .0317$). No differences were found between atopic and nonatopic patients for the remaining professions.

Table 3 shows the complete allergen series and the positive results. The most frequent allergens from the standard series in patients with HE were nickel sulfate

Table 1 Epidemiological and Clinical Characteristics of Patients with Hand Eczema.

	Total	Atopic dermatitis (*n* = 326)	No atopic dermatitis (*n* = 1140)	*P* value
No.	5007	326 (22)	1140 (78)	
Female sex, No. (%)		234 (72)	762 (67)	.0931
Mean (SD) age, y		38 (14.7)	46.8 (14.3)	**.0000**
Age > 40 y, %		138 (42)	771 (68)	**.0000**
Mean (SD) duration of symptoms, mo		45.8 (67)	35.7 (57.6)	**.0001**
Occupational factors, %		118 (38)	558 (53)	**.0000**
Other locations, %		24 (7)	57 (5)	.1008

Values shown in bold are statistically significant.

Table 2 Occupational History of Hand Eczema in Atopic Patients and Nonatopic Patients.[a]

Health workers	Atopic dermatitis		OR (95% CI)	*P* value
	Yes, No. (%)	No, No. (%)		
No	288 (88)	1040 (91)		
Yes	38 (12)	100 (9)	1.37 (0.90–2.01)	.1316
Administrative				
No	287 (88)	1043 (91)		
Yes	39 (12)	97 (9)	1.46 (0.96–2.19)	0.0655
Retired				
No	309 (95)	1026 (90)		
Yes	17 (5)	114 (10)	0.49 (0.27–0.84)	**.0079**
Hairdresser				
No	308 (94)	1034 (91)		
Yes	18 (6)	106 (9)	0.57 (0.32–0.96)	**.0317**
Homemaker				
No	305 (94)	1040 (91)		
Yes	21(6)	100 (9)	0.72 (0.42–1.18)	.2091
Cleaner				
No	312 (96)	1066 (94)		
Yes	14 (4)	74 (6)	0.65 (0.33–1.17)	.1851
Student				
No	281 (86)	1099 (96)		
Yes	45 (14)	41 (4)	4.29 (2.69–6.86)	**.0000**
Other				
No	192 (59)	632 (55)		
Yes	134 (41)	508 (45)	0.87 (0.67–1.12)	.2821

[a] The OR can be interpreted as the OR of AD for this profession or the OR for this profession in patients with AD.
Values shown in bold are statistically significant.

(20%), methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) (11%), cobalt chloride (5%), potassium dichromate (4%), fragrance mixes I and II (4%), and formaldehyde (4%). Results were positive with ethylenediamine more frequently in atopic patients with HE (3.56 [0.94–13.39]), whereas results were more frequently positive to nickel sulfate (0.70 [0.51–0.95]) and carba mix (0.30 [0.08–0.83]) in nonatopic patients with HE.

The main diagnoses after patch testing in atopic patients with HE were, in order, AD alone (147/326 [45% of the total]), allergic contact dermatitis, and irritant contact dermatitis (Table 4). The other diagnoses included psoriasis and dyshidrotic eczema.

Discussion

Our study showed that HE was a frequent reason for consultation among atopic patients. This association has been reported elsewhere.[4] In fact, 1152 patients from the general

Table 3 Sensitization in Patients with Hand Eczema.

