ORIGINAL ARTICLE

Prevalence of Atopic Dermatitis in the Adult Population of Catalonia, Spain: A Large-Scale, Retrospective, Population-Based Study

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Abstract

Background: Studies on the prevalence of atopic dermatitis (AD) in adults in general populations are scarce worldwide. We performed a retrospective population-based observational cohort study of 537 098 adult patients diagnosed with AD in Catalonia, Spain, a larger population than in previous studies.
Objectives: To study the prevalence of AD by age, sex, disease severity, multimorbidity, serum total immunoglobin E (tIgE), and appropriate medical treatment (AMT) for the population of Catalonia.
Methodology: The study population comprised adult individuals (≥18 years) diagnosed with AD according to medical records at different health care levels (primary, hospital, emergency) in the Catalan Health System. Statistical analyses were conducted to evaluate sociodemographic characteristics, prevalence, multimorbidity, serum tIgE, and AMT.
Results: The prevalence of AD in the adult Catalan population was 8.7%, being higher for nonsevere disease (8.5%) than for severe disease (0.2%) and in females (10.1%) than in males (7.3%). Topical corticosteroids were the most prescribed drug (66.5%), and treatment was prescribed more frequently in severe AD patients, especially systemic corticosteroids (63.8%) and immunosuppressants (60.7%). More than half of severe AD patients (52.2%) had serum tIgE ≥100 kU/L, and higher values were observed for those with multimorbidity. The most frequent comorbid respiratory diseases were acute bronchitis (13.7%), allergic rhinitis (12.1%), and asthma (8.6%).
Conclusions: We provide new and robust evidence of the prevalence of AD and related characteristics in adults using a large-scale population-based study and a more significant cohort of individuals.

Key words: Atopic dermatitis. Epidemiological study. Population-based. Prevalence. Severity. Multimorbidity. Total serum IgE.

Resumen

Antecedentes: Existen pocos estudios de prevalencia de dermatitis atópica (AD) con cohortes de población adulta a nivel mundial. Realizamos un estudio poblacional de cohortes retrospectivo observacional con 537.098 pacientes adultos diagnosticados de AD en Cataluña (España), una población mayor que en estudios previos.
Objetivos: Estudiar la prevalencia de la AD por edad, sexo, gravedad de la enfermedad, comorbilidades, inmunoglobina E total sérica (tIgE) y con un uso adecuado del tratamiento médico (ATM) en la población catalana.
Metodología: Se incluyeron personas adultas (≥18 años) diagnosticadas de AD por historia clínica en los diferentes niveles asistenciales (primaria, hospitalario, urgencias) del Sistema Catalán de la Salud. Se realizaron análisis estadísticos para evaluar características sociodemográficas, prevalencia, comorbilidades, tIgE sérica y ATM.
Resultados: La prevalencia global de AD diagnosticada en la población adulta catalana fue del 8,7%, siendo mayor la AD no grave (8,5%) que la AD grave (0,2%) y en el sexo femenino (10,1%) con respecto al masculino (7,3%). Los corticoides tópicos fueron el fármaco más prescrito (66,5%), y el uso de todos los tratamientos prescritos fue mayor en pacientes con AD grave, especialmente corticoides sistémicos (63,8%) e inmunosupresores (60,7%). Más de la mitad (52,2%) de los pacientes con AD grave presentaron tIgE sérica ≥100 kU/L, y se observaron valores más altos en aquellos con múltiples comorbilidades. La bronquitis aguda (13,7%), la rinitis alérgica (12,1%) y el asma (8,6%) fueron las enfermedades respiratorias concomitantes más frecuentes.
Conclusiones: Nuestro estudio proporciona evidencia nueva y sólida de la prevalencia de la AD y las características relacionadas en adultos utilizando un estudio poblacional a gran escala y una cohorte de individuos más significativa que los estudios previamente publicados.

Palabras clave: Dermatitis atópica. Estudio epidemiológico. Poblacional. Prevalencia. Gravedad. Comorbilidades. IgE sérica total.

