



Severity of atopic dermatitis in relation to food and inhalant allergy in adults and adolescents

J. Čelakovská & J. Bukač

To cite this article: J. Čelakovská & J. Bukač (2017) Severity of atopic dermatitis in relation to food and inhalant allergy in adults and adolescents, Food and Agricultural Immunology, 28:1, 121-133, DOI: [10.1080/09540105.2016.1228838](https://doi.org/10.1080/09540105.2016.1228838)

To link to this article: <https://doi.org/10.1080/09540105.2016.1228838>



Published online: 15 Sep 2016.



Submit your article to this journal [↗](#)



Article views: 105



View related articles [↗](#)



View Crossmark data [↗](#)



Citing articles: 1 View citing articles [↗](#)



Severity of atopic dermatitis in relation to food and inhalant allergy in adults and adolescents

J. Čelakovská^a and J. Bukač^b

^aDepartment of Dermatology and Venereology, Faculty Hospital and Medical Faculty of Charles University, Hradec Králové, Czech Republic; ^bDepartment of Medical Biophysics, Medical Faculty of Charles University, Hradec Králové, Czech Republic

ABSTRACT

The aim of this study is the evaluation of the relationship between the severity of atopic dermatitis (AD) and the occurrence of IgE-mediated food allergy, food sensitization, and sensitization to inhalant allergens. The complete dermatological and allergological examinations were performed and the severity of AD was evaluated with the SCORing Atopic Dermatitis index. The statistical evaluation of the relationship between the occurrence of IgE-mediated food allergy, food sensitization, sensitization to inhalant allergens, and the severity of AD was performed. Two hundred and eighty-three patients were examined, 89 men and 194 women, average age 26.2 (s.d. 9.5). The significant relation was recorded between the severity of AD and sensitization to tested inhalant allergens. The significant relation was also found between the severity of AD and IgE-mediated food allergy. It turns out that the higher time to reaction, the higher the severity of AD.

ARTICLE HISTORY

Received 9 February 2016
Accepted 7 August 2016

KEYWORDS

Atopic dermatitis;
IgE-mediated food allergy;
cow milk; wheat; egg; soy;
peanuts; sensitization to
mites; feather; animal
dander; dust; severity of
atopic dermatitis; SCORAD
index

Introduction

Atopic dermatitis (AD), a common chronic inflammatory skin disease, is characterized by pruritus and eczematous plaques. The prevalence of AD in children varies worldwide from approximately 10% to 20% and AD may persist into adolescence or adult life in up to 10% of patients (Spergel, 2010; Zeppa, Bellini, & Lisi, 2011). Some hypotheses have been put forward to explain this trend, including diet, air pollution, and the hygiene hypothesis. New insights into the genetics and pathophysiology of AD indicate the important role of structural abnormalities in the epidermis, as well as immune dysregulation (Boguniewicz & Leung, 2011; Howell et al., 2007; van den Oord & Sheikh, 2009; Weidinger et al., 2006). Defect of the skin barrier facilitates penetration and sensitization to food or airborne allergens, as well as infections by *Staphylococcus aureus*, herpes simplex virus, or other microbes. The study of animals suggests that the environmental allergen, such as mites and food proteins, can make contact with the immune system via antigen-presenting cells in the superficial epidermis, leading to sensitization, which could potentially make existing AD worse and may also be an important precursor of food and respiratory allergies (Barker et al., 2007; Bussmann, Böckenhoff, Henke,

Werfel, & Novak, 2006; Fallon et al., 2009; Howell et al., 2007; Jeong et al., 2008; Kim, Leung, Boguniewicz, & Howell, 2008; Nemoto-Hasebe et al., 2009). The theory describing atopic diseases as highly IgE dependent has persisted over a long time; however, a subgroup of atopic patients exhibits normal IgE levels and mechanisms contributing to the so-called intrinsic or nonallergic form have been the matter of intensive research work in the last few years and new data have raised the question of the precise role of IgE in atopy. Some authors think that a strict distinction of intrinsic and extrinsic variant is impossible because intrinsic AD may develop into extrinsic over time (Roguedas Contios & Misery, 2011). The hypothesis of a dynamic relationship between the two forms of AD is supported by the data in a study investigating the persistence of AD during the development of respiratory allergic diseases (Novembre et al., 2001). The level of total IgE is one of the main factors determining the variant of AD.

