

# Epidemiologic, Clinical and Socioeconomic Factors of Atopic Dermatitis in Spain: *Alergológica-2005*

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## ■ Abstract

*Objective:* To analyze the clinical and epidemiologic characteristics of the population with atopic dermatitis (AD) consulting in Allergology services in Spain.

*Materials and Methods:* The study was a multi-center, observational, descriptive, cross-sectional epidemiologic study with prospective collection of data on patients consulting for the first time in Allergology services in Spain. By means of a data collection record, personal and specific variables were collected during the calendar year 2005 from a total of 4991 patients with AD.

*Results:* AD was diagnosed in 171 patients (3.4% of patients seen in Allergology services), which represented no significant change with regard to the *Alergológica-1992* study. In 72% of cases, AD was associated with other allergic disorders. The mean age of the onset of clinical manifestations of AD was 1 year and 4 months. During the first consultations, the suspected diagnosis of AD was established in 83% of cases. In 58% of cases the cause was considered idiopathic and 42% were associated with sensitization to allergens. In 10% of patients with AD the triggering allergens were foods and in 26% aeroallergens. Most patients (94%) received hydrating skin and drug treatment (anti-histamines 73%, topical corticoids 49%, calcineurin inhibitors 31%). Only 10% of patients followed an exclusion diet.

*Conclusions:* No significant increase in the demand for AD consultations was observed in comparison with *Alergológica-1992*. AD was frequently associated with other allergic disorders. In few cases was food involved in the etiology of the disease. In most cases nothing more than topical drug treatment was indicated.

**Key words:** Atopic dermatitis. Epidemiology. Treatment.

## ■ Resumen

*Objetivo principal:* Analizar las características clínicas y epidemiológicas de la población con Dermatitis Atópica (DA) que acude a las consultas de alergología en España.

*Material y métodos:* Estudio multicéntrico epidemiológico observacional descriptivo transversal, con recogida prospectiva de información sobre pacientes atendidos por primera vez en consultas de alergología de España durante un año natural, incluyendo un total de 4991 pacientes. Mediante cuaderno de recogida de datos se recogieron variables personales y específicas sobre la DA.

*Resultados:* Se diagnosticó de DA a 171 pacientes (3,4% de los pacientes atendidos en las consultas de alergología), sin diferencia significativa con respecto al estudio previo *Alergológica-1992*. En el 72% se asoció a otras enfermedades alérgicas. La edad media de inicio de las manifestaciones clínicas de la DA fue de un año y cuatro meses. En la primera consulta se estableció el diagnóstico de sospecha de DA en el 83% de los casos. El 58% se consideró de causa idiopática y el 42% asociada a sensibilización a alérgenos. En el 10% de los pacientes con DA se consideraron como alérgenos causales los alimentos y en el 26% los aeroalérgenos. La mayoría de los pacientes (94%) recibió tratamiento cutáneo hidratante y farmacológico (antihistamínicos: 73%, corticoides tópicos: 49%, inhibidores de calcineurina: 31%). Sólo un 10% siguió una dieta de eliminación de alimentos.

*Conclusiones:* No se observó un aumento significativo en la demanda asistencial por DA respecto al estudio *Alergológica-1992*. Con frecuencia se asoció a otras patologías alérgicas. En pocos casos se consideró la implicación etiológica de los alimentos. En la mayoría se indicó exclusivamente tratamiento tópico.

**Palabras clave:** Dermatitis atópica. Epidemiología. Tratamiento.

## Introduction

Atopic dermatitis (AD) is an inflammatory skin disease characterized by intense pruritus, chronic and relapsing course and where the morphology of lesions and pattern of distribution have no specific characteristics and so is not differentiated from other types of dermatitis. Currently no objective laboratory test exists and diagnosis is based on association with a series of clinical features. In 1980, Hanifin and Rajka [1] established the major and minor criteria which are still the norm for the diagnosis of this disease.

AD is a common health problem in children and adolescents throughout the world. The prevalence of AD varies widely from country to country and even within the same country [2], which indicates that environmental factors play an important role in the expression of the disease.

