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Research Article

Fungal Sensitization in Bronchial Asthma: Epidemiological Insights and Clinical Correlates from an Indian Cohort

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Abstract

Background: Fungal sensitization is increasingly recognized as an important contributor to poor asthma control and disease severity, particularly in patients with severe asthma. Data from Indian populations remains limited, necessitating region-specific epidemiological and clinical insights.

Objectives: To determine the prevalence of fungal sensitization in patients with bronchial asthma and to evaluate its association with clinical severity, spirometric parameters, and immunological markers.

Methods: This cross-sectional study was conducted in the Department of Respiratory Medicine at a tertiary care center in western India. About 70 diagnosed bronchial asthma patients aged ≥12 years were enrolled. Clinical assessment, spirometry with bronchodilator reversibility testing, skin prick testing for fungal allergens, absolute eosinophil count, and serum IgE levels were performed. Asthma severity scores were correlated with lung function and immunological parameters using appropriate statistical analyses.

Results: Fungal sensitization was identified in 11 patients (15.7%). *Aspergillus fumigatus* was the most common sensitizing fungus (11.43%), followed by *Mucor mucedo* (5.71%), while no sensitization was observed to several other fungal species. Spirometric indices showed significant improvement post-bronchodilator, confirming reversible airflow obstruction. Fungal sensitization demonstrated a strong positive correlation with asthma severity and an inverse relationship with lung function parameters, particularly FEV_1/FVC. Absolute eosinophil count and serum IgE levels showed significant positive correlations with both fungal sensitization and asthma severity, highlighting an underlying IgE-mediated inflammatory mechanism.

Conclusion: Fungal sensitization, especially to *A. fumigatus*, is present in a significant subset of asthma patients and is associated with increased disease severity and impaired lung function. Early identification of fungal sensitization, along with immunological profiling, may aid in better phenotyping and targeted management of bronchial asthma in the Indian setting.

Keywords: Asthma control, Fungal sensitization, *Aspergillus fumigatus*, Spirometry, Serum IgE, Absolute eosinophil count, Skin prick test.

Introduction

According to the Global Initiative for Asthma (GINA), asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.[1,2]

In 2019, asthma affected approximately 262 million people and resulted in 0.45 million deaths globally.[3] The disease manifests with varying severity, ranging from mild to life-threatening symptoms.[4] Typical signs include nighttime

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cough, wheezing, breathlessness even at rest, and chest tightness.[5] These symptoms can severely impair sleep, daily activities, lung function, and overall quality of life.

The occurrence of asthma is multifactorial, with contributing elements including genetic, socioeconomic, environmental, and contextual factors (Figure 1). Among environmental triggers, fungal allergens, particularly molds, are gaining attention due to their role in severe asthma with fungal sensitization (SAFS). Molds like *Aspergillus fumigatus*, *Penicillium*, *Alternaria alternata*, and *Cladosporium herbarum* are known to trigger severe hypersensitivity reactions and increase disease severity. Fungal sensitization elevates IgE levels and is often confirmed via skin prick tests.[6]

SAFS is defined as asthma accompanied by allergic bronchopulmonary aspergillosis. Though recognized since 1726, the condition remains underexplored. Up to 70% of severe asthma patients show fungal sensitization, especially to *Aspergillus*, correlating with higher ICU admissions and mortality. The immunopathology, biomarkers, and standardized diagnostic tools for SAFS remain inadequately characterized, demanding urgent clinical attention.[7]

In India, asthma management is further challenged by underdiagnosis, stigma, outdated epidemiological data, and limited access to treatment. Furthermore, fungal sensitization has been increasingly recognized as a contributing factor affecting disease severity and control. This study was therefore designed to assess the prevalence of fungal sensitization in individuals with bronchial asthma, with a view to improving diagnosis, Treatment, and long-term outcomes, along with understanding the relation between the severity of asthma and fungal sensitization.

Methods

This cross-sectional study was conducted in the Department of Respiratory Medicine at our institute. The study population included diagnosed bronchial asthma patients who were receiving regular treatment and attending either the outpatient or inpatient departments. Patients aged over 12 years who were compliant with their asthma medications were eligible for inclusion.

