

Prevalence of Allergic Bronchopulmonary Aspergillosis in Severe Asthma Patients Presenting to a Tertiary Care Hospital in North West India



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Received: 29 December 2024; Accepted: 15 April 2025

ABSTRACT

Background/introduction: The Indian subcontinent faces a substantial healthcare challenge with allergic bronchopulmonary aspergillosis (ABPA). While numerous investigations have explored ABPA's occurrence in the general asthmatic population, there remains a significant knowledge gap regarding its specific prevalence among individuals with severe asthma. Current Indian research demonstrates considerable variation in reported ABPA prevalence rates among severe asthmatics, highlighting the need for more comprehensive investigation.

Objective: This research initiative aimed to determine the precise prevalence of ABPA among severe asthma patients seeking treatment at a tertiary healthcare institution in northwestern India, with the goal of enhancing our understanding of this complex condition's burden in this specific patient population.

Methodology: We conducted a comprehensive cross-sectional investigation spanning August 2022 through July 2023. The study encompassed 247 patients diagnosed with severe asthma. Each participant underwent thorough clinical evaluation and provided blood samples for comprehensive analysis, including absolute eosinophil count measurement, total IgE quantification, and specific testing for *Aspergillus fumigatus*-related IgE antibodies. When clinically indicated, additional diagnostic procedures included *Aspergillus*-specific IgG testing and detailed chest imaging through X-ray or high-resolution computed tomography (HRCT).

Results: Our investigation revealed that 63.2% (156 out of 247) of severe asthma patients met the diagnostic criteria for ABPA. The affected population showed a mean age of 41.6 years, with a relatively balanced gender distribution (80 females, 76 males). Among those diagnosed with ABPA, we observed a notably higher prevalence of ABPA-B (92.3%, 144 patients) compared to ABPA-S (7.7%, 12 patients).

Conclusion: This research represents one of the most extensive investigations to date documenting such a high ABPA prevalence (63.2%) among severe asthma patients in northern India. These findings underscore the critical need for expanded research initiatives to investigate the underlying factors contributing to such elevated ABPA rates in this geographical region, ultimately aiming to develop and implement effective preventive strategies at the community level.

Journal of The Association of Physicians of India (2025): 10.59556/japi.73.1097

INTRODUCTION

The global healthcare landscape has witnessed a significant transformation in respiratory disease patterns, with bronchial asthma emerging as a critical concern characterized by chronic airway inflammation and variable airflow limitation.¹ This respiratory condition demonstrates increasing prevalence across all demographic groups worldwide, with recent decades showing a marked upward trend that healthcare experts project will continue to escalate.^{1,2} The evolving nature of this condition presents mounting challenges for healthcare systems globally, emphasizing the urgent need for enhanced understanding of its complexities and the development of more effective management strategies.

Environmental factors play a crucial role in asthma progression, with fungal spore

exposure emerging as a significant contributor to both symptom deterioration and declining pulmonary function. The *Aspergillus* species, in particular, represents a notable environmental trigger.³ The interaction between fungal elements and severe asthma manifests through multiple pathways: direct triggering of asthma exacerbations through spore inhalation, development of fungal sensitization characterized by immediate cutaneous hyperreactivity or elevated specific IgE antibodies, and in severe cases, the emergence of allergic bronchopulmonary mycosis leading to permanent bronchopulmonary damage.³

Among fungal pathogens, *Aspergillus fumigatus* demonstrates particular clinical significance in asthma patients. This organism can affect the respiratory system through various mechanisms, including allergic

bronchopulmonary aspergillosis (ABPA), aspergilloma formation, and invasive aspergillosis.^{3,4} ABPA represents a complex hypersensitivity response to *A. fumigatus*, characterized by a distinctive combination of clinical features: asthma exacerbations, recurrent pulmonary infiltrates, elevated eosinophil counts, increased total serum IgE levels, and elevated *Aspergillus*-specific IgE or IgG, with or without central bronchiectasis.⁴

The International Society for Human and Animal Mycology (ISHAM) established comprehensive diagnostic criteria for ABPA in 2013, requiring the presence of two mandatory criteria alongside at least two of three additional criteria.⁵ However, despite these standardized diagnostic guidelines, the actual prevalence of ABPA among asthmatic populations remains subject to considerable variation across different studies and geographical regions.

