

ORIGINAL ARTICLE

[Translated article] Clinical–Epidemiological Profile, and Treatment Response in Relation to Associated Atopic Comorbidity in Atopic Dermatitis. Experience From the BIOBADATOP Registry

V. Peris-Espino^{a,*}, M. Munera-Campos^{a,b}, P. Chicharro^c, A. González Quesada^d,
Á. Flórez Menéndez^e, P. de la Cueva Dobao^f, A.M. Giménez Arnau^g,
Y. Gilaberte Calzada^h, M. Rodríguez Sernaⁱ, T. Montero-Vilchez^j,
J.F. Silvestre Salvador^k, R. Ruiz-Villaverde^l, M. Elosua-González^m,
E. del Alcázar-Viladomiu^{a,b}, J. Sánchez-Pérez^c, G. Carretero Hernández^d,
A. Batalla^e, H.J. Suh Oh^e, C. Couselo-Rodríguez^e, C. Mauleón Fernández^f,
L. Curto-Barredo^g, M. Bertolín-Colilla^g, A. Navarro-Bielsa^h, A. Ballano Ruiz^h,
R. Botella Estradaⁱ, S. Arias-Santiago^j, R. Sanabria-de-la-Torre^j, I. Betlloch-Mas^k,
F.J. Navarro-Triviño^l, G. Roustán Gullón^m, A. Rosell-Díaz^m, M. Loro-Pérez^m,
J. Suárez-Pérezⁿ, I. García-Doval^{o,p}, M.Á. Descalzo-Gallego^p, J.M. Carrascosa Carrillo^{a,b}

^a Servicio de Dermatología, Hospital Universitari Germans Trias i Pujol, Germans Trias i Pujol Research Institute (IGTP), Badalona, Barcelona, Spain

^b Departament de Medicina, Universitat Autònoma de Barcelona (UAB), Barcelona, Spain

^c Servicio de Dermatología, Hospital Universitario de la Princesa, Madrid, Spain

^d Servicio de Dermatología, Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria, Spain

^e Servicio de Dermatología, Complejo Hospitalario Universitario de Pontevedra, Pontevedra, Spain

^f Servicio de Dermatología, Hospital Universitario Infanta Leonor, Madrid, Spain

^g Servicio de Dermatología, Hospital del Mar de Barcelona, Hospital del Mar Research Institute, Barcelona, Spain

^h Servicio de Dermatología, Hospital Universitario Miguel Servet, Zaragoza, Spain

ⁱ Servicio de Dermatología, Hospital Universitario y Politécnico La Fe, Universidad de Valencia, Valencia, Spain

^j Servicio de Dermatología, Hospital Universitario Virgen de las Nieves, Instituto de Investigación IBS, Granada, Spain

^k Servicio de Dermatología, Hospital General Universitario Dr. Balmis, Alicante, Spain

^l Servicio de Dermatología, Hospital Universitario San Cecilio, Granada, Spain

^m Servicio de Dermatología, Hospital Universitario Puerta de Hierro, Madrid, Spain

ⁿ Servicio de Dermatología, Hospital Clínico de Málaga, Málaga, Spain

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* Corresponding author.

E-mail address: vicente.peris@hotmail.com (V. Peris-Espino).

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° Servicio de Dermatología, Complejo Hospitalario Universitario de Vigo, Vigo, Spain
P Unidad de Investigación, Fundación Piel Sana AEDV, Madrid, Spain

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atópicas;
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Tratamientos

Abstract

Background: Despite advances made in treatments for atopic dermatitis (AD), information on its impact and interaction with atopic comorbidities, such as asthma, rhinoconjunctivitis, and ocular disease is limited. This study aims to assess the clinical-epidemiological characteristics of patients with AD – treatment response included – while taking into consideration atopic comorbidities like these.

Materials and methods: Data were analyzed from the multicenter BIOBADATOP registry (a prospective cohort of AD patients initiating systemic treatment). We conducted a descriptive analysis of the main characteristics collected in the registry in relation to atopic comorbidity.

Results: We included a total of 509 patients, mostly adults (81.9%) with severe AD (73.7%). Patients with personal atopic comorbidity (64%) more frequently exhibited flexural dermatitis (89.7% vs. 81.5%), a higher mean of previous systemic treatments (1.6 vs. 1.3), and higher baseline values on the POEM scale (19.6 vs. 17.9). Patients with familial atopic comorbidity (40.7%) had a higher incidence of pediatric/adolescent patients (24.2% vs. 13.9%) and a history of allergic rhinoconjunctivitis (61.1% vs. 47.1%). No differences regarding treatment response were observed at the 6- and 12-month follow-ups based on the presence or absence of atopic comorbidities.

