ORIGINAL ARTICLE

Prevalence, Burden, and Risk Factors of Atopic Eczema in Schoolchildren Aged 10-11 Years: A National Multicenter Study

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Abstract

Background: Little is known about the epidemiology of atopic eczema (AE), and studies from the Mediterranean region and the Middle East are limited.
Objective: We investigated the frequency, burden, and risk factors of AE in a developing country.
Methods: The International Study of Asthma and Allergies in Childhood Phase II questionnaire was used to survey a representative sample of 10 to 11-year-old children in Turkey. Children were examined by allergists, and parents completed standardized questionnaires.
Results: Among 6755 children, the prevalence of having eczema during one's lifetime or currently was 17.1% and 8.1%, respectively. The prevalence of visits to the doctor, nocturnal awakening, school absenteeism, and drug usage was 36.3%, 56%, 9.7%, and 28.7%, respectively. Associated factors were current rhinoconjunctivitis (odds ratio [OR], 2.53; 95% confidence interval [CI], 1.99-3.21), current wheezing (OR, 2.10; 95% CI, 1.58-2.79), family history of allergic disease (OR, 1.62; 95% CI, 1.21-2.18), low birth weight (OR, 1.79; 95% CI, 1.08-2.94), and exposure to animals in the first year of life (OR, 1.47; 95% CI, 1.06-2.03).
Conclusions: In a developing Mediterranean country, the prevalence of AE is comparable to that of developed countries in the same region and lower than that observed in developed countries elsewhere. The course of the disease and risk factors of AE probably differ in developing countries.

Key words: Atopic eczema. Atopy. Allergy. Prevalence. Burden. Children. Risk factors. Epidemiology. Treatment. ISAAC.

Resumen

Antecedentes: No se dispone de muchos datos sobre la epidemiología del eccema atópico (EA) y los estudios llevados a cabo en la región del Mediterráneo y Oriente Medio son limitados.
Objetivo: Se investigaron la frecuencia, la carga y los factores de riesgo del EA en un país en desarrollo.
Métodos: Se utilizó el cuestionario de la fase II del estudio ISAAC para entrevistar a una muestra representativa de niños de entre 10 y 11 años en Turquía. Los niños fueron examinados por alergólogos y los padres rellenaron los cuestionarios estandarizados.
Resultados: En 6.755 niños, la frecuencia de padecer eccema a lo largo de la vida o en el momento del estudio fue del 17,1% y el 8,1%, respectivamente. La frecuencia de visitas al médico, despertar nocturno, absentismo escolar y uso de fármacos fue del 36,3%, 56%, 9,7% y 28,7%, respectivamente. Los factores asociados fueron la rinoconjuntivitis existente (oportunidad relativa [OR]: 2,53; intervalo de confianza [IC] del 95%: 1,99-3,21), las sibilancias existentes (OR: 2,10; IC del 95%: 1,58-2,79), los antecedentes familiares de enfermedad alérgica (OR: 1,62; IC del 95%: 1,21-2,18), el bajo peso al nacer (OR: 1,79; IC del 95%: 1,08-2,94) y el contacto con animales durante el primer año de vida (OR: 1,47; IC del 95%: 1,06-2,03).
Conclusiones: En un país mediterráneo en desarrollo la prevalencia de EA es comparable a la de países desarrollados de la misma región, y menor que la observada en países desarrollados de otras áreas. El curso de la enfermedad y los factores de riesgo de EA probablemente difieren en los países en desarrollo.

Palabras clave: Eccema atópico. Atopia. Alergia. Prevalencia. Carga. Niños. Factores de riesgo. Epidemiología. Tratamiento. ISAAC.

Introduction

Atopic eczema (AE), also known as atopic dermatitis, is a chronic inflammatory skin disorder, characterized by cutaneous dryness, intense itching, scratching, skin damage, and secondary infections. In chronic AE, flexural eczema becomes more prominent. The disease is closely associated with asthma and allergic rhinitis [1] and results in significant morbidity, leading to school absenteeism and emotional stress in children. Its cause remains unknown, although it is probably a combination of genetic, environmental, and immunologic factors [2]. The prevalence of AE has risen substantially in many countries in recent decades, and this increase has been attributed mainly to changes in lifestyle, nutrition, and environmental factors [3-5].

