

Sensitization to fungi in atopic dermatitis patients 14 year and older – Association with other atopic diseases and parameters

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Abstract

Background: Fungi as a source of allergen are still largely neglected in basic research as well as in clinical practice. This study aimed to highlight the impact of fungal allergens in a group of patients suffering from atopic dermatitis (AD). **Aims and Objectives:** The evaluation of the sensitization to fungi in AD patients aged 14 year and older and the evaluation of the relation of fungal sensitization to the occurrence of other atopic diseases and parameters. **Materials and Methods:** All patients satisfying inclusion criteria attending our hospital between 2008 and 2017 were included in the study. The complete dermatological and allergological examinations were performed in all included patients including examination of specific immunoglobulin E, skin prick test to mixture of fungi and inhalant allergens, evaluation of asthma bronchiale, rhinitis, onset of AD, family history about atopy, duration of eczematous lesions, severity of AD. Pairs of these categories were entered in the contingency tables and the Chi-square test for relationship of these variables was performed with the level of significance set below 5%. **Results:** Three hundred and thirty-one patients were included in the study; the average age was 26.8 years. The sensitization to fungi was recorded in 100 patients (30%). In these patients, the occurrence of asthma bronchiale, rhinitis, family history about atopy, sensitization to grass and trees was significantly higher than in patients without sensitization to fungi. We did not find any significant relation between the sensitization to fungi

and the severity of AD, no relation was also found between the sensitization to fungi and sensitization to mites, animal dander, bird feather, and dust. Conclusion: The occurrence of asthma bronchiale, rhinitis, family history about atopy, sensitization to grass and trees was significantly higher in AD patients with sensitization to fungi. No relation was found between the severity of AD and the sensitization to fungi.

Keywords: Asthma bronchiale, atopic dermatitis, persistent eczematous lesions, rhinitis, sensitization to fungi

➤ Introduction



Allergic diseases are considered the epidemics of the twentieth century and are estimated to affect >30% of the population in industrialized countries with a still increasing prevalence.^{[1],[2]} It has been largely revealed that fungi are potent sources of allergenic molecules covering a vast variety of molecular structures including enzymes, toxins, cell wall components, and phylogenetically highly conserved cross-reactive proteins.^{[1],[2]} Fungi can have adverse effects on human health, causing infection, immunoglobulin E (IgE)-mediated allergy, non-IgE-mediated hypersensitivity, and toxicity or irritation. The incidence of fungal diseases has risen rapidly over the past two decades and fungal allergy is one of the common health problems worldwide.^{[1],[2]} Indoor and outdoor exposure to fungal components, including spores, is a recognized triggering factor for respiratory allergy and asthma as well as for atopic dermatitis (AD).^{[3],[4]} Among over 100 thousand fungal species, only a few hundreds have been described as opportunistic pathogen causing human illness through three-specific mechanisms: direct infection of the host, elicitation of deregulated immune responses, and toxic effects due to secondary metabolites.^{[5],[6],[7],[8]} The exact prevalence of fungal sensitization among the general population is still unknown.^[9] The contribution of different fungal allergens to allergic diseases is not identical, but species-specific. *Alternaria* and *Cladosporium* species are considered to be important outdoor allergens and sensitization and exposure to the species of these genera are related to the development of asthma and rhinitis, as well as epidemics of asthma exacerbation, including life-threatening asthma exacerbation. In contrast, xerophilic species of *Penicillium* and *Aspergillus*, are implicated in allergic diseases as indoor allergens. *A. fumigatus* has a high capacity to colonize the bronchial tract of asthmatic patients, causing severe persistent asthma and low lung function, and sometimes leading to allergic bronchopulmonary aspergillosis.^{[5],[6],[7],[8],[9],[10],[11]} Clinically, the IgE-mediated sensitization to fungal allergens can manifest as allergic rhinitis and rhinosinusitis, allergic asthma, and AD.^{[12],[13],[14]} AD is a chronic relapsing and highly pruritic inflammation of the skin with a worldwide prevalence of 10%–20% in children and of 1%–3% in adults.^{[4],[15],[16]} Recently, *Malassezia sympodialis*, a lipophilic yeast colonizing the skin of both AD and healthy individuals, has been shown to induce IgE-mediated sensitization exclusively in patients suffering from AD.^[4] The main reason for this specific sensitization may be the disrupted skin barrier facilitating allergen uptake which may contribute to the perpetuation of the disease.^[4]

Aim of the study

The aim of this study was the evaluation of sensitization to mixture of fungi in AD patients aged 14 year and older and to show the relation to the occurrence of asthma bronchiale, rhinoconjunctivitis, onset of AD, family history about atopy, duration of eczematous lesions, sensitization to inhalant allergens (mites, animal dander, dust, bird feather, mixture of grass, and mixture of trees), and to the severity of AD.

