Atopic dermatitis in specialised centres in Spain: a retrospective analysis of incidence and costs (2000-2017)

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Abstract

Background: Atopic dermatitis is a chronic inflammatory skin disease that has substantial effects on patients' quality of life, with a prevalence between 2.2% and 17.6% worldwide. This study aimed to evaluate the use of specialised care resources generated by children and adults with atopic dermatitis, and the associated direct medical costs.

Methods: Admission details from patients admitted in specialised healthcare centres (inpatient and outpatient care) in Spain between 1 Jan 2000 and 31 Dec 2017 were analysed in a retrospective multicentre study.

Results: Records corresponded to 3036 patients, 1266 aged 5 years or younger. Comorbid conditions corresponded to skin infections and respiratory difficulties (asthma, bronchiectasis). Hospital incidence of atopic dermatitis was 5.8 per 100,000 persons, stable over the study period, and 30.0 per 100,000 in those aged 5 years and younger. Mean annual direct medical cost per patient was €2469. Overall, direct medical costs per patient increased significantly over the study period ($p<0.0001$).

Conclusion: Hospital incidence of atopic dermatitis remained stable over the study period, which is in contrast with the increasing incidence reported by the Spanish government in primary care centres. The increase in direct medical costs of specialised care responded to the increase in treatment costs.

Keywords: atopic dermatitis; incidence; comorbidity; specialised care; direct medical costs.

1. Introduction

Atopic dermatitis is a chronic inflammatory skin disease characterised by pruritus, dry skin and eczematous lesions [1,2]. Disease onset is usually in early childhood, before 3-5 years of age, and it often persists during adulthood, having substantial effects on patients' quality of life [2-4]. Treatment is focused on improving the skin condition, alleviating pruritus and inflammation in order to improve life quality [5]. Mild atopic dermatitis is generally managed with topical steroids or calcineurin inhibitors, while more severe cases may be treated with phototherapy and systemic immunomodulators, or the recently developed antibody-based treatments [6,7].

The prevalence of atopic dermatitis is variable among different populations and for its different severity levels; its general prevalence is estimated to be between 2.2% and 17.6%, with the highest self-reported prevalence found in Spain [8]. Atopic dermatitis represents a significant burden for patients and healthcare systems in direct medical costs and social, academic and indirect costs, especially when considering the paediatric population [9]. Admissions into specialised care centres could contribute significantly to this burden; in fact, a study developed in the United States analysing paediatric dermatology inpatient services indicated that 86% of all admissions were for atopic dermatitis in 2009-2010 [10]. Thus, the interest in understanding the profile and needs of the patients with atopic dermatitis treated in specialised care centres.

The Spanish healthcare system consists of an extended network of primary healthcare centres, the first contact point with the patient, and a secondary care setting that includes outpatient specialised care, inpatient care and emergency care. The analysis of real-world evidence provides a clear image of current practice, which can assist resource allocation decisions in public health [11,12].

72 This study aimed to evaluate the use of specialised care resources generated by children
73 and adults with atopic dermatitis and the associated direct medical costs. In addition,
74 patient characteristics and hospital incidence were analysed.

75 2. Methods

76 *2.1 Study setting*

77 Admission records of patients that were admitted in specialised healthcare centres
78 (inpatient and outpatient care) between 1 Jan 2000 and 31 Dec 2017 were analysed in
79 a retrospective multicentre study. Records were extracted from a Spanish National
80 discharge database including public and private hospitals, which covers 90% of hospitals
81 in Spain and is representative of all Spanish regions. Data is codified at the hospital level
82 by means of the International Statistical Classification of Diseases and Related Health
83 Problems, 9th version (ICD-9) prior to 2016 and 10th version (ICD-10) after the year 2016
84 [13,14]. The database is validated internally and subjected to periodic audits; in this
85 process, errors and unreliable data are eliminated. Equally, the Spanish Ministry of
86 Health registers admission data from primary care centres, used to obtain data on
87 pharmaceutical consumption; this database is codified using the International
88 Classification of Primary Care, Second edition (ICPC-2).

