## Monaldi Archives for Chest Disease International Journal of Cardiopulmonary Medicine and Rehabilitation

eISSN 2532-5264

https://www.monaldi-archives.org/

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Monaldi Arch Chest Dis 2021 [Epub ahead of print]

Citation

Monika Bansal, Komaldeep Kaur, Aditi Gupta, Deepak Goyal, Nidhi Girdhar, Vishal Chopra, Sanjeev Bhagat, Akhil D. Goel. **Prevalence of aspergillus skin hypersensitivity in allergic rhinitis.** 

Monaldi Arch Chest Dis 2021;91:1416. doi: 10.4081/monaldi.2021.1416

## Prevalence of aspergillus skin hypersensitivity in allergic rhinitis

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Key words: Allergic rhinitis; Aspergillus fumigatus; skin prick test.

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Final version of the paper was approved by all the authors.

All authors agreed for the accountability for all aspects of the work regarding accuracy and integrity of study work.

**Conflict of interest:** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**Declarations about ethics approval, informed consent:** Approval for the study was taken from Research and institutional ethical committee, Government Medical College, Patiala, Punjab and informed consent for study was taken from each patient.

### Abstract

Allergic rhinitis (AR) is a chronic allergen specific, IgE-mediated hypersensitivity disorder which significantly impairs the quality of life in affected patients. Many aeroallergens and molds are responsible for AR. This study was conducted to find prevalence of *Aspergillus fumigatus* skin hypersensitivity in patients of AR by skin prick test (SPT). 150 clinically diagnosed AR patients visiting our OPD were enrolled. Skin hypersensitivity for *Aspergillus f.* was done by SPT in all the enrolled patients. Chi square test and Student's *t*-test were applied for statistical analysis. Out of 150 patients, 60 (40%) were positive for *Aspergillus fumigatus* SPT. Majority of the positive patients had persistent AR and among those 39/60 (65%) had moderate to severe persistent AR and 12/60 (20%) had mild persistent AR. Our study concluded that there is high (40%) prevalence of *Aspergillus f.* was found more in severe AR patients and it was statistically significant.

#### Introduction

Allergic rhinitis (AR), is an inflammatory condition of the nasal mucosa, which is associated with an IgE-mediated immune response against allergens. It is characterized by nasal symptoms including anterior or posterior rhinorrhoea, sneezing, nasal blockage and/or itching of the nose.[1] It is one of the most common chronic disorders, with reported prevalence ranging from 2% to 25% in children and 1% to >40% in adults, globally, whereas in India, prevalence of AR ranges from 20 to 26%.[2,3] Symptoms occur during two or more consecutive days for more than 1 hour on most days. Based on duration, symptoms can be intermittent (<4 days/week or <4 weeks/year) or persistent (>4 days/week or >4 weeks/year). Based on the absence or presence of sleep disturbance and impairment in daily activities, it can be graded as mild AR or moderate to severe AR, respectively [1].

Various aeroallergens including molds are responsible for causing and triggering AR.[1,3] Molds are ubiquitous and responsible for causing a broad spectrum of type I-IV hypersensitivity reactions.[4] Skin prick test (SPT) is the standard test used to diagnose IgE-mediated allergy.[1,3] Indications for SPT include AR, asthma, atopic dermatitis, suspected food allergies, latex allergy, and conditions in which specific IgE is hypothesised to play a role. Using SPT, this study was performed with the aim to determine the prevalence of *Aspergillus fumigatus* skin hypersensitivity in diagnosed AR patients.

#### **Material and Methods**

It was a cross-sectional study, conducted after taking approval from ethical committee. 150 patients of clinically diagnosed AR were enrolled by simple random sampling from the department of Pulmonary Medicine, G.M.C. Patiala. Patients of all age groups with 2 or more clinical features of AR (nasal congestion, rhinorrhea, postnasal drip, sneezing, and/or nasal itchiness) were included. Patients were classified clinically as per Allergic Rhinitis and its Impact on Asthma [ARIA] 2008 Update. Patients taking drugs that may interfere with SPT within one week of test were not enrolled. These drugs include antihistamines, H2 receptor blockers, tricyclic antidepressants, steroids, beta blockers.

SPT was performed in these patients to look for *Aspergillus fumigatus* hypersensitivity. A single droplet of solution containing *Aspergillus fumigatus* reagent was pricked on the skin of volar aspect of forearm. Histamine dichloride (10mg/ml)

and buffered glycerinated saline were used as positive and negative controls, respectively. Evaluation of skin reactivity was done by calculating the mean diameter as (D+d)/2; where D=longest diameter and d= perpendicular diameter at the largest width of D. Redness and swelling i.e. wheal with flare, equal to or more than 3 mm than negative control was considered positive after 20 minutes.

Statistical analysis was conducted with statistical package for social science system (SPSS version 23). Chi-square test and student's t-test were applied and P-value less than 0.05 was considered significant.