Little is known about the epidemiology of AE. However, geographical variations in prevalence among children have been described and findings closely match regional variations in hay fever [6]. In practice, there have been no internationally accepted criteria for defining AE in epidemiological surveys. A list of major and minor criteria proposed by Hanifin and Rajka [7] in the 1970s has been further evaluated and widely applied in clinical studies, although these criteria have not been defined and standardized in a manner suitable for field surveys [8].

The International Study of Asthma and Allergies in Childhood (ISAAC) Phase II method made it possible to determine symptom frequency and to check for objective markers of asthma and allergy using pulmonary function tests, bronchial reactivity measurements, and the presence of atopy and flexural dermatitis. The use of objective tools has improved the validity of results by minimizing the detection bias due to variations in language, awareness, perception, and accessibility to health services. Moreover, supplementing standardized inquiries with objective measures has made it possible to enhance validity and reliability [9].

A number of studies on the prevalence of AE have been conducted, although few were performed in Mediterranean and Middle Eastern populations [10-14]. In 2006, a cross-sectional multicenter study based on the same objective markers as proposed in ISAAC Phase II was performed in Turkey. This paper discusses the findings of this study in terms of risk factors, prevalence, and burden of AE among schoolchildren.

Materials and Methods

Study Population and Design

The study protocol has been described in detail elsewhere [15]. In summary, this cross-sectional study was conducted between 15 September 2005 and 30 May 2006 using the ISAAC Phase II option B method on a group of randomly selected schoolchildren representative of their peers and residing in each of 5 cities in Turkey (Van, Manisa, Ankara, Antalya, Trabzon), each of which is in a different part of the country. Representative samples of fifth-grade school children in the target population were selected in each province according to data from the Turkish Institute of Statistics, using a cluster sampling method, where clusters were individual schools.

The study is not registered by the international ISAAC study group, as it was conducted after completion of the ISAAC studies. All questions on the ISAAC Phase II questionnaire modules were applied [16].

Questionnaires were distributed to all fifth grade students in the selected schools to be completed at home, preferably by the parents.

Eczema ever was defined as a positive response to the question *Have you ever had an itchy rash which was coming and going for at least 6 months?* and a positive response by parents to *Has your child ever had eczema?* was accepted as physician-diagnosed AE. Current eczema symptoms were investigated on the basis of positive answers to 2 questions: *Has your child had this itchy rash at any time in the past 12 months?* and *Has this itchy rash at any time affected any of the following places: folds of the elbows; behind the knees; in front of the ankles; under the buttocks; or around the neck, ears, or eyes?* To investigate the burden of eczema, parents were asked *In the last 12 months, how often, on average, has your child been kept awake at night by this itchy rash?*

Current wheezing symptoms were investigated based on a positive answer to the question *Has your child had wheezing or whistling in the chest in the past 12 months?* Current rhinoconjunctivitis symptoms were evaluated as positive if the answer to both of the following questions was yes: *In the past 12 months, has your child had a problem with sneezing or a runny or blocked nose when you (he/she) did not have a cold or the flu? In the past 12 months, has this nose problem been accompanied by itchy/watery eyes?*

The AE diagnosed on physical examination by physicians was labeled point eczema. All study participants were examined by a pediatric allergy specialist or a pediatric allergy fellow who was specifically trained to perform the study.

Flexural Dermatitis

Examination for flexural dermatitis was performed according to an illustrated manual, and the presence of dermatitis signs was recorded for the following areas: around the eyes, sides/front/back of the neck, ankles and elbows, and antecubital and popliteal regions [9].

Determination of Potential Risk Factors

The potential personal and familial risk factors that were investigated for current AE included the following: gender, birth weight, delivery time, parental asthma and/or allergic rhinitis, exposure to animals in the first year of life and within the last year, exposure to smoke in the first year of life and within the last year at home, maternal smoking in the first year of life, vaccination history, duration of breastfeeding, duration of weaning period, number of older siblings, dampness and mold in the house in the first year of life and within the last year, number of rooms in the house resided in during the last year, number of members of the household in the first year of life and in the last year, family income, educational status of the parents, atopic status, and presence of allergic rhinitis.