Materials and Methods



During the period of 2008–2017, 331 patients suffering from AD at the age of 14 year and older had attended. All these patients were examined at 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.^[17] Exclusion criteria were long-term therapy with cyclosporin or systemic corticoids, pregnancy or breastfeeding. Patients with AD having other systemic diseases were excluded from the study as well. Complete dermatological and allergological examinations were performed in patients included in the study. The following parameters were studied: - sensitization to fungi, the occurrence of asthma bronchiale, rhinitis, onset of AD, family history about atopy, duration of eczematous lesions, sensitization to inhalant allergens (mites, animal dander, dust, bird feather, mixture of grass, and mixture of trees), and the severity of AD. The statistical evaluation of the relation between the sensitization to fungi and these parameters was performed.

The study was approved by Ethics committee of Faculty Hospital Hradec Králové, Charles University in Prague, Czech Republic. There was no conflict of interest. CONSORT statement and STROBE statement guidelines were followed.^[18]

Evaluation of parameters monitored

Sensitization to fungi (mixture): It was determined according to the specific IgE level (sIgE) and the skin prick test (SPT) results. Commercial extracts Alyostal (Stallergens, France) was used for SPT (Mixture of *Alternaria tenuis*, *A. fumigatus*, *Candida albicans*, *Cladosporium herbarum*, *Mucor racemosus*, *Penicillium notatum*). The serum level of the sIgE was measured with the method of CAP (system FEIA-Pharmacia Diagnostics, Uppsala, Sweden). The level of sIgE >0.35 U/ml was assessed as positive. The diagnosis of sensitization to fungi was made in the case of positive results in sIgE and/or SPT examination.

Sensitization to dust (mixture), mites (mixture), animal dander (mixture), feather (mixture), grass (mixture), and trees (mixture): It was determined according to the sIgE level and the SPT results for these allergens. Commercial extracts Alyostal (Stallergens, France) were used for SPT. The serum level of the sIgE has been measured with the method of CAP (system FEIA-Pharmacia Diagnostics, Uppsala, Sweden). The level of sIgE >0.35 U/ml was assessed as positive. The diagnosis of sensitization to these aeroallergens was made in the case of positive results in sIgE and/or SPT examination.

The diagnosis of asthma bronchiale

It was made according to the results in spirometry at allergological department.

The evaluation of rhinitis (seasonal or perrenial)

It was made according to the anamnestical data.

The evaluation of the duration of atopic dermatitis

The AD lesions were evaluated as persistent or occasional according to the dermatologist's examination during one previous year and according to the patient information. Persistent lesions were defined as eczematous lesions on the different parts of the body appearing in the period shorter than 1 month. Occasional lesions were defined as episodes of eczematous lesions; the patient had been without lesions of AD at least 1 month during 1 year. It was evaluated according to the SCORAD index with the evaluation of affected skin area and intensity.

The onset of atopic dermatitis

It was evaluated according to the patient history (the onset of AD under 5 year of age or later).

The family history

The family history of atopy was evaluated according to the patient information (the occurrence of allergy, AD, asthma bronchiale, rhinoconjunctivitis in parents, brothers or sisters, children).

Severity of atopic dermatitis

Severity of AD was scored in agreement with SCORAD with the assessment of topography items (affected skin area), intensity criteria, and subjective parameters. This examination was performed during 1 year every 3 months and the average SCORAD index was recorded.^[19]

Statistical analysis

We evaluated whether there was some relation between the sensitization to mixture of fungi and followed parameters (the occurrence of asthma bronchiale, rhinitis, onset of AD, duration of eczematous lesions, family history about atopy, sensitization to mites, animal dander, dust, bird feather, mixture of grass, mixture of trees, and severity of AD according to the SCORAD index). We analyzed the data to determine whether the occurrence of sensitization to fungi was associated with the occurrence of mild, moderate, or severe form of AD. Pairs of these categories were entered in the contingency tables and the Chi-square test for relationship of these variables was performed with the level of significance set to less than 5%. We used the Excel program and macros to enter the data. We also used the NCSS package for analysis.

