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Aeroallergen Sensitizations with Special Reference to Fungi Sensitization among the Community of Sultan Idris Education University, Malaysia

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Abstract: The present study is aimed to profile the prevalence and determine the risk of aeroallergen sensitization including fungi on gender, ethnicity, and age groups. 225 of the university community population were interviewed using a standard questionnaire by allergists to collect information on demographic including gender, ethnicity, and age. To confirm the prevalence of the aeroallergens sensitization, the gold standard procedure, i.e. skin prick testing was performed using commercial aeroallergens. Of the subjects, 93 (41.3%) were categorised as atopic. The most prevalent positive SPT among the general and the atopic population were house dust mites, (32.4%; 78.5%), followed by German cockroach (20%; 48.3%), fungal (7.55%; 18.2%), and cat dander (4.8%; 11.8%) respectively. The prevalence of fungi sensitization among the atopic population is doubled to the general population and considerably high compared to the World Allergy report. Among the 17 fungal sensitized subjects, 9 (52.9%) were monosensitized to *Aspergillus fumigatus*, 4 (23.5%) to *Penicillium notatum*, 2 (11.8%) to *Candida albicans*, and one (5.9%) to *Alternaria alternata*. One (5.9%) subject was oligosensitized to both *Alternaria alternata* and *Aspergillus fumigatus*. Male subjects were with the higher risk to fungi sensitization compared to female, Chinese ethnicity subjects to other ethnicities, and subjects with \geq 20 years of age to other age groups. Sensitization is high to both *Aspergillus fumigatus* and *Penicillium notatum*. Thus, it is an indicator not to be taken lightly as these fungi are also highly prevalent at UPSI and have been associated with the sick building syndrome.

Keywords: Indoor aeroallergen sensitization, Fungi sensitization, Risk group sensitization

The incidence of allergic diseases has been on the rise in recent decades all over the world (Sharma et al 2012, Soegiarto et al 2019). Aeroallergens are various airborne substances or inhalants, such as pollen, spores, and other biological or non-biological airborne particles that can cause allergic disorders. Inhalation or cutaneous contact with aeroallergens can trigger a release of proteins in the form of an allergic reaction on the skin and mucous membranes (Chapman 2008). Aeroallergens play a great role in the pathogenesis of respiratory allergic diseases. Pollens, molds, and pets are the main sources of allergens, the number and types of aeroallergens an individual is sensitized to vary across geographic regions (Assarehzadegan et al 2013, Ahmed et al 2019). Sensitization to aeroallergens is the most important factor causing allergic symptoms such as allergic rhinitis (Alvarez Cuesta et al 2006). Many studies have shown that the distribution and pattern of aeroallergens are significantly different from one country to another (Bousquet et al 2007). Identification of the most common aeroallergens to which the patients are sensitized has an important role in the diagnosis and treatment of allergic

symptoms. Selecting the most appropriate panel of allergen extracts for diagnostic testing and finding the best formulation of allergen immunotherapy depends on information about the most important aeroallergens in a specific area. Likewise, allergen avoidance cannot be properly achieved without identifying the allergens that are associated with allergic symptoms for every patient (Aburuz et al 2011).

Fungi are ubiquitous and, as a consequence of this, sensitization to fungi can be found throughout the world. The exact prevalence of mold sensitization is not known but is estimated to range from 3 to 10% in the general population, 12 to 42% of the atopic patients (Wiszniewska et al 2013). Fungi of the genera i.e. *Mucor, Penicillium, Aspergillus, Rhizopus, Alternaria,* and *Cladosporium* dominate the fungi isolated from dust mites which are the indoor fungi (Sabariego et al 2012). Allergens of indoor fungi are present in the air space throughout the year. Sensitivity is mostly detected to the genera of *Alternaria, Cladosporium, Aspergillus, Penicillium, and Fusarium.* In the tropical and other hot, humid regions, spore counts typically exceed