Patients with asthma-COPD overlap, those who were current smokers, or had active infections such as tuberculosis or bronchiectasis, were excluded from the study. Additionally, individuals already on oral corticosteroids or on antihistamine therapy for more than 7 days prior to recruitment were not included. Ethical clearance was obtained from the Institutional Research Ethics Board, and written informed consent was collected from all participants. A comprehensive clinical history and physical examination were carried out, and the details were recorded in a structured case proforma.

The sample size was determined based on statistical guidelines to estimate prevalence within a 95% confidence interval and a 5.5% margin of error, which yielded a final sample of 60 participants.

All enrolled participants underwent a standardized evaluation protocol. Spirometry was performed using a computerized spirometer in accordance with American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines, ensuring acceptability and reproducibility criteria. Pre- and post-bronchodilator measurements were obtained, with post-bronchodilator values recorded 15 minutes after administration of 400 µg inhaled salbutamol, and reversibility was defined as an increase in FEV_1 of ≥12% and ≥200 mL. Skin prick testing (SPT) was carried out using a standardized fungal allergen panel (Allergo SPT Kit, Allergopharma/Creative Diagnostics, India) on the volar aspect of the forearm following international guidelines. A wheal diameter ≥3 mm greater than the negative control after 15–20 minutes was considered positive. Asthma severity (AST) was assessed based on symptom frequency, nocturnal awakenings, reliever medication use, and spirometric impairment, in line with GINA-based severity classification. Serum total IgE levels were measured using an enzyme-linked immunosorbent assay (ELISA) technique, with values <100 IU/mL considered normal; elevated levels were interpreted as indicative of atopy. Absolute eosinophil count (AEC) was determined from peripheral blood samples using an automated hematology analyzer, with counts >500 cells/µL considered abnormal.

All data collected were organized using Microsoft Excel. Categorical variables were expressed as frequencies and percentages, while continuous variables were summarized using means, standard deviations, medians, or interquartile ranges, depending on the distribution. Statistical tests like the student's t-test were used to compare means between groups, and the Chi-square test was used to assess relationships between categorical variables. A *p-value* less than 0.05 was considered statistically significant. Pearson's correlation coefficient was used to assess the strength and direction of linear relationships between variables, helping to understand how strongly two clinical parameters were associated.

Results

The study analyzed gender distribution across different age groups among 70 bronchial asthma patients, with 36 females and 34 males. The highest number of patients was in the 28 to 37 years age group, followed by the 38 to 47 years. While age-wise variation was observed, the gender distribution showed no significant difference ($p = 0.87$), indicating asthma affects both sexes similarly across age groups (Figure 1). The distribution of patients based on BMI categories is shown in Table 1. Among the 70 patients, 4% were underweight, 22.7% had normal BMI, 16.7% were overweight, and 3.3% were classified as obese. No patients fell into the very high or extreme obesity categories. A statistically significant association was observed between BMI and the study population ($\chi^2 = 87.88$, $p < 0.01$), indicating BMI may influence disease severity and management in bronchial asthma.

The study found cough to be the most reported respiratory symptom (57.14%) among patients, though it lacked statistical

significance. In contrast, wheezing, shortness of breath, and chest tightness, though less prevalent, showed significant associations with bronchial asthma, highlighting the variability of symptom presentation (Table 2).

The study demonstrated a significant improvement in spirometry parameters following bronchodilator administration in bronchial asthma patients. Mean FEV_1 increased from 1.36 L to 1.83 L, FVC from 1.88 to 2.29 L, and FEV_1/FVC ratio from 72.17 to 79.20%, all with statistically significant *p-values*. These findings highlight the importance of spirometry in confirming reversible airflow obstruction, a hallmark of asthma (Table 3 and Figure 2a and b).

The skin prick test (SPT) results revealed that fungal sensitization among bronchial asthma patients was relatively infrequent. *A. fumigatus* showed the highest sensitization rate (11.43%), followed by *Mucor mucedo* (5.71%), while *A. flavus*, *Helminthosporium*, and *Trichoderma* each showed sensitization in only one patient (1.43%). No sensitization was observed for the remaining fungal strains (Table 4). These findings suggest a possible role of specific fungi, especially *A. fumigatus*, in worsening asthma symptoms and influencing disease management.

