

Clinical Features and Disease Management in Adult Patients With Atopic Dermatitis Receiving Care at Reference Hospitals in Brazil: the ADAPT Study

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Abstract

Background: Atopic dermatitis is a chronic inflammatory skin disease with a prevalence of 0.02% to 8.1% in adults. Adult patients with moderate-to-severe atopic dermatitis are affected by frequent relapses and a significant disease burden.

Objective: To determine the clinical, immunological, and therapeutic profile of Brazilian adults with atopic dermatitis.

Methods: A multicenter, observational, retrospective, descriptive registry-based study was conducted at reference hospitals between December 2016 and October 2017. The data collected were demographics, personal and family history of atopic diseases, clinical manifestations, laboratory tests, disease severity and management.

Results: Of the 187 patients included in the analysis, 56.1% were female and 71.7% were White, with a mean age of 24.7 years. Mean follow-up was 9 years. Asthma or other allergic diseases were reported by 80.2% of patients. The main comorbidity was hypertension (10.2%), and common disease manifestations included pruritus and erythema. Lesions generally affected flexural and nonflexural areas, with typical morphology. Around 83% of patients had moderate-to-severe disease, and 8.6% reported at least 1 hospitalization. Most patients received topical and/or systemic pharmacological therapies, including omalizumab (5.9%); 4.3% received phototherapy. Moreover, 66.8% of patients received adjuvant therapy, and 79.1% changed or discontinued treatment for atopic dermatitis due to remission (46.5%), poor effectiveness (33.7%), or lack of adherence (12.9%). Most patients presented characteristics of type 2 inflammation, with immunoglobulin E levels above 100 IU/mL (94.4%) and peripheral blood eosinophils above 5% (55.9%).

Conclusion: Brazilian adult patients with severe atopic dermatitis need treatment to efficiently control the disease and improve quality of life.

Key words: Atopic dermatitis. Epidemiologic study characteristics. Disease management. Adult. Tertiary care centers.

Resumen

Antecedentes: La dermatitis atópica es una enfermedad inflamatoria crónica de la piel con una prevalencia, en adultos, del 0,02% al 8,1%. Los pacientes adultos con dermatitis atópica moderada o grave tienen reagudizaciones frecuentes y una sintomatología importante.

Objetivos: Describir las características clínicas e inmunológicas, así como las opciones terapéuticas de los pacientes brasileños adultos con dermatitis atópica.

Métodos: Estudio multicéntrico, observacional, retrospectivo, descriptivo y basado en registros, realizado en hospitales de referencia, entre diciembre de 2016 y octubre de 2017. Se recopilaron datos demográficos, antecedentes personales y familiares de enfermedades atópicas, manifestaciones clínicas, pruebas de laboratorio, gravedad y manejo de la enfermedad.

Resultados: De los 187 pacientes incluidos en el análisis, el 56,1% fueron mujeres y el 71,7% caucásicos, con una edad media de 24,7 años. La duración media del seguimiento fue de 9 años. El 80,2% de los pacientes referían asma u otras enfermedades alérgicas. La principal comorbilidad fue la hipertensión (10,2%) y las manifestaciones más frecuentes de la enfermedad fueron el prurito y el eritema. Las lesiones se distribuyeron tanto en flexuras como en áreas no flexurales, con una morfología típica. Alrededor del 83% de los pacientes tenían enfermedad moderada a grave y el 8,6% notificó al menos una hospitalización. La mayoría de los pacientes recibieron tratamientos

farmacológicos tópicos y/o sistémicos, incluyendo omalizumab (5,9%). El 4,3% recibió fototerapia. Además, el 66,8% de los pacientes recibió terapia adyuvante y el 79,1% cambió o suspendió el tratamiento para la dermatitis atópica debido a la remisión (46,5%), poca efectividad (33,7%) o falta de adherencia terapéutica (12,9%). La mayoría de los pacientes presentaron características de inflamación tipo 2, con niveles de inmunoglobulina E superiores a 100 UI/ml (94,4%) y cifras de eosinófilos en sangre periférica superiores al 5% (55,9%).

Conclusión: Los pacientes brasileños adultos con dermatitis atópica necesitan tratamiento continuo para controlar la enfermedad de manera eficiente y mejorar la calidad de vida.

Palabras clave: Dermatitis atópica. Adulto. Estudio epidemiológico. Tratamiento. Hospital terciario.

Introduction

Atopic dermatitis (AD) is a chronic inflammatory disease with an estimated global prevalence of 0.02%-8.1% in adults [1-4]. Epidemiologic data show that the prevalence, clinical presentation, and severity of AD vary between different populations, as does access to health care and treatment. These variations reflect multifactorial interactions between genetic, immune, and environmental features of the disease [3-8].

As a predominantly pediatric dermatosis, AD and the burden it generates during adolescence and early adulthood are poorly characterized. This disease can be persistent, with an early onset or first manifest late during adulthood [2,9]. Adult patients with moderate-to-severe AD may have frequent recurrences, with a marked impact on quality of life, affecting personal, family, and social dimensions [10].