pollen counts by 100-fold. In Malaysia, studies among allergic rhinitis patients reported the prevalence of Aspergillus and Penicillium sensitization were 21.2 and 16% respectively (Hamilos 2010). House dust mites (HDM) have been described as important allergen sources causing respiratory allergies, such as asthma and rhinitis. More than 30 allergens from HDM have been described are responsible for over 50% of IgE reactivity in patients sensitized to HDM (Resende et al 2019). Clinical studies in patients demonstrated that allergy to HDM and cat allergens were the most common aeroallergens in Malaysia (Lim et al 2015). One study suggested that sensitization to one allergen (monosensitization) versus sensitization to multiple allergens (polysensitization) constitute two different phenotypes of allergic rhinitis (Ciprandi & Cirillo 2011). Moreover, polysensitization seems to be associated with a more severe form of respiratory allergy (Migueres et al 2009). Understanding sensitization patterns in certain geographic areas helps target specific interventions like allergen reduction and/or avoidance and encourages the use of specific immunotherapy towards the most common allergens (Ciprandi et al 2008, Casset & Braun 2010). Due to the lack of published studies on sensitization towards aeroallergens in Malaysia, the prevalence of common aeroallergens is still not fully understood in this region.

MATERIAL AND METHODS

There was a total of 225 subjects made up of students, lecturers, supporting staff, and volunteers undergoing SPTs to common aeroallergens for evaluation of allergy. The inclusion criteria were that the subject must be between 18-60 years of age and able to provide self consent for participation in the study. The exclusion criteria were pregnant women and those who drew negative results in the histamine test. All the subjects also completed a questionnaire. In this study, 6 commercial fungi allergen extracts were included namely; Alternaria alternata, Aspergillus fumigatus, Candida albicans, Aspergillus niger, Mucor mucedo, and Penicilliumnotatum purchased f rom Inmunotek, a pharmaceutical company based in Madrid. Allergens of SPT routinely used for allergy testing comprising of environmental insect allergens German cockroach (Blattella germanica), house dust mites (HDM) (Dermatophagoides pteronyssinus and Dermatophagoides farinae), and animal dander (cat dander) were also included. The prevalence of immunoglobulin E (IgE) to various common aeroallergens was determined by the skin-prick test (SPT) performed by two trained investigators following the recommendations of the European Academy of Allergy and Clinical Immunology (Mbatchou Ngahane et al 2016).Skin prick testing relies on the introduction of a very small amount of allergen extract into the epidermis using a sterile lancet along with the negative control (saline) and positive control (Histamine) (10 mg/mL). Results of the skin prick testing were examined after 15 mins of testing. The diameters of the resulting wheal and erythema in mm were recorded. By convention, a positive test is in which the mean of the two wheal diameters is at least 3 mm, greater than the negative control (saline). The atopic population was defined as having at least one positive to the test. Monosensitization was defined as sensitization to one of the four aeroallergens groups, namely; HDM, Cockroach, Cat Dander, and Fungi. Oligosensitizationrefers to sensitization to 2-3 groups. and polysensitization to all the 4 groups. This study was approved by the Ethical Committee of Universiti Pendidikan Sultan Idris (code:2019-005-01) and informed consent was obtained from all the participants.Data were analyzed using IBM SPSS Statistics version 23 (Armonk, NY, USA: IBM Corp). Descriptive statistics were presented as frequencies, mean, and standard deviation while the inferential statistics involved correlation and odds-ratio for risk factor analysis. Group differences were studied using the chi-squared test for categorical variables or independent t-test for continuous variables.

RESULTS AND DISCUSSION

Of the 225 general subjects (167 females, 58 males, the age range of 18-60 years), 93 (41.3%) had responded to at least one aeroallergen and epithet as the atopic population. **General population:** The most prevalent positive SPT was house dust mites (78%), followed by German cockroach (48.3%), fungal (18.2%), and cat dander (11.8%). The fungi sensitization prevalence in the general population was 7.55%. Among the 17 fungal sensitized subjects, 9 (52.9%) were sensitized only to *Aspergillus fumigatus*, 4 (23.5%) to *Penicillium notatum*, 2 (11.8%) to *Candida albicans*, and one (5.9%) to *Alternaria alternata*. One (5.9%) subject was sensitized to both *Alternaria alternata* and *Aspergillus fumigatus* (Table 1).