The correlation analysis among asthma patients showed several significant associations linking lung function, symptom severity, and immunological markers. Spirometry findings demonstrated strong positive correlations, with pre- and post-bronchodilator (BD) FEV_1 and FVC closely related ($r = 0.94$ and $r = 0.95$, $p < 0.001$), as well as a strong relationship between pre- and post-BD FEV_1 ($r = 0.95$, $p < 0.001$). This consistency suggests similar patterns of lung performance both before and after bronchodilation. In contrast, indices of airway obstruction correlated negatively with the asthma Severity (AST), where pre-BD FEV_1/FVC showed a strong inverse association ($r = -0.71$, $p < 0.001$), and weaker but significant negative correlations were observed between AST and both pre- and post-BD FEV_1 as well as post-BD FEV_1/FVC. These patterns indicate that poorer spirometric values are linked with increased symptom burden. Fungal sensitisation (FS) also demonstrated meaningful associations, showing a strong positive correlation with AST ($r = 0.65$, $p < 0.001$) and a negative relationship with pre-BD FEV_1/FVC ($r = -0.31$, $p = 0.01$), implying that sensitisation to fungi may contribute to worsening respiratory function and heightened symptom severity. Immunological markers further reinforced this link, as absolute eosinophil count (AEC) and serum IgE were highly correlated ($r = 0.89$, $p < 0.001$), and both were positively associated with AST and FS. Specifically, AEC correlated with AST ($r = 0.78$) and FS ($r = 0.66$), while IgE demonstrated strong associations with both AST ($r = 0.84$) and FS ($r = 0.71$). These results underscore the immunopathological interplay between eosinophilia, IgE-mediated responses, and fungal sensitisation, suggesting that sensitisation-driven immune activation plays a major role in symptom severity and disease burden in asthma patients (Tables 5 and 6).

Table 1: Distribution of patients in the current study according to BMI

Category	*BMI range*	*Number of patients*	*Chi-square and p-value*
Underweight	<18.5	6	Chi square = 87.88, p =<0.01**
Normal	18.5–24.9	34	
Overweight	25–29.9	25	
Obesity	30–34.9	5	
Very high obesity	35–39.9	0	
Extreme obesity	>40	0	

N = 70, *p-value* was calculated using $\chi 2$ test, df = 5

Table 2: Symptoms observed in the study population

Symptoms	*Number of patients*	*Percent*	*Chi-square value*	*p-value*
Shortness of breath	25	35.71	5.71	0.016*
Wheezing	17	24.28	18.51	<0.01**
Cough	40	57.14	1.42	0.23
Chest tightness	25	35.71	5.71	0.016*
Total	70	100		

N = 70, *p-value* was calculated using Chi square test, df = 1

Table 3: Mean values of pre BD and post BD – FEV1, FVC and FEV1/FVC (%)

	Pre-BD	*Post- BD*	*Mean differences*	*p-value*
FEV1	1.36 ± 0.75	1.83 ± 0.86	0.46 ± 0.28	0.0009**
FVC	1.88 ± 0.93	2.286 ± 0.98	0.41 ± 0.22	0.01*
FEV1/FVC (%)	72.17 ± 15.6	79.20 ± 11.18	7.04 ± 2.30	0.002**

N = 70, *p value* is calculated by student's t test

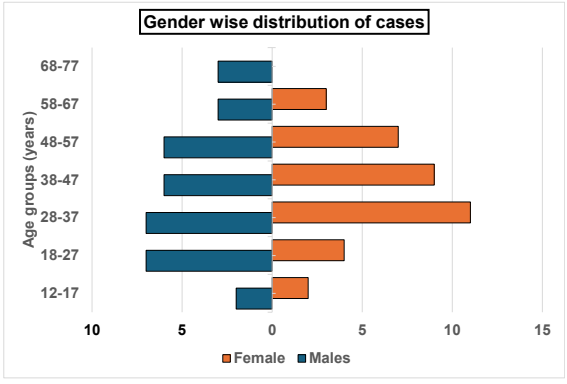

Figure 1: Graph showing the distribution pattern of patients in the current study according to age and sex. (N= 70, data is represented by the number of patients)