Conclusions: Results suggest that a history of atopic comorbidity is associated with an early onset and persistent course of AD. Although no differences were reported in the short-term treatment response, further follow-up is required to better understand the impact of comorbidities on AD.

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Perfil clínico, epidemiológico y respuesta al tratamiento, en función de la comorbilidad atópica asociada en la dermatitis atópica. Experiencia del registro BIOBADATOP

Resumen

Antecedentes: Pese al avance terapéutico en la dermatitis atópica (DA), la información sobre el impacto y la interacción con las comorbilidades atópicas (como el asma, la rinoconjunctivitis y la afección ocular) es limitada. Este estudio pretende evaluar las características clínicas y epidemiológicas de los pacientes con DA, así como la respuesta al tratamiento, considerando dichas comorbilidades.

Material y métodos: Se realizó un análisis descriptivo de los datos del registro multicéntrico BIOBADATOP, una cohorte prospectiva de los pacientes con DA, que inician tratamiento sistémico, según la comorbilidad atópica.

Resultados: Se incluyeron 509 pacientes, siendo mayoritariamente adultos (81,9%), con DA grave (73,7%). Los pacientes con comorbilidad atópica personal (64%) presentaron con mayor frecuencia dermatitis flexural (89,7 vs. 81,5%), mayor media de tratamientos sistémicos utilizados (1,6 vs. 1,3) y valores basales mayores en la escala POEM (19,6 vs. 17,9). Entre los pacientes con comorbilidad atópica familiar (40,7%) hubo mayor número de pacientes pediátricos/adolescentes (24,2 vs. 13,9%) y con antecedente de rinoconjunctivitis alérgica (61,1 vs. 47,1%). No se observaron diferencias en la respuesta a los tratamientos a los 6 y 12 meses, en función de la presencia o ausencia de comorbilidades atópicas.

Conclusiones: Los resultados sugieren que el antecedente de comorbilidad atópica se asocia con inicio temprano y curso persistente de la DA. Aunque no se observaron diferencias en la evolución a corto plazo, se destaca la necesidad de mayor seguimiento para comprender mejor el impacto de las comorbilidades en la DA.

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Introduction

Atopic dermatitis (AD) is a chronic inflammatory disease characterized by recurrent and unpredictable episodes of eczematous lesions. While symptoms commonly appear before the age of six, it is not uncommon for the disease to begin in adulthood, highlighting the variability of its clinical presentation.¹ AD affects approximately 15% of the pediatric population in developed countries^{2,3} and is closely related to the concept of atopic status, which includes various conditions such as food allergies, asthma, allergic rhinoconjunctivitis, and eosinophilic esophagitis. The interconnection among these conditions suggests a genetic basis and an altered immune response as key factors in the development and persistence of AD.^{4,5}

The prevalence of rhinitis and/or asthma in individuals with AD is estimated at 40.5% (25.7% for rhinitis and 14.2% for asthma),⁶ though significant variations may occur depending on the age at which the condition is assessed.⁷ Nationwide, results from the EpiChron cohort³ indicate that the most common chronic comorbidities in the pediatric population with AD were asthma (13.1%), psychosocial disorders (7.9%), visual impairment (7.8%), congenital limb anomalies (5.8%), and developmental disorders (3.2%), among others. Additionally, different published cohorts have shown that individuals with more severe clinical presentations of AD are at higher risk of developing comorbidities, which tend to show with greater intensity,^{6,8} which underscores the importance of adequately screening for associated comorbidities in these patients for optimal overall management of AD.⁹

In addition to the impact of skin lesions and comorbidities, persistent pruritus and the associated pain can lead to sleep disorders, anxiety, and/or depression, exacerbating the emotional burden on affected individuals. The need for a comprehensive approach becomes evident once again to provide complete care and improve the quality of life for those living with AD.¹⁰

In recent years, advancements in AD treatment have emerged, thanks to the introduction of innovative therapies with diverse mechanisms of action.¹¹ These new therapeutic options open the possibility of extending beneficial effects to atopic comorbidities. However, the safety profile of these treatments may be influenced by the presence of such comorbidities.^{12,13}

Despite these advancements, limited information exists on the effect and interaction of new treatments with atopic comorbidities. Most information comes from randomized clinical trials supporting the commercial approval of drugs. While these trials are crucial for understanding the expectations of drug efficacy, they include selection criteria that do not always reflect the diversity of patients encountered in the routine clinical practice. Patients with severe comorbidities are often excluded.