The prevalence of HDM sensitization (78%) in this study is within the range demonstrated among the adult population of Southeast Asian countries, reported to be 80% for Malaysia, 33.3%-68.5% for Singapore, 64.7% for Thailand, and the Philippines showed the prevalence was 33.3%-97%. The present study indicates higher value compared to other of the recent studies conducted among office workers in Malaysia (Lim et al 2015) with the prevalence of *D. pteronyssinus*, *D. farinae* were 50.3% and 49.0% respectively. Several HDM surveys suggested that *Dermatophagoides* species are an important source for the allergic sensitization, but *Blomia tropicalis* has recently been

identified as the most common and abundant species of HDM (Ahmed et al 2019). The prevalence of fungi sensitization (18.9%) in this study is relatively low compared to 72.8% among the Filipinos (Navarro et al 2009, Navarro & Lim-Jurado 2018). There is a great discrepancy between studies about allergies affecting male subjects more than the female. The male subjects showed a high prevalence (46.55%) of sensitization to all the allergens tested in this study in comparison to the female (39.52%). The male subjects also showed high sensitization to HDM and cat dander, in line with the previous study conducted in Malaysia in 2015, among Malaysia's office workers (Siti Nadzrah et al 2015, Lim et al 2015). This study also supported Psenka (2015), findings that demonstrated the male exhibit higher sensitivity to 11 common allergens including mold. Ahmed et al (2019) revealed male is more sensitive to common environmental aeroallergens than female. In Vietnam, where sensitization to house dust mites is common in both rural and urban areas, specific rates for HDM D. pteronyssinus to male 16.5%, female 10.6%, and for D. farinae, male15.3% and female 6.3% (Lâm et al 2014). Some studies concluded that the allergy prevalence found to be more among females than males as reported by a meta-analysis study that reviewed 591 studies (Kelly & Gangur 2009). In the contrast, a huge study involving 14 million blood tests showed that males exhibit higher sensitivity to 11 common allergens including mold (Psenka 2015). Among different ethnicities subjects, Indian ethnicity subjects showed the highest sensitization (35.0%) to HDM. The Malay ethnicity demonstrated high sensitization to cockroach (22.2%) and cat dander (7.1%). Subjects from the Chinese ethnicity were highly sensitized to fungi (25.0%) compared to others. The subjects with age group ≤20 years showed the highest sensitization to HDM (38.0%) and cat dander (4.7%), while the age group 21-30 was highly prevalent to cockroach (21.3%) and fungi (9.2%) (Table 1). It is interesting to note that the age group \geq 31 years old did not show a high prevalence of any aeroallergen compared to other age groups.

Understanding how groups with high risk differ from other groups with lower risk is an important step that can lead to an understanding of aetiology. Racial disparities are present in many facets of health and disease, allergy and asthma are no exceptions (Chen et al 2018). Genetics is unlikely to be the sole or major cause of the observed differences (Wegienka et al 2016). Some studies suggested disparity in allergic sensitization by race might be primarily a result of environmental factors rather than genetic differences (Yang et al 2008). In this study, the high prevalence of fungi among Chinese subjects may due to environmental factors especially many recent studies reported that in China the overall incidence of invasive fungal continued to rise especially Aspergillus have propagated in recent years. The drastic socioeconomic lifestyle transformation among Chinese people may have altered the epidemiological characteristics of fungal infections in the country (Chen et al 2016, 2018). However, in another study which was conducted in Singapore Chinese ethnicity subjects also showed high fungal sensitization compared to Malay, Indian, and other ethnicities (Goh et al 2017). Chinese subjects showed significant risk between atopic and general population OR= 1.33; 95% CI: (0.962-1.848). Generaly in the allergy systematic review studies, subjects within the ages of 2 and 17 years demonstrated sensitization to 1 or more allergens. From the age of 18 onwards, mold sensitization steadily declined in patients after the age of 12 (Psenka 2015). This is similar to our results in which the age group \leq 20 showed high sensitization to both HDM and cat dander. In this study, the age group ≤ 20 has significant risk between atopic and general population OR=1.750 95% CI: 1.413 -2.167.

Parameter		General population (n)	Fungi sensitized subjects (%)	HDM sensitized subjects (%)	Cockroach sensitized subjects (%)	Cat dander sensitized subjects (%)
Gender	Male	58	18.9	41.3*	20.6	6.8
	Female	167	3.5	29.3	19.7	4.1
Ethnicity	Malay	153	5.8	33.3	22.2*	7.1*
	Chinese	12	25.0*	33.3	8.3	0
	Indian	20	5	35.0*	10	0
	Others	40	10	27.5	20	0
Age	≤ 20	63	6.3	38.0*	19	4.7*
	21-30	131	9.2*	32.0	21.3*	3.0
	≥31	31	3.2	22.5	16.1	3.0