Skin Tests

All participants underwent skin prick tests (SPT) for

Dermatophagoides pteronyssinus, *Dermatophagoides farinae*, *Alternaria alternata*, cat, grass mix (*Phleum pratense*, *Poa pratensis*, *Dactylis glomerata*, *Lolium perenne*, *Festuca pratensis*, *Avena eliator*), tree mix (*Betula verrucosa, Alnus glutinosa, Coryllus avellena*), *Olea europaea*, horse, *Blatella germanica*, milk, egg white, hazelnut, peanut, walnut, histamine, and negative controls [9]. The tests were applied using a multiprick test device (Quantitest, Panatrex Inc, Placentia, California, USA) on the volar surface of both forearms. The results were recorded after 15 minutes and considered positive if the mean wheal diameter was ≥3 mm compared to the negative control. Atopy was defined as having at least 1 positive skin test response to any of the aeroallergens tested.

Permission to perform the study was obtained from the Ethics Committee of Hacettepe University Medical School, the Ministry of Health, the central and provincial directors of the Ministry of Education, and the governors of the 5 selected cities. Written parental and student consent was obtained separately for each objective of the survey.

Statistical Analysis

Statistical analyses were conducted using SPSS version 15.0 (SPSS Inc. Chicago, Illinois, USA). The complex samples module was used to obtain weighted estimates and robust estimates for the cluster sampling design used. Weights were calculated as inverses of the sampling fractions. Statistical analyses included univariate, bivariate, and multivariate analyses, and odds ratios (OR) with relevant 95% confidence intervals (CIs) were calculated to evaluate the potential associations between risk factors and AE. Statistical significance was set at $P<.05$.

Results

A total of 7623 children received the questionnaire. Of the 6963 children/families that agreed to take part, 6755 completed the AE question module. The overall completion rate was 88.6%. The flexural dermatitis examination and SPT were successfully performed in a mean (range) of 79.0% (range, 74.9%-83.3%) and 80.5% (range, 75.2%-85.7%) of the children, respectively.

Characteristics of Atopic Eczema

The frequency of eczema ever was 17.1% (14.7%-27.2%) and that of current eczema 8.1% (6.5%-13.7%), whereas physician-diagnosed AE was reported in only 2.6% (2.1%-4.5%) of the participants. Among children with symptoms of current eczema, the percentage of physician-reported cases was 7.3%.

On physical examination, flexural dermatitis (point eczema) was observed in 3.6% (1.0%-9.9%) of the participants. Of the children with current eczematous symptoms, 93.6% were free of flexural dermatitis, whereas 77.1% of those with flexural dermatitis did not report any symptoms.

The distribution of affected regions in children with and without current eczema is shown in Figure 1.

Of the children with current eczema, 50.8% were male and 47.5% had a family history of atopy. The frequency of atopy was 20.4%, whereas the frequency of current wheezing and rhinoconjunctivitis was 33.4% and 47.1%, respectively. The descriptive characteristics of children according to current AE are presented in the Table.

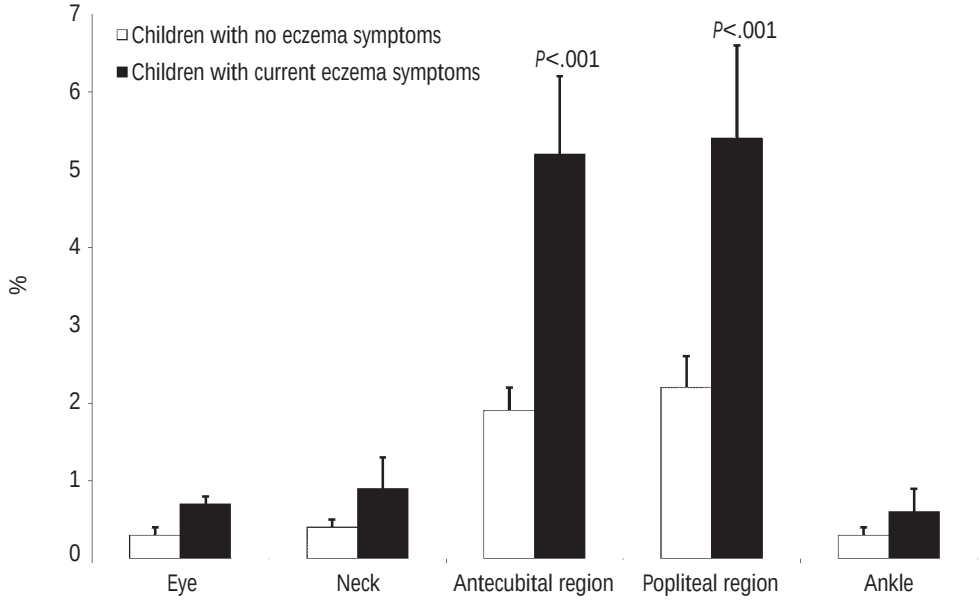

Figure 1. Distribution of affected regions in students with and without current eczema.