89 *2.2 Data extraction*

90 Records of admissions in which atopic dermatitis was registered as the admission motive
91 were identified from the database using the ICD-9 and ICD-10 codes: 691.8 and L20. The
92 medication prescribed to these patients was obtained for the year 2017, and categorized
93 according to the Anatomical Therapeutic Chemical (ATC) classification, identifying the
94 patients with the ICPC-2 code S87 [15,16].

95 All parameters identifying healthcare centres or medical history were re-coded within
96 healthcare centres to maintain records anonymised, in accordance with the principles
97 of Good Clinical Practice and the Declaration of Helsinki. This research did not involve
98 human participants and there was no access to identifying information; in this context
99 the Spanish legislation does not require patient consent and ethics committee approval
100 [17].

101 ***2.3 Study variables***

102 The variables extracted for analysis were: patients' sex and age, date of admission, type
103 of admission, date of discharge, type of discharge (including death), readmission rate
104 (defined as a subsequent readmission for the same cause within 30-days after
105 discharge), admission motive, secondary diagnoses registered during the admission and
106 admission costs. Pharmaceutical prescription data was obtained from primary care
107 records.

108 ***2.4 Data analysis***

109 Patient characteristics were analysed in the first admission registered per patient. All
110 the admission files were used to analyse the nature of admission, length of stay,
111 readmission rate, medical procedures and admission costs. An independent analysis was
112 performed considering the patients aged 5 years and younger, considering the typical
113 age of disease onset, comparing in all cases to patients older than 5 years of age.
114 Hospital incidence was calculated as the number of cases of atopic dermatitis registered
115 in the specialised care database within the total number of patients. Direct medical cost
116 of specialised care was calculated based on the admission costs that are registered in
117 the database; these are assigned according to the standardised average expenses of
118 admissions and medical procedures determined by the Spanish Ministry of Health

(include all expenses related to the admission: examination, medication, surgery, diet, costs associated to personnel, medical equipment and resources). The costs of prescribed medication were not available.

Frequencies are presented for dichotomous variables and mean and range were calculated for quantitative variables. Normality was tested with the Kolmogorov-Smirnov test. A Cochran-Armitage trend test was performed to assess temporal trends in the incidence of atopic dermatitis and the Mann-Kendall trend test was used to assess temporal trends in the length of stay and direct medical costs. Two-tailed T-student or one-way analysis of variance were used as appropriate to compare characteristics between patient groups, with null hypothesis “patient characteristics are independent from age”. Two-sample Z tests were used to test for differences in sample proportions between age groups. In all cases, a $p<0.05$ was considered statistically significant.

Statistical analyses were performed using Microsoft Excel© Professional Plus 2016 (Microsoft Corporation, Redmond, WA, USA) and StataSE 12 for Windows (StataCorp LP. 2011. Stata Statistical Software: Release 12. College Station, TX, USA).

3. Results

Admission records corresponded to 3,036 patients, admitted in specialised care centres in Spain between 2000 and 2017; 1266 of the patients were aged 5 years or younger (Table 1). A history of allergies was registered in 22.4% of all admissions and 16.8% of admissions of patients aged 5 years and younger. Overall, 15.7% of admissions of all patients registered chronic obstructive pulmonary disease, namely asthma and bronchiectasis. In addition, skin infections and other bacterial infections were found in a number of admissions. The frequency of diagnosis of all relevant comorbidities varied significantly between age groups ($p<0.0001$).