In Brazil, a comprehensive characterization of the adult population with AD is limited. Three Brazilian studies described the profile of adults with skin disorders and the impact of their disease on quality of life [11-13] and found that both patient journey and disease management are very challenging. Adult patients with AD present heterogeneous and relapsing-remitting disease due to triggering factors, infections (eg, by *Staphylococcus aureus*), and other allergic/atopic comorbidities (eg, asthma) [14-15].

Clinical guidelines for diagnosis and treatment of AD have been published in Brazil [16,17]. Relapses can be controlled with topical corticosteroids and calcineurin inhibitors, in addition to adjuvant treatment for pruritus [18]. Second-line therapies include phototherapy and systemic immunosuppressants (eg, oral cyclosporine, methotrexate). Recently, immunobiological and targeted disease-modifying therapies were developed to provide effective control of moderate-to-severe AD [19,20].

Hence, it is crucial to understand the clinical course of AD and how to improve its management in adults, especially those with refractory forms of the disease. This epidemiological registry-based study aimed to examine the clinical, immunological, and therapeutic characteristics of adult patients with AD receiving care at tertiary institutions in Brazil.

Methods

Patients and Study Design

This multicenter, observational, retrospective, descriptive registry-based study was conducted between December 2016

and October 2017. Adult participants with AD were followed in 7 reference hospitals in southern and southeastern Brazil (Paraná, São Paulo, and Rio de Janeiro). Data were collected from the medical records of patients who had been receiving care at the hospital for at least the previous 36 months. The selection criteria required that participants had attended at least 3 visits to the site during the retrospective study period, including the admission visit (designated as the first visit), an intermediate follow-up visit during the previous 36 months, and a final visit within the 12 months before entering the study (designated as the last visit). The local ethics committees approved the study protocol, and all procedures complied with the Declaration of Helsinki and Good Epidemiological Practices. Eligible patients who met the selection criteria described in Table 1 were enrolled retrospectively and consecutively to minimize possible selection bias.

Study Outcomes

The primary outcome measure was the distribution of demographic and clinical features and disease management of adult AD patients who had received care within the previous 36 months at the participating sites. Data were retrospectively collected, as follows: demographics (age, sex, and ethnicity); personal and family history of AD; and clinical characteristics

Table 1. Selection Criteria for Patients in the ADAPT Study

Inclusion Criteria
– Age >18 years (at enrollment)
– Participants receiving care at the hospital in the previous 36 months (at least)
– Diagnosis of AD in the previous 36 months
– Participants who attended at least 3 visits to the site during the retrospective study period (ie, admission visit, intermediate follow-up visit during the last 36 months, and a final visit within 12 months before study entry)
Exclusion Criteria
– Other severe skin conditions not related to AD that may have affected AD management (according to investigator criteria)
– Primary or secondary immunodeficiency with skin manifestations similar to AD
– Patients who participated in clinical trials during the last 36 months that may have affected management of AD

(age of onset, lesion distribution and morphology, comorbidities and/or laboratory changes, manifestations, and severity).

We assessed the severity of AD by applying the following scores: SCORing Atopic Dermatitis (SCORAD), 5-point Investigator's Global Assessment (IGA) Scale, and the Eczema Area and Severity Index (EASI) [21-25]. We also took into account the investigator's assessment of severity. All scales had been previously translated into Portuguese and validated for the Brazilian population. Our Overall Severity AD Index was determined as the highest degree of severity among all available assessments for each patient during the study. Severity assessed with each scale was determined at different time points.

Regarding disease management and treatment, we assessed the number of hospitalizations due to AD, the mean length of stay per patient, the mean follow-up time, and the number of medical appointments per patient. We also collected information on the AD treatments prescribed and other adjuvant therapies for AD. Patients were also characterized according to their immune response profile [26], considering as elevated IgE levels >100 IU/mL (measured using nephelometry or fluoroenzymatic assay) and peripheral blood eosinophil counts >5% [13] during the previous 36 months.

Sample Size

Given the descriptive nature of this study, the sample size was calculated to ensure a robust and representative population. Assuming losses of approximately 15%, a total of 200 patients were required to achieve 171 eligible patients. This estimation was based on an expected rate of hospitalizations of 56% [13], considering a 95%CI and a margin of error of less than 7.5%. The sample size was computed using nQuery Advisor, version 7.0.

Statistical Analysis

Multiple answers were allowed for most of the collected data, implying that more than 1 option could be reported for the same patient. For descriptive options, such as "Other", terms were analyzed using a standard approach, according to the Medical Dictionary for Regulatory Activities. All results were summarized as number (nonmissing data), mean, standard deviation, minimum and maximum values for continuous variables, and counts and percentages for categorical variables. All analyses were conducted using SAS, version 9.4.

