



The Pattern of Allergic Bronchopulmonary Aspergillosis (ABPA) in Asthmatic Patients

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Abstract

Introduction: Asthma is a heterogeneous disease and *Aspergillus fumigatus* (*A. fumigatus*) is the one that is strongly associated with asthma which majorly affects the lung. The present study was done to find the prevalence of ABPA in adult asthmatics in tertiary care hospitals using the ISHAM criteria for ABPA.

Method: A cross-sectional study was conducted among 165 asthma patients using ISHAM criteria for ABPA.

Result: Out of 165 cases, 36 (21.81%) patients had ABPA according to ISHAM criteria.

Conclusion: ABPA is frequently misdiagnosed as pulmonary tuberculosis in India results in delaying the diagnosis of ABPA. Clinicians should be sensitized to the problem burden, timely diagnosis and management to prevent lung tissue damage.

Significance of result: A separate guideline can be formulated to diagnose and manage ABPA in asthmatic patients.

Keywords: Allergic Bronchopulmonary aspergillosis; ABPA; Asthma; ISHAM criteria

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Introduction

Asthma is a heterogeneous disease with respiratory symptoms such as wheezing, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation [1]. At times it can even be fatal [2,3].

Asthma prevalence has been in a rising state. Asthma involves interactions between host variables (obesity, nutritional factors, infections), environmental exposures, (pollens, mold, other aeroallergens), and genetic factors (asthma susceptibility loci on genes) [4,5].

The cause of asthma symptoms is airway inflammation, which also leads to the development of mucus, remodeling of the airway wall, and Bronchial Hyper-Responsiveness (BHR), i.e., the propensity of smooth muscle cells to respond to unspecific stimuli like cold air [6]. Symptoms can be aggravated in the presence of additional insults like smoking, CHF, fungal infection/infestation etc.

Among various fungal infections, *Aspergillus fumigatus* is strongly associated with asthma though it can also affect our lungs in various ways like Allergic Bronchopulmonary Aspergillosis (ABPA), aspergilloma (fungal ball) and invasive aspergillosis etc.

Allergic Bronchopulmonary Aspergillosis (ABPA) is an allergic symptom and is further classified as Serological ABPA (ABPA-S) and ABPA with Bronchiectasis (ABPA-B) depending on High-Resolution Computed Tomography (HRCT) chest findings [7].

The International Society for Human and Animal Mycology (ISHAM) criteria has 2 classifications that have 'obligatory' criteria and the 'other' criteria [8]. The obligatory criteria's two attributes are as follows: (1) raised total IgE levels >1000 IU/mL and (2) positive acute (type I) cutaneous hypersensitivity to *Aspergillus* antigen or elevated IgE levels against *Aspergillus fumigatus* (*A. Fumigatus*). The presence of both of these attributes is required to make the diagnosis of ABPA

or alternatively a minimum of two out of the three additional criteria, which includes precipitating IgG antibodies against *A. Fumigatus* in blood, radiographic pulmonary opacities consistent with ABPA, and a total eosinophil count in steroid-naïve individuals greater than 500 cells/L.

Also, In India, ABPA is misdiagnosed as pulmonary TB in as many as 17% to 58% of cases, as per several studies [9].

Since ABPA is the most common form of pulmonary aspergillosis, which is also a significant developing illness in India [8,10] and it affects the lifestyle and quality of life therefore frequent absenteeism from work has been also reported. The present study was done to find the prevalence of ABPA in adult asthmatics in tertiary care hospitals using the ISHAM criteria for ABPA.

Aim and Objectives

1. To find the prevalence of Allergic Bronchopulmonary Aspergillosis (ABPA) in adult asthmatics in tertiary care hospital by using ISHAM criteria.

Material and Methods

After ethical clearance from the Institutional Ethical Committee, a hospital-based cross-sectional study was conducted from March 20th, 2021 to June 30th, 2022. Subjects were taken from the outpatient and in-patient Department of Respiratory Medicine at the tertiary care center of Delhi-NCR using a systematic sampling method, every K patient with bronchial asthma was included in the study (k=4).

Sample size

Based on the study done by Bhankhur et al., considering the prevalence of ABPA was found to be 70% with a margin of error considered as 7% and a confidence interval of 95%, by using the formula:

$$N = \frac{Z^2 PQ}{l^2},$$

Z=1.96 (confidence level), P=88% (prevalence), Q=1-P, l = (margin of error), the sample size calculated to 165.

Inclusion criteria

All Bronchial asthma patients of age 18 to 80 years, who have given consent to be the part of study, irrespective of their economic status, educational status, residential status, caste, creed or religion were included in the study.

Exclusion criteria

All the patients aged less than 18 years or more than 80 years of age, non-cooperative, COPD, Asthma-COPD overlap case (ACOS), active tuberculosis case and pregnant females.