The question of our study is whether the severity of AD is in some relation to the occurrence of IgE-mediated food allergy, food sensitization, and sensitization to inhalant allergens. The immune response in food allergy can be classified into IgE-mediated, non-IgE-mediated, or a mixture of both. IgE-mediated food allergy requires food allergen sensitization (with the development of serum-specific IgE antibody – sIgE to a food allergen), and secondly the development of signs and symptoms on exposure to that food. Symptoms of food allergy usually start within minutes of exposure to the trigger food and must occur within two hours to classify as an IgE-mediated response; any combination of local oral, dermatological, gastrointestinal, and respiratory symptoms can occur. Non-IgE-mediated food allergy includes a wide range of diseases from AD to food protein-induced enterocolitis and from eosinophilic esophagitis to coeliac disease. The immune mechanisms underlying these conditions are not well understood, though TNF α has been heavily implicated. A recent study has also found a possible link with the T_H2-type response found in IgE-mediated allergy, in that whilst there is no production of IgE, T cells are skewed towards a T_H2-type response (Morita, Nomura, Matsuda, Saito, & Matsumoto, 2013; Tan & Smith, 2014; Turnbull, Adams, & Gorard, 2015). The development of AD before six months of age, and severe AD within the first year of life are associated with the development of egg, milk, and peanut allergies (Hill et al., 2008; Wassmann & Werfel, 2015). Approved tests of value in diagnosing IgE-mediated food allergy are the skin prick test (SPT) and measuring of the food-specific IgE antibody levels. The double-blind placebo-controlled food challenge remains the gold standard in food allergy testing, but is not frequently performed due to its inherent risks, inconvenience, and cost. The main difficulty with both sIgE testing and SPTs is that they cannot distinguish between an individual who is merely sensitized to the allergen (has detectable circulating sIgE) and one who is clinically allergic (has mast cell-bound IgE leading to immediate mediator release). This is why it is essential to target allergy testing based on leads in the patient's history, and it is ideal to complement the tests with a definitive food challenge (Stiefel & Roberts, 2012). The atopy patch test (APT) is defined as a patch test procedure to assess the delayed type of hypersensitivity reactions against those protein allergens known to elicit IgE-mediated type I reactions in atopic patients. This patch test procedure uses intact protein allergens instead of haptens in an optimized test setting and with a special reading key. APTs detect delayed reactions and can also show immediate urticarial reactions. Patch testing involves applying food extract directly to skin on a patient's back and then assessing for erythema, infiltration, and papules after 48–72 hours. There is

currently no official role for the APT in IgE-mediated food allergy, but there is some support that it may reflect late phase clinical reactions (Boyce et al., 2010).

There is a lack of reports focusing on the course of AD with respect to its evolution and association with IgE-mediated food allergy or sensitization to foods and to aeroallergens in adolescent and adult patients suffering from AD. Only a few reports demonstrate the comorbidity of IgE-mediated food allergy and inhalant allergy and the severity of AD evaluated with the SCORing Atopic Dermatitis (SCORAD) index. The SCORAD index has been developed on consensus by the European Task Force on Atopic Dermatitis in 1993. The acronym SCORAD was proposed by Arnold Oranje, and stands for SCORing Atopic Dermatitis (European Task Force on Atopic Dermatitis, 1993). The use of this instrument makes different studies more comparable in routine practice, as well as in observational or double-blind randomized clinical trials (Gelmetti & Colonna, 2004).

In this study, we evaluate the relation between the severity of AD evaluated with the SCORAD index and the occurrence of IgE-mediated food allergy and food sensitization to cow milk, wheat, egg, soy, peanuts, and sensitization to mites, feather, animal dander, and dust. In patients with IgE-mediated food allergy, we evaluate the severity of AD in patients with early, combined, and late food reactions.

Method

In the period 2008–13, 283 patients suffering from AD at the age of 14 years or older were examined. All these patients were examined in the Department of Dermatology, Faculty Hospital Hradec Králové, Charles University of Prague, Czech Republic. The diagnosis of AD was made with the Hanifin–Rajka criteria (Hanifin & Rajka, 1980). Exclusion criteria were long-term therapy with cyclosporin or systemic corticoids, pregnancy, and breastfeeding. Patients with AD having other systemic diseases were excluded from the study as well. Complete dermatological and allergological examination was performed in patients included in the study. This study was approved by Ethics Committee of Faculty Hospital Hradec Králové, Charles University of Prague, Czech republic. The following parameters were examined: IgE-mediated food allergy, food sensitization (wheat flour, cow milk, egg, peanuts, and soy), and sensitization to inhalant allergens (mites, animal dander, feather, and dust). In patients suffering from IgE-mediated food allergy, we evaluated the occurrence of early, combined, and late food reactions. The statistical evaluation of the relation between the occurrence of IgE-mediated food allergy, food sensitization, sensitization to inhalant allergens and the severity of AD evaluated with the SCORAD index was performed.

Severity of AD

Severity of AD was scored in agreement with SCORAD (European Task Force on Atopic Dermatitis, 1993) with the assessment of topography items (affected skin area), intensity criteria, and subjective parameters. This examination was performed during one year every three months and the average SCORAD index was recorded.

To measure the extent of AD, the rule of nines was applied on a front/back drawing of the patient's inflammatory lesions. The extent was graded 0–100 points. The intensity part

of the SCORAD index consists of six items: erythema, oedema/papulation, excoriations, lichenification, crusts, and dryness. Each item was graded on a scale 0–3. The subjective items included daily pruritus and sleeplessness. Both subjective items were graded on a 10-cm visual analogue scale and the maximum subjective score was 20 points. All items were filled out in the SCORAD evaluation form. The SCORAD index formula was $A/5 + 7B/2 + C$. In this formula, *A* is defined as the extent (0–100 points), *B* as the intensity (0–18 points), and *C* as the subjective symptoms (0–20 points). The severity of AD was evaluated with SCORAD as a mild form to 25 points, as moderate over 25–50 points, as a severe form over 50 points.

The diagnosis of IgE-mediated food allergy to wheat flour, cow milk, egg, peanuts, and soy was made according to the results in sIgE, SPTs, APT, and open exposure tests (OETs; Celakovska, Ettlerova, Ettler, Vaněčková, & Bukač, 2015b). Patients with the positive result in the OET (early and/or late reactions) with examined food and with the positive result at least in one of the diagnostic methods (sIgE, APT, and SPT) to this food were considered as the patients with IgE-mediated food allergy. Early reactions were defined as clinical symptoms within two hours after the ingestion of this dose in OET and late symptoms if occurring after more than two hours (Celakovska et al., 2015b). The severity of AD in patients with early reactions, combined, and late food reactions was evaluated.