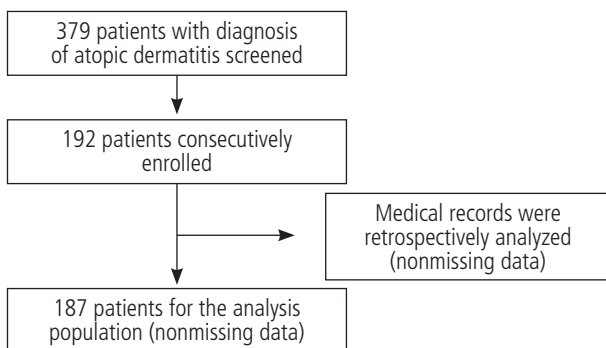


Figure 1. Flow chart of the study population.

Results

Study Participants

Of the 192 patients enrolled, 5 (2.6%) were excluded from the analysis due to missing data, with the analysis population comprising 187 patients (Figure 1).

Table 2. Demographic Data, Family and Personal History of Atopic Dermatitis (AD), and Asthma or Allergic Disease of the Study Patients^a

Characteristics of AD Patients	n = 187
<i>Demographic data</i>	
Age (years) ^b	
Mean (SD [95%CI]) age at first visit	24.7 (13.4 [22.8-26.6])
Mean (SD [95%CI]) age at last visit	33.7 (13.0 [31.9-35.6])
Sex, No. (%)	
Male	82 (43.9%)
Female	105 (56.1%)
Ethnicity, No. (%)	
White	134 (71.7%)
Mixed	21 (11.2%)
Black	12 (6.4%)
Asian	1 (0.5%)
Missing data	19 (10.2%)
<i>Family and personal history of AD</i>	
Onset of AD	
Age (years), mean (SD [95%CI])	13.1 (13.6 [10.9-15.3])
Median age (range), y	7.0 (0.5-59)
Missing data	45 (24.1%)
Family history of AD, asthma or allergic disease	
Patients with family history of any	
allergic disease	70 (37.4%)
Allergic rhinitis	44/70 (62.8%)
Asthma	36/70 (51.4%)
Atopic dermatitis	18/70 (25.7%)
Other ^c	5/70 (7.1%)
No family history	5 (2.7%)
Missing data	112 (59.9%)
Personal history of asthma or allergic disease	
Patients with personal history of asthma or any allergic disease	
Allergic rhinitis	150 (80.2%)
Asthma	125/150 (83.3%)
Conjunctivitis	96/150 (64.0%)
Food allergy	13/150 (8.6%)
Other ^d	7/150 (4.6%)
22/150 (14.6%)	
No personal history	2 (1.1%)
Missing data	35 (18.7%)

Abbreviation: AD, atopic dermatitis.

^aMultiple answers were allowed during the data collection. Missing data or unknown responses were not considered for calculation of the percentage (unless otherwise specified).

^bIf "<1", then age was set as "0.5".

^cOther: Drug hypersensitivity (1.1%), anxiety disorder (0.5%), and contact dermatitis (0.5%).

^dOther: Contact dermatitis (2.7%), drug hypersensitivity (2.1%), and angioedema (1.6%).

Table 3. Comorbidities and Laboratory Changes in the Study Population, at the First Visit and During the Last 36 Months^a

Comorbidities and Laboratory Changes	First Study Visit	Last 36 Months n = 187 Patients
Any comorbidity and/or laboratory change	40 (21.4%)	46 (24.6%)
Hypertension	10 (5.3%)	19 (10.2%)
Diabetes mellitus	4 (2.1%)	9 (4.8%)
Mood disorders (depression, anxiety, suicidal ideation)	7 (3.7%)	5 (2.7%)
Change in renal function	1 (0.5%)	1 (0.5%)
Change in hepatic function	0 (0.0%)	1 (0.5%)
Other ^b	37 (19.8%)	36 (19.3%)

^aMultiple answers were allowed during the data collection. Missing data or unknown responses were not considered for calculation of the percentage (unless otherwise specified).

^bOther comorbidities: at first visit, allergic rhinitis (4.3%), asthma (2.1%), contact dermatitis (2.1%); at last visit, contact dermatitis (4.3%), blood cortisol decrease (1.1%), keratoconus (1.1%), neurodermatitis (1.1%), and primary adrenal insufficiency (1.1%).

Among this analysis population, 105 (56.1%) were women and 134 (71.7%) were White. The mean (SD) age at enrollment was 24.7 (13.4) years (range, 18-69.5 years). Patient demographics, as well as family and personal history of AD, asthma, and allergic diseases are presented in Table 2. Four women (3.8%) were pregnant at enrollment or during the study. The mean age at onset of AD was 13.1 years, and the condition started between the ages of 1 and 7 years in 57 patients (38.8%).

Seventy patients (37.4%) had a family history of allergic rhinitis (62.8%; 44/70), asthma (51.4%; 36/70), and atopic dermatitis (25.7%; 18/70). Regarding the personal history, 150 patients (80.2%) had mainly allergic rhinitis (83.3%; 125/150), asthma (64.0%; 96/150), conjunctivitis (8.6%; 13/150), and food allergy (4.6%; 7/150). The proportion of patients who had at least 1 comorbidity and/or laboratory changes increased by 3.2% between the first and last study visits (Table 3).