Results



Patients

A total of 331 patients were examined, 110 men and 221 women with the average age 26.8 years (minimum 14 year and maximum 63 year, standard deviation (SD) 9.2 years) and with the average SCORAD 33.1 points, SD 13.1 points.

The sensitization to mixture of fungi was found in 100 (30%), no sensitization to fungi was recorded in 231 patients (70%). Asthma bronchiale was confirmed in 146 patients (44%), rhinitis in 165 patients (50%), onset of AD under 5 year of age in 250 patients (75%), (the youngest age of onset was 6 month of age), positive family history about atopy in 190 patients

(57%), persistent eczematous lesions in 203 patients (61%), sensitization to mites in 202 patients (61%), to dust in 82 patients (25%), to animal dander in 158 patients (48%), to bird feather in 47 patients (14%), to mixture of grass in 225 patients (68%) and to mixture of trees in 167 patients (51%). Mild form of AD was recorded in 99 patients (30%, the average SCORAD was 14.6), moderate form in 205 patients (62%, the average SCORAD was 34.7) and severe form in 27 patients (8%, the average SCORAD was 52.4). The characteristic of patients were displayed in [Table 1]. The percentage of positive sIgE, SPT and both and the percentage of patients with positive family history about atopy in patients with sensitization to fungi, mites, dust, animal dander, bird feather, mixture of grass, and mixture of trees are shown in [Table 2]. The relations between the occurrence of sensitization to fungi and the occurrence of asthma bronchiale, rhinitis, duration of eczematous lesions during 1 year, family history about atopy, and the onset of AD are shown in [Table 3]. A significant relation was found between the occurrence of sensitization to fungi and the occurrence of asthma bronchiale ($P=0.002$), rhinitis ($P<0.0001$), and positive family history about atopy ($P=0.01$). No relation was found between the sensitization to fungi and the onset of AD ($P=0.084$) and duration of eczematous lesions ($P=0.377$). The relations between the occurrence of sensitization to fungi and the occurrence of sensitization to mites, animal dander, bird feather, dust, mixture of grass and trees are shown in [Table 4]. No relation was recorded between the sensitization to fungi and the sensitization to mites ($P=0.168$), animal dander ($P=0.089$), bird feather ($P=0.580$), and dust ($P=0.847$). The significant relation was confirmed between the sensitization to fungi and the sensitization to mixture of grass ($P=0.001$) and trees ($P<0.001$).

Parameters	Number of patients from 331 patients n (%)
Sensitization to fungi	
Yes	100 (30)
No	231 (70)
Asthma bronchiale	
Yes	146 (44)
No	185 (56)
Rhinitis	
Yes	255 (77)
No	76 (23)
Onset of AD	
Under 5 years	250 (75.5)
Above 5 years	81 (24.5)
Family history	
Positive	190 (58)
Negative	141 (43)
Duration of lesions during last 1 year	
Persistent	203 (61)
Occasional	128 (39)
Sensitization to mites	
Yes	202 (61)
No	129 (39)
Sensitization to dust	
Yes	82 (25)
No	249 (75)
Sensitization to animal dander	
Yes	158 (48)
No	173 (52)
Sensitization to bird feather	
Yes	47 (14)
No	284 (86)
Sensitization to trees	
Yes	167 (51)
No	164 (49)
Sensitization to grass	
Yes	225 (68)
No	106 (32)