In this context, registries collecting data from patients from the routine clinical practice become particularly valuable. These registries not only complement the evidence from clinical trials but also provide a broader and more representative perspective on the safety and efficacy profile of treatments in real-world conditions.¹⁴

The present study aims to describe the clinical and epidemiological characteristics of patients with AD, as well as their treatment responses, based on the presence or absence of atopic comorbidities and family history of atopic comorbidities.

Materials and methods

The study included patients from the Spanish Registry of Atopic Dermatitis (BIOBADATOP), which has already been previously described.¹⁴ Briefly, it is a prospective, multicenter observational cohort that, since its inception in March 2020, includes pediatric, adolescent, and adult patients with AD initiating systemic immunomodulatory therapy. Baseline visits collect demographic data, diagnostic information, and disease severity metrics using the Eczema Area and Severity Index (EASI), the Dermatology Life Quality Index (DLQI), and the Patient-Oriented Eczema Measure (POEM). Similarly, data on comorbidities and prior treatments are recorded. Follow-up visits document changes in AD severity, main systemic treatments, and any concomitant treatments. Adverse events, if any, are recorded using the MedDRA dictionary.

Patient data mining in the registry is conducted using a pseudonymized unique identification code, employing the Research Electronic Data Capture (REDCap) online system.

We conducted a descriptive analysis of patients included from the start of the registry (March 2020) to the current cutoff (September 2023) based on the presence or absence of atopic comorbidities, which were defined as either the patient exhibiting asthma, allergic rhinoconjunctivitis, or atopic ocular disease, or having a first-degree relative with AD, asthma, allergic rhinoconjunctivitis, or atopic ocular disease.

Statistical analysis was performed using Stata software (version 17.0, StataCorp, Texas, United States). Demographic and clinical data were described using conventional statistics (means and standard deviations, absolute and relative frequencies). Differences across groups were compared using the chi-square test, Student's *t*-test, or the Mann-Whitney test, as appropriate. Box plots illustrated treatment responses at 6 and 12 months based on the presence or absence of atopic comorbidity. *P*-values <0.05 were considered statistically significant.

The BIOBADATOP registry received approval from the Clinical Research Ethics Committee of Aragón (Spain) (PA18/051). This approval process adheres to the principles set forth in the Declaration of Helsinki and complies with current ethical and clinical research legislation. All patients provided written consent to be included in the study.

Results

Clinical characteristics of study patients

In the present study, a total of 509 patients with AD were included from the BIOBADATOP registry. Most patients were adults (81.9%), with a median age of 29.5 years and an interquartile range of 20.9–44.5 years. The registry median follow-up time at the time of the cutoff was 9.6 months (IQR,

Table 1 Clinical characteristics of patients included in the study.

Clinical characteristics	N	Percentage
<i>Total patients</i>	509	100.0
<i>Type of patients</i>		
Pediatric/adolescent (0–17 years)	92	18.1
Adults (≥ 18 years)	417	81.9
<i>Age at inclusion</i>		
Mean (SD)	33.2	16.8
Median (Q1–Q3)	29.5	20.9–44.5
<i>Sex</i>		
Male	273	53.6
Female	236	46.4
<i>Atopic comorbidities</i>		
No	183	36.0
Yes	326	64.0
<i>Familial atopic comorbidities</i>		
No	302	59.3
Yes	207	40.7
<i>Combined atopic comorbidities</i>		
None	131	25.7
Family only	52	10.2
Patient only	171	33.6
Both	155	30.5
<i>AD severity (EASI and/or IDLQ/CDLQ/IDLQ)</i>		
Mild–moderate	128	26.3
Severe	358	73.7
<i>Scales</i>		
Pruritus VAS (0–10), mean (SD)	7.4	2.4
Pruritus VAS, median (Q1–Q3)	8	6–9
EASI total score (0–72), mean (SD)	21.4	11.8
EASI, median (Q1–Q3)	21.3	12.2–27.4
POEM total score (0–28), mean (SD)	19.0	6.5
POEM, median (Q1–Q3)	20	15–24
Baseline quality of life (DLQI/CDLQI/IDLQI: 0–30), mean (SD)	13.2	7.5
Baseline quality of life, median (Q1–Q3)	12	7–19
<i>Status</i>		
Under follow-up (on systemic treatment)	452	88.8
Under follow-up (without systemic treatment)	20	3.9
Lost to follow-up	36	7.1
Death	1	0.2

AD: atopic dermatitis; CDLQI: Children’s Dermatology Life Quality Index; DLQI: Dermatology Life Quality Index; EASI: Eczema Area Severity Index; VAS: Visual Analogue Scale; IDLQI: Infant’s Dermatology Life Quality Index; POEM: Patient-Oriented Eczema Measure; Q1: first quartile; Q3: third quartile; SD: standard deviation.