Clinical Characterization of AD

Data on the distribution and morphology of skin lesions were collected retrospectively from medical records at the first and last visits, within 36 months of follow-up. All patients (100%) had at least 1 type of skin lesion at the first visit, compared with 181 patients (96.8%) at the last visit (note that each patient could present more than 1 condition). Most skin lesions were nonflexural and flexural (Table 4). Nonflexural lesions were located mostly on the legs, trunk, and arms. Among affected patients, 17 (9.1%) (first visit) and 15 (8.0%) (last visit) also had lesions on extensor surfaces that were equally distributed between the elbows and knees. Flexural lesions were distributed mainly on the popliteal, antecubital, and neck areas.

Regarding morphology, most lesions were typical, with a lichenified/exudative eczematous pattern (Figure 2).

AD manifestations (any kind) were reported by 162 patients (86.6%) at the first visit and by 149 (79.7%) at the last visit. The main manifestations, including pruritus, erythema, and dry skin, are described in Figure 3.

To determine the severity of AD, a total of 941 assessments were performed, including 1 of the 5 scoring options mentioned

Table 4. Distribution of Skin Lesions on the Body at the First Visit and During the Last 36 Months^a

Location of Skin Lesions	First Study Visit	Last 36 Months No. (%)
Patients with some kind of lesion	187 (100%)	181 (96.8%)
Missing data	44 (23.5%)	53 (28.3%)
Flexural	92 (49.2%)	70 (37.4%)
Popliteal	64 (34.2%)	50 (26.7%)
Antecubital	65 (34.8%)	42 (22.5%)
Neck	38 (20.3%)	31 (16.6%)
Ankles	12 (6.4%)	19 (10.2%)
Axillae	13 (7.0%)	14 (7.5%)
Wrists	13 (7.0%)	13 (7.0%)
Extensors	17 (9.1%)	15 (8.0%)
Nonflexural	114 (61.0%)	101 (54.0%)
Legs	65 (34.8%)	53 (28.3%)
Trunk	55 (29.4%)	45 (24.1%)
Arms	55 (29.4%)	41 (21.9%)
Face	45 (24.1%)	36 (19.3%)
Eyelids	19 (10.2%)	16 (8.6%)
Hands	10 (5.3%)	22 (11.8%)
Feet	13 (7.0%)	14 (7.5%)
Ears	13 (7.0%)	6 (3.2%)
Lips	7 (3.7%)	9 (4.8%)
Scalp	5 (2.7%)	8 (4.3%)
Nipples	7 (3.7%)	6 (3.2%)
Retroauricular area	5 (2.7%)	6 (3.2%)
Anogenital	2 (1.1%)	3 (1.6%)
Others	19 (10.2%)	14 (7.5%)

^aMultiple answers were allowed during data collection. Missing data or unknown responses were not considered for calculation of the percentage (unless otherwise specified).

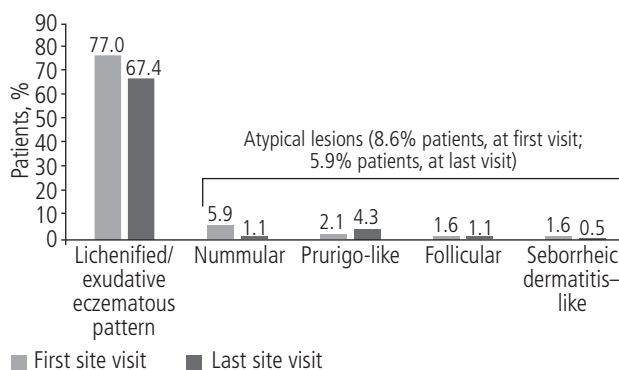


Figure 2. Clinical characteristics of atopic dermatitis lesions in ADAPT patients.

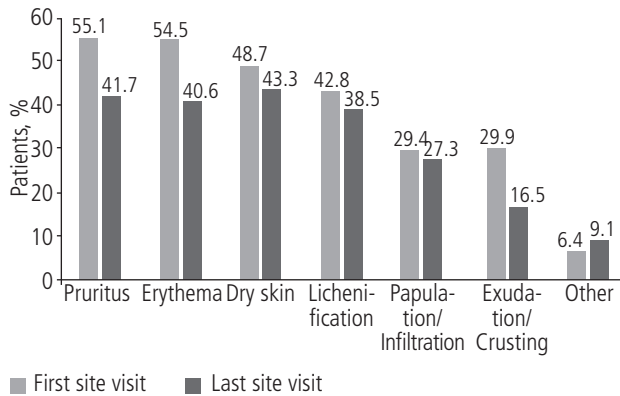


Figure 3. Manifestations of atopic dermatitis in the study population, considering the first and the last visits of the study period (percentage of patients). Percentages were calculated with $N_{total} = 187$ as the denominator. ("Other" includes skin exfoliation, skin hyperpigmentation, and excoriation).

in the Methods section. According to the Overall AD Severity Index, defined as the worst severity obtained among the scores applied to each patient, 27 patients (16.9%) were classified as mild, 28 (17.5%) as moderate, and 105 (65.6%) as severe. Among the subpopulation using immunosuppressants, 48.5% of patients were classified as severe. The investigator classification available in medical records was used to assess severity in 137 patients (73.3%) (799 measurements) and the SCORAD was used in 98 patients (52.4%) (280 measurements). IGA and EASI scores were available for 31 patients (16.6%) and 32 patients (17.1%), respectively. Nonetheless, IGA (total measurements, 148) was used more frequently than EASI (total measurements, 48). AD severity scores, defined as the worst score during the study period, are presented in Table 5.