Standard series in patients with hand eczema, No. of patches		Atopic dermatitis		No atopic dermatitis		OR (exact 95% CI)	*P* value (Bonferroni)
		Positive, No. (%)	Negative, No. (%)	Positive, No. (%)	Negative, No. (%)		
Nickel sulfate	1448	65 (20)	255 (80)	302 (27)	826 (73)	0.70 (0.51–0.95)	**.0198**
Lanolin alcohol	1450	3 (1)	317 (99)	3 (0)	1127 (100)	3.60 (0.47–26.64)	.1255
Neomycin sulfate	1454	2 (1)	322 (99)	8 (1)	1122 (99)	0.87 (0.09–4.40)	.0000
Potassium dichromate	1452	13 (4)	309 (96)	49 (4)	1081 (96)	0.93 (0.46–1.76)	.0000
Caine mix	1455	3 (1)	320 (99)	11 (1)	1121 (99)	0.96 (0.17–3.65)	.0000
Fragrance mix I	1439	12 (4)	303 (96)	44 (4)	1080 (96)	0.97 (0.46–1.90)	1.0000
Colophony	1455	4 (1)	320 (99)	16 (1)	1115 (99)	0.87 (0.21–2.73)	1.0000
Parabens mix	1459	1 (0)	323 (100)	5 (0)	1130 (100)	0.70 (0.01–6.29)	1.0000
Balsam of Peru	1454	6 (2)	316 (98)	35 (3)	1097 (97)	0.60 (0.20–1.45)	.3388
Ethylenediamine	1461	6 (2)	318 (98)	6 (1)	1131 (99)	3.56 (0.94–13.39)	**.0310**
Cobalt chloride	1451	17 (5)	305 (95)	56 (5)	1073 (95)	1.07 (0.57–1.90)	.7743
p-Tert butylphenol formaldehyde resin	1454	6 (2)	316 (98)	18 (2)	1114 (98)	1.18 (0.38–3.12)	.8038
Epoxy resin	1454	1 (0)	322 (100)	10 (1)	1121 (99)	0.35 (0.01–2.46)	.4729
Carba mix	1449	4 (1)	316 (99)	46 (4)	1083 (96)	0.30 (0.08–0.83)	**.0139**
Black rubber mix/IPPD	1457	3 (1)	321 (99)	10 (1)	1123 (99)	1.05 (0.18–4.11)	1.0000
Methylchloroisothiazolinone/ methylisothiazolinone	1456	34 (11)	286 (89)	116 (10)	1020 (90)	1.05 (0.68–1.58)	.8353
Quaternium-15	1461	5 (2)	319 (98)	14 (1)	1123 (99)	1.26 (0.35 3.73)	.5888
Methyldibromo glutaronitrile	1460	9 (3)	314 (97)	33 (3)	1104 (97)	0.96 (0.40–2.08)	1.0000
Paraphenylenediamine	1453	9 (3)	314 (97)	45 (4)	1085 (96)	0.70 (0.29–1.45)	.4043
Formaldehyde	1458	13 (4)	309 (96)	41 (4)	1095 (96)	1.12 (0.55–2.17)	.7383
Mercapto mix	1457	0 (0)	324 (100)	8 (1)	1125 (99)	0 (0–1.67)	.2115
Thiuram mix	1454	5 (2)	318 (98)	45 (4)	1086 (96)	0.38 (0.11–0.96)	.0367
Diazolidinyl urea	1461	3 (1)	320 (99)	6 (1)	1132 (99)	1.77 (0.28–8.33)	.4233
Tixocortol pivalate	1458	1 (0)	324 (100)	4 (0)	1129 (100)	0.87 (0.02–8.84)	1.0000
Imidazolidinyl urea	1461	1 (0)	323 (100)	3 (0)	1134 (100)	1.17 (0.02–14.63)	1.0000
Budesonide	1457	1 (0)	324 (100)	7 (1)	1125 (99)	0.50 (0.01–3.89)	.6927
Mercaptobenzothiazole	1457	4 (1)	320 (99)	4 (0)	1129 (100)	3.53 (0.65–19.03)	.0786
Methylisothiazolinone	1272	28 (10)	265 (90)	130 (13)	849 (87)	0.70 (0.43–1.07)	.1058
Sesquiterpene lactone mix	1253	2 (1)	284 (99)	2 (0)	965 (100)	3.40 (0.24–47.01)	.2254
Fragrance mix II	1283	11 (4)	286 (96)	37 (4)	949 (96)	0.99 (0.45–2.01)	1.0000
Lyral	1285	3 (1)	293 (99)	7 (1)	982 (99)	1.44 (0.24–6.34)	.7050
Phenoxyethanol	1272	0 (0)	293 (100)	0 (0)	979 (100)	NA	NA

Values shown in bold are statistically significant.

Table 4 Main Final Diagnosis in Atopic Patients Assessed for Hand Eczema.