AD: Atopic dermatitis

Table 1: The number of patients with the occurrence of the followed parameters

	Number of patients with recorded sensitization of 331 patients; n (%)	Positive sIgE (%)	Positive SPT (%)	Positive sIgE + SPT (%)	Positive family history (%)
Fungi	100 (30)	16 (4.8)	60 (18.12)	24 (7.2)	69 (20.8)
Mites	202 (61)	22 (6.6)	155 (46.8)	25 (7.5)	132 (39.8)
Dust	82 (24.7)	5 (1.5)	15 (4.5)	62 (18.7)	57 (17.2)
Animal dander	158 (48)	5 (1.5)	120 (36.2)	33 (9.9)	104 (31.4)
Bird feather	47 (14)	15 (4.5)	27 (8.1)	5 (1.5)	29 (8.7)
Grass	225 (68)	15 (4.5)	180 (54.3)	30 (9)	142 (42.9)
Trees	167 (51)	9 (2.7)	120 (36.2)	38 (11.4)	108 (32.6)

sIgE: Specific immunoglobulin E, SPT: Skin prick test

Table 2: The percentage of positive sIgE, skin prick test and both and the percentage of patients with positive family history about atopy in patients with sensitization to fungi, mites, dust, animal dander, bird feather, mixture of grass, and mixture of trees

Parameters	AB+ (%)	AB- (%)	RC+ (%)	RC- (%)	Persistent (%)	Occasional (%)	Family history+ (%)	Family history- (%)	Onset of AD under 5 year (%)	Onset of AD after 5 year (%)
Sensitization to fungi+	58 (18)	42 (13)	90 (27)	10 (3)	66 (20)	34 (10)	69 (21)	31 (9)	76 (23)	24 (7)
Sensitization to fungi-	88 (26)	143 (43)	165 (50)	66 (20)	137 (41)	94 (28)	121 (37)	110 (33)	174 (53)	57 (17)
Total number of patients	146 (44)	185 (56)	255 (77)	76 (23)	203 (61)	128 (39)	190 (58)	141 (42)	250 (76)	81 (24)
P	0.002		0.00001		0.377		0.010		0.0843	

AB+: Asthma bronchiale yes, AB-: Asthma bronchiale no, RC+: Rhinitis yes, RC-: Rhinitis no, AD: Atopic dermatitis

Table 3: The relation between the occurrence of sensitization to fungi and the occurrence of asthma bronchiale, rhinitis, duration of eczematic lesions during 1 year, family history about atopy, and the onset of atopic dermatitis

Parameters	Mites+ (%)	Mites- (%)	Animal dander+ (%)	Animal dander- (%)	Bird feather+ (%)	Bird feather- (%)	Dust+ (%)	Dust- (%)	Trees+ (%)	Trees- (%)	Grass+ (%)	Grass- (%)
Sensitisation to fungi+	68 (20)	32 (10)	56 (17)	44 (13)	17 (5)	83 (25)	25 (8)	75 (23)	69 (21)	31 (9)	81 (24)	19 (6)
Sensitisation to fungi-	134 (40)	97 (30)	102 (31)	129 (39)	30 (9)	201 (61)	57 (17)	174 (52)	98 (30)	133 (40)	144 (43)	87 (26)
Total number of patients	202 (60)	129 (40)	158 (48)	173 (52)	47 (14)	284 (86)	82 (25)	249 (75)	167 (51)	164 (49)	225 (68)	106 (32)
P	0.168		0.089		0.580		0.847		0.00001		0.001	

+= Sensitization; - = Sensitization absent

Table 4: The relation between the occurrence of sensitization to fungi and the occurrence of sensitization to mites, animal dander, bird

feather, dust,
grass, and tress

The relations between the occurrence of sensitization to fungi and the occurrence of mild, moderate, and severe forms of AD is depicted in [Table 5]. The relation between the sensitization to fungi and the occurrence of mild, moderate, and severe forms was not confirmed ($P=0.128$).

Number of patients	Severity of atopic dermatitis		
	Mild (%)	Moderate (%)	Severe (%)
Sensitization to fungi+	28 (8.4)	58 (17.5)	14 (4.2)
Sensitization to fungi-	71 (21.4)	147 (44.4)	13 (4)
Total number of patients	99 (29.8)	205 (61.9)	27 (8.2)
<i>P</i>	0.128		

Table 5: The relation between the occurrence of sensitization to fungi and the occurrence of mild, moderate, severe form of atopic dermatitis according to the SCORAD index

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Discussion



There is a lack of reports focusing on the course of AD with respect to its evolution and association with other allergic diseases and parameters.