Table 1. Demographical prevalence of aeroallergens sensitization among the general population

*Ranked as the highest

Degree of sensitization: Among the general population, 53 3.56%) were monosensitized, 37 (14.44%) oligosensitized, and 3 (1.33%) polysensitized. Polysensitization as evidenced by SPT is common among the general population worldwide. Based on the studied population by Miguires et al (2014), reported monosensitization was between 16.2 and 19.6%, 12.8 to 25.3% oligosensitization, and 38.8% polysensitized. The sensitization degree disparities between these studies due to the definition of mono-, oligo-, and polysensitization. In our study, we are referring to the allergens' groups, whereas Miguires et al (2014) to the allergens in the test panel.

Atopic population: Among the atopic population, there is an increment of allergy prevalence as compared to the general population for the most common allergen (house dust mites, 32.4 to 78.5%; German cockroach, 20 to 48.3%; cat dander, 4.8 to 11.8% and fungi, 7.5 to 18.2%). Similar house dust mites prevalence result was demonstrated by Gendeh et al (2000) among their rhinitis patients (72%) compared to the general population (22.2%). HDM sensitization is also highly related to atopic patients with asthma with mean of 76% (range 50 - 90%) and more than 80% of asthmatic and rhinitis patients (Sinniah and Thakachy 2014). The female atopic population showed a higher prevalence compared to males (70.99%: 29.01%). Subjects from Malay ethnicity showed the highest sensitization to cockroach allergen, whereas subjects from Chinese ethnicity showed the highest sensitization to fungi and HDM. SPT found highest in the age group 21-30 years old followed by ≤ 20 , and ≥ 31 (Table 2).

Degree of sensitization: Among the atopic subjects, 53 (57%) were monosensitized, 37 (39.7%) oligosensitized, and 3 (3.22%) polysensitized. Interestingly, all the polysensitized were male subjects. Other studies revealed a higher prevalence of polysensitization (from 31.0% to 74.3%)

among allergic rhinitis patients. The discrepancy in the degree of prevalence between this study as reported by other studies may be due to fewer allergens were included in the test kit panel. Nevertheless, other factors such as the allergen extracts are varied markedly from one country to another. Age groups are also to be considered as polysensitized increased with age (Fasce et al 2007).

Fungal sensitization: Seventeen subjects (18.2%) found to be positive to at least one fungal allergen. Among the fungi sensitized subjects, the highest sensitization was to *Aspergillus fumigatus* (n=9, 58.8%) followed by *Penicillium notatum* (n=4, 23.5%), *Alternaria alternata*,and *Candida albicans* (n=2, 11.7%). No positive reactivity for both *Aspergillus niger*, and *Mucor mucedo*as as presented in Table 3.

Gender: In the general population, the male demonstrated a higher prevalence compared to females. The prevalent showed 2.15 folds higher in males of the atopic population compared to the general population (40.7%: 18.9%). Among the female, it was even greater up to 2.57 folds (3.5%: 9.0%) in the atopic population (Table 4).

Table 3. SPT reactivity to a panel of fungi allergens a	mong
the atopic population	

Allergen	Number positive (n=17)	Percent positive (%)
All fungi allergens		
Alternaria alternata	2	11.7
Aspergillus fumigatus	10	58.8
Candida albicans	2	11.7
Aspergillus niger	0	0
Mucor mucedo	0	0
Penicillium notatum	4	23.5

Table 2. Demographical	prevalence of aeroallergens	sensitization amond	the atopic population

Parameter		Fungi sensitized subjects (N=17)		HDM sensitized subjects (N= 73)		Cockroach sensitized subjects (N=45)		Cat dander sensitized subjects (N= 11)	
		n	(%)	n	(%)	n	(%)	n	(%)
Gender	Male	11	40.7	24	88.8*	12	44.4	4	14.8
	Female	6	9.0	49	74.2	33	50	7	10.6
Ethnicity	Malay	9	14	51	79.6	34	53.1*	11	17.1*
	Chinese	3	75*	4	100*	1	25	0	0
	Indian	1	11.1	7	77.7	2	22.2	0	0
	Others	4	25	11	68.7	8	50	0	0
Age	≤ 20	4	14.8	24	88.8*	12	44.4	3	11.1
	21-30	12	21.4*	42	75	28	50*	4	7.1
	≥31	1	10	7	70	5	50*	4	40*

*Ranked as the highest

Ethnicity: Chinese subjects in the general population were higher prevalent for fungal sensitization (25%) followed by other ethnicities (10%), Malay (5.8%), the least was Indian (5%). Among the atopic population, the highest prevalence was also among the Chinese subjects (75%) with 3 folds higher than the general population. Other ethnicity subjects showed 25% prevalent among the atopic population and 2.5 folds higher than the general population. Indian ethnicity prevalent was the least (11.1%) among the atopic population and 2.2 folds higher compared to the general population (Table 4).