Allergic contact dermatitis	Atopic dermatitis		OR (95% CI)	*P* value
	Yes, No. (%)	No, No. (%)		
No	248 (76)	792 (69)		
Yes	78 (24)	348 (31)	0.71 (0.53–0.96)	**.0224**
Irritant contact eczema				
No	266 (82)	746 (65)		
Yes	60 (18)	394 (35)	0.43 (0.31–0.58)	**.0000**
Psoriasis				
No	321 (98)	999 (88)		
Yes	5 (2)	141 (12)	0.11 (0.35–0.27)	**.0000**
Dyshidrotic eczema				
No	305 (94)	1016 (89)		
Yes	21 (6)	124 (11)	0.56 (0.33–0.92)	**.0202**

Values shown in bold are statistically significant.

registry had a history of atopy; therefore, patients with HE accounted for 28% of all atopic patients. Compared with the nonatopic patient, the profile of the atopic patient with HE was that of a younger person with a longer duration of symptoms. This profile is coherent with the endogenous nature of AD, which is often present from childhood, with eczematous lesions at various sites, including the hands.[6,14] In addition, the longer mean duration of symptoms before patch testing in this population could be explained by the fact that a diagnosis of AD itself is a plausible explanation for HE that often rules out the indication for patch testing.

The distribution by age is consistent with that of AD, with more students and, albeit to a lesser extent, retirees than among the nonatopic patients. By profession, the only differences were found for hairdressing, with a lower percentage of HE in atopic patients, compared with dermatitis that was mainly allergic or irritant. This seemingly paradoxical observation could be due to the bias arising from the nature of the REIDAC, which does not usually include patients with occupational skin diseases. However, some authors have reported an occupational history associated with hairdressing and HE where no differences were found for sensitization to allergens among patients with and without a history of AD.[15] Working as a hairdresser is a standard indication for patch testing and an independent factor for positive patch test results with present relevance independently of a history of AD.[16] Furthermore, having a history of AD from childhood, especially the severe forms, might be expected to affect a person's occupational history and choice of a particular profession,[17] thus modifying the results.

The most frequent allergens in atopic patients with HE—nickel, MCI/MI, cobalt, potassium dichromate, fragrances, and formaldehyde—are generally the most commonly reported allergens in HE in various studies.[18–22] The difference with respect to sensitivity to nickel in both atopic and nonatopic patients is noteworthy. The greater or lesser sensitization to nickel in atopic patients is controversial. While some authors report mutations in the filaggrin gene to be responsible for greater sensitization to nickel,[23,24] others conclude that the frequency of sensitization to nickel and other allergens is similar to or even lower in atopic than in nonatopic patients.[18,25] It is important to remember that the present study only took into account allergens included in the GEIDAC standard series. It is reasonable to assume that these findings could vary with the increasing frequency of other allergens, such as acrylates, which are especially present in some occupational settings.

Although the profile of positive allergy results was similar in both atopic and nonatopic patients, the interpretation of the relevance and the final diagnosis varied. Therefore, a final diagnosis of allergic contact dermatitis or irritant hand dermatitis was less common in atopic patients, probably because, in a certain percentage, the dermatologist thought that the endogenous dermatosis itself accounted for the symptoms, with some resistance toward explaining that a positive patch test result could be playing a role beyond that of the trigger. Thus, a final diagnosis of AD was the most frequent (45% of all the cases studied).

Dyshidrosis, which was diagnosed in some cases, was more frequent in nonatopic patients, consistent with its nonspecific nature as hand involvement associated with various types of eczema, also including, albeit nonexclusively, AD.[26]

Our study is subject to a series of limitations. The first is that of selection bias, since we only included patients whose reason for attending the clinic was to undergo patch testing. Atopic patients may be overrepresented, since they often undergo patch testing more frequently, even when the main suspected diagnosis is endogenous eczema, especially in adults. However, patch testing could also be delayed in some patients with AD, since a history of AD has been considered the main reason for the cutaneous symptoms. Furthermore, given that the participating centers belong to the Spanish National Health System, many working patients are excluded because they were assessed by their occupational health

insurer, thus affecting the results for occupational exposure. Finally, we only took into account allergens included in the standard GEIDAC series. While this points to a degree of homogeneity between centers, it may limit the identification of emerging allergens such as acrylate and linalool in the study groups.

In conclusion, this multicenter study from Spain revealed that patients who undergo patch testing for HE commonly have a history of AD. Among HE patients as a whole, atopic patients are younger, with a mean duration of dermatitis that is greater than in nonatopic patients, and, apparently, with no broad variations between most of the professions studied. Overall, the sensitization profile was also similar to that observed in patients with HE. These findings could vary with the emergence of new allergens.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ad.2022.02.015.

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