Summary box

- **What do we know about this topic?**
  Atopic dermatitis (AD) has an estimated global prevalence of 2% to 8% in adults, with a high impact on an individual's quality of life. AD is the most common cutaneous disease in children. Severe cases may persist over time and are more common during adulthood.
- **How does this study impact our current understanding and/or clinical management of this topic?**
  To our knowledge, this is the first population-based epidemiological study performed in a large population of AD patients. We provide more robust prevalence results for Spanish adults overall and by age group, as well as data on disease severity, multimorbidity, medical treatments, and biomarkers.

Introduction

Atopic dermatitis (AD) and its related states (atopic eczema, eczema, neurodermatitis) is a noncontagious, pruritic, inflammatory skin condition characterized by defects in the epidermal barrier. It is a chronic relapsing condition, often occurring in families with atopic diseases, namely, AD, bronchial asthma, and/or allergic rhinoconjunctivitis [1]. According to the European Academy of Allergy and Clinical Immunology, atopy is defined as a personal or familial tendency to produce IgE antibodies in response to low doses of allergens, usually proteins, and to develop typical symptoms such as asthma, rhinoconjunctivitis, and eczema/dermatitis [2].

The pathogenesis of AD is multifactorial [3]. The genetic component plays a significant role, as do the skin microbiome and environmental factors. Onset is usually during childhood. AD is the most common cutaneous disease in children, with a high impact on an individual's quality of life. Infants with AD may develop the atopic march, which comprises simultaneous development of atopic disorders, including food allergy, allergic rhinitis, and asthma [3-5]. Severe cases may persist over time and are more common during adulthood.

Reports on the epidemiology of AD have estimated the global prevalence to be about 2% to 8% in adults [1]. In Europe, 4.4% of the population is estimated to have AD. In the USA, numbers vary between 4.9% [6] and 10.2% [7]. Evidence of the estimated prevalence for Spanish adults is scarce, and results vary between 1.9% [8,9] and 7.2% [6], with vast differences between geographical regions. The prevalence estimates for severe AD range between and 0.07% [9] and 0.09% [10].

We performed a retrospective epidemiological study using a large-scale population-based database for the period 2013-2017. We aimed to investigate the prevalence of AD, overall and by age and sex in a cohort of adults with AD from Catalonia, Spain. We also assessed disease severity, multimorbidity, total serum IgE levels, and medical treatments. To our knowledge, this is the first population-based epidemiological study to be performed in a large population of AD patients and to provide richer patient information than previously reported in the literature. Therefore, we provide more robust prevalence results for Spanish adults overall and by age groups, as well as data on disease severity, multimorbidity, medical treatments, and biomarkers for Spain.

Materials and Methods

Study Population

We analyzed all residents of Catalonia, the second most populated region in Spain, with coverage in the National Health Service (NHS) and included in the Agency for Health Quality and Assessment of Catalonia (AQuAS) database. The inclusion criteria were age ≥18 years and a diagnosis of AD established by medical records at any care level covered by the NHS (primary, hospital, outpatient, and emergency care) at any point in time from January 2013 until December 2017 (different follow-up period for everyone in the dataset). The exclusion criteria were transfer to other regions in Spain and permanent institutionalization (ie, patients in nursing homes, psychiatric care, and other care facilities). The study was based on 537 098 patients diagnosed with AD during 2013-2017.

The data obtained were confidential, anonymous, and dissociated according to the Spanish Organic Law on Data Protection (Law 15/1999 of December 13). The Spanish Agency for Medicines and Medical Devices classified the study as No-EPA (ie, no drug postauthorization), as this is a retrospective observational study of the epidemiological characteristics of AD. It was approved by the Clinical Research Ethics Committee, the International University of Catalonia (Barcelona), and the Ethics Committee of Hospital Clínic de Barcelona.