Age group: Subjects in 21-30 years age group was the highest fungal sensitized (21.4%) with 2.32 folds higher compared to the general population (9.2%) (Table 4). The incidence of fungal allergy ranges from 6 to 24% in the general population (Simon-Nobbe et al 2008). In this study, the prevalence of fungal allergy was 7.55% among the general population and 18.27% among the atopic population. Many of systematic review studies reported the highest prevalence of fungi sensitization in Spain (20%), the lowest in Portugal (3%) (Twaroch et al 2015). In this study fungi sensitization prevalence is high compared to prevalence in many European cities (Newson et al 2014) and also higher than Turkey 14.8% (Hamilos 2010), and relatively less compared to the asthmatic population in Africa countries 23% (Kwizera et al 2019). The results of fungi sensitization prevalence in this study nearly similar to the prevalence in Singapore and Iran (19%). The latter has subtropical weather conditions while the climate of the south is tropical (Kidon et al 2004, Moghtaderi et al 2017). Chinese ethnicity subjects have higher reactivity to SPT to both fungal and house dust mite (HDM) allergens. This could be extensive exposure to HDM in most Chinese households. According to many studies which reported that HDM considers as major allergens in overall China (Zheng et al 2015, Zhang & Zhang 2019). The individuals in the age group 21-30 years showed the highest sensitization (5.33%), whereas the age group ≥31 years were the least likely to have fungi sensitization (Table 4). This agrees with the data from the European Community Respiratory Health Survey (ECRHS) which demonstrated that among adults aged 20-44 years within the same population, fungi sensitization ranged from 0.2 to 14.4% (Bousquet et al 2007). Uysal et al (2016) also reported that the number of sensitized allergens in the majority of children, who have been sensitized until the age of 4, rises by time and detected at age 10 and 18 years. Sensitization to some fungi species tends to decrease with age, following the general recognition that atopic asthma is more common in younger patients. However, the frequency of Aspergillus fumigatus did not decrease with age, most likely because

populations						
Patient groups according to	Per cent of the general population (N=225)	Per cent of the atopic population (N=93)				
Sex						
Male	11 (18.96)	11 (40.74)				
Female	6 (3.59)	6 (9.09)				
Ethnicity						
Malay	9 (5.88)	9 (14.06)				
Chinese	3 (25.0)	3 (75.0)				
Indian	1 (5.0)	1 (11.1)				
Others	4 (10.0)	4 (25.0)				
Age (years)						
≤20	4 (6.34)	4 (14.81)				
21–30	12 (9.02)	12 (21.42)				
≥31	1 (3.33)	1 (10.00)				

 Table 4. Prevalence offungi sensitized subjects by gender, ethnicity and age groups in the general and atopic populations

sensitization to this species is associated with severe persistent asthma with long disease duration (Fukutomi & Taniguchi 2015). Among fungi sensitized subjects 9 were mono-sensitized to *Aspergillus fumigates* which was also highly detected at UPSI buildings, reported in our previous study (Hadi et al 2019). Therefore, *Aspergillus* could be considered as a potential and hazardous aeroallergen that could elicit serious upper respiratory tract infection among UPSI community. *Aspergillus* sp., the dominating genera (Barathy et al 2020) is also known as one of the major causes of the disease among the pathogenic Aspergilli. The frequency of *Aspergillus fumigatus* sensitization did not decrease with age, most likely because sensitization to this species is associated with severe persistent asthma with long disease duration (Fairs et al 2010).

Degree of sensitization: Among 17 fungal sensitized subjects 6 (35.29%) were mono-sensitized only to fungi group 8 (47.06%) were oligo-sensitized to two to three groups, while 3 (17.65%) were poly-sensitized to all aeroallergen groups (Fig. 1). Prevalence on polysensitization among AR patients was reported in the range of 27.5 to 74.3% (Ciprandi et al 2008, Migueres et al 2009, Didier et al 2010, Baatenburg et al 2011). Many studies confirmed that polysensitized subjects are more likely to have a more severe and persistent respiratory allergic disease (Ciprandi et al 2008, Ciprandi & Cirillo 2011, Gelardi et al 2015).