202 4.8–21.6 months). A total of 73.7% of the patients presented
203 severe AD vs. 26.3% with mild or moderate AD. Additionally,
204 64% of the patients included in the registry had personal
205 atopic comorbidities and 40.7%, familial atopic comorbidities.
206 More clinical characteristics of the patients included in
207 the study are shown in [Table 1](#).¹

208 The most common presentations of AD were flexural der-
209 matitis (86.8%), followed by facial-eyelid dermatitis (84.4%)
210 and hand dermatitis (60.1%). Regarding treatments prior to

211 registry inclusion, the most widely used were oral corticosteroids
212 (33.1%) and cyclosporine (32.3%). Notably, 23.9% of
213 the patients had not used any prior treatment.

214 A total of 749 systemic treatments were initiated, with
215 dupilumab (37.1%) and cyclosporine (29.2%) being the most
216 common ones. Additionally, 532 topical therapies were
217 recorded, with topical corticosteroids (50.4%) being the
218 most widely used. For a more detailed overview of the sys-
219 temic and topical treatments used, see [Table 2](#).

Table 2 Systemic and topical therapies used at the follow-up.

Previous systemic treatments	N	Percentage
Corticosteroids	166	33.1
Cyclosporine	162	32.3
None	120	23.9
Methotrexate	26	5.2
Azathioprine	10	2.0
Other	7	1.4
Upadacitinib	4	0.8
Baricitinib	3	0.6
Dupilumab	3	0.6
Omalizumab	1	0.2
Initiated systemic treatments	N	Percentage
Dupilumab	278	37.1
Cyclosporine	219	29.2
Upadacitinib	89	11.8
Corticosteroids	56	7.4
Tralokinumab	55	7.3
Baricitinib	19	2.5
Methotrexate	17	2.2
Abrocitinib	11	1.4
Omalizumab	1	0.1
Other	4	0.5
Initiated topical therapies	N	Percentage
Corticosteroids	490	50.4
None	441	45.3
Calcineurin inhibitors	37	3.8
Other	5	0.5

Relationship between clinical variables and the patients' atopic comorbidities

Patients with atopic comorbidities were more likely to exhibit flexural dermatitis as a clinical form (89.7% vs. 81.5%; $P=0.010$), less likely to exhibit nodular prurigo (8.5% vs. 18.1%; $P=0.001$), had used more systemic therapies previously (1.6 vs. 1.3; $P=0.010$), and had higher baseline POEM scores (19.6 vs. 17.9; $P=0.021$) vs. those without atopic comorbidities.

No significant differences were reported between the presence or absence of atopic comorbidities and other clinical forms of AD, baseline EASI severity, quality of life, or the EVA Pruritus scale (Table 3). Similarly, no other differences were reported in the initiation of systemic therapies, whether first- or second-line therapies.

Finally, no differences were identified regarding personal atopic comorbidity histories in terms of discontinuation of the drugs prescribed first or later on, reasons for discontinuation or change, dosages used, or responses to systemic therapies at the 6- and 12-month follow-up (Fig. 1).⁴

Relationship between clinical variables and familial atopic comorbidities

Among patients with familial atopic comorbidities, there was a higher proportion of pediatric/adolescent patients

(24.2% vs. 13.9%; $P=0.003$) and a higher frequency of allergic rhinoconjunctivitis history (61.1% vs. 47.1%; $P=0.002$) vs. those without familial atopic comorbidities (Table 4).

No differences were found between the two groups for other evaluated variables or in response to systemic therapies at the 6- and 12-month follow-up (Fig. 2).

Discussion

In our study on AD and atopic comorbidities, we observed similarities in most clinical characteristics between patients with and without these past medical histories. However, those with atopic comorbidities more frequently exhibited flexural dermatitis, an earlier onset of AD, a higher prior use of systemic therapies, and higher baseline POEM scores. These findings suggest a clinical profile characterized by early onset and extensive therapeutic trajectories, potentially increasing the likelihood of systemic therapy-related side effects. The greatest POEM impact could reflect greater perceived disease burden by the patient despite similar clinical characteristics and severity vs. those without atopic comorbidities. The cumulative physical, psychological, and inflammatory burden of the skin disease may play a significant role in shaping the patient's expectations and perspectives over their lifetime, a phenomenon described as cumulative life course impairment (CLCI).¹⁵ Of note, most

Table 3 Comparison of clinical characteristics of patients based on the presence or absence of personal atopic comorbidities.