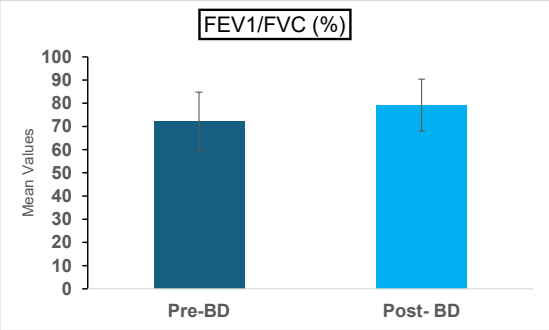

Figure 2a: Graph showing the mean value of FEV1/FVC(%) in the current study. (n = 70, data are represented as mean ± SEM)

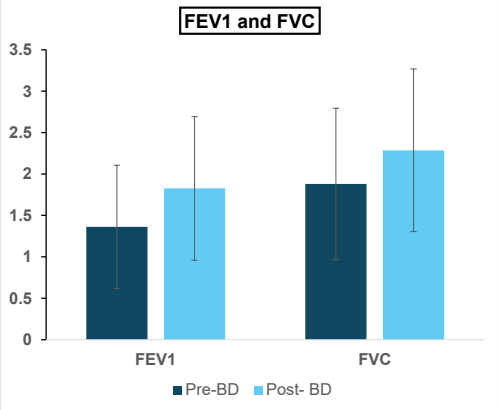

Figure 2b: Graph showing the mean value of pre-BD and post-BD FEV1 and FVC in the current study. (n = 70, data are represented as mean ± SEM)

Table 4: Distribution of patients in the current study according to fungal sensitization using skin prick test

	Number of patients positive	*Percent*
Alternaria tenius	0	0
A. flavus	1	1.42
A. fumigatus	8	11.42
A. niger	0	0
A. tamarii	0	0
A. versicolor	0	0
Candida albicans	0	0
Cladosprium herbarum	0	0
Curvularia lunata	0	0
Fusarium solani	0	0
Helminthosporium	1	1.42
Mucor mucedo	4	5.71
Penicillum	0	0
Rhizopus nigricans	0	0
Trichoderma	1	1.42

Discussion

This study explored the association between fungal sensitization and asthma control in bronchial asthma patients, providing critical insights into immunologic, clinical, and functional parameters involved in disease severity.

Fungal sensitization, particularly to *A. fumigatus*, has been increasingly recognized as a key contributor to poorly controlled asthma. In our study, *A. fumigatus* was the most frequently identified sensitizer (11.43%), followed by *M. mucedo* (5.71%). No sensitization was detected for several other fungal strains. These findings echo previous literature: Savio *et al.*[8] reported *A. fumigatus* sensitization in 32.2% of asthma patients, while Franconi *et al.*[9] and Lamoth[10] also confirmed *A. fumigatus* as the predominant species implicated in allergic asthma.

The demographic distribution in our cohort showed asthma prevalence peaking in middle-aged adults (28–47 years), likely due to prolonged environmental exposure. Gender distribution was nearly equal, and no significant association was found between gender and disease distribution ($p = 0.87$). BMI analysis revealed that 22.7% had normal BMI, with no patients in extreme obesity categories. A significant association was noted between BMI and asthma control ($p < 0.01$), aligning with Zheng *et al.*[11] and contrasting with Munoz *et al.*,[12] who observed higher mean BMI in asthmatic populations.

Symptomatically, cough was the most prevalent complaint (57.14%), significantly associated with asthma severity ($p = 0.001$). This supports findings from Agarwal *et al.*[13] and Savio *et al.*[8], who also reported high prevalence of cough and chest tightness in asthma patients.

Pulmonary function testing showed significant reversibility in airflow obstruction post-bronchodilator: FEV_1 ($p = 0.0009$), FVC ($p = 0.0131$), and FEV_1/FVC ratio ($p = 0.0026$). These results affirm the reversibility characteristic of asthma and are consistent with Singh *et al.*[14], who reported significant post-bronchodilator improvements in FEV_1.

Statistical correlation analysis revealed strong interrelationships among spirometric indices, clinical symptom scores, and immunologic markers. FEV_1 and FVC showed a strong positive correlation both pre and post-bronchodilation. Importantly, FEV_1/FVC ratio inversely correlated with symptom severity. These findings align with Singh *et al.*[15], who found significant negative correlations between spirometry parameters and symptom scores (e.g., FEV_1 $r = -0.809$; FVC% $r = -0.735$).