AD generally begins in infancy and its frequency and intensity diminish with age. Consequently, its prevalence is greatest in the first six months of life.

In 1992, the Spanish Society of Allergology and Clinical Immunology (SEAIC) carried out a wide-scale study, which was published in 1995, into the epidemiologic, clinical and socioeconomic factors of the main allergic disorders in Spain [3], among them AD. In 2005, this study was repeated (*Alergológica-2005* [4]) with the general aim of obtaining information about current clinical practice in allergology from patients consulting allergy services for the first time and of identifying any relevant changes that could have taken place in the intervening decade, thus replicating the main objectives of the *Alergológica-1992* study.

The objective of *Alergológica-2005* was to analyze the epidemiologic and clinical characteristics of the population with AD who consulted in Allergy Services in Spain and to determine the prevalence of this disorder. Other objectives were to investigate the possible current differences in the regional distribution of AD in Spain, analyze the possible seasonal variability in the demand for allergy care in Spain, to describe the diagnostic and therapeutic procedures followed by specialists in this disease and the preventive measures adopted, to estimate the social and healthcare repercussions of AD on the quality of life of the patients and on their school and/or work activities and to describe the functional and organizational aspects of health services specialized in Allergy in the Spanish healthcare system in 2005 (source of referral of patients, time on waiting lists, duration of consultations or pressure on resources)

## Material and Methods

This was a multi-center, observational, descriptive, cross-sectional epidemiologic study with prospective collection of data on patients consulting for the first time in a broad sample of public and private Allergology services in Spain.

The materials and methods used in the study are as described in the relevant section of this issue of the journal [5].

Using a data collection booklet, both general and specific variables were collected from patients on each of the disorders they presented with. Figure 1 shows the questionnaire specifically used for AD.

Qualitative variables were described by calculating relative frequencies (%) and 95% confidence intervals. Quantitative variables were described by measures of centrality and dispersion (means and standard deviations). Differences between percentages of qualitative variables were compared by calculating the 95% confidence interval of the difference in the percentages found or by using the chi-square test (or Fisher exact test). Comparison of mean values in quantitative variables was made using the Student t test (or the Mann-Whitney test) or the analysis of variance (or Kruskal-Wallis test).

## Results

A total of 4991 patients, 2860 males (57.3%) and 2131 females (42.7%) were included in the study. Their distribution by age is shown in Figure 2.

### Prevalence

The number of patients diagnosed with AD by an allergist was 171 (63.9% children and 36.1% adults), which corresponds to 3.4% (95% CI, 2.9%-3.9%) of the total of the sample (Table 1). A significant difference in the distribution of AD was seen according to age group: 16.9% in the 0-5 years old group; 7.9% in the 6-15 years old group, and 1.5% in the group of over 15 years of age.

### Age

Sixty-three percent of the patients diagnosed with AD were younger than 15 years old with a mean age of  $15.3 \pm 14.2$  years. This was significantly lower ( $P < .0001$ ) than that of the total sample ( $32.7 \pm 18.2$  years).

### Gender

There was a clear predominance among females, with a female:male ratio of 1.5:1, similar to that observed in the overall sample (1.3:1), but significantly different ( $P < .0001$ ) to that of the general population (1:1).

### History of Atopy

Seventy-four percent of AD patients reported a family history of atopic disease. The most frequent were rhinitis (42%), bronchial asthma (36%) and AD (30%). Fifty-five percent of patients had a personal history of other allergic disorders (rhinitis 26%, bronchial asthma 19%, and food allergies 12%).