Disease Management and Treatment

Patients were followed for approximately 9 years. Sixteen patients (8.6%) were hospitalized at least once because of AD, and 2 of these were hospitalized more than once (Table 6).

Patients received both pharmacological and nonpharmacological treatments for AD, in addition to adjuvant therapies for complications of the disease. Each patient could receive more than 1 treatment. Topical treatments were prescribed for 183 patients (97.9%) and systemic treatments for 171 (91.4%); 183 patients were simultaneously taking more than 1 treatment during the course of the study. Immunobiological therapies were prescribed to 17 (9.1%) patients, including 5.9% of patients receiving anti-IgE therapy with omalizumab, and phototherapy was indicated in 8 patients (4.3%). Most patients received systemic and/or topical pharmacological therapy (Figure 4). Topical treatments were mainly corticosteroids (88.2%, 165/187) and emollients (85.6%, 160/187), while the most frequently used systemic disease-modifying treatment was oral corticosteroids (32.6%, 61/187). Seventy patients took systemic corticosteroids (oral corticosteroids, 61; injectable corticosteroids, 4; and a combined formulation of corticosteroid with antihistamine, 5).

Table 5. Scores of Severity of Atopic Dermatitis (AD) During the Entire Study

Severity Scores	n = 187 Patients
Patients with at least one recorded evaluation of AD severity; No of measurements	160 (85.6%); 941
Patients with any data on need of immunosuppressant therapy	165 (88.2%)
Severity score, n/N1 (%) ^a	
No assumption of severity score	85/165 (51.5%)
Severe	80/165 (48.5%)
Investigator classification available in the medical records	137 (73.3%)
Severity score, n/N1 (%) ^a	
Mild	30/137 (21.9%)
Moderate	35/137 (25.5%)
Severe	72/137 (52.6%)
SCORAD ^b	98 (52.4%)
Severity score, n/N1 (%) ^a	
Mild (<25)	13/98 (13.3%)
Moderate (25-50)	38/98 (38.8%)
Severe (>50)	47/98 (48.0%)
IGA ^c	31 (16.6%)
Severity score, n/N1 (%) ^a	
Clear (no inflammatory signs of AD)	0/31 (0.0%)
Almost clear (just perceptible erythema, and just perceptible papulation/infiltration)	2/31 (6.5%)
Mild (mild erythema and papulation/infiltration)	4/31 (12.9%)
Moderate (moderate erythema and papulation/infiltration)	9/31 (29.0%)
Severe (severe erythema and papulation/infiltration)	7/31 (22.6%)
Very severe (very severe erythema and papulation/infiltration)	9/31 (29.0%)
EASI ^d	32 (17.1%)
Severity score, n/N1 (%) ^a	
Clear (0)	0/32 (0.0%)
Almost clear (0.1-1.0)	0/32 (0.0%)
Mild (1.1-7.0)	8/32 (25.0%)
Moderate (7.1-21.0)	13/32 (40.6%)
Severe (21.1-50.0)	8/32 (25.0%)
Very severe (50.1-72.0)	3/32 (9.4%)

^aAD severity defined as worst score during the entire study period, based on the total number of patients who completed the score.

^bSCORAD, Scoring Atopic Dermatitis. SCORAD values ranged from 0 to 96 in the present study.

^cIGA, Investigator Global Assessment scale.

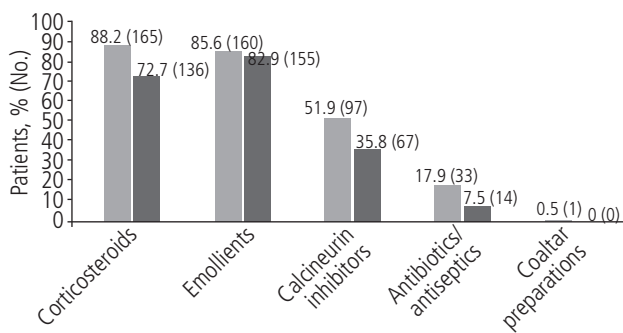
^dEASI, Eczema Area and Severity Index. EASI values ranged from 3 to 57 in the present study.

Of the 66 patients who took oral corticosteroids/oral corticosteroid combined with antihistamine in the same formulation, data on treatment duration were available for 51 patients. Duration of oral corticosteroid treatment varied widely, from 3 to 1765 days, with a mean duration of 65.4 (208.3) days and a median duration of 15 (6.7-31) per course.