Immunologically, strong positive correlations were identified between absolute eosinophil count (AEC), serum IgE, fungal sensitization (FS), and asthma severity (AST). This underlines the immunopathogenic link between eosinophilic inflammation and IgE-mediated responses in asthma, supporting the view that elevated AEC and IgE levels contribute to increased flare frequency and symptom burden.

Table 5: Correlation coefficient of different parameters for asthma severity test

Pearson's correlation coefficient	*PRE BDR FEV1/FVC*	*PRE FEV1*	*PRE FVC*	*POST FEV1/ FVC*	*POST FEV1*	*POST FVC*	*FS*	*AST*
PRE BDR FEV1/FVC	1.00	0.47	0.19	0.66	0.35	0.17	-0.31	-0.71
PRE FEV1	0.47	1.00	0.94	0.37	0.95	0.90	-0.06	-0.32
PRE FVC	0.19	0.94	1.00	0.17	0.94	0.97	0.01	-0.14
POST FEV1/FVC	0.66	0.37	0.17	1.00	0.42	0.14	-0.22	-0.53
POST FEV1	0.35	0.95	0.94	0.42	1.00	0.95	-0.08	-0.28
POST FVC	0.17	0.91	0.97	0.14	0.95	1.00	0.00	-0.13
FS	-0.31	-0.06	0.01	-0.23	-0.08	0.00	1.00	0.65
AST	-0.71	-0.32	-0.14	-0.53	-0.28	-0.13	0.65	1.00
p-values								
PRE BDR	FEV1/FVC	PRE FEV1	PRE FVC	POST FEV1/FVC	POST FEV1	POST FVC	FS	AST
PRE BDR FEV1/FVC	0.00**	0.00**	0.12	0.00**	0.00**	0.16	0.01*	0.00**
PRE FEV1	0.00**	0.00**	0.00**	0.00**	0.00**	0.00**	0.65	0.01*
PRE FVC	0.12	0.00**	0.00**	0.15	0.00**	0.00**	0.95	0.25
POST FEV1/FVC	0.00**	0.00**	0.15	0.00**	0.00**	0.25	0.06	0.00**
POST FEV1	0.00**	0.00**	0.00**	0.00**	0.00**	0.00**	0.52	0.02*
POST FVC	0.16	0.00**	0.00**	0.25	0.00**	0.00**	0.98	0.27
FS	0.01*	0.65	0.95	0.06	0.52	0.98	0.00**	0.00**
AST	0.00**	0.01*	0.25	0.00**	0.02*	0.27	0.00**	0.00**

*p <0.05 and **p <0.01

Table 6: Correlation between AST, FS, AEC and IgE

Pearson's correlation coefficient	*AEC*	*S. IgE*	*FS*	*AST*
AEC	1.00	0.89	0.66	0.78
S. IgE	0.89	1.00	0.71	0.84
FS	0.66	0.71	1.00	0.65
AST	0.78	0.84	0.65	1.00
p-values for the correlation coefficients				
	AEC	S. IgE	FS	AST
AEC	0.00**	0.00**	0.00**	0.00**
S. IgE	0.00**	0.00**	0.00**	0.00**
FS	0.00**	0.00**	0.00**	0.00**
AST	0.00**	0.00**	0.00**	0.00**

**p <0.01
AST – Asthma Severity Test, FS – Fungal Sensitization, AEC – Absolute Eosinophil Count, S. IgE – Serum Immunoglobulin E, FEV_1 – Forced Expiratory Volume in one second, FVC – Forced Vital Capacity, FEV_1/FVC – Ratio of Forced Expiratory Volume in one second to Forced Vital Capacity, BD – Bronchodilator, Pre-BD – Pre-bronchodilator, Post-BD – Post-bronchodilator

The consistent correlation between FS and AST further supports their utility in comprehensive asthma evaluation and phenotyping.

Conclusion

This study substantiates the role of fungal sensitization, particularly to *A. fumigatus*, as a contributing factor to asthma severity. It emphasizes the interrelation between immunologic markers and pulmonary function, reinforcing the value of integrating clinical, functional, and immunological assessments in asthma management. These findings advocate for early detection of fungal sensitization to guide targeted interventions and improve disease outcomes.

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