Outdoor allergens are an important part of the exposures that lead to allergic disease and outdoor allergens have been the subject of only limited studies with respect to the epidemiology of asthma. According to the literature, there are only a few studies that evaluated the sensitization to fungi and much remains to be studied with respect to prevalence patterns, exposure, and disease relationships.^[20]

The clinical history that represents one of the most important diagnostic criteria for an allergy is difficult to elicit for patients with a fungal allergy. In contrast to other allergies (seasonal pollen-derived allergies, food allergies) most patients sensitized to fungi are not aware of the source of exposure and can only report that the symptoms are more or less perennial. In our study, we evaluated the sensitization to fungi according to the results of SPT and/or to the specific IgE level. Sensitization to fungi was recorded in 100 patients out of 331 (30%). Regarding the evaluation of the relation between the sensitization to fungi and the occurrence of other atopic diseases and parameters, we found that patients suffering from sensitization to fungi suffered significantly more often from asthma bronchiale, from rhinitis, and about positive family history of atopy. On the other hand, a significant relation between the sensitization to fungi and the severity of AD according to the SCORAD index was not detected. Regarding the relation between the sensitization to fungi and other inhalant allergens, we found the significant relation only between the sensitization to fungi and the sensitization to a mixture of grass and trees. The relation between the sensitization to fungi and other inhalant allergens such as mites, dust, bird feather, and animal dander was not detected. The explanation might be in the nature of outdoor allergen-bearing particles, the distributions of their source, and the nature of the aerosols (particle types, sizes, and dynamics of concentrations). Primary sources for outdoor allergens included vascular plants (pollen, fern spores, soy dust), and fungi (spores, hyphae).^[20] Nonvascular plants, algae, and arthropods contributed small numbers of allergen-bearing particles. Pollen and fungal spore exposures had

both been implicated in acute exacerbations of asthma and sensitivity to some fungal spores predicted the existence of asthma.^[20] No official standards existed for interpretation of pollen or fungal data. The American Academy of Asthma, Allergy, and Immunology published guidelines for interpretation of pollen data that were based on national averages for groups of pollen types. Outdoor fungal aerosol concentrations were also listed. Whether these guidelines were related to a disease in any way remained unknown.^[21] Jariwala et al. performed a study to better understand the contribution of pollen and fungi to asthma severity in Bronx. According to their results, there existed a significant association between spring asthma bronchiale and tree pollen concentrations in a highly urbanized area such as Bronx.^[22] The following were predictors of asthma: presence of rhinitis and/or eczema, positive prick test for certain aeroallergens, especially *Alternaria* and grass pollen, and family history of asthma.^[23]

The prevalence of fungal sensitization displays wide geographical variability. Data from the European Community Respiratory Health Survey demonstrated that among adults aged 20–44 years in the general population, the prevalence of positive skin tests using *Alternaria* and *Cladosporium* extracts ranged from 0.2%–14.4%, to 0%–11.9%, respectively.^[24] Prevalence of positive SPT for mixture of fungi in our study was higher-25%; the probable explanation for the difference was that we evaluated this sensitization in patients suffering from AD and the prevalence of sensitization to fungi could be higher in this group of patients suffering from atopic disease. According to a study in Japan, sensitization to *Malassezia*, *Alternaria*, and *Cladosporium* tended to decrease with age, which was in accordance with the general conception that atopic asthma was more common in younger patients.^[25] However, the frequency of *A. fumigatus* did not decrease with age most likely because sensitization to this species was associated with severe persistent asthma with a long disease duration.^[26] This phenomenon highlighted the potential significance of these indoor fungal species in middle-aged and elderly patients. This finding was similar to that of a study by Chou et al.^[27] According to Cramer, the incidence of fungal sensitization was high and clinically relevant. However, the problems related to the in vitro and in vivo diagnosis of fungal and other allergies were far from being solved.^[28] Any in vivo diagnosis of allergy based on skin tests as well as any in vitro diagnosis of allergy based on the determination of allergen-specific IgE depended on the quality of the material used for testing. Although standardized extracts approved by the FDA were available for some allergenic sources, no fungal extracts had been approved to date.^{[29],[30]}