#### Results

Majority of the patients were in 21 to 30 year age group and the mean age of presentation was 26.8 years (age ranging from 11 to 70 years). Male to Female ratio was 0.82, with female preponderance. Family history of AR was present in only 24 (16%) patients and nearly one third (42/150) had history of asthma. Moderate to severe persistent AR (65.3%) was the most common type of AR observed. 60 patients out of 150 patients (40%) had positive SPT and 20 out of them had history of bronchial asthma (BA). Out of these SPT positive patients, 39 (65%) had moderate to severe persistent AR, 12 (20%) had mild persistent AR and 9 (15%) had moderate to severe intermittent AR. None of the patients with mild intermittent AR were SPT positive for *Aspergillus fumigatus*. Hence, majority of SPT positive patients had persistent AR and among them majority had moderate to severe persistent AR. Relationship between severity of AR and presence of skin hypersensitivity to *Aspergillus fumigatus* was statistically significant (p<0.05) [Table 1].

### Discussion

Allergic rhinitis is an IgE-mediated hypersensitivity disorder affecting the nasal lining and characterized by nasal congestion, rhinorrhea, sneezing, nasal itchiness, and/or post nasal drip. Different type of aeroallergens including molds have dominant role in etiopathogenesis of AR.

Fungus *Aspergillus* comprises of 132 different species which are distributed ubiquitously in the environment and it releases large quantities of small conidiospores of  $2-3 \mu m$ . It represents a dominant indoor as well as outdoor pathogen. Because of its thermo-tolerance, it can grow at human body temperature, and has resistance to oxidative killing and produces small metabolites and enzymes with proteolytic and

immunosuppressive activity. Human disorders caused by *Aspergillus* range from colonization of the respiratory tract, hypersensitivity pneumonitis, allergic rhinitis, sinusitis, allergic bronchopulmonary aspergillosis and asthma, to life-threatening systemic invasive aspergillosis, about 80% of *Aspergillus* related infections are caused by *A. fumigatus*.[4]

The diagnosis of allergic rhinitis is based upon the history of allergic symptoms and supportive diagnostic tests. Diagnostic tests include serum total IgE level, allergen specific IgE level and immediate hypersensitivity skin test. Serum IgE assay is more specific but costly as well as results are not available immediately and in contrast skin hypersensitivity testing is cheap, quick and sensitive.[5] Total serum IgE measurement has a poor predictive value for allergy screening in rhinitis. Various skin hypersensitivity testing methods are used including scratch test, prick and puncture test, intradermal skin test, prick-prick tests and atopy patch tests.[1]

In this study, majority of AR patients were having moderate-severe persistent AR, while few had mild intermittent AR in concordance with results of other authors.[6] The severity of AR has great impact on quality of life (QOL) and there are tools available to access health related quality of life (HRQoL) in patients of AR and/or BA eg RAPP (Rhinitis and Asthma Patient's perspective), CARAT (concomitant asthma and rhinitis) and ACT (Asthma Control Test).[7] In the present study, 60 (40%) patients were hypersensitive to *Aspergillus fumigatus* by SPT [Table 1]. Aggarwal et al observed SPT positivity for fungi in AR patients being 9.7%, Sharma et al found in 8.3% and by Chogtu et al in 13.92%.[3,8,9] The percentage of skin prick hypersensitivity to *Aspergillus fumigatus* has been found to be higher in our study. This can be attributed to the fact that majority of our patients were from rural population with farming background.

Special attention is needed in management of patients with concomitant AR and BA as the coexistence may impair asthma control causing more frequent asthma exacerbations and asthma-related hospitalizations. Prevalence of BA in AR was 28% (42/150), whereas other authors reported prevalence ranging from 16% to 55%.[3,10–13] Out of 60 SPT positive patients, 20 had concomitant BA and AR. Prevalence of BA in AR was found more in our study as patients were enrolled from a tertiary care chest hospital.

As the study sample size was small, thus the results cannot be generalized, this is the limitation of our study.

# Conclusion

Identification of particular allergen may be important for treatment of AR by avoidance of allergen and immunotherapy. We found a high prevalence of *Aspergillus fumigatus* hypersensitivity among AR patients and there was a statistically significant correlation between severity of AR and hypersensitivity to *Aspergillus fumigatus* by SPT, thus AR patients having hypersensitivity to *Aspergillus fumigatus* are more likely to have moderate to severe form of allergic rhinitis. It is suggested that all moderate to severe AR patients should be screened for *Aspergillus fumigatus* hypersensitivity.

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Table 1. Distribution of Aspergillus fumigatus skin hypersensitivity by SPT in allergic rhinitis patients.

Aspergillus		Type of Allergic Rhinitis				
fumigatus skin		Mild	Mild	Moderate To	Moderate	N = 150
hypersensitivity by				Severe	To Severe	
Skin prick test		mermillem	Feisistein	Intermittent	Persistent	
Negative	Ν	10	15	6	59	90(60%)
		(11.1%)	(16.7%)	(6.7%)	(65.6%)	
Positive	Ν	0	12	9	39	60(40%)
		(0.0%)	(20.0%)	(15.0%)	(65.0%)	
Chi-Square	9.391					
р	0.025					
Significance	Significant					