Sensitization to wheat flour, cow milk, egg, peanuts, and soy was confirmed in patients with the positive results in sIgE and/or SPT and/or APT, but with the negative results in the OET to this food allergen (Celakovska et al., 2015b).

Sensitization to dust (mixture), mites (mixture), animal dander (mixture), or feather (mixture) was determined according to the sIgE level and SPT for these allergens (Celakovska, Ettlerová, Ettler, Vaněčková, & Bukač, 2015c). Commercial extract Alyostal (Stallergens, France) was used for SPT. SPTs were placed on the volar side of the forearm according to the extent of AD. SPT was carried out by a standardized method using the lancet with a 1-mm tip. The results were read after 15 minutes and assessed by comparison with the wheal induced with histamine (10 mg/ml) and a negative control. A wheal with a diameter greater than 3 mm in comparison with a negative control was scored as a positive one. The serum level of the sIgE has been measured with the method of CAP (system fluorescens enzymatic immunoassay (FEIA CAP) – Pharmacia Diagnostics, Uppsala, Sweden). The level of sIgE higher than 0.35 U/ml was assessed as positive (Celakovska et al., 2015c).

Statistical analysis

We analysed the data to determine whether the occurrence of IgE-mediated food allergy, food sensitization, and sensitization to aeroallergens is associated with the occurrence of mild, moderate, or severe form of AD according to the SCORAD index.

Pairs of these categories were entered in contingency tables and the chi-square test of independence of these classifications was performed with the level of significance set to 5%.

The patients suffering from IgE-mediated food allergy were subdivided into three categories, depending on the time to reaction, that is, early, combined, and late. We formed a contingency table to study the dependence between the time to reaction and severity of AD. We also studied the direction of the dependence using the Goodman–Kruskal test.

Results

Patients and tested parameters

Two hundred and eighty-three patients were examined – 89 men and 194 women with the average age 26.2 years (s.d. 9.5 years) and with the average SCORAD 32.9 (s.d. 14.1) points. The characteristic of patients and the survey of our results with the tested parameters are shown in Table 1.

IgE-mediated food allergy and severity of AD

IgE-mediated food allergy was confirmed in 78 patients (27%). Out of these patients, 24 patients (8%) suffer from mild form of AD, 46 patients (16%) suffer from moderate form, and 8 patients (2.8%) suffer from severe form. Out of 205 patients without confirmed IgE-mediated food allergy, 65 patients (23%) suffer from mild form, 123 (44%) suffer from moderate form, and 17 patients (6%) suffer from severe form. The relation between the occurrence of IgE-mediated food allergy in general (without subdividing these patients according to the kind of reaction as early, combined, and late) and the severity of AD was not confirmed (p value = .873) (Table 2). The occurrence of early, combined, and late food reactions in the 78 patients suffering from IgE-mediated food allergy to wheat, cow milk, egg, soy, and peanuts is recorded in Table 3. The early allergic reaction

Table 1. The characteristics of patients and the occurrence of the tested parameters in 283 patients with AD.

The characteristics of patients:		
283 patients were examined – 89 men, 194 women		
the average age 26.2 years (s.d. 9.5 years)		
the average SCORAD 32.9 (s.d. 14.1) points		
Monitored parameter	Number of patients from 283 (100%)	
<i>IgE-mediated food allergy</i>	78 confirmed (28%)	205 not confirmed (62%)
Wheat flour	6 (2%)	
Cow milk	2 (0.7%)	
Peanuts	57 (20%)	
Egg	14 (5%)	
Soy	9 (3%)	
Reactions		
Early	30 patients (11%)	
Combined	35 patients (12%)	
Late	13 patients (5%)	
<i>Food sensitization</i>	148 confirmed (52%)	135 not confirmed (48%)
Wheat flour	31 (11%)	
Cow milk	29 (10%)	
Peanuts	38 (13%)	
Egg	56 (20%)	
Soy	56 (20%)	
<i>Sensitization to inhalant allergens</i>	235 (83%) confirmed	48 not confirmed (17%)
Mites	171 (60%)	
Feather	38(13%)	
Animal dander	126 (44%)	
Dust	62 (22%)	
Mild form of AD	89 (31%)	
Moderate form of AD	169 (60%)	
Severe form of AD	25 (9%)	

Table 2. The number of patients with and without IgE-mediated food allergy (FA) to examined food allergens and the severity of AD according to SCORAD.

Food allergy	Mild form	Moderate form	Severe form	Total number of patients
No. of patients FA+	24 (8%)	46 (16%)	8 (3%)	78 (27%)
No. of patients FA–	65 (23%)	123 (44%)	17 (6%)	205 (72%)
Total number of patients	89 (31%)	169 (60%)	25 (9%)	283 (100%)
<i>p</i> Value			.873	

Notes: Pairs of these categories were entered in contingency tables and the Chi-square test for the relationship of these variables was performed with the level of significance set to 5%.
FA+: food allergy confirmed; FA–: food allergy not confirmed.

(oral allergy syndrome, anaphylaxis, and pruritus) was recorded in 30 patients, the combined reaction in 35 patients and the late reaction (gastrointestinal symptoms, worsening of AD, and pruritus) in 13 patients.

In evaluating the severity of AD and the occurrence of early, combined, and late IgE-mediated food reactions in 283 patients included in the study, the relation was confirmed (*p* value = .005) (Table 4). The relation between the time of food reaction and the severity of AD was also evaluated; the relation was confirmed (*p*- value = .002), the higher the time to reaction, the higher the severity of AD (complement to Table 4).