Nolles et al. investigated the prevalence of sensitization to different fungi in atopic children in relation to age and other aeroallergens. A total of 137 atopic children were studied. In this study in atopic children total IgE showed a significant linear relation with age, whereas specific IgE against outdoor fungi, indoor fungi, and house dust mite showed significant nonlinearity with respect to age. Specific IgE for indoor and outdoor fungi was associated with the presence of specific IgE for aeroallergen and milk. The conclusion of the study was that the sensitization to fungi was prevalent in childhood with an age-dependent distribution reaching maximum values at 7.7–7.8 years, followed by a decline for all fungal sensitization with increasing age. The importance and relative contribution of fungal sensitization to airway disease, compared with the other allergens, remained to be established.^[31] Reijula et al. evaluated the prevalence of IgE-mediated allergy and clinical outcomes caused by sensitization to fungal allergens in patients with suspected allergy. The conclusion of the study was, that in the Finnish population with allergic symptoms, IgE-mediated sensitization to 2 common fungal allergens was rare and of minor clinical importance. SPT reactions to fungi were mostly observed in patients with multiple sensitivity to various allergens.^[32] The aim of another study was the analysis of specific IgE against *Alternaria alternata* in AD and asthma patients. A total of 50 AD patients (17 males and 33 females) and 50 asthma patients (males 20 and females 30) were included in the study. This study suggested that *A. alternata* was a major aeroallergen. Some previous studies had shown that *A. alternata* was one of the most common indoor and outdoor airborne

fungi, so it could permanently present some allergic reaction to susceptible individuals. Therefore, control of *A. alternata* growth in indoor areas and avoidance with *A. alternata* could play an important role in reducing allergic reaction in susceptible individuals.^[33] According to Cramer, airborne fungal spores had been implicated as causative factors in respiratory allergy, particularly asthma. However, the prevalence of fungal sensitization was not known mainly due to the lack of standardized fungal extracts and to the overwhelming number of fungal species able to elicit IgE-mediated reactions. Recent work based on high-throughput cloning of fungal allergens revealed that fungi were able to produce extremely complex repertoires of species-specific and cross-reactive allergens. There was evidence that fungal sensitization also contributed to auto-reactivity against self-antigens due to shared epitopes with homologous fungal allergens.^[9] The significant relation between the sensitization to fungi and the severity of AD was not found in our study. According to some studies, *Malassezia sympodialis* had been reported as the most frequent skin-colonizing yeast in both AD patients and healthy individuals. Approximately 50% of the AD patients show immediate-type skin reactions or have specific serum IgE against *Malassezia sympodialis*. The main cause for this specific sensitization might be the disrupted skin barrier facilitating allergen uptake.^{[10],[14]} *Malassezia* might interact with the local skin immune responses and barrier function. Sensitization against this skin-colonizing yeast could correlate with disease activity. Furthermore, antifungal therapy shows beneficial effects in some patients. However, the pathogenetic mechanism and mutual interaction between *Malassezia* spp and AD still remained partly unclear and needed further investigation.^[34] In our study, we did not observe the higher risk of fungal infections in patients with positive test (SPT, sIgE) to mixture of fungi. We found the significant relation between the sensitization to fungi and the occurrence of asthma bronchiale and rhinitis. In patients with sensitization to fungi the occurrence of asthma bronchiale and rhinitis was significantly higher than in patients without sensitization to fungi. The epidemiologic studies had failed to demonstrate a direct relationship between fungal allergy and allergic rhinitis via either outdoor or indoor exposure.^[35] It was known, that fungal allergy was clearly linked to a subset of chronic rhinosinusitis known as allergic fungal rhinosinusitis.^[35] In the patient's mucus, fungal hyphae were detectable and patients showed hypersensitivity to specific fungal allergens along with specific IgE and IgG antibodies against the sensitizing fungus and an increased total serum IgE level.^[36] Regarding the asthma bronchiale, there was a compelling evidence that fungal allergy is associated with severe asthma.^{[9],[37],[38]} However, with exception of special cases such as workplace exposure or allergic bronchopulmonary aspergillosis, which were well documented, the contribution of fungal sensitization to the severity of asthma remained to be investigated.^[9] The relation of food allergens and aeroallergens to the severity of AD was evaluated in our previous studies.^[39] We found that the sensitization to mites, animal dander, bird feather and dust was in significant relation to the severity of AD.^[39] We also found, that AD patients with sensitization to mites and animal dander suffered significantly more often from asthma bronchiale, rhinitis, persistent eczematous lesions and had positive data about atopy in their family history.^[40] In another previous study, we evaluated the dependence between the severity of AD evaluated with the SCORAD index and the occurrence of other atopic diseases and parameters. The statistical evaluation of the dependence between the occurrence of bronchial asthma, rhinitis, and duration of the skin lesions, and the severity of AD was performed. Two hundred and eighty-three patients were examined; the significant relationship was recorded between the severity of AD according to the SCORAD index and bronchial asthma, the occurrence of rhinitis, and the duration of the skin lesions.^[41]