Table. Characteristics of the Study Population According to the Presence of Atopic Eczemaa

	No Eczema, %	Current Eczema, %
Male sex	50.6	51.3
Prematurity (<37 wk)	4.4	2.6
Birth weight <2500 g	11.0	15.1[b]
Family history of allergic disease	32.8	47.5[d]
Incomplete vaccination	18.9	28.2[c]
House with a single room	3.9	2.9
Shared bedroom with other people last year	79.5	84.1
Shared bedroom with other people in the first year of life	88.4	89.5
Contact with animals last year	47.5	59.4[c]
Contact with animals in the first year of life	58.1	70.7[d]
Mold and dampness at home last year	6.3	11.7[d]
Mold and dampness at home in the first year of life	10.5	18.6[d]
Monthly income <500 TL ($350)	43.1	52.2[c]
Maternal smoking in the first year of life	18.2	18.4
Maternal smoking during pregnancy	12.5	13.9
Smoke exposure at home	58.2	69.6[c]
Moving house	14.1	33.4[d]
Current wheezing	21.3	47.1[d]
Current rhinoconjunctivitis	3.2	7.8[d]
Atopy (>3 mm)	18.9	20.4
Inhalant atopy (>3 mm)	18.9	20.4
Pollen atopy (>3 mm)	7.0	5.7
House dust mite atopy (>3 mm)	7.0	7.9
Food sensitization	4.6	4.5
Bronchial hyperreactivity	23.4	27.9
Maternal education <6 years	70.2	76.8[b]
Paternal education <6 years	46.7	56.7[c]
Patients with eosinophilia >4%	16.8	13.1
Patients with total immunoglobulin E >100 kU_A/L	29.6	34.9
Duration of breast feeding, mo	11.7	11.0
Duration of weaning, mo	5.9	6.0
No. of household members last year	5.0	5.5
No. of household members in the first year of life	5.0	5.8
No. of older siblings	1.2	1.5
Eosinophils, %	2.7	2.6
Immunoglobulin E levels, kU_A/L	128.9	167.8

[a]The χ^2 test was used for categorical variables and the *t* test was used for mean values.
[b]P<.05
[c]P<.01
[d]P<.001

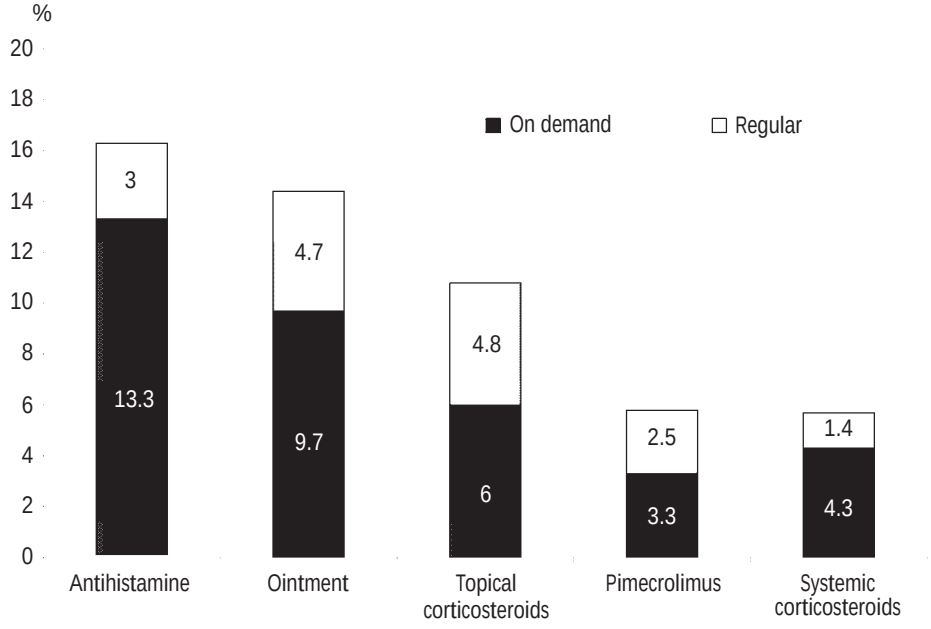

Figure 2. Types of drugs used and frequency (regular vs on demand) in children with current atopic eczema.