143 The hospital incidence of atopic dermatitis was 5.8 per 100,000 persons over the study
144 period, 30.0 per 100,000 in those aged 5 years and younger. The incidence registered
145 in specialised care centres decreased significantly over the study period for the patients
146 aged 5 years and younger ($p<0.0001$), while in the total patient population it was stable
147 (Figure 1a).
148 Patients aged 5 years and younger registered a higher percentage of urgent admissions
149 (84.3% in patients age 5 years and younger vs. 61.2% in those over 5 years; $p<0.0001$)
150 (Table 2). Up to 99.6% of all admissions were inpatient admissions and mean length of
151 hospital stay (LOHS) was of 5.7 days. Patients aged 5 years or younger required shorter
152 stays, with a mean of 4.3 days (vs. 6.5 days in patients over 5 years; $p<0.0001$) and the
153 LOHS decreased significantly over time in both age groups ($p<0.0001$) (Figure 1b).
154 The most common medical procedures registered on admission included blood
155 microscopic examination, which included the examination of IgE levels, the injection of
156 steroids and antibiotics and skin biopsies. Additionally, pharmacological interventions
157 registered in primary care centres showed a majority of antibiotics, non-steroid anti-
158 inflammatory products, antihistamines and corticosteroids (Table 2).
159 Total annual direct medical costs were €465,565 for the patients registered in the
160 database (N=3036). Mean annual direct medical cost per patient was €2469. No
161 differences were observed per age groups in this cost: €2310 in patients aged 5 years
162 and younger, and €2549 in patients older than 5 years of age ($p=0.3724$). Significant
163 shifts appeared in the costs per patient over time: a major increase is observed between
164 the years 2009 and 2010 ($p<0.0001$) (Figure 2a). Mean admission cost reached the €3052
165 between 2010 and 2013.

166 Subsequently, the diagnosis of comorbid conditions over time was analysed. An increase
167 in the diagnosis of asthma and bronchiectasis, and skin infections was observed
168 between 2009 and 2010 ($p<0.0001$) (Figure 2b). The registry of allergy history peaked
169 the year 2008 and after 2012 ($p<0.0001$); other relevant comorbidities did not exhibit
170 any major trends.

171 4. Discussion

172 This study evaluated the burden of atopic dermatitis in specialised care centres in Spain
173 over a large time period (2000-2017) aiming to provide a description of patients' needs
174 in terms of specialised healthcare and the associated medical costs.
175 The 3036 patients included in the study had a mean age of 18.8 years; in addition, 41.7%
176 (1266) of the patients hospitalised due to atopic dermatitis were aged 5 years or
177 younger. Hospital incidence of atopic dermatitis was 5.8 per 100,000 persons between
178 2000 and 2017, increasing to 30.0 per 100,000 in those aged 5 years and younger.
179 Prevalence studies show significantly higher figures in children, a population group in
180 which atopic dermatitis is often present preceding the diagnosis of other allergic
181 disorders later in life [18].
182 Overall, the prevalence of atopic dermatitis continues to increase, especially in low-
183 income countries [18]. In this study, hospital incidence of atopic dermatitis remained
184 stable over time, while the portion of patients aged 5 years and younger decreased over
185 the study period; this trend was likely to respond to differences in the treatment of this
186 condition. The Spanish Ministry of Health registered an increasing incidence of atopic
187 dermatitis in primary care centres between 2011 and 2017 (223 per 10,000 persons in
188 2011 to 464 per 10,000 persons in 2017) [15].

189 A history of allergies was registered in 22.4% of all patients; in addition, patients were
190 diagnosed with skin infections and respiratory conditions. The association with
191 cutaneous infections has been previously analysed in patients with atopic dermatitis,
192 often colonised with *Staphylococcus aureus* [19]. Asthma was identified in 12.1% of
193 patients with atopic dermatitis in a previous study in Spain, in which it was associated
194 with a more intensive use of medical resources [20]. Anxiety disorders were present in
195 patients with atopic dermatitis in previous studies, registered in up to 31.9% when self-
196 reported [21].
197 Most of the admissions analysed were inpatient admissions, with a LOHS that decreased
198 over the study period. The injection of steroids appeared underrepresented in this
199 patient group; however, drugs registered herein did not necessarily coincide with acute
200 manifestations of this condition. A previous study in Spain indicated that cyclosporine
201 was the most frequent immunosuppressant [22].
202 The mean direct medical cost of specialised care of atopic dermatitis was €2469. A
203 significant increase was registered in patient costs between 2009 and 2010. The
204 diagnosis of several comorbid conditions increased between 2010 and 2013; however,
205 a causal relation cannot be confirmed since this raise could respond to an increased
206 registration rate of such conditions. In addition, mean unit costs of medical procedures
207 and for the treatment of conditions as declared by the Spanish Ministry of Health
208 increased over the study period: major and minor skin disorders had a mean cost of
209 €4164, €3997, €7829 and €5549 the years 2002, 2008, 2011 and 2015, respectively;
210 similarly, the treatment of bronchitis and asthma had a mean cost of €3913, €3799,
211 €4785 and €4240 the same years [23].