Table 6. Management of AD Including Medical Appointments and Hospitalizations During the Study

Management of AD	n = 187 Patients
Mean (SD) total follow-up period, mo	108.4 (64.9)
Mean (SD [range]) number of medical appointments	10.1 (5.6 [2-28])
Mean (SD [range]) time between medical appointments, mo	6.7 (6.7 [1.3-36])
Patients with at least 1 hospitalization	16 (8.6%)
Mean (SD [range]) duration of hospitalization per patient, d	5.8 (6.3 [1-23])

A



B

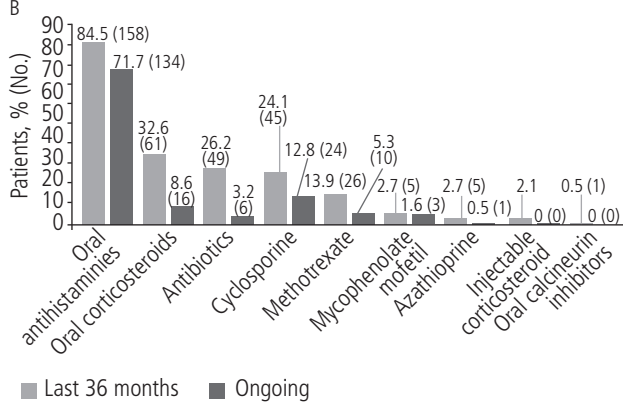


Figure 4. Pharmacological treatment for atopic dermatitis (A, Topical; B, Systemic) administered over the last 36 months and ongoing prescriptions at the last study visit. Percentages were calculated with $N_{\text{total}} = 187$ as the denominator.

Oral anti- H_1 antihistamines were also used by most patients (84.5%, 158/187) to control AD symptoms.

Regarding nonpharmacological treatment, 22 (11.8%) patients received other therapies or psychological support, including psychotherapy (95.4%, 21/22), participation in AD support groups (18.1%, 4/22), and psychiatric monitoring (4.5%, 1/22). Additionally, 125 (66.8%) patients were prescribed adjuvant therapy for complications associated with AD (Figure 5).

As presented in Figure 6, 148 patients (79.1%) discontinued or switched AD treatment, mainly due to disease remission

(46.5%, 87/187), poor effectiveness (33.7%, 63/187), or lack of adherence (12.9%, 24/187). Other reasons (13.9%, 26/187) included treatment time (5.3%, 10/187), dose reduction (2.7%, 5/187), and drug shortage (1.6%, 3/187). It should be highlighted that patients could have 1 or more reasons to stop or change pharmacological treatment of AD.

Not all patients stopped pharmacological therapies for AD during the study. For instance, 144 patients (77.0%) maintained topical corticosteroids, with a mean duration of 41.3 months per patient, and 77 (41.2%) were taking topical calcineurin inhibitors for a mean duration of 33.2 months per patient. As for systemic therapies, 45 participants (24.1%) were treated with cyclosporine for an average of 13.2 months per patient and, lastly, 25 participants (13.4%) were treated with methotrexate for an average of 7.9 months per patient.

Immune Pathway of AD Patients

Laboratory findings of 89 patients with at least 1 registered measure were assessed to define the immune profile of AD patients (Table 7). Of those, 84 (94.4%) presented IgE levels >100 IU/mL, while 76 (64.4%) had eosinophil counts $>5\%$.

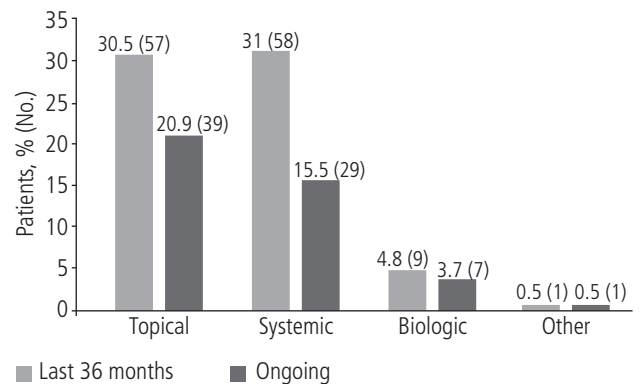


Figure 5. Adjuvant treatment for complications of atopic dermatitis administered over the last 36 months and ongoing prescriptions at the last study visit. Percentages were calculated with $N_{\text{total}} = 187$ as the denominator.

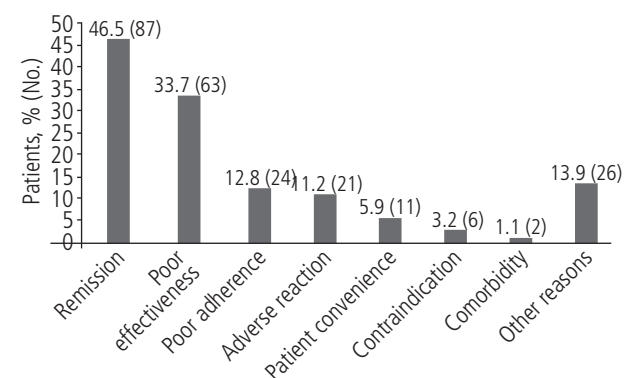


Figure 6. Reasons for stopping or changing pharmacological treatment for atopic dermatitis. Percentages were calculated with $N_{\text{total}} = 187$ as the denominator.