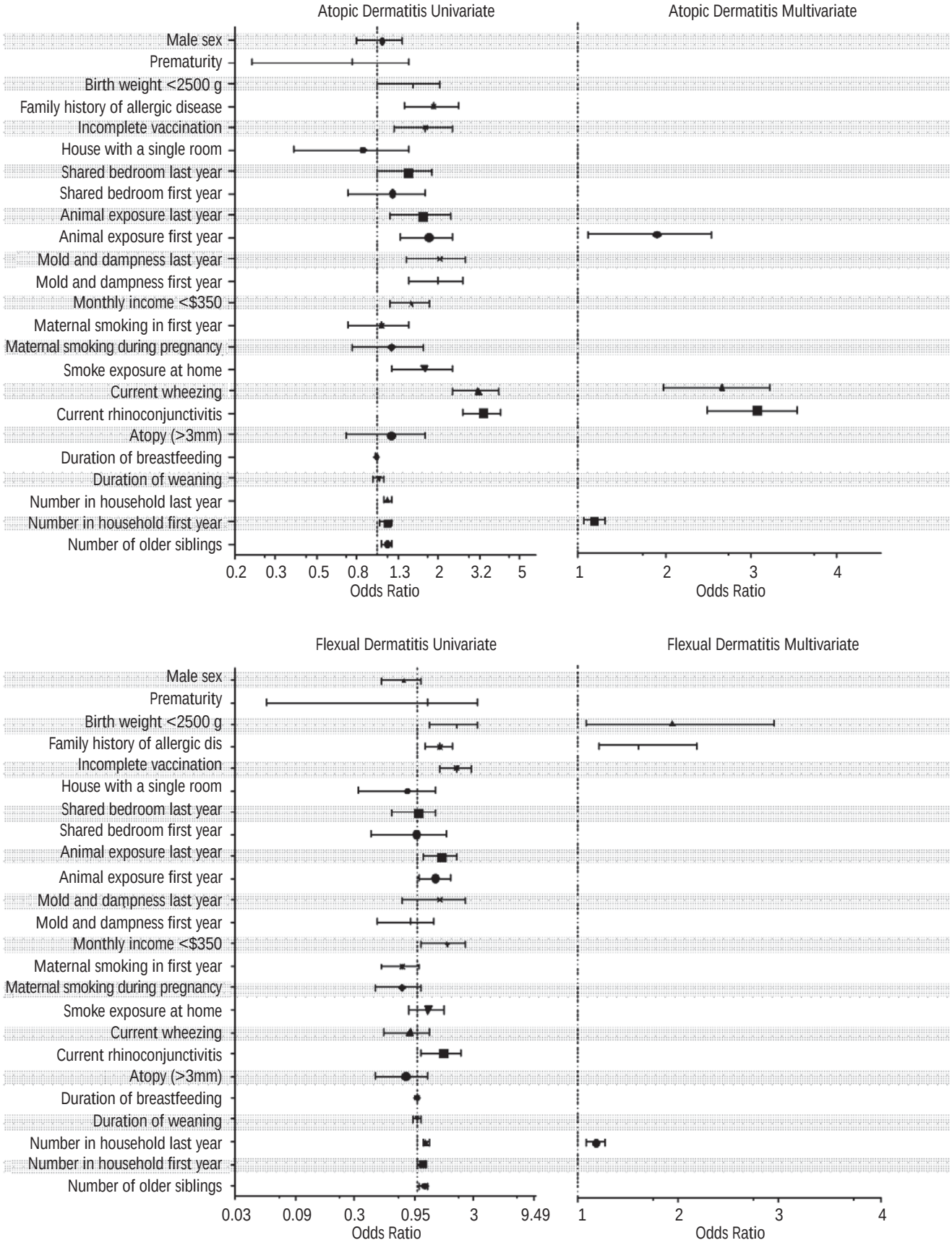

Figure 3. Potential risk factors of atopic dermatitis and flexural dermatitis based on individual effect sizes in bivariate analyses and potential risk factors found to be independent significant predictors in multivariate analyses.

Burden of Atopic Eczema

Only 36.3% of the children had consulted a physician due to eczema in the previous year. The percentages of children with current eczema who declared nocturnal awakening and had at least 1 awakening per week due to eczema were 56% and 13.6%, respectively. About 10% of the children with current eczema had reported at least 1 day of absenteeism because of eczema symptoms during the past year.