Study Design

The database was provided by AQuAS and contains details of all administrative medical registers on available admissions to primary care, hospital care, outpatient care, and emergency care at the individual-patient level of residents in Catalonia with coverage in the NHS.

AD was recorded in the database from records based on medically certified diagnoses coded according to the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*. The *ICD-9-CM* codes considered were as follows: 691.8 - Atopic dermatitis and related states - Other atopic dermatitis and associated conditions: AD, eczema, neurodermatitis; 692.9 - Contact dermatitis and another eczema, unknown cause. Including the second code might have led us to overestimate the prevalence, because it comprises irritant and allergic contact dermatitis and other nonatopic dermatoses. Nevertheless, not considering that code would lead to the exclusion of a consistent number of AD registered as such.

The type of AD therapies prescribed (topical corticosteroids, antihistamines, topical and systemic immunosuppressants, and systemic corticosteroids) available in the database for the period under study can be found in the supplementary material.

See supplementary material for further description of the database and prescribed treatment codes.

Outcomes

Demographic characteristics

The socioeconomic and demographic characteristics obtained were sex, age, and annual income levels (adjusted for household size).

Epidemiology

The overall prevalence of AD in the general adult population was calculated based on all individuals from the study population diagnosed with AD over the total adult population in Catalonia (6 155 980 residents in 2017). Since the database encompasses the entire population of Catalonia, prevalence results do not represent estimated values. Instead, data should be interpreted as the diagnosed prevalence in Catalonia during 2013-2017.

Disease severity

Since data on symptoms were not available in the dataset, no information was available for the SCORAD scale [1,11], and disease severity (nonsevere, severe) was classified based on drug prescription following the existing literature [9,10]. The degree of severity was based on drug prescription over the previous 2 years. Individuals were classified as presenting severe AD if they had been prescribed immunosuppressants (cyclosporine, azathioprine, cyclophosphamide, methotrexate, alitretinoin, mycophenolic acid, interferon α-2a, interferon α-2b) at least once during the previous 2 years or if they had been hospitalized/attended the emergency department during the previous 2 years with AD as a first diagnosis. Disease was considered nonsevere in all other situations.

Total serum IgE biomarker

Atopy and its associated allergic responses correlate with increased serum total IgE (tIgE) production. Therefore, tIgE was also provided in the AQuAS dataset and used to calculate the median (confidence interval) and number of individuals above and below the cut-off value (≥100 kU/L was considered high) for the total adult population by disease severity and by comorbid condition. The maximum value reported during 2016-2017 was recorded.

Multimorbidity

Comorbid conditions of AD, including respiratory disease/allergy and systemic/general conditions, were also analyzed (supplementary material).

Statistical Analysis

We performed an observational, multicenter, longitudinal, retrospective study based on a review of all available medical records related to AD in Catalonia (from 2013 to 2017) using computerized databases with dissociated data.

The statistical analyses were conducted using the statistical package Stata 16. A descriptive study reported frequencies and proportions of individuals in the overall population and by disease severity for confounders, comorbid conditions, treatment characteristics, and biomarkers. The Pearson χ^2 test was performed to assess independence between categorical variables, as well as mean differences by disease severity. OR (95%CI) and *P* values were reported for the multivariate logistic regression analysis performed to determine the probability of having severe AD against multimorbidity and confounders. The overall prevalence of AD was reported, as was the prevalence by disease severity, by sex, and by age groups. A *P* value <.05 was considered statistically significant.

Results

Descriptive Characteristics

Even though the population under study comprises adults, it is worth noting that most AD cases were recorded during childhood, up to age 15 years (Figure 1 online supplementary figures). After that, the population shrank, with fewer AD cases among adults, although sufficient to be the object of study.

AD was diagnosed in 537 098 adults out of 6 155 980 Catalan residents in 2017. Of these, 2.4% (12 860 individuals) were classified as having severe AD, and 97.6% (524 238 individuals) as having nonsevere AD (Figure 2 online supplementary figures).