### Feeding during lactation

Seventy-five percent of patients with AD were breastfed (59% exclusively for more than 3 months), a percentage similar to that of the overall sample. No significant difference in the diagnosis of AD was seen with regard to type of feeding. Only 10% of patients with AD received special formulas (hypoallergenic, extensive hydrolyzed, soy)

### Patient background

Ninety-four percent of patients were from a mean

## ATOPIC DERMATITIS

### DIAGNOSIS

Involvement

Only cutaneous

Associated with:

- |  |   |
|--|---|
| <input type="checkbox"/> Rhinitis<br><input type="checkbox"/> Food allergy<br><input type="checkbox"/> Eczema on hand/foot<br><input type="checkbox"/> Dyshidrosis<br><input type="checkbox"/> Cheilitis<br><input type="checkbox"/> Staphylococcus infection<br><input type="checkbox"/> Asthma | <input type="checkbox"/> Pulpitis<br><input type="checkbox"/> Prurigo<br><input type="checkbox"/> Ichthyosis<br><input type="checkbox"/> Pityriasis alba<br><input type="checkbox"/> Herpes infection<br><input type="checkbox"/> Other |
|--|---|

Cause

Idiopathic Allergen     Inhalants     Others  
 Foods

Age of onset in months

-----

How long (days) have you had the symptoms in your present episode/attack?

-----

In which month did the first symptoms appear?

Spring                       Autumn  
 Summer                       Winter

How many months have you had these symptoms?

-----

How many acute episodes/attacks of your illness have you had in the last year?

-----

### DIAGNOSTIC TESTS

Involvement

- |  |  |
|--|--|
| <input type="checkbox"/> Clinical history and examination<br><input type="checkbox"/> Blood tests<br><input type="checkbox"/> Oral/physical challenge tests<br><input type="checkbox"/> Type 1 skin tests<br><input type="checkbox"/> Biopsy | <input type="checkbox"/> Immunoglobulins <input type="checkbox"/> Total IgE <input type="checkbox"/> Others<br><input type="checkbox"/> Specific IgE |
| <input type="checkbox"/> Epicutaneous tests  | <input type="checkbox"/> Neumoallergens <input type="checkbox"/> Others<br><input type="checkbox"/> Foods  |

How many days has it taken for the diagnosis to be made in the Allergy Service?

-----

SEVERITY (IGA) General Evaluation of the Researcher	
<input type="checkbox"/>	No involvement —————> With no inflammatory signs of atopic dermatitis
<input type="checkbox"/>	With almost no involvement —————> Erythema, infiltration and formation of papules that are hardly perceptible
<input type="checkbox"/>	Slight disease —————> Slight erythema and infiltration and formation of papules that are hardly perceptible
<input type="checkbox"/>	Moderate disease —————> Moderate erythema. Infiltration and moderate formation of papules
<input type="checkbox"/>	Severe disease —————> Severe erythema. Infiltration and severe formation of papules
<input type="checkbox"/>	Very severe disease —————> Severe erythema. Infiltration and severe formation of papules with suppuration and formation of crusts

### THERAPEUTIC APPROACH

- |   |   |   |  |
|---|---|---|--|
| <input type="checkbox"/> Hydration<br><input type="checkbox"/> Antihistamines   | <input type="checkbox"/> Topical<br><input type="checkbox"/> Systemic | <input type="checkbox"/> First generation<br><input type="checkbox"/> Second generation<br><input type="checkbox"/> New | <input type="checkbox"/> Keratolytics<br><input type="checkbox"/> Calcineurin inhibitor (tacrolimus, pimecrolimus)<br><input type="checkbox"/> Cyclosporine<br><input type="checkbox"/> Antibiotics<br><input type="checkbox"/> Antifungals<br><input type="checkbox"/> Others |
| <input type="checkbox"/> Topical steroids<br><input type="checkbox"/> Systemic steroids<br><input type="checkbox"/> Dietary measures<br><input type="checkbox"/> Allergen avoidance |   |   |  |

Figure 1. Questionnaire specifically used for atopic dermatitis patients.

socioeconomic background. Seventy-one percent lived in urban areas, with a dry environment in 78% of cases. Thirty-nine percent reported living with animals.

### Quality of life

School-aged children with AD missed a mean of 11 days of class in the preceding year. AD or an associated illness was the cause of time off work in 19% of parents of patients, with a mean of 4 days per year.

The percentage of adults with AD who were off sick from work in the previous year (1.4%) was significantly lower ( $P < .05$ ) than the corresponding figure for the overall sample (5.5%).