A comprehensive systematic review conducted by Agarwal and colleagues revealed that ABPA prevalence in Indian asthma patients ranges from 3 to 41%, with an aggregate prevalence of 16.2%.⁶ When specifically examining severe asthma cases, the reported prevalence demonstrates even greater variability. Previous research by Agarwal et al. documented ABPA prevalence rates ranging from 12.9 to 27.2% in severe asthma patients,^{5,7} while another study reported a prevalence of 38.6% among patients hospitalized with acute severe asthma.⁸

The substantial burden of ABPA in India, evidenced by these varying prevalence estimates, underscores the critical importance

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How to cite this article: Gupta S, Garg A. Prevalence of Allergic Bronchopulmonary Aspergillosis in Severe Asthma Patients Presenting to a Tertiary Care Hospital in North West India. J Assoc Physicians India 2025;73(10):24–26.

of establishing precise epidemiological data, particularly among individuals with severe asthma. Accurate prevalence data can significantly inform the development and implementation of targeted screening protocols and management strategies within asthma care settings. Current literature reveals a notable gap in understanding ABPA prevalence specifically within the severe asthma population in the Indian context.

This research initiative aims to address this knowledge gap by conducting a detailed investigation into ABPA prevalence among severe asthma patients presenting to a tertiary care institution in northwestern India. The findings from this study will contribute valuable insights into the burden of ABPA in this high-risk population and help inform future screening and management approaches, ultimately working toward improving care outcomes for individuals with severe asthma in India.

METHODOLOGY

This was a prospective institutional study, and a total of 247 patients presenting with a diagnosis of severe asthma to the outpatient clinic or emergency department were consecutively enrolled from August 2022 to July 2023. The patients were classified as severe asthma as per the Global Initiative for Asthma guidelines, 2022.¹ After taking informed consent, patients' detailed case history, examination, and other relevant workup were done.

Collection of Sample

Under aseptic conditions, a venous blood sample was collected and serum was separated for further testing. Absolute eosinophil count and total IgE levels were tested in all 247 patients. Chemiluminescence immunoassay (CLIA)-based tests were performed for total IgE, and fluorescent enzyme immunoassay (FEIA)-based tests were done for *A. fumigatus*-specific IgE and IgG using the ImmunoCap Diagnostics kit.

Patients were diagnosed with ABPA according to ISHAM criteria and further classified into ABPA-B and ABPA-S. The results of all these tests were recorded and compiled.

Data analysis was performed using SPSS software (version 27.0; SPSS Inc., Chicago, IL,

USA). We employed descriptive statistical methods appropriate to the data distribution, presenting continuous variables as either mean with standard deviation or median with range, depending on the underlying distribution patterns.

Inclusion Criteria

- Patients presenting to the outpatient clinic or emergency department who had been diagnosed with severe asthma.
- Older than 15 years.

Exclusion Criteria

- Patients who had already been diagnosed with ABPA in the past or were currently being treated for ABPA.
- Pregnant women.
- Those who did not give consent.

RESULTS

Among the 247 patients enrolled, 55.5% ($n = 137$) were female and 44.5% ($n = 110$) were male, and the mean age of the patients was 46.3 ± 16.3 years. The mean AEC recorded was 901.8 ± 940.8 cells/ μ L, and mean IgE was 2874.9 ± 2701.5 IU/mL among the total 247 patients enrolled in the study.

Of the 247 severe asthma patients, 63.2% ($n = 156$) were diagnosed with ABPA, while 36.8% ($n = 91$) patients had no ABPA, according to ISHAM criteria. The mean age of the patients diagnosed with ABPA was 41.6 ± 15.2 years. Of these 156 ABPA patients, 80 (51.3%) were female and the remaining 76 (48.7%) were male. Twelve (7.7%) patients were diagnosed with ABPA-S and 144 (92.3%) patients with ABPA-B.

The mean absolute eosinophil count (AEC) in our patients was 1097.9 ± 951.9 cells/ μ L. The mean AEC values were higher in the ABPA-B group (1141.4 ± 974.6) as compared to the ABPA-S group (577.1 ± 317.2), and this difference was statistically significant ($p = 0.05$) (Table 1).

The mean IgE in our ABPA patients was 3867.9 ± 2782.2 IU/mL. The mean IgE values were higher in the ABPA-B group (4041.4 ± 2798.2 IU/mL) as compared to the ABPA-S group (1785.9 ± 1470.2 IU/mL), and this difference was statistically significant ($p < 0.01$) (Table 1).