More women than men had a diagnosis of AD for both nonsevere disease (1.46:1) and severe disease (1.52:1). The diagnosis of AD is more frequent (65%) in young adults (18-59) than in patients aged ≥60 years, and the same is true among the nonsevere and severe subgroups. More than half of the adult AD cohort (70%) had annual incomes <€18 000€ (Table 1).

Prevalence of AD

The diagnosed prevalence of AD was 8.7%. Prevalence was higher in the nonsevere than in the severe group (8.5% vs 0.2%) (Figure 3 online supplementary figures). By sex, the overall prevalence was higher for females than males (10.1% vs 7.3%, *P*<.0001). The prevalence was highest for women aged 18-29 years (11.2%). The prevalence increased over time for both sexes, especially in men, where it was highest (9.6%) for those aged ≥60 years (Figure 4A online supplementary figures). Differences in prevalence between males and females were statistically significant (*P*<.0001) from age 30 years onward. A similar pattern for both sexes was observed for nonsevere AD (Figure 4B online supplementary figures). However, the prevalence for females with severe AD increased slightly with age.

Treatment Prescribed

During 2013-2017, topical corticosteroids were the most prescribed drugs in the population as a whole (66.5%) and in each severity group (66.3% for nonsevere and 77.9% for severe). These were followed by antihistamines (53.2%)

Table 1. Sociodemographic Characteristics of the Adult Atopic Dermatitis Cohort.[a]

	Overall cohort	Cohort by severity	
Sociodemographic characteristics	**N=537 098 (100%)**	**Nonsevere n=524 238 (97.6%)**	**Severe n=12 860 (2.4%)**
Sex, No. (%)			
Males	217 999 (40.6)	212 895 (40.6)	5104 (39.7)
Females	319 099 (59.4)	311 343 (59.4)	7756 (60.3)
χ^2 (4.42; *P*=.036)			
Age, y, No. (%)			
18-59	349 335 (65)	341 503 (65.1)	7832 (60.9)
≥60	187 763 (35)	182 735 (34.9)	5028 (39.1)
χ^2 (99.28; *P*<.0001)			
Income, €, No. (%)			
Exempt	26 071 (4.9)	25 359 (4.8)	712 (5.5)
<18 000	380 118 (70.8)	370 852 (70.7)	9266 (72.1)
18 000-100 000	129 273 (24.1)	126 420 (24.1)	2853 (22.2)
>100 000	1636 (0.3)	1607 (0.3)	29 (0.2)
χ^2 (37.83; *P*<.0001)			

[a]Number of individuals in each phenotype (total, nonsevere, and severe). The proportion of individuals over the total adult population in each phenotype is in parenthesis. *P* values are for the Pearson χ^2 test of independence between categorical variables. Data on income were only available for 2017.

and systemic corticosteroids (24.9%). All medications were more frequently prescribed in patients with severe disease than in those with nonsevere AD; this difference is especially significant for systemic corticosteroids (63.8% vs 24%, respectively) and immunosuppressants (60.7% vs 4.5%). No AD treatment was prescribed in 16% of individuals, whose disease was considered mild (Table 2).

Total Serum IgE

During the last 2-year period (2016-2017), information on serum tIgE was available for 14 841 individuals (Table 3). Of these, 6320 (42.6%) had serum tIgE values ≥100 kU/L. This proportion was higher in severe than in nonsevere disease (52.2% vs 42.1%, *P*<.0001), and for those AD patients with comorbid conditions (asthma, 60.8%; nasal polyps [NP], 45.9%; and both asthma and NP, 60.7%) than those without (38.4%, *P*<.0001) (Figure 5 online supplementary figures).

Serum tIgE values were significantly higher (*P*<.05) in severe than in nonsevere AD (110 kU/L vs 72.3 kU/L, respectively). Concerning multimorbidity, patients with asthma, NP, or both had higher levels of serum tIgE than those without multimorbidity (Table 3).