### Diagnosis

The mean age at the onset of clinical manifestations of AD was one year 4 months. In almost half of patients (46%) manifestations had begun in the first 6 months of life and in all cases before the age of 8. The mean age at the first visit was 15 years, and patients reported having symptoms for an average of 2.5 years and experiencing a mean of 3.5 acute attacks in the previous year.

Seventy-two percent of patients with AD had consulted their primary care physician in the previous 4 months for allergic disease in comparison with 58.5% of patients from the full sample, which represented a significant difference ( $P < .05$ ).

Cutaneous symptoms were the initial cause of consultation in 66% of patients and only 14% reported a suspected adverse reaction to foods.

In the first consultation, a diagnosis of AD was established in 83% of cases with a median of 5 days to complete the diagnosis. Table 2 lists the diagnostic tests performed in the analysis of patients with AD. The tests most frequently used were skin prick tests (86% of patients) followed by

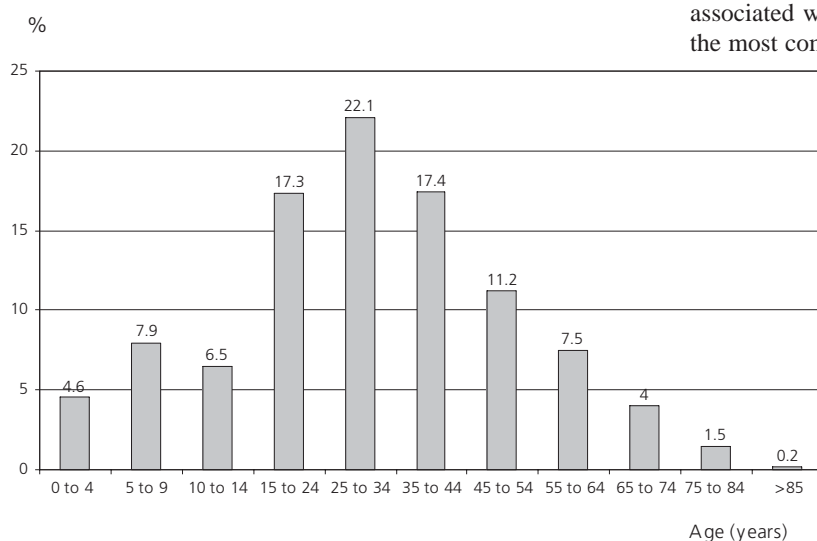


Figure 2. Distribution of the Overall Sample of Alergológica-2005 in Percentages (%) of Patients by Age Group.

Table 1. Prevalence of Disorders Treated in Allergy Services\*

Disorder	Prevalence	95% CI
Rhinitis/conjunctivitis	55.5%	54.1-56.9%
Bronchial asthma	27.9%	26.7-29.2%
Allergy to drugs	14.7%	13.7-15.7%
Urticaria/angioedema	11%	10.2-11.9%
Allergy to foods	7.4%	6.7-8.1%
Others non-allergy-related	5.8%	5.2-6.5%
Contact dermatitis	4.2%	3.7-4.8%
Atopic dermatitis	3.4%	2.9-3.9%
Hypersensitivity to insects	1.5%	1.2-1.9%
Other diagnoses	6.7%	6.0-7.4%

\* CI indicates confidence interval.

Table 2. Diagnostic Tests Performed on Patients With Atopic Dermatitis\*

Diagnostic Test	N° patients	%
Blood tests and analyses	59	34.5%
Biopsy	1	0.6%
Skin prick tests	147	86%
Epicutaneous tests (foods)	14	8.2%
Epicutaneous tests (aeroallergens)	9	5.2%
Epicutaneous tests (contactants)	15	8.8%
Total serum IgE	93	54.7%
Serum specific IgE	90	52.9%
Oral challenge test	8	4.7%

\* IgE indicates immunoglobulin E.

determination of total serum immunoglobulin E (IgE) (54.7%) and specific IgE (52.9%).

Twenty-eight percent of patients were diagnosed as having exclusively AD and in the remaining patients (72%) AD was associated with other disorders, with rhinitis (59.1%) being the most common, followed by bronchial asthma (50%) and food allergies (23.1%).