Food sensitization and severity of AD

Out of 148 patients with food sensitization, 44 patients (15%) suffer from mild form of AD, 91 patients (32%) suffer from moderate form, and 13 patients (4.5%) suffer from severe form of AD. From 135 patients without food sensitization, 45 patients (16%) suffer from mild form, 78 (28%) suffer from moderate form, and 12 patients (4%) suffer from severe form. The relation between the occurrence of food sensitization and the severity of AD was not confirmed, (*p* value = .797) (see Table 5).

Sensitization to mites, animal dander, feather, dust versus severity of AD

Mild form of AD is recorded in 89 patients, from these patients 36 patients suffer from sensitization to mites, 9 patients to feather, 28 patients to animal dander, and 7 patients

Table 3. Symptoms of IgE-mediated food allergy (FA) in 78 (27%) patients from 283 (100%).

Food	Symptoms of IgE-mediated food allergy in 78 patients					
	FA confirmed	OAS	Pruritus	Worsening of AD	GIT symptoms	Anaphylactic reaction
Milk	2 (0.7%)	1	1	1	0	0
Wheat	6 (2%)	0	6	6	0	0
Peanut	57 (20%)	45	12	3	9	3
Soy	9 (3%)	4	4	4	4	0
Egg	14 (6%)	4	9	9	0	1
The total number of patients	78 (27%)	55 (19%)	30 (10%)	19 (7%)	12 (4%)	4 (1.4%)

Notes: from 78 patients with confirmed food allergy, 12 patients suffer from allergy to two and more foods, 66 patients suffer from allergy to one of examined food. The early reactions are recorded in 30 patients, combined in 35 patients and late reactions in 13 patients.
OAS: oral allergy syndrome; AD: atopic dermatitis; GIT symptoms: gastrointestinal symptoms; FA: total number of patients with confirmed FA.

Table 4. The number of patients with and without IgE-mediated food allergy (FA) to examined food allergens and the severity of AD according to SCORAD.

IgE-mediated food allergy	Mild form	Moderate form	Severe form	Total number of patients
Early reactions	15 (5%)	14 (5%)	1 (0.3%)	30 (10%)
Combined reactions	5 (2%)	27 (9%)	3 (1%)	35 (12%)
Late reactions	4 (1.4%)	5 (1.7%)	4 (1.4%)	13 (4.5%)
No of patients without FA	65 (23%)	123 (44%)	17 (6%)	205 (72%)
Total number of patients	89 (31%)	169 (60%)	25 (9%)	283 (100%)
<i>p</i> Value			.005*	

Seventy-eight patients with early, combined and late IgE-mediated food allergy to examined foods and the relation to the severity of AD according to SCORAD.

Food allergy	Mild form	Moderate form	Severe form	Total number of patients
Early reactions	15 (5%)	14 (5%)	1 (0.3%)	30 (10%)
Combined reactions	5 (2%)	27 (9%)	3 (1%)	35 (12%)
Late reactions	4 (1.4%)	5 (1.7%)	4 (1.4%)	13 (4.5%)
Total number of patients with FA	24 (8.4%)	46 (16%)	8 (2.8%)	78 (27%)
<i>p</i> Value			.002*	

Notes: The patients suffering from IgE-mediated food allergy are subdivided into three categories according to the time of reaction.

Pairs of these categories were entered in contingency tables and the Chi-square test for the relationship of these variables was performed with the level of significance set to 5%.

The significant dependence is shown extra bold*.

Table 5. The number of patients with and without food sensitization (FS) to examined food allergens and the severity of AD according to SCORAD.

Food sensitization	Mild form	Moderate form	Severe form	Total number of patients
No. of patients FS+	44 (15%)	91 (32%)	13 (4.5%)	148 (52%)
No. of patients FS–	45 (16%)	78 (28%)	12 (4.5%)	135 (48%)
Total number of patients	89 (31%)	169 (60%)	25 (9%)	283 (100%)
<i>p</i> -Value			.797	

Notes: Pairs of these categories were entered in contingency tables and the Chi-square test for the relationship of these variables was performed with the level of significance set to 5%.

FS+: food sensitization confirmed; FS–: food sensitization not confirmed. The significant dependence is shown in bold.

Table 6. The number of patients with sensitization to mites, feather, animal dander, and dust and the relationship to the severity of AD according to SCORAD.

Inhalant sensitization	Mild form	Moderate form	Severe form
<i>Mites+</i>	36 (40%)	115 (68%)	20 (80%)
<i>Mites–</i>	53 (60%)	54 (32%)	5 (20%)
Total	89 (100%)	169 (100%)	25 (100%)
<i>p</i> -Value		.0000*	
<i>Feather+</i>	9 (10%)	20 (12%)	9 (36%)
<i>Feather–</i>	80 (90%)	149 (88%)	16 (64%)
Total	89 (100%)	169 (100%)	25 (100%)
<i>p</i> -Value		.002 *	
<i>Animal dander+</i>	28 (32%)	84 (50%)	14 (56%)
<i>Animal dander–</i>	61 (68%)	85 (50%)	11 (44%)
Total	89 (100%)	169 (100%)	25 (100%)
<i>p</i> -Value		.009*	
<i>Dust+</i>	7 (8%)	41 (24%)	14 (56%)
<i>Dust–</i>	82 (92%)	128 (76%)	11 (44%)
Total	89 (100%)	169 (100%)	25 (100%)
<i>p</i> -Value		.000*	

Notes: The occurrence sensitization to inhalant allergens in mild, moderate, and severe form of AD. The number of patients suffering from sensitization to inhalant allergens in percentage is calculated for mild form (100% patients), moderate form (100%), and severe form (100% patients).