Multimorbidity

The most frequent respiratory/allergic comorbid conditions were acute bronchitis (13.7%), allergic rhinitis (12.1%), and asthma (8.6%). The most prevalent nonrespiratory comorbid conditions were hypertension (28.2%), anxiety (20.9%), and overweight (19.2%) (Table 4). The proportion of all comorbid conditions was higher in severe than in nonsevere AD, with a significant difference between those with severe AD and asthma (15%) for nonsevere AD (8.4%) and those with allergies and severe AD (9.2%) than in those with nonsevere AD (4.8%) and acute bronchitis.

Along the same lines, asthma, nonspecified allergies, and food allergy should be highlighted among the remaining respiratory and allergic comorbid conditions for having the strongest associations with severe AD (OR, 1.83, 1.95, and

Table 2. Adult Atopic Dermatitis Cohort According to Disease Severity by Treatment Prescribed.[a]

	Overall cohort	Cohort by disease		
Treatment prescribed No. (%)	**N=537 098 (100%)**	**Nonsevere n=524 238 (97.6%)**	**Severe n=12 860 (2.4%)**	***P* Value**
Drugs				
Topical CS	357 362 (66.5)	347 349 (66.3)	10,013 (77.9)	<.0001
Systemic CS	133 766 (24.9)	125 565 (24.0)	8201 (63.8)	<.0001
Antihistamines	285 591 (53.2)	276 215 (52.7)	9376 (72.9)	<.0001
Immunosuppressants	31 650 (5.9)	23 849 (4.5)	7801 (60.7)	<.0001
No drugs	87 533 (16.3)	87 533 (16.7)	-	-

Abbreviation: CS, corticosteroids.

[a]In parenthesis, the proportion of individuals over the total adult population in each phenotype (total, nonsevere, and severe). *P* values are based on the test of differences in means between the degrees of severity for each treatment under study at a 95%CI of significance (null hypothesis [Ho], ie, no statistically significant differences between degrees of severity. Reject Ho if *P*<.05). No drug data were available for 87 533 individuals, who were assumed to have nonsevere AD. Drugs are not mutually exclusive, as 1 individual can be simultaneously prescribed more than 1 group of medications.

Table 3. Total IgE Values for the Adult Atopic Dermatitis Cohort Over the 2016-2017 Period.[a]

Biomarkers, median and mean values (95%CI)	Total population	By disease severity		Cohort by disease			
		Nonsevere	Severe	AD alone	AD + asthma	AD + NP	AD + asthma + NP
Serum total IgE	N=14 841	n=14 172	n=669	n=11 887	n=2472	n=268	n=214
Median, kU/L	73.4 (71.09-76.1)	72.3 (70-74.9)	110[b] (94.8-132.4)	62.8 (60.2-64.8)	153[b] (143-166)	86[b] (62.15-106)	132.6[b] (112-171.9)
Mean, kU/L	275.4 (0.1-1513.1)	259.5 (0.1-1405.6)	582.1 (0.1-2903.1)	227.8 (0.1-1286.9)	474.9[b] (0.8-2246.9)	270.0[b] (0.2-1327.1)	441.4[b] (2.2-2039.4)

Abbreviations: AD, atopic dermatitis; NP, nasal polyposis.

[a]For IgE, median and mean values are calculated and reported across the maximum value reported for everyone with available information on the biomarker during 2016-2017. The 95%CIs are reported in parenthesis for the median value and the test of statistically significant differences in means across degrees of severity and among multimorbidity phenotypes. Median values were preferred above average, as the kernel distribution for each biomarker was very asymmetric with extremely high skewness and kurtosis.

[b]$P<.05$.

1.54, respectively), as should rheumatoid arthritis among systemic conditions (OR, 22.63; $P<.0001$) (Table 4).