212 Overall, public expenditure on specialised care in Spain increased at least a 10% over the
213 past 20 years [24]. However, the direct medical cost of specialised care of atopic
214 dermatitis displayed a decreasing tendency between 2011 and 2017.
215 A number of limitations may have influenced the results of this study. The characteristics
216 of patients and comorbid conditions were limited to those registered in the database.
217 The analysis was limited by the ICD-9 and ICD-10 codification; for instance, all blood
218 examination procedures were clustered in a single code. The revision of pharmaceutical
219 interventions included all drugs in primary care registries, which impeded the evaluation
220 of interventions specific for acute or severe manifestations of atopic dermatitis; in
221 addition, medication was only available for the year 2017. Further studies will be
222 required to evaluate the indirect costs of this condition at the Spanish level.

223 5. Conclusions

224 The incidence of atopic dermatitis measured in specialised care centres was stable over
225 the study period, contrarily to the incidence reported by the Spanish Ministry of Health
226 in primary care centres. Direct medical costs of specialised care increased considerably
227 over the study period as a result of the increase of treatment costs of asthma and skin
228 disorders.

229 6. Declarations

230 ***Ethics approval and consent to participate***

231 Ethics committee approval and consent were not required for this study.

232 ***Data Availability Statement***

233 The data that support the findings of this study is available from the Spanish Ministry of
234 Health via the Unit of Health Care Information and Statistics (Spanish Institute of Health

Information) for researchers who meet the criteria for access to confidential data at https://www.mscbs.gob.es/estadEstudios/sanidadDatos/home.htm

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Declaration of financial and other interest

The authors declare that they have no competing interests.

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Papers of special note have been highlighted as:

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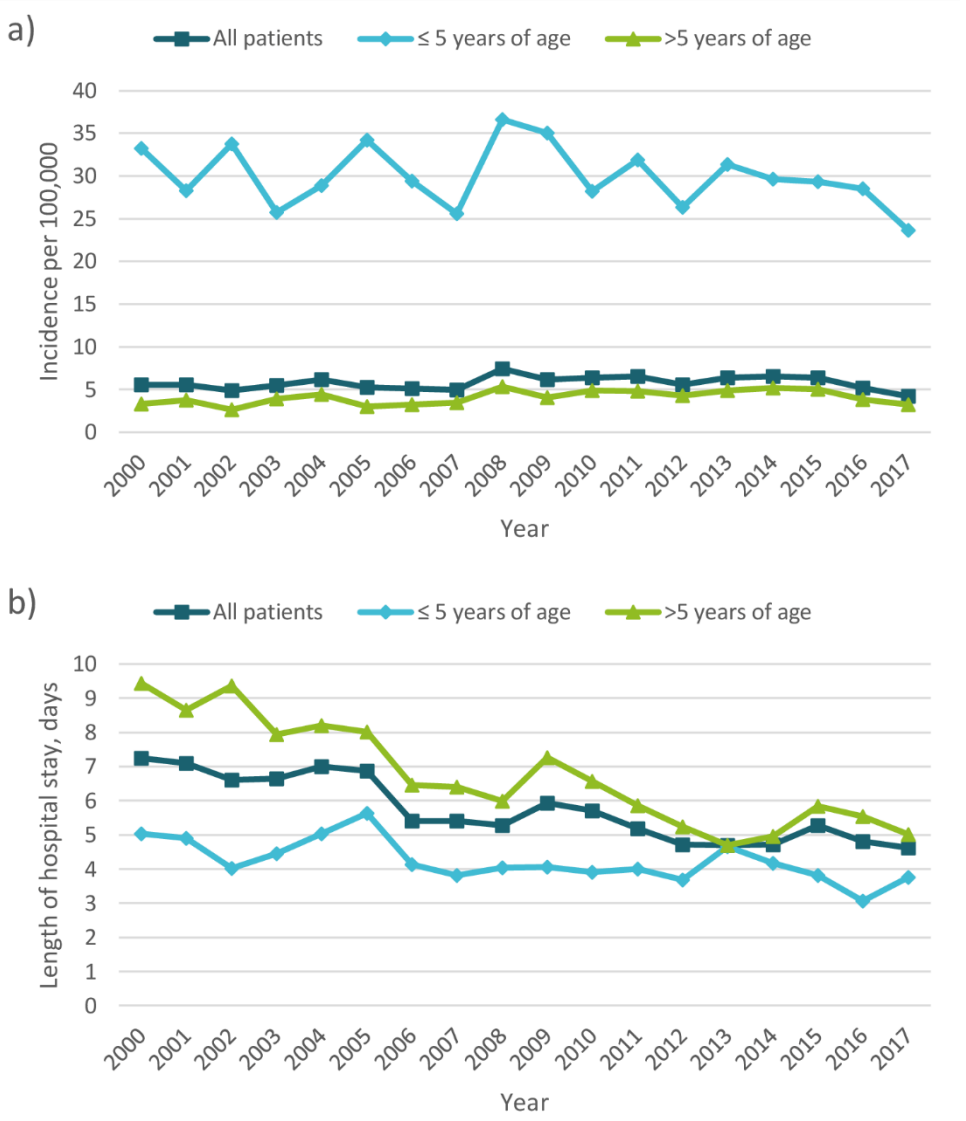
** of considerable interest

