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Prevalence of cutaneous hypersensitivity to *Aspergillus fumigatus* in patients with asthma in the central part of Karnataka and its impact on asthma severity

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Abstract

Introduction: Severe asthma is particularly linked to atopic conditions, especially to mold allergens like *Aspergillus fumigatus*. Allergic bronchopulmonary aspergillosis is an immunological lung disorder, with initial phase of hypersensitivity to Aspergillus (AH). This study aimed to assess Aspergillus sensitization among asthmatic patients through cutaneous hypersensitivity testing at our tertiary care center in central Karnataka.

Material and methods: This hospital-based cross-sectional study included 100 asthmatic patients attending the outpatient department at SS Institute of Medical Sciences, Davangere, Karnataka, from 2022 to 2024. Patients with acute exacerbations, COPD, bronchiectasis, recent antihistamine use, or pregnancy were excluded; asthma was diagnosed as per GINA guidelines using clinical history and spirometry.

Results: In our study we found that the prevalence rate of AH is 22% in asthma patients diagnosed by skin prick test (SPT). The most common symptom among the patients with AH was cough (100%), shortness of breath (95.5%) and wheeze (86.4%). Patient's with AH had more severe asthma ($p<0.001$), cough ($p=0.04$), shortness of breath ($p<0.001$), wheeze ($p=0.017$) and night awakenings ($p = 0.003$) compared to patients without AH, which were statistically significant.

Conclusion: Cutaneous hypersensitivity to *Aspergillus fumigatus* was found in 22% of asthmatics. Early detection and targeted management strategies for patients sensitized to *Aspergillus fumigatus* can potentially improve disease outcomes.

Keywords*:* asthma; Aspergillus hypersensitivity; skin prick test; *Aspergillus fumigatus*

Introduction

People with asthma can develop sensitivity to allergens such as pollen, dust mites, animal dander, and molds. Severe asthma is particularly associated with atopic conditions, especially mold allergens like *Aspergillus fumigatus* [1]. Aspergillus is one of the most prevalent molds, accounting for approximately 0.1–22% of sampled airborne spores. Among more than 250 species of Aspergillus, only a small number are capable of causing diseases in humans [2].

Allergic bronchopulmonary aspergillosis (ABPA) is a spectrum of disease characterized by chronic asthma, recurrent pulmonary infiltrates, and bronchiectasis. It is an immunological lung disorder in which the initial phase involves hypersensitivity to Aspergillus (AH) [3]. AH can be identified by a skin prick test (SPT) demonstrating heightened sensitivity to Aspergillus antigens [4]. Lung fibrosis and bronchiectasis represent severe, advanced stages that typically have unfavorable

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clinical outcomes. Therefore, it is essential to determine the frequency of sensitization to Aspergillus antigens among asthmatic patients in our population.

Studies conducted in northern India report that the prevalence of type I Aspergillus cutaneous sensitization among asthmatic patients ranges from 28% to 50% [1]. However, there is a notable scarcity of data from South India.

The present study was undertaken to screen asthmatic patients for Aspergillus sensitization by cutaneous hypersensitivity testing at our tertiary healthcare center in central Karnataka.

Materials and methods

This hospital-based cross-sectional study was conducted on 100 asthmatic patients attending the outpatient department at SS Institute of Medical Sciences, Davangere, Karnataka, over a period of two years, from 2022 to 2024 after getting approval from institutional ethics committee. Asthma was diagnosed based on clinical history and spirometry criteria as per the Global Initiative for Asthma (GINA) guidelines [5].

Asthmatic patients with acute exacerbations, chronic obstructive pulmonary disease (COPD), bronchiectasis, a history of antihistamine use within one week, or pregnancy were excluded from the study. Written informed consent was obtained from all participants.

SPT was performed on all participants. Histamine dihydrochloride (10 mg/mL or 0.1%) was used as the positive control, and normal saline was used as the negative control. Each allergen site was marked with a pen on the forearm after cleaning the test area. SPT was performed on the volar aspect of the forearm, 2–3 cm from the wrist and 5 cm from the antecubital fossa, with a minimum distance of 2 cm between test sites. A drop of each test solution was placed on the skin in an identical order for each patient and immediately pricked.

A single-head metal lancet was pressed through the drop of Aspergillus allergen extract (commercially available) and held against the skin for at least one second. The results were read 15–20 minutes after application. The largest diameter of the wheal was measured, and a wheal size ≥3 mm compared to the negative control was considered positive [6].

Based on the SPT results, participants were divided into two groups: SPT-positive and SPT-negative. Clinical symptoms and spirometry values were compared between the two groups. The severity of asthma was assessed according to GINA recommendations, and patients were categorized as having mild, moderate, or severe asthma [5]. Mild obstruction was defined as forced expiratory volume in one second (FEV1) ≥80% of the predicted value, moderate obstruction as FEV1 between 60% and 80% predicted, and severe obstruction as FEV1 ≤60% predicted [7].