Discussion

This is the first retrospective population-based epidemiological study of a large population of adult AD patients. Its main strength is that it offers abundant information for Spain, based on a total sample of 6.1 million residents. The main findings were as follows. First, the overall diagnosed prevalence of AD for the adult population of Catalonia was 8.7%, being higher for nonsevere disease (8.5%) than for severe disease (0.2%). Second, AD was more frequent among females than among males for the overall AD population and irrespective of disease severity and age range. Third, the prevalence of AD decreased during the lifespan for females and increased for males overall and by severity, except for females with severe AD, where it increased slightly with age. Fourth, in general, drug prescription was more frequent in severe than in nonsevere AD for all treatments, with more frequent prescription of systemic corticosteroids and immunosuppressants. Fifth, serum tIgE values were higher for severe than for nonsevere disease (52.2% vs 42.1%, $P<.0001$), and for AD patients with comorbid conditions (asthma, 60.8%; NP, 45.9%; and asthma and NP, 60.7%). Sixth, a higher proportion of individuals with severe AD had respiratory and allergic comorbid conditions, as well as systemic conditions, especially anxiety (20.9%) and hypertension (28.2%). There was also a strong association between rheumatoid arthritis and the probability of severe AD (OR, 22.63; $P<.0001$).

Our study is based on medical records from the Catalan health care system at the primary, hospital, and emergency care levels; this made it possible to identify a cohort of 537 098 adults with a diagnosis of AD established by medical records covered by the whole NHS, ie, 8.7% of the study population in Catalonia. This prevalence is very similar to recently reported data (2018) [6] for Spanish adults aged up to 65 years (7.2%), which were recorded using questionnaires on the diagnoses of AD in a sample of 9924 individuals.

Prevalence rates in this study are higher than those reported in the literature for Spain [9,10]. One cause of overestimation in the present study is the inclusion of the *ICD-9-CM* code 692.9. However, in our case, not including that code would have led the overall prevalence to be underestimated at 1.61% (99 062 individuals), possibly because of methodological differences between the studies cited and ours. The previous studies relied on a smaller population from 7 regions in Spain, whereas the current study is based on the Catalan adult population.

Moreover, the inclusion criteria for previous studies were more restrictive than for the present study. A recent report from Spain [10] used medical register data for adults aged >18 years, including only those individuals who met all the following inclusion criteria: prescription of any medication for AD with a minimum of 2 drugs during the follow-up period and ≥2 health records including 1 dermatology visit (38 475 individuals). These criteria considerably restricted the population and generated a lower prevalence result (1.9%) and a possible sample bias. Another difference in this result is the age group classification compared to previous studies [10], which is >18 years (ie, not including patients aged ≥18 years, thus potentially increasing prevalence). Yet, to date, the present population-based study is the first to analyze the prevalence of AD in the adult population using a much larger database and including all public medical registers of individuals with a diagnosis of AD during the study period in Catalonia, Spain, thus constituting a much larger sample of individuals with severe AD.

On the other hand, the prevalence of severe AD (0.21%) was more significant than reported in the literature, that is, 0.08% [8] and 0.07% [10], for the same reasons explained above. In addition, given the nature of the disease, the severity of AD is based on the medication prescribed instead of on the medical diagnosis. In the case of Spain [8-11], the medication used was directly associated with treatment of AD. In contrast, it was impossible in the present study to distinguish whether the drugs were explicitly prescribed to treat AD or other concomitant diseases.

In line with earlier studies [6,7], we found significant sex differences, with prevalence being higher in females (10.1%)

Table 4. Comorbid Conditions in the Adult Atopic Dermatitis Cohort.