	Personal atopic comorbidities			
	No		Yes	
	N	Percentage	N	Percentage
<i>Total patients</i>	183	100.0	326	100.0
<i>Patient type</i>				
Pediatric/adolescents (0–17 years)	41	22.4	51	15.6
Adults (≥ 18 years)	142	77.6	275	84.4
		<i>P-value</i>	0.057	
<i>Sex</i>				
Male	93	50.8	180	55.2
Female	90	49.2	146	44.8
		<i>P-value</i>	0.340	
<i>Nummular eczema</i>				
No	153	90.0	280	89.5
Yes	17	10.0	33	10.5
		<i>P-value</i>	0.851	
<i>Nodular prurigo</i>				
No	140	81.9	292	91.5
Yes	31	18.1	27	8.5
		<i>P-value</i>	0.001	
<i>Palmoplantar eczema</i>				
No	147	86.5	276	87.3
Yes	23	13.5	40	12.7
		<i>P-value</i>	0.785	
<i>Fold dermatitis</i>				
No	32	18.5	33	10.3
Yes	141	81.5	288	89.7
		<i>P-value</i>	0.010	
<i>Face and eyelids</i>				
No	24	17.8	41	14.5
Yes	111	82.2	241	85.5
		<i>P-value</i>	0.393	
<i>Genitals</i>				
No	97	72.4	175	63.2
Yes	37	27.6	102	36.8
		<i>P-value</i>	0.064	
<i>Hands</i>				
No	60	44.8	104	37.5
Yes	74	55.2	173	62.5
		<i>P-value</i>	0.160	
<i>Erythroderma</i>				
No	110	85.3	229	83.6
Yes	19	14.7	45	16.4
		<i>P-value</i>	0.664	
<i>Previous systemic treatment</i>				
No	50	27.9	70	21.7
Yes	129	72.1	253	78.3
		<i>P-value</i>	0.115	
<i>Number of previous systemic treatments (SD)</i>	1.3	1.2	1.6	1.5
		<i>P-value</i>	0.010	

Table 3 (Continued)

	Personal atopic comorbidities			
	No		Yes	
	N	Percentage	N	Percentage
<i>Previous phototherapy</i>				
No	129	71.7	202	63.5
Yes	51	28.3	116	36.5
		<i>P</i> -value	0.064	
<i>Severity of AD (EASI and/or DLQI/CDLQI/IDLQI)</i>				
Mild–moderate	50	29.4	78	24.7
Severe	120	70.6	238	75.3
		<i>P</i> -value	0.259	
<i>Pruritus last week (VAS 0–10) mean (SD)</i>	7.2	2.6	7.5	2.2
		<i>P</i> -value	0.248	
<i>EASI total score (0–72) mean (SD)</i>	20.7	11.2	21.8	12.1
		<i>P</i> -value	0.339	
<i>POEM total score (0–28) mean (SD)</i>	17.9	6.9	19.6	6.3
		<i>P</i> -value	0.021	
<i>Baseline quality of life (DLQI/CDLQI/IDLQI: 0–30) mean (SD)</i>	12.3	7.8	13.6	7.3
		<i>P</i> -value	0.122	

CDLQI: Children’s Dermatology Life Quality Index; DA: atopic dermatitis; SD: standard deviation; DLQI: Dermatology Life Quality Index; EASI: Eczema Area Severity Index; VAS: Visual Analog Scale; IDLQI: Infant’s Dermatology Life Quality Index; POEM: Patient-Oriented Eczema Measure.