Table 7. Analyses of Total IgE and Peripheral Blood Eosinophils, in the Last 36 Months and at the Most Recent Study Visit

Immunological Parameters	Last 36 Months ^a n = 187 Patients	Last Measurement ^b n = 187 Patients
Serum total IgE, IU/mL		
Any measurement (Patients; No. [%])	89 (47.6%)	
IgE >100 IU/mL, (n/N1) ^c	84/89 (94.4%)	
Mean IgE (95% CI)	13 316.3 (8232.4-18 400.3)	10 688.9 (6006.9-15 370.9)
Median (range)	5000.0 (2-184 000)	3133.0 (2-184 000)
Eosinophil counts (%)		
Any measurement (Patients; No. [%])		118 (63.1%)
Blood eosinophilia >5%	76 (64.4%)	66 (55.9%)
Mean value (95% CI)	9.6 (8.1-11)	7.6 (6.3-8.9)
Median (range)	7.9 (0-47.1)	5.4 (0-45.6)

^aHighest value observed.

^bValue collected during the most recent study visit.

^cn/N1 = number of patients who met the laboratory criterion/ number of patients assessed.

Considering the last registered value, 66 patients (55.9%) showed increased levels of eosinophils (>5%). The results suggested that most patients presented characteristics indicating type 2 immune pathway activation [26,27].

Discussion

Adults with AD frequently experience intense flare-ups due to lack of disease control [10]. AD is often chronic, with a low decrease in prevalence (1%) after the age of 12 [28]. Several studies report a high patient burden and a relevant impact on mental health, work absenteeism, and daily activities [29-31], similar to psoriasis [32]. Effective treatments lead to lower discontinuation rates and fewer adverse effects, while their absence represents an unmet need in patients with AD, especially those with moderate-to-severe disease. Hence, optimization of both patient journey and disease course must become a priority for adult patients.

The ADAPT study sought to define the characteristics of adults with AD in terms of demographic and clinical features, disease management, and laboratory findings. Most patients were female and White, with a mean age of 24.7 years. These characteristics were similar in patients from Europe, the USA, and Canada, where the prevalence of AD was higher in adults aged 25 to 44 years and in females [1]. Around 80% of the patients had a personal history of asthma and/or allergic rhinitis, although only 37.4% reported a family history of AD, asthma, or allergic disease. These characteristics were comparable to those of other populations, where most adults had an associated respiratory disease (asthma, rhinitis, or both) [13,33]. Approximately 21% of patients had at least 1 comorbidity, mainly hypertension and/or changes in laboratory values. Our results are consistent with those of an Italian population-based study, in which hypertension was also frequent (7.1%) [33], and with a Spanish study that showed high associated morbidity, especially hypertension, in adults with severe AD (37.6%) [3].

The frequency of hypertension in our study (10.2%) was lower than the prevalence reported in adults from the general population in Brazil (30.5%-52.5%) [34,35]. However, adult patients with AD in the present study were younger (mean age, 24.7 years) than those included in studies of hypertension in the general Brazilian population (median age of 41 and mean age of 52 years) [34,35]. A systematic review of 40 studies comprising over 120 000 individuals (mostly aged ≥ 18 years) estimated the prevalence of hypertension in Brazil to be 28.7% (95%CI, 26.2-31.4) [36]. In the French population, common comorbidities in AD patients included atopic, allergic, autoimmune, and cardiovascular diseases [14].

In our study population, the skin lesions presented mainly a lichenified/exudative eczematous pattern. Such lesions were described as a distinct form in adults with AD, although adults may characteristically present heterogeneous mixed forms of pediatric AD [2]. In an Italian cohort, flexural lesions (upper limbs) were more frequent (47.8%), followed by lesions on the eyelid and periocular area, with an erythematous-desquamative pattern (74.3%) [33]. The distribution of nonflexural rash and atypical morphology are also common in adults, for example, on the head and neck or extensor surfaces of the limbs and trunk [2,14,31]. In our study, flexural rash was mostly distributed on the popliteal, antecubital, and neck areas, while nonflexural rash was generally present on the legs, arms, and trunk. Furthermore, clinical features may vary according to age, age of disease onset, and characteristics of acute/chronic AD [14]. Patients with persistent AD (pre-adult onset) show increased disease severity, intensity of pruritus, and comorbidities (eg, hypertension), compared with adult-onset AD [33]. In addition, the location of skin lesions might vary according to age of onset [37]. Patients in the ADAPT study mainly had pre-adult onset AD, with a mean age of onset of 13.1 years, which is comparable to data reported elsewhere [30,37].