Statistical analysis

Data were collected using a structured proforma and entered into a Microsoft Excel sheet, then analyzed using SPSS version 22.0 (IBM, USA). Qualitative data were expressed as proportions, while quantitative data were presented as mean and standard deviation. Associations between qualitative variables were tested using the Chi-square test or Fisher's exact test. Differences in means between the two groups were analyzed using an unpaired t-test to assess statistical significance. Descriptive statistics for each variable included mean, standard deviation, and standard error of the mean. A p-value of <0.05 was considered statistically significant, and a p-value of <0.001 was considered highly significant.

Results

The mean age of the participants was 32.35 ± 11.04 years. The majority were between 20 and 40 years of age. Of the 100 patients, 50 were male and 50 were female. The most common symptom was cough (87%), followed by shortness of breath (65%) and wheeze (65%).

Among the participants, 51% had mild obstruction with a mean FEV1% of 90.4 ± 4.80, 34% had moderate obstruction with a mean FEV1% of 72.4 ± 5.2, and 15% had severe obstruction with a mean FEV1% of 55.2 ± 3.3. The clinical profile of the participants is summarized in Table 1.

Out of the 100 participants, 22 had a positive SPT to *Aspergillus fumigatus*, indicating a prevalence of Aspergillus hypersensitivity (AH) of 22%. Among them, 10 were male and 12 were female.

Of the patients with AH, 50% (11 out of 22) had moderate obstruction, and 40.9% (9 out of 22) had severe obstruction. There was a statistically significant association between spirometry results and SPT positivity to *Aspergillus fumigatus* (Pearson Chi-Square, $p < 0.001$). Although the mean FEV1 was lower in SPT-positive participants compared to SPT-negative participants, the difference was not statistically significant ($p = 0.891$).

Table 1: Clinical profile of study participants.

Clinical profile		*Study participants, n=100 (%)*
Mean age (years)		32.35 ± 11.04
Mean duration of asthma (years)		2.9 ±1.04
Cough		87
Shortness of Breath		65
Wheeze		65
Chest Tightness		42
Allergic Rhinitis		45
Eczema		15
Conjunctivitis		9
Night Awakening		33
Family history of asthma		46
Spirometry	Mild obstruction	51
	Moderate obstruction	34
	Severe obstruction	15

All 22 individuals who tested positive on SPT reported cough, and this association was statistically significant (p = 0.040), suggesting a strong link between SPT positivity and the presence of cough. Shortness of breath was reported in 95.5% of SPT-positive patients compared to 56.4% of SPT-negative patients, which was also statistically significant (p < 0.001). Wheeze was present in 86.4% of SPT-positive patients compared to 59.0% of SPT-negative patients (p = 0.017). Night awakenings were significantly more common in SPT-positive patients (p = 0.02).

The mean duration of asthma in SPT-positive participants was shorter compared to SPT-negative participants, and this difference was statistically significant (p = 0.02). A comparison of clinical parameters between the two groups is provided in Table 2.

Discussion

Aspergillus hypersensitivity (AH) and allergic bronchopulmonary aspergillosis (ABPA) are common among asthmatic patients and often lead to poorly controlled asthma, adversely affecting quality of life and increasing morbidity. This underscores the importance of screening for Aspergillus sensitization in patients with uncontrolled asthma, given its clinical and therapeutic implications.

Table 2: Comparison of clinical parameters between SPT positive and SPT negative patients.

	SPT positive (n = 22)	*SPT negative (n = 78)*	*P value*
Mean Age (yrs)	35.9 ± 12.6	31.3 ± 10.4	0.276
Mean FEV1	67.4 ± 12.1	82.2 ± 12.4	0.891
Severe form of asthma (moderate and severe asthma)	20 (91%)	29 (37.1%)	< 0.001
Duration of asthma (yrs)	2.32 ± 0.99	3.09 ± 1.47	0.02
Cough	22 (100%)	65(73.8%)	0.05
Dyspnea	21 (95.5%)	44 (56.4%)	<0.001
wheeze	19 (86.4%)	46 (58.9%)	0.017
Night awakenings	13 (59.1%)	19 (25.6%)	0.003
Chest tightness	11(50%)	31 (39.7%)	0.389
Allergic rhinitis	12 (54.5%)	13 (16.6%)	0.308
Eczema	2 (9%)	13 (16.6%)	0.379
Conjunctivitis	0 (0%)	9 (11.5%)	0.095
Family history	14(63%)	32 (41%)	0.348

In our study, the prevalence of AH among asthma patients was 22%, as diagnosed by SPT. Studies conducted in North India have reported that the prevalence of type I Aspergillus cutaneous sensitization among asthmatic patients ranges from 28% to 50%. In bronchial asthma, the prevalence of AH detected via skin prick testing is approximately 28%.

The prevalence of ABPA in asthma patients ranges from 12.9% to 21.7%, as reported by Agarwal et al [2] and Nath et al [8] Bansal et al. found a high prevalence (40%) of *Aspergillus fumigatus* skin hypersensitivity in patients with allergic rhinitis, particularly those

with moderate to severe persistent symptoms[4]. In cases of post-tuberculosis fibrocavitary disease, 32% of patients exhibited Aspergillus sensitization, which was significantly associated with airflow obstruction, as reported by Dhooria et al [9].