Already in early disease stages, a defective epidermal barrier is known to contribute to the pathogenesis of AD. Central elements in the epidermal barrier are antimicrobial peptides (AMPs), which are secreted by keratinocytes, sweat gland cells but also by infiltrating immune cells. AMPs function as endogenous antibiotics and are able to kill bacteria, viruses, and fungi. The probably best-studied AMPs in human skin are the defensins and cathelicidin. In atopic

diseases the functions of AMPs such as cathelicidin might be impaired and the resultant microbial superinfections could serve as cofactors for allergic sensitization. A variety of functions have been attributed to plant defensins. While many have antifungal activity, plant defensins have also been described with functions in antibacterial activity, zinc tolerance, and blocking of ion channels as well as inhibition of protein translation machinery, α -amylases, and proteases. Plant defensins with antifungal activity have shown promise for use in both agricultural and therapeutic settings.^[42] According to Peterson et al., peanut was one of the most hazardous sources of food allergens. They performed detection, isolation, and characterization of novel peanut allergens from lipophilic peanut extract. According to their results, on microbial cell cultures, the peanut defensins showed inhibitory effects on the mold strains of the genera *Cladosporium* and *Alternaria* but none on bacteria. The conclusion of their study was that they identified defensins as novel peanut allergens (Ara h 12 and Ara h 13) that reacted in particular with IgE of patients with severe peanut allergy. Their antimicrobial activity was solely antifungal.^[43] In our previous study we confirmed that patients suffering from sensitization to fungi suffered significantly more from food hypersensitivity reactions to nuts and fishes.^[44] The antifungal effect of plant proteins (defensins and lipid transfer proteins) probably cannot be applied, as also the antifungal effect of fatty acids methyl esters in fish.^[44] In India, Bains and Dogra determined the prevalence of positive SPT in patients with chronic allergic skin disorders.^[45] Fifty patients with chronic allergic disorders were recruited in this study. They were evaluated by SPT with both food and aeroallergens. In this study, SPT positivity in AD patients was 77.78%. Among nine patients with AD, maximum SPT positivity was seen with *Dermatophagoides farinae*, pollen *Amaranthus spinosus*, grain dust wheat, and cotton mill dust; each comprising 22.2% of patients. The conclusion of this study was that a significant number of patients of chronic allergic disorders showed sensitivity to dust, pollen, insects, *D. farinae*, and fungi on SPT. Fungus was positive in 12.2% of patients and included *Fusarium solanii* (7.32%) and *Rhizopus nigricans* (4.88%). In the present study with evaluation of sensitization to fungi, our results were similar – sensitization to fungi was in significant relation to the occurrence of asthma bronchiale, rhinitis, and positive family history about atopy.

Despite its importance in the management of allergic diseases, precise recognition of species-specific IgE sensitization to fungal allergens is often challenging because the majority of fungal extracts exhibits broad cross-reactivity with taxonomically unrelated fungi. Recent progress in gene technology has contributed to the identification of specific and cross-reactive allergen from different fungal sources. However, data revealing the clinical relevance of IgE reactivity to these allergen components are still insufficient.^[5]

❖ Conclusion



The sense of this study was to find the occurrence and the importance of the sensitization to fungi in the group of patients suffering from AD and to show the relation to other atopic diseases and parameters. The conclusion of our study was that the sensitization to fungi occurred in 30% of patients suffering from AD. In these patients, the occurrence of asthma bronchiale, rhinitis, family history about atopy, sensitization to grass and trees was significantly higher than in patients without sensitization to fungi. The severity of AD was not in a significant relation to the sensitization to fungi.

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Conflicts of interest

There are no conflicts of interest.

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