AD-related comorbid conditions	Total population N=537 098	Population by disease severity[c]				
		Nonsevere n=524 238 (97.61%)	Severe n=12 860 (2.39%)	*P* Value	Logit regression Pr (severe)	
					OR (95% CI)	*P* Value[d]
Respiratory and allergy, No. (%)						
Asthma	45 934 (8.6)	44 009 (8.4)	1925 (15.0)	<.0001	1.83 (1.74-1.94)	<.0001
Allergic rhinitis	64 993 (12.1)	63 498 (12.1)	1495 (11.6)	.047	0.85 (0.80 -0.90)	<.0001
Acute bronchitis	73 608 (13.7)	71 225 (13.6)	2383 (18.5)	<.0001	1.12 (1.07-1.19)	<.0001
Nasal polyposis	4849 (0.9)	4689 (0.9)	160 (1.2)	<.0001	1.16 (0.98-1.37)	.085
COPD	8318 (1.5)	7985 (1.5)	333 (2.6)	<.0001	1.04 (0.92-1.18)	.536
Nonspecified allergy	26 295 (4.9)	25 113 (4.8)	1182 (9.2)	<.0001	1.95 (1.83-2.08)	<.0001
Food allergy	1747 (0.3)	1661 (0.3)	86 (0.7)	<.0001	1.54 (1.22-1.93)	<.0001
Systemic and general, No. (%)						
Hypertension	151 486 (28.2)	147 021 (28.0)	4465 (34.7)	<.0001	1.16 (1.1-1.22)	<.0001
Overweight	103 080 (19.2)	100 375 (19.1)	2705 (21.0)	<.0001	0.93 (0.89-0.98)	.005
Dyslipidemia	57 399 (10.7)	55 467 (10.6)	1932 (15.0)	<.0001	1.18 (1.12-1.25)	<.0001
Diabetes	58 871 (11.0)	57 027 (10.9)	1844 (14.3)	<.0001	1.15 (1.08-1.22)	<.0001
Ischemic heart disease	21 087 (3.9)	20 384 (3.9)	703 (5.5)	<.0001	1.06 (0.97-1.16)	.191
Alcohol-related disease[a]	16 721 (3.1)	16 105 (3.1)	616 (4.8)	<.0001	1.36 (1.24 -1.49)	<.0001
Smoking-related diseases[b]	75 756 (14.1)	73 577 (14.0)	2179 (16.9)	<.0001	1.16 (1.10-1.22)	<.0001
IBD	6943 (1.3)	6758 (1.3)	185 (1.4)	.07	0.98 (0.84-1.14)	.775
Rheumatoid arthritis	4418 (0.8)	2913 (0.6)	1505 (11.7)	<.0001	22.63 (21.12-24.24)	<.0001
Heart/liver/kidney failure	6108 (1.1)	5839 (1.1)	269 (2.1)	<.0001	1.58 (1.38-1.80)	<.0001
Anxiety	112 084 (20.9)	109 207 (20.8)	2877 (22.4)	<.0001	1 (0.95-1.04)	.944
Depression	25 679 (4.8)	24 829 (4.7)	850 (6.6)	<.0001	1.12 (1.03-1.21)	.005

Abbreviations: COPD, chronic obstructive pulmonary disease; IBD, inflammatory bowel disease.

[a]Alcohol-related diseases include alcohol-induced mental disorders, alcohol dependence and abuse, alcoholic polyneuropathy, alcoholic cardiomyopathy, alcoholic fatty liver, acute alcoholic hepatitis, alcoholic cirrhosis of the liver, excessive blood level of alcohol, toxic (acute) effect of alcohol, alcoholic gastritis with or without bleeding, fetal alcohol syndrome.

[b]Smoking-related diseases include chronic pharyngitis, uncomplicated chronic bronchitis, and leukoplakia of the oral mucosa, including the tongue.

[c]The number of AD individuals in each phenotype (total, nonsevere, and severe) by related comorbid conditions. The proportion of individuals over the total adult population in each phenotype is in parenthesis.

[d]*P* values are for the test of differences in means between degrees of severity (nonsevere vs severe) for each comorbid condition under study at a 95%CI of significance (null hypothesis [Ho]: No statistically significant differences between severity degrees. Reject Ho if *P* value < .005). Logistic regression analysis for the probability of severe disease. The model includes sociodemographic characteristics as control variables.

than in males (7.3%), and differences in severity and over the lifespan, where prevalence tends to decrease for both sexes, except for females with severe AD.