Our study showed that a greater number of patients with AH had moderate to severe asthma as assessed by spirometry. This finding is consistent with Savio et al. [10], who reported increased asthma severity in Aspergillus-sensitized patients. Similar patterns were noted by Bansal et al [4] and Nath et al [8] and suggesting a strong association between *Aspergillus fumigatus* sensitization and more severe respiratory impairment. This implies that asthmatic patients sensitized to *Aspergillus fumigatus* are more likely to experience severe obstruction. Savio et al [10] and Agin et al [11] reported similar findings, reinforcing that Aspergillus sensitization correlates with more severe asthma and impaired pulmonary function. These results highlight the importance of screening asthmatic patients, particularly those with severe respiratory symptoms, for Aspergillus sensitization.

The mean FEV1 value was lower in the SPT-positive group compared to the SPT-negative group. These findings are in line with those of Maurya et al [12] and Hendrick et al [13], who reported that Aspergillus sensitization is associated with reduced lung function and increased asthma severity. The significant difference in FEV1 values underscores the impact of Aspergillus sensitization on lung function and highlights the need for early detection and management to prevent further deterioration.

This study also revealed significant associations between cutaneous hypersensitivity to *Aspergillus fumigatus* and various respiratory symptoms. Statistically significant associations were found between SPT positivity and the presence of cough, wheeze, shortness of breath, and night awakenings.

Cough was significantly associated with AH in our study. This aligns with findings from Savio et al [10], who also reported that Aspergillus sensitization is linked to increased asthma severity and persistent cough. The chronic cough in SPT-positive individuals may result from an inflammatory response triggered by *Aspergillus fumigatus*, leading to airway hyperresponsiveness.

Shortness of breath was also significantly associated with SPT positivity, with 95.5% of positive individuals reporting this symptom compared to 56.4% of SPT-negative individuals. Agin and Namavary [11] similarly reported heightened respiratory distress in Aspergillus-sensitized patients, suggesting that fungal allergens exacerbate asthma symptoms by promoting airway inflammation and obstruction.

Wheeze was another symptom significantly associated with SPT positivity. Among those who tested positive, 86.4% reported wheezing, compared to 59.0% of those who tested negative. This observation is consistent with the findings of Nath et al [8], indicating that Aspergillus sensitization contributes to more frequent and severe wheezing episodes. The increased wheezing could be attributed to the allergenic properties of *Aspergillus fumigatus*, which may intensify airway constriction and mucus production.

Night awakenings were also significantly associated with SPT positivity, with 59.1% of SPT-positive individuals experiencing this symptom compared to 25.6% of SPT-negative individuals. This is in line with the study by Agarwal et al [1], which noted increased nocturnal symptoms in Aspergillus-sensitive asthmatics. Night awakenings may result from nocturnal bronchospasm and airway inflammation triggered by fungal allergens.

On the other hand, the study found no significant association between SPT status and symptoms such as chest tightness, allergic rhinitis, eczema, and conjunctivitis. These non-significant findings could be attributed to the multifactorial nature of these symptoms, which are likely influenced by a variety of environmental and genetic factors beyond Aspergillus sensitization. For instance, allergic rhinitis and eczema are often associated with other common allergens such as dust mites and pollens, which may have overshadowed the influence of *Aspergillus fumigatus* in this cohort.

The significant association between the duration of asthma and SPT results observed in this study aligns with findings from several existing research works. Participants with negative SPT results had a longer mean duration of asthma (3.09 years) compared to those with positive SPT results (2.32 years). This suggests that individuals with long-standing asthma might exhibit reduced allergen sensitization over time.

One study supporting this finding is by Wang et al. [14], which reported that the prevalence of atopy, as determined by SPT, was lower in patients with a longer duration of asthma. The authors suggested that chronic inflammation and ongoing treatment in long-standing asthma could alter the immune response, resulting in reduced skin reactivity to allergens.

Limitations of the study: Sample size of the study was small. We require a larger sample size to confirm the

above findings. We chose only SPT as a marker of aspergillus hypersensitivity, serum immunoglobulin E for *Aspergillus fumigatus* was not done. Confounding factors like age, past treatment, occupational or residential exposure to aspergillus antigens are not considered in the study.

Conclusion

The prevalence of cutaneous hypersensitivity to *Aspergillus fumigatus* antigen in the study population of asthmatic patients was 22%. Asthmatic patients sensitized to *Aspergillus fumigatus* are more likely to experience severe airway obstruction and more troublesome respiratory symptoms compared to non-sensitized patients. Additionally, patients with AH are at higher risk of developing ABPA over the course of the disease. Early detection and targeted management strategies for individuals sensitized to *Aspergillus fumigatus* can potentially improve clinical outcomes, reduce symptom severity, and prevent further deterioration in lung function.

Conflicts of interest

Authors declare no conflicts of interest.

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