Overall drug usage was 28.7% among children with current eczema. The most frequently used drugs were antihistamines, followed in decreasing order by moisturizers, topical corticosteroids, systemic corticosteroids, and topical calcineurin inhibitors. Frequency of drug use (on demand or on a regular basis) and proportion of each drug in treatment regimens are presented in Figure 2.

Risk Factors for Eczema

The association between potential risk factors and current eczema or flexural dermatitis was analyzed using bivariate tables and multivariate logistic regression modeling. The factors found to be associated with an increased risk of eczema were current rhinoconjunctivitis (OR, 2.53; 95% CI, 1.99-3.21; *P*<.001), current wheezing (OR, 2.10; 95% CI, 1.58-2.79; *P*<.001), exposure to animals in the first year of life (OR, 1.47; 95% CI, 1.06-2.03; *P*=.022), and number of household members in the first year of life (OR, 1.09; 95% CI, 1.03-1.15; *P*=.005).

The factors found to be independent predictors of flexural dermatitis were birth weight <2500 g (OR, 1.79; 95% CI, 1.08-2.94; *P*=.024), family history of allergic disease (OR, 1.62; 95% CI, 1.21-2.18; *P*=.002), and number of household members sharing the house over the last year (OR, 1.17; 95% CI, 1.08-1.27; *P*<.001). Details of the analysis of the potential risk factors are presented in Figure 3.

Discussion

We found that AE was common in Turkey: based on parental reports, prevalence rates were 17.1% and 8.1% for eczema ever and current eczema, respectively. The prevalence of point eczema was much lower (3.6%). In a developing Mediterranean country, the prevalence of eczema seems to be comparable with relevant rates in developed countries of the region and lower than those observed in developed countries elsewhere [1,3,4,13,14]. As for disease burden, the percentages of children with current eczema who reported nocturnal awakening and had at least 1 awakening per week due to nighttime itching were 56% and 13.6%, respectively. School absenteeism was observed in one-tenth of the children with current eczema. Only one-third of current eczema patients used medication, mostly antihistamines and moisturizers. Current allergic diseases, family history of allergic disease, low birth weight, and exposure to animals in the first year of life were found to be independent risk factors of current eczema and flexural dermatitis. Atopy was found to be less associated with the disease process.

The prevalence of allergic diseases differs with geographic location and climate. The results of this study indicate that eczema is common in Turkish schoolchildren. However, the physician-diagnosed point prevalence of eczema was lower than the prevalence of current eczema (8.1% vs 3.6%). Several factors may be responsible for this difference. First, in the ISAAC questionnaire, current eczema is defined as eczema within the last 12 months; thus, at the time of physical diagnosis, the disease may be in remission and, therefore, missed. A recent study comparing the ISAAC questionnaire and the results of physical examination in patients with eczema showed the questionnaire to be a reliable method for prevalence studies of AE, since the point prevalence determined by the physical diagnosis could underestimate a relapsing and waning chronic disease [17]. Second, the reliability of the questionnaire may be undermined by difficulties in translation. To minimize such a possibility, the previous translation of the questionnaire was used, with some format improvements and minor changes in the ordering of the questions [18]. In addition, the questionnaire was piloted on a convenience sample of schoolchildren before the full survey was undertaken.

Comparison of findings across studies is problematic, because estimates have been shown to vary with disease definition and methods of assessment, age ranges, year of birth of the children studied, period of time in which the study was conducted, and geography [19-23]. However, our results are comparable with those of previous reports from Turkey and reveal that current prevalence of patient-reported eczema has increased slightly [10-12,24]. Current eczema in developed countries with a western lifestyle is more common than in Turkey [1,3,4]. The prevalence for current eczema we found was much lower than the rates of 17.2% reported in a sample of American children [25] and 24.0% reported in Japanese children aged 5-6 years [19]. However, our findings are comparable with results for current eczema rates in Mediterranean populations. Climate may be more important than a western lifestyle with respect to eczema [4,13,14]. In a study from Italy, the prevalence of eczema ever and point eczema were found to be 15.2% and 5.8%; both were comparable to our results [14]. Weiland et al [26] investigated the relationship between climate and atopic diseases and found that prevalence of eczema symptoms in children aged 6-7 years increased with latitude and decreased with indoor relative humidity. The sex ratio for eczema in our study population was approximately equal, as reported in other studies [11,14]; however, it contrasted with that of previous studies, some of which show a female preponderance [8,10,12].