Following the European Guidelines on Treatment for Atopic Dermatitis [1], we recorded more frequent prescription for severe AD than for nonsevere AD, especially in the case of systemic corticosteroids (63.8% vs 24%, respectively) and immunosuppressants (60.7% vs 4.5%).

Higher values for serum tIgE were found for severe AD and individuals presenting with comorbid conditions (asthma and/or NP). Serum tIgE values were ≥100 kU/L in 42.6% of individuals despite the lack of consensus on the use of serum tIgE for the diagnoses of AD [3] and the fact that it might be age-dependent, with tIgE levels decreasing with age [12,13]. This proportion was higher for severe AD (52.2%), as reported elsewhere [14], and for those with comorbid conditions [15,16].

Respiratory and allergy were the most frequent comorbid conditions, especially for those with severe AD compared to those with nonsevere AD. In line with earlier studies [8,10,17,18], the most prevalent comorbid conditions for the total adult AD population were acute bronchitis (13.7%), allergic rhinitis (12.1%), and asthma (8.6%). Among adults with severe disease, the most prevalent were acute bronchitis (18.5%), allergic rhinitis (11.6%), and asthma (15%). However, there are differences in the percentage of

multimorbidity reported in the severe AD population from other studies [10], which is higher (allergic rhinitis, 22.9%; and asthma, 20.8%).

Furthermore, a recent study [18] showed that 82% of patients with moderate-to-severe AD have ≥1 atopic comorbid condition, including allergic rhinitis (63%), asthma (54%), allergic conjunctivitis (44%), food allergy (40%), chronic rhinosinusitis (14%), atopic keratoconjunctivitis (8%), and NP (5%).

It can be concluded that there is a strong correlation between AD and type 2 diseases, which are even more frequent in severe AD patients, and that the proportion of comorbid conditions in this study could be lower owing to the restrictive inclusion criteria.

The most frequent systemic comorbid conditions were hypertension (28.2%), anxiety (20.9%), and overweight (19.2%), which were found in lower proportions, as reported elsewhere [10,20,21]. Moreover, although the frequency of patients with rheumatoid arthritis (0.8%) was lower than that of other systemic comorbid conditions, it had one of the strongest associations with severe AD (OR, 22.63), in line with previous studies [22].

Our study is subject to a series of limitations. First, the design was retrospective, and the severity of treatment was based on the medication prescribed instead of the medical diagnosis. Prescribed medication is understood as prescribed and purchased by the individual. However, information on whether this is taken is not available. Note that ruling out oral corticosteroids as a criterion of severity could have introduced bias between the severe and nonsevere clusters. Biological treatment was not considered, given its low implementation during the study period and because the reasons for this treatment were unknown. Second, we do not know whether some drugs, such as oral corticosteroids, were prescribed to treat AD or other, concomitant diseases specifically. Therefore, oral corticosteroid intake was not used as a severity criterion. On the other hand, the prevalence for severe AD patients could also be underestimated, by assuming that patients with no drug information present nonsevere AD, which might or might not always be the case. And third, the absence of individuals diagnosed and treated outside the NHS in private hospitals or medical centers could lead us to underestimate prevalence and disease severity.

In summary, evidence regarding the prevalence of AD in children is more plentiful than in adults. This paper aimed to contribute to the literature by providing new evidence based on a larger number of AD patients than in previous studies, including richer information on most of the patients diagnosed with AD from the general adult population of Catalonia. Our findings show an overall prevalence of 8.72%, with higher values for females than males overall and irrespective of severity and age range. The prevalence for severe AD was 0.21%, and this tended to increase slightly across age groups for females and decrease for males. Serum tIgE ≥100 was found in 42.6% of individuals and was more frequent in patients with severe AD and patients with comorbid conditions. Finally, the most frequent allergic and respiratory comorbid conditions were acute bronchitis and allergic rhinitis, and the most frequent systemic and nonallergic conditions were hypertension, anxiety, and obesity.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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