Our findings are in line with those of previous studies on the manifestations of AD, since pruritus, erythema, and dry skin were reported by most patients [1,30,38]. A slight

variance was found between patients who reported pruritus (55.1% at the first visit; 41.7% at the last visit) and dry skin (48.7% at the first visit; 43.3% at the last visit). This difference might reflect a variation in patient perception about how such major symptoms impact their daily activities [30]. Our results also demonstrated that 83.1% had moderate-to-severe disease, as assessed using 5 different scores. Of these, only the SCORAD index includes 2 patient-reported outcomes, which are related to pruritus and impact on sleep [30]. This high proportion of patients with moderate-to-severe disease should be interpreted with caution, as the study population included patients followed in tertiary care, who present a more severe disease form. Differences in the severity of AD were observed in other countries, with France, Italy, Japan, and Spain reporting higher proportions of mild AD, while Canada, Germany, and the USA reported higher scores of severe AD [1]. Additionally, in a multicenter study from Spain, 41.6% of the adults diagnosed with moderate-to-severe AD had poor disease control [10].

Regarding disease management, it should be highlighted that after 9 years of follow-up, 16 (8.6%) patients had been hospitalized at least once owing to AD. Compared with another study of Brazilian patients, where 56% had been hospitalized at least once since diagnosis [13], our study reported a lower number of hospitalizations. Nonetheless, an increased use of health care resources has been outlined in other populations with AD [29,39].

In Brazil, patients with severe AD need more effective therapies and well-established treatment goals to improve their care. In the ADAPT study, we characterized the treatment patterns of Brazilian patients with AD and found that, overall, most patients received systemic and/or topical pharmacological therapy, followed by immunobiological treatments (eg, omalizumab) and phototherapy. In other studies assessing therapeutic trends in AD, patients frequently used topical pharmacological treatments, such as corticosteroids, calcineurin inhibitors, and antihistamines [10,33,39]. A relevant percentage of ADAPT patients (36.2%) received oral corticosteroids, as reported in other real-life studies [13,30,33,39]. Despite this evidence, oral corticosteroids are recommended in treatment guidelines only for a short period to control severe exacerbations [19,20]. Oral corticosteroids can be prescribed through a family physician or taken as self-medication, which is possible in Brazil [40]. A recent global survey found that AD was generally diagnosed by dermatologists, but also by a family physician or, eventually, by the patient him/herself [1]. Only 48.2% of patients who self-diagnosed with AD had their diagnosis confirmed by a physician [1]. In our study, oral antihistamines, frequently administered to manage pruritus [19], were the most used systemic treatment (84.5%).

According to guidelines, systemic treatments, including corticosteroids and cyclosporine, have limited indications for AD and may not be suitable for long-term use, potentially due to serious adverse effects [20]. In the ADAPT study, adverse reaction was the reason for stopping or changing any pharmacological treatment for AD in 11.2% of patients. Most importantly, patients discontinued or switched AD treatment due to poor effectiveness (33.7%) and lack of adherence (12.8%). Still, almost half of the patients stopped treatment

due to remission. Comparison of the duration of topical and systemic treatments revealed that 77.0% of patients maintained treatment with topical corticosteroids, while only 24.1% maintained treatment with cyclosporine. Besides pharmacological treatment, approximately 12% of patients were receiving psychological support, thus highlighting the burden of this disease.

Finally, considering that IgE and eosinophil cut-offs were >100 IU/mL and >5%, respectively, most patients presented characteristics of type 2 inflammation [27]. Extrinsic AD is characterized by a predominant type 2 immune response, defined by a T_H2 - and ILC-2-based pathophysiology, as well as IgE-mediated sensitization [41,42]. Eosinophilia is also present in areas of skin inflammation, resulting from secretion of cytokines and other proinflammatory mediators. Our results suggest extrinsic-type AD, which is characterized by elevated IgE levels and high eosinophil blood counts [3,13]. A positive correlation has been reported between disease severity and blood eosinophil counts and high serum IgE levels [13]. Therefore, controlling this immune response is of the utmost importance for preventing exacerbations, particularly in patients with moderate-to-severe AD.

Despite its epidemiologic significance, this study presents limitations inherent to its design and retrospective nature. Since data were collected from different types of medical charts and participating sites, data were missing in some cases, and inconsistencies were found in the information collected. In addition, we did not evaluate the efficacy of treatment modalities, or whether patients were also taking other medications for respiratory comorbidities. Based on this registry study, future prospective studies could incorporate quality of life measurements and apply patient-reported outcomes to assess patient perspectives on disease burden and use of health care resources.

Conclusion

When managing adult patients with AD, we need to consider several issues, such as substantial use of systemic corticosteroids, presence of multiple comorbidities, and need for psychological and mental health support. New investigations should focus on patients with moderate-to-severe AD, for whom more effective and targeted treatments may improve disease control and quality of life and reduce healthcare costs.

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Conflicts of Interest

L Karla Arruda: Investigator for the ADAPT Study (Sanofi); Speaker for Sanofi, Novartis, Shire, and Chiesi at medical conferences.

Ariana C Yang: Investigator for the ADAPT Study (Sanofi); Speaker for Sanofi and Danone.

Valéria Aoki: Investigator for the ADAPT Study (Sanofi).

Roberta FJ Criado: Investigator for the ADAPT Study (Sanofi); Speaker for Novartis, and GlaxoSmithKline.

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