The correlation is shown extra bold*.

to dust. Moderate form of AD is recorded in 169 patients and from these patients, 115 patients suffer from sensitization to mites, 20 patients to feather, 84 patients to animal dander, and 41 patients to dust. Severe form of AD is recorded in 25 patients, from these patients 20 patients suffer from sensitization to mites, 9 patients to feather, 14 patients to animal dander, and 14 patients to dust.

Regarding the evaluation of the occurrence of sensitization to mites, feather, animal dander, dust versus the severity of AD, the significant relationship was confirmed between all tested inhalant allergens and the severity of AD (see Table 6).

The significantly rising occurrence of sensitization to mites, feather, animal dander, and dust in mild, moderate, and severe form of AD is shown in this table.

Discussion

This study evaluates the relation of IgE-mediated food allergy, food sensitization, and sensitization to inhalant allergens versus the severity of AD evaluated with the SCORAD index.

There are few studies dealing with this question in adolescents and adults suffering from AD according to the databases in Medline, PubMed, and Web of science.

In this study, the significant relation was confirmed between the sensitization to the tested inhalant allergens and the severity of AD. Patients suffering from moderate and severe form of AD suffer significantly more often from sensitization to mites, animal dander, dust, and feather in comparison to patients with mild form of AD. Regarding the IgE-mediated food allergy, without distinguishing the early, combined, and late food reactions, no significant relation was recorded between the severity of AD and the occurrence of IgE-mediated food allergy in general. But if we restrict ourselves to patients with IgE-mediated food allergy, the situation is different. The patients suffering from IgE-mediated food allergy were subdivided into three categories, depending on the time to reaction, that is, early, combined, and late. The significant dependence between the time to food reaction and severity of AD was confirmed. We also studied the direction of this dependence and it turns out that the higher the time to reaction, the higher the severity of AD.

The occurrence of food sensitization (patients with positive results of sIgE and/or SPT and/or APT without the clinical symptoms) is not in significant relation to the severity of AD.

If we compare the significance of the food and inhalant allergens, it seems that inhalant allergens play more important role in the severe form of AD than IgE-mediated food allergy. Severe form of AD is recorded in 25 patients (9%) in our study; among these patients, 8 patients suffer from IgE-mediated food allergy and 17 patients are without IgE-mediated food allergy, but all these 17 patients suffer from sensitization to one or more of the inhalant allergens. Sensitization to house dust mites seems to be important and clinically relevant for AD. However, the importance of inhaled allergens is still under investigation. Early epicutaneous sensitization to aeroallergens may be enhanced by damage of the skin barrier function, which is one of the major manifestations of AD and a key contributor to its pathogenesis. Abnormal expression of epidermal proteins caused by T_H2 -type cytokines or protease allergens may increase the risk of sensitization to allergens and contribute to the development of AD (Barker et al., 2007; Bussmann et al.,

2006; Fallon et al., 2009; Howell et al., 2007; Jeong et al., 2008; Kim et al., 2008; Nemoto-Hasebe et al., 2009). Airborne proteins have the ability to penetrate into the epidermis and worsen AD severity through the following three mechanisms: inherent proteolytic enzyme activity, activation of proteinase-activated receptors-2, and immunoglobulin E (IgE) binding, leading to increased inflammation (Bussmann et al., 2006; Jeong et al., 2008). Food allergens have a well-known contribution to disease activity of AD, especially in infants and young children. For clinical implication, identification of individualized allergens is an ideal strategy for better control of AD and avoidance of atopic march (Dai, 2007). According to Schäffer et al., the degree of sensitization is directly associated with the severity of AD and the sIgE response seems to contribute to the severity of the disease in a dose-dependent fashion (1999). In their study, a nested case-control analysis on AD was performed on the basis of a cross-sectional study of 2201 East German school-children aged 5–14 years. Total and allergen-sIgE antibodies to grass and birch pollen, *Cladosporium herbarum*, *Dermatophagoides pteronyssinus*, and cat epithelium in serum were determined and additional information was obtained by means of a standardized questionnaire. Multiple linear regression analyses showed significant associations between the severity score of AD and concentrations of allergen-sIgE to dust mite allergens after adjustment for sex, age, location, and parental predisposition (Schäfer et al., 1999). According to another study, there are conflicting data regarding whether dust mite allergens have their primary role through direct contact with skin or whether inhalation and absorption through the respiratory tract is equally important (Bieber & Leung, 2002). It has been known that patients with AD have increased sensitivity to irritant. Further, house dust mite allergen is a cysteine proteinase which may function not only as an allergen (Deleuran, Ellingsen, Paludan, Schou, & Thestrup-Pedersen, 1998). Carswell found that serum concentration of mite-sIgE were greater in children with AD than in children with bronchial asthma. They concluded that increased exposure to mite allergens was a result of skin inflammation and thus the high level of mite-sIgE provided an evidence for cutaneous sensitization (Carswell & Thompson, 1986). Kutlu et al. evaluated 45 children with AD and found that patients with strong SPT positivity to mites had a higher total SCORAD score (2013). In the study of Laske and Niggemann, children with high SCORAD levels showed a sensitization to aeroallergens significantly more often; their results suggest that serum IgE levels seem to be associated with the degree of AD. Their results indicate a significant correlation between SCORAD and serum IgE levels, but the standard deviation was large (Laske & Niggemann, 2004). Tupker demonstrated a double-blind, randomized, placebo-controlled trial, which showed that inhalation of house dust mite could induce new skin lesions and exacerbation of existing lesions in AD (Tupker, De Monchy, Coenraads, Homan, & van der Meer, 1996).