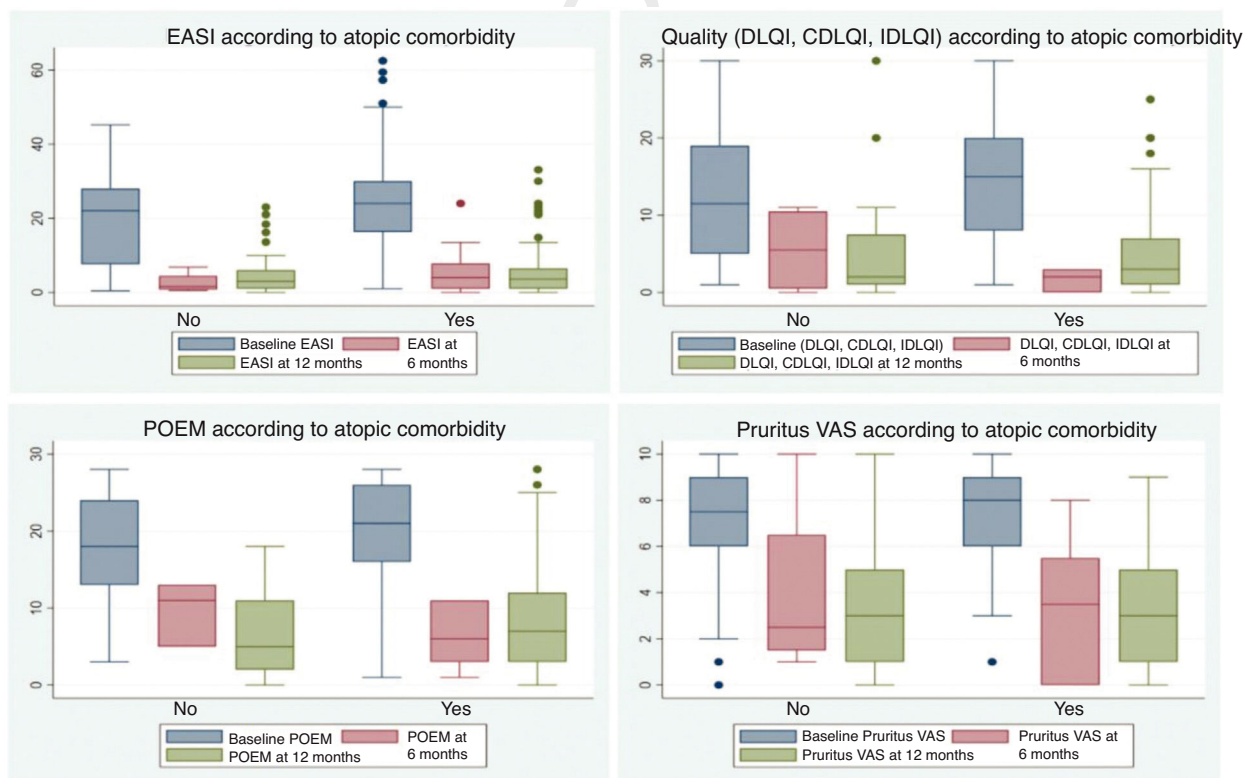


Figure 1 Box plots showing response to systemic treatments at 6 and 12 months, based on the presence or absence of personal atopic comorbidities. Responses were evaluated using scales measuring the severity of atopic dermatitis, including EASI, quality of life scales (DLQI/IDLQI/CDLQI), POEM, and EVA Pruritus (over the last week). No significant differences were observed between patients with and without personal atopic comorbidities.

Table 4 Comparison of clinical characteristics of patients based on the presence or absence of familial atopic comorbidities.

	Familial atopic comorbidities			
	No.		No.	
	<i>N</i>	Percentage	<i>N</i>	Percentage
<i>Total patients</i>	302	100.0	207	100.0
<i>Patient type</i>				
Pediatric/adolescents (0–17 years)	42	13.9	50	24.2
Adults (≥ 18 years)	260	86.1	157	75.8
		<i>P</i> -value	0.003	
<i>Sex</i>				
Male	164	54.3	109	52.7
Female	138	45.7	98	47.3
		<i>P</i> -value	0.714	
<i>Asthma</i>				
No	167	58.8	107	52.2
Yes	117	41.2	98	47.8
		<i>P</i> -value	0.146	
<i>Allergic rhinoconjunctivitis</i>				
No	147	52.9	79	38.9
Yes	131	47.1	124	61.1
		<i>P</i> -value	0.002	
<i>Atopic eye disease</i>				
No	234	86.3	164	80.8
Yes	37	13.7	39	19.2
		<i>P</i> -value	0.102	
<i>Nummular eczema</i>				
No	257	91.1	176	87.6
Yes	25	8.9	25	12.4
		<i>P</i> -value	0.203	
<i>Nodular prurigo</i>				
No	251	86.9	181	90.0
Yes	38	13.1	20	10.0
		<i>P</i> -value	0.281	
<i>Palmoplantar eczema</i>				
No	253	88.8	170	84.6
Yes	32	11.2	31	15.4
		<i>P</i> -value	0.175	
<i>Fold dermatitis</i>				
No	44	15.1	21	10.3
Yes	247	84.9	182	89.7
		<i>P</i> -value	0.122	
<i>Face and eyelids</i>				
No	37	15.5	28	15.7
Yes	202	84.5	150	84.3
		<i>P</i> -value	0.944	
<i>Genitals</i>				
No	160	68.1	112	63.6
Yes	75	31.9	64	36.4
		<i>P</i> -value	0.345	
<i>Hands</i>				
No	89	38.0	75	42.4
Yes	145	62.0	102	57.6
		<i>P</i> -value	0.373	