349 # 8. Figures

350 **Figure 1 (a) Hospital incidence of atopic dermatitis in Spain and (b) length of hospital**

351 **stay (2000-2017).**



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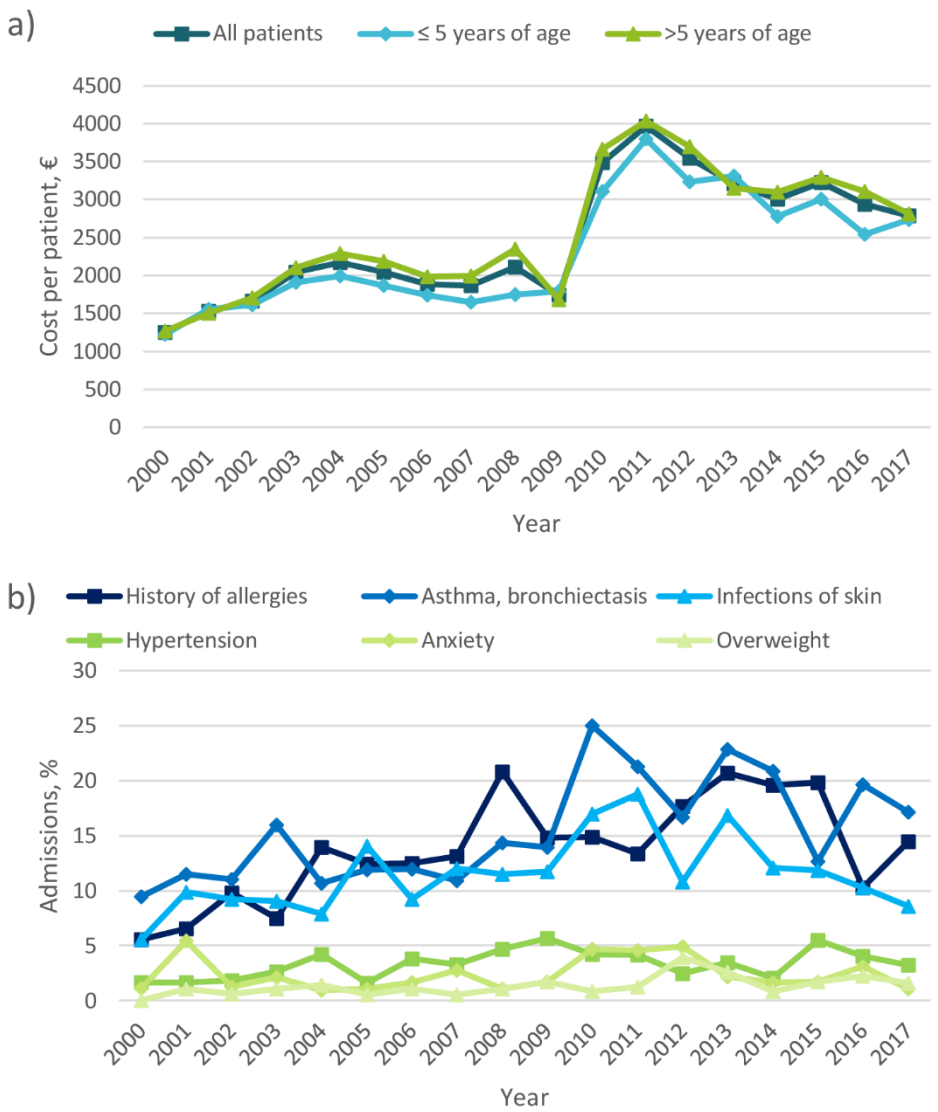
357 **Figure 2 (a) Direct medical cost per patient over time and (b) percentage of admissions**