Regarding the food allergens, a similar study was done by Röckemann et al., they evaluated the food sensitization in adults with AD in relation to the severity of the disease: 211 adult patients were examined and the severity of AD was determined; food allergy was defined as convincing history taken by a physician and sensitization to the corresponding allergen. There was no association between the severity of AD and frequency of food sensitization or history of food allergy. But the percentage of sensitization to animal food allergens was significantly higher in severe AD patients and sensitization to *nAra h 1* was significantly more frequent in patients with severe AD (Röckmann et al., 2014). In some previous studies, the problem of severity of AD and the occurrence of IgE-mediated

food allergy, food hypersensitivity reactions had been dealt, as well as the occurrence of concomitant allergic diseases and parameters, such as the family history about atopy and the onset of AD (Celakovska, 2015; Celakovska & Bukač, 2011; Celakovska & Bukač, 2015a, 2015b; Celakovska & Ettlerova, 2009; Celakovska, Bukac, & Ettler, 2015; Celakovska, Ettlerova, Ettler, & Bukač, 2015; Celakovska, Ettlerova, Ettler, & Krčmová, 2010; Celakovska, Ettlerova, Ettler, Vaněčková, & Bukač, 2015a; Celakovska, Ettlerová, Vaněčková, & Ettler, 2011a; Celakovska, Ettlerová, Vaněčková, & Ettler, 2011b). According to these results, IgE sensitization to animal dander, dust, and mites may increase the risk of developing asthma or rhinitis. Persistent lesions of AD occur more often in patients with sensitization to animal dander, mites, and dust (Celakovska et al., 2015c). The significant relationship between the severity of AD and the occurrence of food hypersensitivity reactions was confirmed; 96% of patients with severe form of AD suffer from food reactions. The occurrence of asthma bronchiale, rhinitis, pollen allergy, persistent eczematic lesions, and positive data in the family history are recorded more often in adolescent and adults AD patients who suffer from IgE-mediated food allergy; patients with sensitization without clinical symptoms of IgE-mediated food allergy suffer significantly more often from rhinitis and pollen allergy; wheat, soy, and peanuts are of great importance. Patients suffering from food hypersensitivity reactions, in general, suffer significantly more often from rhinitis and from persistent eczematic lesions; the relationship was confirmed in patients with hypersensitivity reactions to nuts, kiwi, fishes, and apple (Celakovska, 2015; Celakovska & Bukač, 2011; Celakovska & Bukač, 2015a, 2015b; Celakovska & Ettlerova, 2009; Celakovska et al., 2010, 2011a, 2011b, 2015a; Celakovska, Ettlerova, & Ettler, 2015; Celakovska, Ettlerova, Ettler, & Bukač, 2015).

There are other studies dealing with the question of severity of AD. In Ong's study, the levels of food and staphylococcal superantigen-sIgE were measured by Phadia ImmunoCAP system. Of the five common food allergens (cow's milk, egg white, soybean, wheat, and peanut), only IgE levels to egg white were associated significantly with the severity of AD in young children with AD. IgE sensitization to egg white was significantly associated with IgE sensitization to staphylococcal superantigens in older children (Ong, 2014). Another study was designed to evaluate an inner-city urban birth cohort to identify early environmental factors associated with AD and food allergy, as well as the incidence of wheezing during the first year of life. This study supports the following recommendations: (i) longer breastfeeding, (ii) avoid pets during gestation, (iii) avoid too frequent house cleaning, and (iv) living in an area with decreased traffic density (Stelmach et al., 2014). Manam conducted a systematic literature search for studies investigating the link between AD and food sensitization or clinically significant allergy in adults to assess the strength of the association between the two diseases in both general and selected populations. Adult AD patients show much higher rates of sensitization to foods than healthy individuals, in particular to food proteins cross-reactive with airborne allergens, rather than the food allergens that typically predominate amongst children with AD. The conclusion of this study is that challenge-proven food allergy in adults with AD is uncommon. The incidence of new-onset food allergy in adult AD patients is currently unknown, as are the main routes of sensitization (Manam, Tsakok, Till, & Flohr, 2014).

Conclusion

The significant relation was recorded between the severity of AD and sensitization to inhalant allergens such as mites, animal dander, dust, and feather. The significant relation was also found between the severity of AD and the occurrence of early, combined, and late IgE-mediated food allergy reaction. It turns out that the higher the time to food reaction, the higher the severity of AD.

Disclosure statement

No potential conflict of interest was reported by the authors.

Notes on contributors

Jarmila Celakovska works as the specialist for atopic dermatitis at the Department of Dermatology and Venereology Faculty Hospital and Medical Faculty of Charles University, Hradec Králové, Czech Republic. She works in the research of atopic dermatitis in the following of some immunological parameters in patients suffering from atopic dermatitis; especially she is interested in examination of food allergy in patients suffering from this disease.

Josef Bukac is the mathematician, and works as a specialist for the statistical analysis at the Department of Medical Biophysics, Medical Faculty of Charles University in Hradec Králové, Czech republic.