Table 4 (Continued)

	Familial atopic comorbidities			
	No.		No.	
	N	Percentage	N	Percentage
<i>Erythroderma</i>				
No	187	81.7	152	87.4
Yes	42	18.3	22	12.6
		<i>P</i> -value	0.121	
<i>Previous systemic treatment</i>				
No	74	25.0	46	22.3
Yes	222	75.0	160	77.7
		<i>P</i> -value	0.490	
<i>Number of previous systemic treatments</i>	1.5	1.4	1.5	1.3
		<i>P</i> -value	0.732	
<i>Previous phototherapy</i>				
No	198	66.9	133	65.8
Yes	98	33.1	69	34.2
		<i>P</i> -value	0.807	
<i>Severity of AD (EASI and/or IDLQ/CDLQ/DLQI)</i>				
Mild–moderate	74	25.9	54	27.0
Severe	212	74.1	146	73.0
		<i>P</i> -value	0.781	
<i>Pruritus last week (VAS 0–10) mean (SD)</i>	7.4	2.3	7.3	2.5
		<i>P</i> -value	0.554	
<i>EASI total score (0–72) mean (SD)</i>	22.1	11.9	20.4	11.5
		<i>P</i> -value	0.137	
<i>POEM total score (0–28) mean (SD)</i>	19.4	6.2	18.6	7.0
		<i>P</i> -value	0.239	
<i>Baseline quality of life (DLQI/CDLQI/IDLQI: 0–30) mean (SD)</i>	13.4	7.4	12.9	7.6
		<i>P</i> -value	0.500	

CDLQI: Children’s Dermatology Life Quality Index; DA: atopic dermatitis; SD: standard deviation; DLQI: Dermatology Life Quality Index; EASI: Eczema Area Severity Index; VAS: Visual Analog Scale; IDLQI: Infant’s Dermatology Life Quality Index; POEM: Patient-Oriented Eczema Measure.

literature supports the idea that atopic comorbidities are associated with greater disease perception and quality of life impacts.¹⁶ However, registries such as the Italian Atopy-Reg cohort¹⁷ made totally different findings, possibly due to a lower prevalence of atopic comorbidities in late-onset AD patients who tend to score higher on evaluation scales.

For patients with familial atopy histories, our study reveals a higher proportion of pediatric/adolescent patients, indicating, similar to personal atopic comorbidities, a greater likelihood of early onset and a long course of the disease. Furthermore, these patients more frequently had allergic rhinoconjunctivitis histories, which is consistent with previous studies highlighting the association between allergic rhinitis and early-onset AD.¹⁸ Nationwide, the EpiChron cohort also demonstrated that there was a significant association between allergic rhinitis and/or asthma in patients with AD, in the age group between 3 and 10 years.¹⁹

Atopic comorbidity histories may function as markers associated with early and prolonged disease, underscoring

the need for individualized management to minimize disease impact. Studies suggest that adults with both AD and asthma exhibit different health care utilization patterns, including higher risks of hospital admission and unscheduled visits vs. those with AD or asthma alone.²⁰ These data suggest that a comprehensive approach to managing AD and its comorbidities could help reduce health care costs.

The impact of these comorbidities on disease progression with treatments used in real-world clinical practice, particularly innovative therapies, remains of interest. Of the available treatments, only dupilumab has indications for atopic comorbidities such as asthma, nasal polyposis, or eosinophilic esophagitis. For other drugs, data is scarce, and the presence of comorbidities may have even limited recruitment in clinical trials.²¹ Therefore, some authors recommend selecting dupilumab for patients with comorbidities.²² In our study, however, no significant differences were observed in treatment choices or responses (at 6 and 12 months) based on the presence or absence of atopic comorbidities.