In this study male subjects with fungi sensitization are more at risk compared to the female OR= 1.688; 95% CI: (1.234 - 2.307), *r*-value 0.573**; OR= 1.100 95% CI: (1.019 -1.187) *r*-value 0.168 (Table 5). The Chinese ethnicity subjects are more at risk compared to other ethnicities OR=

			Fungi sens	Fungi sensitized subjects					
		General population (N=	=225, n=17)	Atopic population (N=93, n=17)					
		OR (95% CI)	<i>r</i> -values	OR (95% CI)	<i>r</i> -values				
Gender	Male	1.234 (1.090 - 1.398)	0.385**	1.688 (1.234 - 2.307)	0.573**				
	Female	1.037 (1.007 - 1.068)	0.098	1.100 (1.019 - 1.187)	0.168				
Ethnicity	Malay	1.063 (1.021 - 1.105)	0.140*	1.164 (1.054 - 1.285)	0.220*				
	Chinese	1.333 (0.962 - 1.848)	0.490**	4.000 (0.733 - 21.838)	0.861**				
	Indian	1.053 (0.952 - 1.164)	0.214**	1.125 (0.893 - 1.417)	.319**				
	Other	1.111 (1.002 - 1.232)	0.289**	1.333 (1.005 - 1.769)	0.465**				
Age groups	≤ 20	1.068 (1.001 - 1.139)	0.216**	1.174 (1.003 - 1.374)	0.331**				
	21-30	1.099 (1.042 - 1.160)	0.197**	0.543 (0.445 - 0.663)	0.313**				
	≥ 31	1.034 (0.968 - 1.106)	0.170*	1.111 (0.904 -1.366)	0.300**				

Table 5. Risk factors for fungi sensitized subjects, including gender, ethnicity, and age groups

*P ≥ 0.05 **P ≥ 0.01

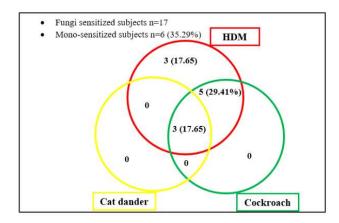


Fig. 1. Degree of sensitizations among fungi sensitized subjects

4.000; 95% CI: (0.733 - 21.838) *r*-value 0.861**. Subjects within the age between 21-30 years are more at risk followed by subjects within the age ≤ 20 , OR= 0.543; 95% CI: (0.445 - 0.663), *r*-value 0.313**; OR= 1.174; 95% CI: (1.003 - 1.374), *r*-value 0.331** respectively (Table5).

Rate of sensitization to fungi is also reported as significantly high among the male than female specifically to *Cladosporium* and *Aspergillus* (Ezeamuzie et al 2000). The prevalence of the Chinese ethnicity fungi sensitization is aligned with the incidence of invasive fungal infections that have continued to rise in China as reported recently (Chen et al 2018). Similarly, the prevalence of *Cladosporium* (60%) was reported among subjects within 8-15 years (Ezeamuzie et al 2000).

CONCLUSION

The SPT results showed a significant proportion of participants are sensitized to common aeroallergens with a

high incidence of sensitization to house dust mites (HDM). The prevalence of fungi sensitization is 7.55% among the general population and 18.27% among the atopic population. Males with fungi sensitization are more at risk compared to the females as Chinese ethnicity subjects to other ethnicities, and subjects within the age between 21-30 years to other age groups. Prevalence of mono-, oligo-, and polysensitization varies but male subjects were more likely to be polysensitized compared to the female. Asp. fumigatus is considered the most causative of sensitization among fungal species. This study implicates that understanding the allergenicity prevalence of the most common indoor aeroallergens can better help to identify patients' sensitization and support immunotherapy for them. Subsequently, enhancing the wellbeing and reducing the medical costs. Further studies are recommended to clarify the role of mono or oligo-, and polysensitization in the development and severity of respiratory allergic conditions. Mechanisms of the Development of Allergy (MeDALL) suggested that monosensitization and polysensitization represent two distinct phenotypes with differences in symptoms and biomarkers.

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