References

- Barker, J., Palmer, C., Zhao, Y., Liao, H., Hull, P. R., Lee, S. P., ... Irwin McLean, W. H. (2007). Null mutations in the filaggrin gene (FLG) determine major susceptibility to early-onset atopic dermatitis that persists into adulthood. *Journal of Investigative Dermatology*, 127, 564–567.
- Bieber, T., & Leung, D. (2002). *Atopic dermatitis* (pp. 365–367). New York, NY: Marcel Dekker.
- Boguniewicz, M., & Leung, D. (2011). Atopic dermatitis: A disease of altered skin barrier and immune dysregulation. *Immunological Reviews*, 242, 233–246.
- Boyce, J., Assa'ad, A., Burks, A., Jones, S. M., Sampson, H. A., ... Schwaninger, J. M. (2010). Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. *Journal of Allergy and Clinical Immunology*, 126, 1105–1118.
- Bussmann, C., Böckenhoff, A., Henke, H., Werfel, T., & Novak, N. (2006). Does allergen-specific immunotherapy represent a therapeutic option for patients with atopic dermatitis? *Journal of Allergy and Clinical Immunology*, 118(6), 1292–1298.
- Carswell, F., & Thompson, S. (1986). Does natural sensitisation in eczema occur through the skin? *The Lancet*, 328, 13–15.
- Celakovska, J. (2015). Atopic March, food allergy and food hypersensitivity in children and adolescents suffering from atopic dermatitis. *Food and Agricultural Immunology*, 26(4), 590–600.
- Celakovska, J., & Bukač, J. (2015a). Food allergy in patients suffering from atopic dermatitis – association with concomitant allergic diseases. *Food and Agricultural Immunology*, 26(3), 325–339.
- Celakovska, J., & Bukač, J. (2015b). The severity of atopic dermatitis and analysis of the food hypersensitivity reactions. *Food and Agricultural Immunology*, 26(6), 896–908.
- Celakovska, J., Bukac, J., & Ettler, K. (2015). Food hypersensitivity reactions in atopic dermatitis patients and analysis of concomitant diseases. *Food and Agricultural Immunology*, 26(2), 260–270.
- Celakovska, J., & Bukač, J. (2011). Food adverse reactions in patients over 14 years of age suffering from atopic eczema. *Food and Agricultural Immunology*, 22(2), 105–114.

- Celakovska, J., & Ettlerova, K. (2009). Could food allergy testing be beneficial in adult patients with atopic dermatitis? Three case-reports. *Revue Française D'Allergologie*, 49(8), 593–599.
- Celakovska, J., Ettlerova, K., Ettler, K., & Bukač, J. (2015). Food allergy, asthma bronchiale, and rhinitis in atopic dermatitis patients with total immunoglobulin E under and above 200 IU/ml. *Food and Agricultural Immunology*, 26(5), 671–681.
- Celakovska, J., Ettlerova, K., Ettler, K., & Krčmová, I. (2010). Food allergy to egg with the onset at adult age. *Revue Française D'Allergologie*, 50(8), 628–633.
- Celakovska, J., Ettlerova, K., Ettler, K., Vaněčková, J., & Bukač, J. (2015a). Evaluation of allergy to soy in patients with atopic dermatitis older than 14 years of age. *Food and Agricultural Immunology*, 26(1), 60–70.
- Celakovska, J., Ettlerova, K., Ettler, K., Vaněčková, J., & Bukač, J. (2015b). Evaluation of food allergy to wheat, cow milk, egg, soy and peanuts in patients suffering from atopic dermatitis. *Food and Agricultural Immunology*, 26(1), 26–37.
- Celakovska, J., Ettlerová, K., Ettler, K., Vaněčková, J., & Bukač, J. (2015c). Sensitization to aeroallergens in atopic dermatitis patients: Association with concomitant allergic diseases. *Journal of the European Academy of Dermatology and Venereology*, 29, 1500–1505.
- Celakovska, J., Ettlerová, K., Vaněčková, J., & Ettler, K., (2011a). Egg allergy in patients over 14 years of age suffering from atopic eczema. *International Journal of Dermatology*, 50, 811–818.
- Celakovska, J., Ettlerová, K., Vaněčková, J., & Ettler, K. (2011b). The peanut allergy in patients suffering from atopic dermatitis over 14 years of age. *Food and Agricultural Immunology*, 22(3), 195–204.
- Dai, Y. (2007). Allergens in atopic dermatitis. *Clinical Reviews in Allergy & Immunology*, 33(3), 157–166.
- Deleuran, M., Ellingsen, A. R., Paludan, K., Schou, C., & Thestrup-Pedersen, K. (1998). Purified Der p1 and p2 patch tests in patients with atopic dermatitis: Evidence for both allergenicity and proteolytic irritancy. *Acta Dermato-Venereologica*, 78, 241–243.
- European Task Force on Atopic Dermatitis. (1993). Severity scoring of atopic dermatitis: The SCORAD index (consensus report of the European task force on atopic dermatitis). *Dermatology*, 186, 23–31.
- Fallon, P., Sasaki, T., Sandilands, A., Campbell, L. E., Saunders, S. P., Mangan, N. E., ... McLean, W. H. I. (2009). A homozygous frameshift mutation in the mouse Flg gene facilitates enhanced percutaneous allergen priming. *Nature Genetics*, 41, 602–608.
- Gelmetti, C., & Colonna, C. (2004). The value of SCORAD and beyond. Towards a standardized evaluation of severity? *Allergy*, 59(Suppl. 78), 61–65.
- Hanifin, J., & Rajka, G. (1980). Diagnostic features of atopic dermatitis. *Acta Dermato-Venereologica*, 92, 44–47.
- Hill, D., Hosking, C., de Benedictis, F., Oranje, A. P., Diepgen, T. L., Bauchau, V., & EPAAC Study Group. (2008). Confirmation of the association between high levels of immunoglobulin E food sensitization and eczema in infancy: An international study. *Clinical & Experimental Allergy*, 38, 161–168.
- Howell, M., Kim, B., Gao, P., Grant, A., Boguniewicz, M., De Benedetto, A., ... Leung, D. Y. M. (2007). Cytokine modulation of atopic dermatitis filaggrin skin expression. *Journal of Allergy and Clinical Immunology*, 120, 150–155.
- Jeong, S., Kim, H., Youm, J., Ahn, S. K., Choi, E. H., Sohn, M. H., ... Lee, S. H. (2008). Mite and cockroach allergens activate protease-activated receptor 2 and delay epidermal permeability barrier recovery. *Journal of Investigative Dermatology*, 128(8), 1930–1939.
- Kim, B., Leung, D., Boguniewicz, M., & Howell, M. (2008). Loricrin and involucrin expression is down-regulated by Th2 cytokines through STAT-6. *Clinical Immunology*, 126, 332–337.
- Kutlu, A., Karabacak, E., Aydin, E., Ozturk, S., Taskapan, O., Aydin, S., ... Bozkurt, B. (2013). Relationship between skin prick and atopic patch test reactivity to aeroallergens and disease severity in children with atopic dermatitis. *Allergologia et Immunopathologia*, 41(6), 369–373.
- Laske, N., & Niggemann, B. (2004). Does the severity of atopic dermatitis correlate with serum IgE levels? *Pediatric Allergy and Immunology*, 15(1), 86–88.