### Etiology

In 58% the cause of the AD was considered to be idiopathic and in 42% to be associated with allergens. In 10% of patients the responsible allergens were foods and in 26% aeroallergens. A significant difference ( $P < .001$ ) was found in the cause (idiopathic/allergens) in relation with the exclusive presence of AD or an association with other diseases. Ninety-five percent of cases of AD which only exhibited dermatitis were considered idiopathic

### Severity

Seventy-three percent of patients did not present with dermatitis lesions or only had minor lesions at the time of diagnosis.

Table 3. Distribution of Patients with Atopic Dermatitis in Relation to the Treatment Recommended by the Allergist in *Alergológica*-1992, *Alergológica*-2005 and the DERTA study\*

Treatment	% patients <i>Alergológica</i> 2005	% patients <i>Alergológica</i> 1992	% patients DERTA study
Hydrating emollient	94.2	83	94.9
Antihistamines	72.5	72	63.8
Topical steroids	49.1	68	87.9
Systemic steroids	4.1	7.4	12.4
Exclusion diet	9.9	36.8	ND
Allergen avoidance	31	34.7	78.6
Keratolytics	1.8	3.2	ND
Calcineurin inhibitors	31	ND	ND
Cyclosporin	0	0	1.8
Antibiotics	1.8	ND	15.3
Antifungals	0	ND	ND
Phototherapy	ND	ND	1.5

\* ND indicates no data was collected on this parameter.

### Treatment

More than 90% of patients received topical hydrating treatment. Treatment with antihistamines was indicated in 72% of AD patients, topical corticosteroids in 49% and calcineurin inhibitors in 31% of patients. In 10% of patients dietary measures were recommended and in 35% patients were advised to avoid certain allergens.

## Discussion

### Prevalence

The prevalence of AD varies widely from country to country and even within the same country. In the International Study of Asthma and Allergies in Childhood [2], the prevalence observed in children varied greatly (from 1% to 17%) depending on the country. In general, a high prevalence of AD symptoms is seen in Australia, the north of Europe and a low prevalence in Asia and central and eastern Europe. The data for Spain show a prevalence of 3.3% in children aged between 6 and 7 years and 4.4% in children aged between 13 and 14 years.

In the present study the percentage of patients consulting with AD was 3.4% and although this is slightly higher than the 2.5% described in the previous *Alergológica* study carried out in 1992 [3], there is no statistically significant difference which indicates that the healthcare demands generated by AD have increased in comparison with other allergic disorders in recent years.

This percentage could appear low given that the study sample corresponds to patients consulting for suspected allergic disease. However, if we stratify the overall sample by age group the results are significantly different: 16.9% in the 0-5 years age group; 7.9% in the 6-15 years age group and 1.5% in the over 15 years age group.

### Age

Sixty-three percent of patients with AD were under 15

years of age compared to 19% of the same age group in the general sample, as corresponds to a disease which primarily affects children.

The mean age of patients with AD was  $15.3 \pm 14.2$  years, similar to the  $13.6 \pm 12.9$  years found in the DERTA study [6], an epidemiologic study carried out by Spanish Academy of Dermatology and Venereology in which 375 dermatologists participated and a total of 1597 patients with AD were included.

### Gender

Distribution by gender shows a clear predominance of females as has been observed in other epidemiologic studies [2]. Gender does not appear to be an independent risk factor for AD [7] and the possibility has been raised that this difference reflects the greater importance given by women to the skin symptoms [8].

### History of atopy

Approximately 70%-80% of patients with AD have personal or family histories of atopy. This constitutes one of the most important signs for diagnosis and expresses the atopic constitution of the patient [1].

However, the percentage of patients reporting food allergies (12%) is lower than that observed in other epidemiologic studies [9].

### Feeding during lactation

The protective effect of breastfeeding on the development of AD is a controversial issue, with some studies showing a benefit and others no effect [10].

In *Alergológica*-2005, 75% of patients with AD had been breastfed and 59% of these exclusively breastfed for more than 3 months. In the rest of the patients from the general sample who did not have AD the same levels of breastfeeding were seen (74%). These data do not reveal any particular tendency as the percentages are similar to the proportion of infants breastfed in the general population [11].