DISCUSSION

Patients with severe asthma with recurrent attacks and those with persistent asthma with irreversible lung changes are at higher risk of fungal colonization and sensitization.⁹

In the current study group, 170 out of 247 patients had total IgE $>1,000$ IU/mL, with a mean value of 3867.9 ± 2782.2 IU/mL. Sarkar et al. reported higher serum total IgE levels in 8 out of 10 patients with ABPA,¹⁰ while Nath et al. reported mean total serum IgE levels as 1970.5 IU/mL.¹¹

In our study cohort, the overall prevalence of ABPA among patients with severe asthma was found to be 63.2% (156 of 247 patients). To date, very few studies have been carried out to estimate the prevalence of ABPA in severe asthma, wherein Bhankhur reported a prevalence of ABPA as high as 70%,⁹ Agarwal reported a prevalence of 38.6% in acute severe asthma,⁸ and Mathur found prevalence of ABPA to be only 2.7% in severe asthmatics.¹²

The mean age in our study was 41.6 years, which was slightly higher than that reported previously. Kumar and Gaur have reported the mean age of ABPA to be 34 years,¹³ Agarwal et al. as 34.4 years,¹⁴ and Sarkar et al. as 33.1 years.¹⁰

In our study, more females (51.3%, $n = 80$) were diagnosed with ABPA than males (43.7%, $n = 76$); however, this difference was not significant. Nath et al. have also reported no significant gender predisposition toward ABPA in their study.¹¹

The mean AEC in ABPA patients in our study was 1097.9 ± 951.9 cells/ μ L, and the mean IgE was 3867.9 ± 2782.2 IU/mL; significantly higher values of both were seen in the ABPA-B variant. In a study done on 31 ABPA patients, Kumar reported significantly higher values of total IgE in ABPA-B than ABPA-S patients.¹⁵ In their study done on 93 patients, Wang et al. reported higher, but not significant, values of both AEC and total IgE in ABPA-B patients when compared to ABPA-S.¹⁶

In our study, the prevalence of ABPA-B (92.3%) was found to be much higher than ABPA-S (7.7%). Kumar and Gaur have reported 75% prevalence of ABPA-B and 25% prevalence of ABPA-S.¹³ Similar findings were reported by Agarwal et al. in their study done on 209 ABPA patients, wherein a high prevalence of ABPA-B (77.5%) was seen compared with ABPA-S (22.5%).¹⁴ On the contrary, in their study

Table 1: Distribution of mean AEC and IgE with respect to types of ABPA

Characteristic	ABPA subcategory	Number of patients	Mean	SD	Minimum	Maximum	Median	p-value
AEC (cells/ μ L)	ABPA—B	144	1141.4	974.6	100	5100	940	0.05
	ABPA—S	12	577.1	317.2	115	1260	500	
IgE (IU/mL)	ABPA—B	144	4041.4	2798.2	189	15856	3200	<0.01
	ABPA—S	12	1785.9	1470.2	269	5630	1291.5	

of 50 ABPA patients, Bhankhur et al. reported a prevalence of ABPA-S (68.5%) much higher than ABPA-B (31.5%).⁹

These diverse findings across multiple studies not only reflect regional variations but also highlight potential environmental and genetic factors that may influence ABPA manifestation in severe asthma patients. The remarkably high ABPA-B prevalence in our study population could be attributed to several factors unique to northwestern India, including climatic conditions, agricultural practices, and indoor air quality characteristics. Additionally, the timing of clinical presentation and diagnosis may play a crucial role, as patients with bronchiectasis often present at later stages of disease progression. The environmental conditions in this region, characterized by significant temperature fluctuations, agricultural activities generating organic dust, and specific housing conditions, might contribute to increased *Aspergillus* exposure and subsequent sensitization. Understanding these regional determinants could be instrumental in developing targeted preventive strategies and optimizing diagnostic protocols for early ABPA detection in severe asthma patients. This observation also raises important questions about the potential role of local environmental modifications and patient education in reducing ABPA burden in this geographical area.

CONCLUSION

Our study highlights a high prevalence (63.2%) of ABPA in patients with severe asthma. Hence, it

seems pertinent to evaluate all such patients for the presence of ABPA using standard guidelines. The importance of creating awareness among the physician community to achieve early diagnosis and institute timely management, so as to achieve better asthma control and avoid permanent lung damage, cannot be undermined. However, studies with a larger sample size are needed to assess the underlying causes of such a high burden of ABPA in this part of the world, so that preventive measures can be instituted at the community level.

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