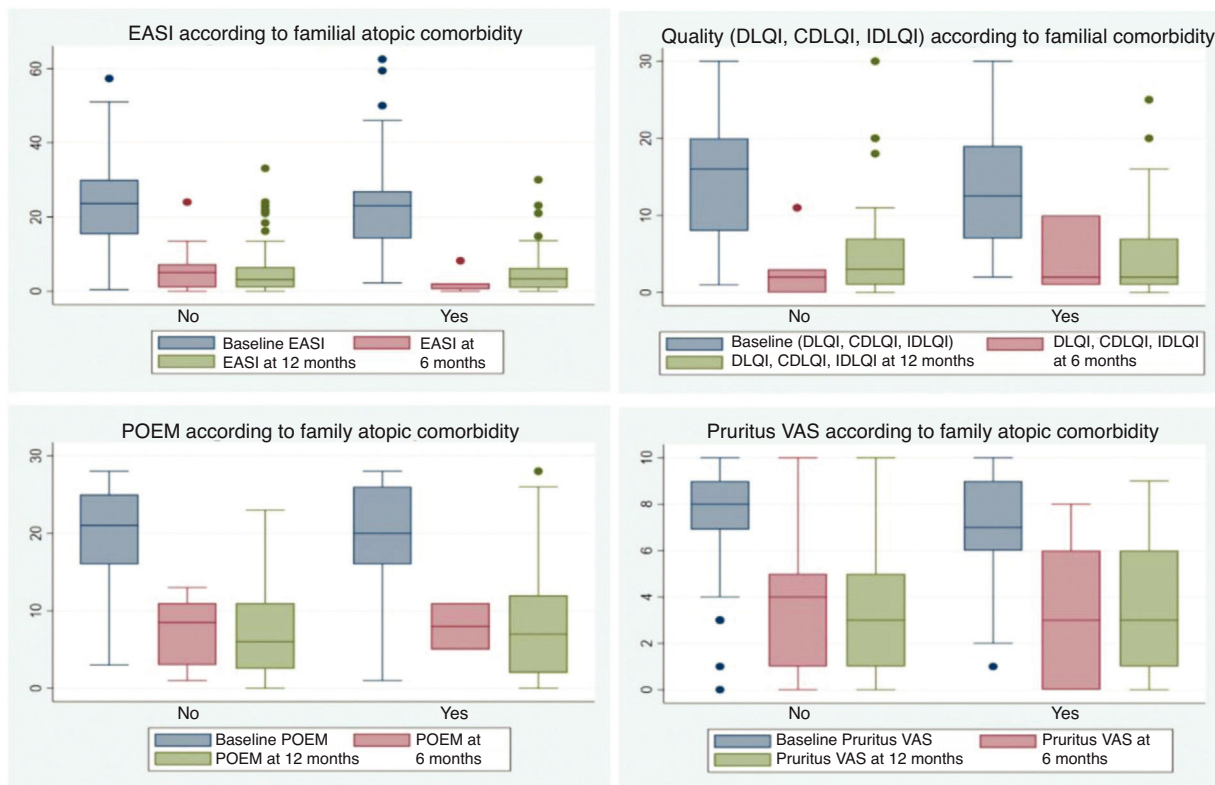


Figure 2 Box plots showing response to systemic treatments at 6 and 12 months, based on the presence or absence of familial atopic comorbidities. Responses were evaluated using scales measuring the severity of atopic dermatitis, including EASI, quality of life scales (DLQI/IDLQI/CDLQI), POEM, and EVA Pruritus (over the last week). No significant differences were observed between patients with and without familial atopic comorbidities.

308 ties. Although short-term differences were not observed,
309 potential long-term effects or specific factors influencing
310 treatment responses warrant further analysis in future stud-
311 ies.

312 This study limitations include those inherent to obser-
313 vational studies, where confounding variables are difficult
314 to control. While multicenter in its design, patients were
315 recruited from specialized centers, likely making them more
316 inclined to participate in research, which could limit gener-
317 alizability. Regarding treatments, it is essential to consider
318 that drugs such as dupilumab were available years before
319 other therapeutic options, potentially influencing patient
320 numbers and prescription patterns beyond the drug inherent
321 characteristics. Additionally, follow-ups were short, with
322 most patients being included in the past year. Informa-
323 tion on the activity and severity of atopic comorbidities,
324 which could significantly influence decision-making, is also
325 unavailable. In fact, it seems plausible, based on the data
326 presented, that the activity of atopic comorbidity – and its
327 need for treatment – is the criterion that can impact the
328 most the choice of treatment, rather than patient’s history
329 *per se*. Among the strengths, we highlight the sample size
330 obtained through the prospective collection of data, rigoro-
331 ously conducted via the BIOBADATOP registry. Similarly, data
332 collection was performed nationwide, obtaining a diverse
333 and extensive sample from the various participant centers,
334 which reinforces the representativeness of the findings and
335 improves the external validity of the study.

336 In conclusion, personal or familial comorbidity histories
337 may be associated with earlier onset and a more persistent
338 course of the disease, a significant factor in real-world clin-
339 ical decision-making. Long-term follow-up will be required
340 to better understand disease progression and responses to
341 new systemic therapies in these patient subgroups.

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Conflicts of interest

355 M. Munera-Campos has participated as an investigator in
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383 served as an advisor for Isdin and Roche Posay, Galderma,
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