358 **in which relevant comorbid conditions were diagnosed over time (2000-2017).**



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367 # 9. Tables

368 **Table 1 Patient characteristics registered upon admission (2000-2017).**

	All patients (N=3036)	≤ 5 years of age (N=1266)	> 5 years of age (N=1770)	p-value [a]
Admission number	3790	1412	2378	-
Males, %	56.6	59.5	54.6	0.0075
Mean age, years (range)	18.8 (0-99)	1.5 (0-5)	31.2 (6-99)	<0.0001
History of allergies (excluding medication), %	22.4	16.8	26.0	<0.0001
Asthma and bronchiectasis, %	15.7	2.6	24.3	<0.0001
Infections of skin and subcutaneous tissue, %	11.9	16.8	8.8	<0.0001
Bacterial infection, %	11.1	13.5	9.5	<0.0001
Other diseases of the upper respiratory tract, %	4.4	1.4	6.3	<0.0001
Essential hypertension, %	3.7	0.0	6.1	<0.0001
Anxiety disorders, %	2.3	0.1	3.8	<0.0001
Overweight and obesity, %	1.4	0.3	2.1	<0.0001

369 [a] ≤ 5 years of age vs. > 5 years of age.

370 **Table 2 Medical procedures and pharmaceutical interventions registered in patients**

371 **with atopic dermatitis (2000-2017).**

	All patients, %	Patients ≤ 5 years of age, %	Patients > 5 years of age, %
Urgent admissions	69.8	84.3	61.2
Mean length of hospital stay, days (range)	5.7 (0-74)	4.3 (0-37)	6.5 (0-74)
Readmission rate	6.4	5.9	6.7
Medical procedures	-	-	-
Microscopic examination of blood	20.6	30.6	13.1
Steroid injection	11.1	18.6	5.8
Antibiotic injection	10.8	12.1	9.6
Skin biopsies	6.8	14.3	1.6
Injection or infusion of other therapeutic or prophylactic substance	6.7	12.5	2.5
Diagnostic ultrasound of abdomen...	6.0	9.0	3.9
Routine chest x-ray, so described	5.8	11.3	1.7
Anatomic and physiologic measurements and manual examinations	4.8	5.1	4.5
Injection or infusion of immunoglobulin	4.1	9.8	0.2
Electrocardiogram	2.6	5.6	0.4
Pharmacological interventions	-	-	-
D06A – Antibiotics for topical use	4.9	8.7	4.2

D07A - Corticosteroids, plain	15.5	25.7	13.8
D07AC14 - Methylprednisolone aceponate	7.2	4.7	6.3
H02A – Corticosteroids for systemic use, plain	7.2	17.8	5.4
H02AB06 - Prednisolone	4.1	14.8	1.9
J01C – Beta-lactam antibacterial, penicillins	20.0	36.1	17.3
J01CA04 – Amoxicillin	12.2	25.0	9.3
J01CR02 – Amoxicillin and beta-lactamase inhibitor	8.8	11.6	8.1
M01A – Antiinflammatory and antirheumatic products, non-steroids	23.5	24.1	23.4
M01AE01 – Ibuprofen	17.6	20.2	16.5
N02B – Other analgesics and antipyretics	19.3	28.3	17.8
N02BE01 – Paracetamol	17.2	27.1	15.4
R03A – Adrenergics, inhalants	10.8	18.0	9.6
R03AC02 – Salbutamol	7.5	15.0	5.8
R06A – Antihistamines for systemic use	16.6	14.3	17.0