- Manam, S., Tsakok, T., Till, S., & Flohr, C. (2014). The association between atopic dermatitis and food allergy in adults. *Current Opinion in Allergy and Clinical Immunology*, 14(5), 423–429.
- Morita, H., Nomura, I., Matsuda, A., Saito, H., & Matsumoto, K. (2013). Gastrointestinal food allergy in infants. *Allergy International*, 62, 297–307.
- Nemoto-Hasebe, I., Akiyama, M., Nomura, T., Sandilands, A., Irwin McLean, W. H., & Shimizu, H. (2009). Clinical severity correlates with impaired barrier in filaggrin-related eczema. *Journal of Investigative Dermatology*, 129, 682–689.
- Novembre, E., Cianferoni, A., Lombardi, E., Bernardini, R., Pucci, N., & Vierucci, A. (2001). Natural history of “intrinsic” atopic dermatitis. *Allergy*, 56(5), 452–453.
- Ong, P. (2014). Association between egg and staphylococcal superantigen IgE sensitizations in atopic dermatitis. *Allergy and Asthma Proceedings*, 35(4), 346–348.
- van den Oord, R., & Sheikh, A. (2009). Filaggrin gene defects and risk of developing allergic sensitisation and allergic disorders: Systematic review and meta-analysis. *BMJ*, 339, b2433.
- Roguedas Contios, A., & Misery L. (2011). What is intrinsic atopic dermatitis? *Clinical Reviews in Allergy & Immunology*, 41(3), 233–236.
- Röckmann, H., van Geel, M., Knulst, A., Huiskes, J., Bruijnzeel-Koomen, C., & de Bruin-Weller, M. (2014). Food allergen sensitization pattern in adults in relation to severity of atopic dermatitis. *Clinical and Translational Allergy*, 4(1), 1–9. doi:10.1186/2045-7022-4-9.
- Schäfer, T., Heinrich, J., Wjst, M., Adam, H., Ring, J., & Wichmann, H. (1999). Association between severity of atopic eczema and degree of sensitization to aeroallergens in schoolchildren. *Journal of Allergy and Clinical Immunology*, 104(6), 1280–1284.
- Spergel, J. (2010). Epidemiology of atopic dermatitis and atopic March in children. *Immunology and Allergy Clinics of North America*, 30, 269–280.
- Stelmach, I., Bobrowska-Korzeniowska, M., Smejda, K., Majak, P., Jerzynska, J., Stelmach, W., ... Hanke, W. (2014). Risk factors for the development of atopic dermatitis and early wheeze. *Allergy and Asthma Proceedings*, 35(5), 382–389.
- Stiefel, G., & Roberts, G. (2012). How to use serum-specific IgE measurements in diagnosing and monitoring food allergy. *Archives of Disease in Childhood – Education & Practice Edition*, 97, 29–36.
- Tan, J., & Smith, W. (2014). Non-IgE-mediated gastrointestinal food hypersensitivity syndrome in adults. *The Journal of Allergy and Clinical Immunology: In Practice*, 2, 355–357.
- Tupker, R., De Monchy, J., Coenraads, P., Homan, A., & van der Meer, J. B. (1996). Induction of atopic dermatitis by inhalation of house dust mite. *Journal of Allergy and Clinical Immunology*, 97, 1064–1070.
- Turnbull, J., Adams, H., & Gorard, D. (2015). Review article: The diagnosis and management of food allergy and food intolerances. *Alimentary Pharmacology & Therapeutics*, 41(1), 3–25.
- Wassmann, A., & Werfel, T. (2015). Atopic eczema and food allergy. *Chemical Immunology and Allergy*, 101, 181–190.
- Weidinger, S., Illig, T., Baurecht, H., Irvine, A. D., Rodriguez, E., Diaz-Lacava, A., ... Liao, H. (2006). Loss-of-function variations within the filaggrin gene predispose for atopic dermatitis with allergic sensitizations. *Journal of Allergy and Clinical Immunology*, 118, 214–219.
- Zeppa, L., Bellini, V., & Lisi, P. (2011). Atopic dermatitis in adults. *Dermatitis*, 22, 40–46.