Several factors affect disease burden. In the present study, one-third of the students with current eczema had consulted a physician for eczema during the previous year. This represented a financial cost to both the family and the population. The design of the study hinders our ability to estimate the direct economic burden of hospital admissions. However, the estimated costs of illness for AE have been estimated to range from US$71 per patient in the Netherlands to US$2559 per patient in Germany, due to variations in study populations and the number of cost components included [27,28].

Sleep difficulties in children with AE may lead to daytime behavioral and disciplinary problems and parental sleep

deprivation. Abnormal sleep patterns documented in children with AE are marked by frequent nighttime awakenings, likely resulting from pruritus. These awakenings persist for many children during disease remissions and many are not associated with scratching [29]. In our study, the percentages of the students with current eczema who reported nocturnal awakening and at least 1 nighttime awakening per week due to eczema were 56% and 13.6%, respectively. In schoolchildren, these awakenings lead to absenteeism. In the present study, 9.7% of the students with current eczema had reported at least 1 day of absenteeism over the past year.

Children with eczema are treated relatively more often with corticosteroids as they get older, while in younger children, moisturizers and relatively less potent corticosteroids are preferred, probably because of concerns regarding the side effects of long-term corticosteroid use. In our study, 28.7% of the current eczema patients took medication. The most frequently used drugs were antihistamines, followed by moisturizers, topical corticosteroids, systemic corticosteroids, and topical calcineurin inhibitors. The preference for antihistamines and moisturizers may reflect the fears of patients and parents regarding corticosteroids. On the other hand, corticosteroids were more common among regular drug users, and this may reflect disease severity.

Our primary objective was to study the association between potential risk factors and eczema and flexural dermatitis in order to identify high-risk groups and priority candidates for preventive and screening efforts. Current rhinoconjunctivitis and current wheezing increased the risk of eczema more than 2-fold, and exposure to animals in the first year of life and number of household members in the first year of life were found to be related with an increased risk of eczema. Having an allergic disease increased the prevalence of having another, probably due to epicutaneous sensitization with subsequent migration of sensitized T cells into the airways and nose, causing asthma and allergic rhinitis [1]. In contrast to the hygiene hypothesis, the prevalence of eczema was higher in children sleeping together within the same household, and those reporting exposure to animals in the first year of life had an increased risk of eczema. These findings were consistent with the findings of Kalyoncu et al [10], who reported that having a pet in the home was associated with AE. For flexural dermatitis, birth weight <2500 g, family history of allergic disease, and number of household members in the last year were found to be independent risk factors. Previously published results considering the association between birth weight and AE are conflicting [1,14,30]. In the development of AE, dysfunction of the skin barrier is an important problem, and in low-birth-weight infants, skin thickness and barrier function are reduced. This might explain the development of flexural eczema in these children. Another finding of the present study was the weak correlation between AE and atopy. Only one-fifth of the children were sensitized to aeroallergens and common foods. A reduction in the degree of atopy in AE patients living in developing countries was recently documented in a review of the association between atopy and AE [31]. Nearly 80% of our cases were nonatopic according to the allergens tested, thus calling into question the validity of the term atopic in atopic eczema.

This study did not find any association between the numerous risk factors that have long been linked to AE, including gender, breastfeeding or stage of weaning, vaccination, moisture, family income, and atopy status. The course of the disease and the risk factors determining AE may differ in developing countries, and further studies are clearly warranted to reveal the factors underlying such differences (if any).

Our study was a cross-sectional study. This design limits our ability to follow disease course, and prevalence of eczema ever and current eczema were estimated based on parental reports. To minimize the potential for information bias, we included a question on physician-diagnosed point eczema in the questionnaire. The large sample size enabled us to control for several potential confounders in multivariate analyses, and the high response rate increased the generalizability of the study results.

Given the representativeness of the sample (5 cities in 5 different geographic regions across Turkey), the high response rate (91.3%), and adequate sample size, the findings of the study seem to be a reliable estimate of the prevalence of eczema among schoolchildren living in urban areas in Turkey.

In summary, in a developing Mediterranean country, the prevalence of eczema seems to be less frequent than in developed countries worldwide but comparable to that observed in developed countries in the same region, suggesting that climate may be more important than western lifestyle in the development of AE. The most important risk factors associated with AE have been found to be current allergic diseases, family history of allergic disease, and number of household members in the first year of life, whereas atopy itself was found to be less associated with the disease process.

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