Only 10% of patients with AD had received special formulas (hypoallergenic, extensive hydrolyzed, soy), which indicates that allergy to proteins in cow milk are very unlikely in these patients.

### Diagnosis

The mean age of onset of the clinical manifestations of AD in the patients in *Alergológica*-2005 was 16 months. In almost half of patients (46%) these had begun in the first 6 months of life and in all cases before 8 years of age. However, the first consultation was made at 15, with a mean time of 2.5 years with symptoms. The delay between the onset of the disease and the first visit to the allergist could be related to the minor nature of the AD in the majority of cases and that patients choose to consult when the AD is associated with other allergic disorders.

Allergic sensitization to allergens was studied by using skin prick tests in 86% and specific IgE in 53% of patients. This contrasts with the DERTA study, which reflects the

dermatologist's point of view, in which skin prick and serum specific IgE tests were performed in only 13% of patients with AD [6], which indicates that, unlike allergists, dermatologists rarely consider the allergic aspects of the problem.

Epicutaneous tests with aeroallergens and foods are novelties in comparison with the previous *Alergológica*-1992 study. The usefulness of these tests for the evaluation of AD is a matter of controversy [12], and they were only used with small numbers of patients (58% with foods and 5% with aeroallergens).

The oral challenge test, which is essential to show the clinical relevance of foods in the dermatitis, was only performed in 5% of patients with AD, which means that in only 8 of 28 patients with food allergies was this test used to confirm the diagnosis.

Eczema is considered by the majority of allergists and dermatologists as a unique entity, usually denominated AD, without taking into account the atopic state of the patient. Currently, it is accepted that, as with asthma, there are at least two variants of eczema: the atopic form which is associated with IgE specific to allergens of the environment, and the non-atopic form.

Recent studies show that in 45%-64% of patients with AD, no allergic sensitization can be proven [13], which are percentages similar to those seen in the present study (58% of idiopathic origin and 42% associated with allergens).

It is very likely that the risk factors and the progression of these two variants of eczema are different and that children with non-atopic eczema are at a lower risk of presenting with asthma than children with atopic eczema [14]. However, the etiologic involvement of food allergens and of aeroallergens in exacerbations of AD is a controversial matter [15, 16]. Some authors, such as Hanifin [17] consider that it is unlikely that more than 10% of patients suffer attacks of AD in relation to foods, and an association has been observed the severity of atopic eczema and the degree of sensitization to aeroallergens.

Although the method of evaluation used in the present study was different to that used in the DERTA study [6], patients consulting allergists seem to have less severe disease (73% with minor disease compared to 22% in the DERTA study). These results could indicate the tendency of patients with more serious skin problems to initially consult a dermatologist and to consult an allergist when AD is associated with other allergic diseases.

### Treatment

Coinciding with the criteria of the dermatologists, in more than 90% of cases allergists prescribed skin hydrating treatments.

In 72% of patients treatment with antihistamines was indicated as was the case in *Alergológica*-1992 [3]. This figure is slightly higher than the percentage of antihistamines recommended by dermatologists in the DERTA study [6] but it must be borne in mind that, apart from dermatitis, 42% of the *Alergológica*-2005 patients presented with symptoms of rhinitis.

Treatment with topical corticosteroids was indicated

in 49% of patients with AD in *Alergológica*-2005, which is lower than the corresponding figure from *Alergológica*-1992 (68%) and the DERTA study (88%). These differences are fundamentally due to the fact that the researchers in *Alergológica*-2005 prescribed calcineurin inhibitors to 31% of patients with AD as an alternative to topical corticosteroids and these drugs were not commercially available when the other two studies were carried out.

In 10% of patients dietary measures were used, which corresponds to the percentage of patients in whom foods were considered to be the triggering allergens. Although this figure is well below the 37% of *Alergológica*-1992, it could even be lower given that only 5% of patients in the *Alergológica*-2005 study were given a challenge test to confirm the clinical relevance of the foods.

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