The study was performed as per ISHAM guidelines. Initially, 180 patients were approached for the study out of which 15 patients were excluded as 2 female patients were tested Urine Pregnancy Test (UPT) positive, 3 patients were diagnosed with active tuberculosis and 10 patients refused to participate in the study. Henceforth, 165 patients full filling the inclusion criteria, finally included in the present study. After taking the written informed consent, a detailed clinical history was taken. All the patients were considered for general examination including anthropometric measurement (height, weight etc.), and systemic examination that includes systems like CVS/CNS/Chest and genitourinary system. In chest examination inspection, palpation, percussion and auscultation were done properly.

All participants were subjected to spirometry, urine pregnancy test, ECG and sputum AFB (2 samples to fulfil the inclusion/exclusion criteria). For the workup of ABPA, serum total IgE, specific IgE for *A. Fumigatus*, blood eosinophilic counts and X-ray chest & HRCT chest were done.

Observations and Results

In the present study, among 165 (100%) patients most of them belonged to 39 to 48 years which is approximately 43.6% (Figure 1).

With a mean age of 48.73 ± 13.50 and Among 165 (100%) patients, 43% were males and 57% were females.

In 33 cases (20%) total IgE was more than 1000 IU/ml, 20 cases (12.2%) positive for specific *Aspergillus* for IgE, 18 cases (11%) were positive for raised AF for IgG, 60 cases (36.4%) with eosinophil more than 500 cells/microL and 55 cases (33.3%) had radiological presentation of ABPA out of total 165 cases taken for study (Table 1).

The overall prevalence of patients according to ISHAM criteria for APBA in Asthma patients was 36 (21.81%) out of total 165 cases (Table 2).

Table 3 shows the radiologically classified ABPA with 13 (7.9%) ABPA-S cases, 5 (3%) ABPA-B cases, 14 (8.5%) ABPA-HAM cases, 10 (6.1%) ABPA-CPF cases and 123 cases with no radiological abnormalities.

The overall prevalence of ABPA according to age was 12.4% in the age group of 18 to 30 years, 21.2% in 31 to 45 years, 33.3% in 46 to 60 years and 33.3% in 61 years and above with gender predilection with 45.4% in male and 54.5% in female (Table 4, 5).

Discussion

Allergy to fungi is found to be associated with increased asthma symptoms and severity. *Aspergillus* is a common environmental mold that is found in both indoor and outdoor air. Severe asthmatic patients with recurrent attacks and persistent asthma symptoms with irreversible lung changes are at higher risk of fungal colonization and sensitization [11,12]. As per Western data, ABPA complicates up to 6% of all chronic cases of asthma.

In a similar study by Banka R, Kamath A reported confirmed ABPA in 73 (66%) patients diagnosed by the ISHAM criteria while in the present study, 36 (21.81%), were diagnosed with ABPA in asthmatics per ISHAM criteria. This difference is probably due to that the former was a UK-based cohort study while the latter is a cross-sectional study on the Indian population.

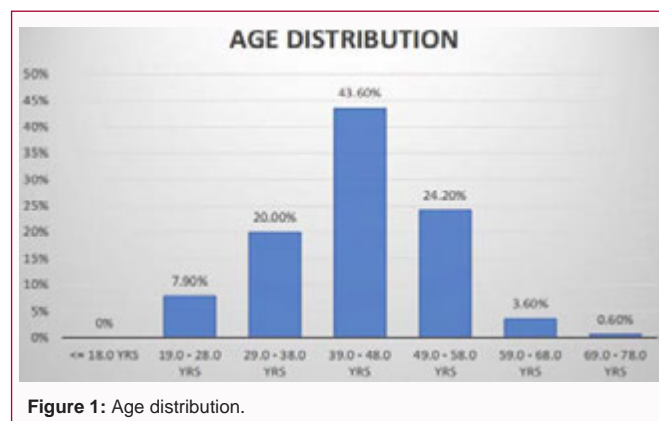


Figure 1: Age distribution.

Table 1: Case findings as per ISHAM criteria.

Total IgE	33 Cases	20%
Positive for specific aspergillus for IgE	20 Cases	12.20%
Positive for specific aspergillus for IgG	18 Cases	11%
Eosinophil >500 cells/micro L	60 Cases	36.40%
Radiological ABPA	55 Cases	33.30%

Table 2: Overall prevalence of ABPA in Asthma.

Obligatory Criteria	N	%
Both	19	11.51
Full diagnostic criteria		
Both obligatory criteria		
With no other criteria	4	2.42
With only 1 other criteria	10	6.06
With only 2 other criteria	24	14.5
With only 3 other criteria	9	5.45
Overall prevalence	36	21.81

Table 3: Distribution of revised classification radiologically of ABPA as per HRCT chest.

	Frequency	%
None	123	74.5
ABPA-S (Serological ABPA)	13	7.9
ABPA-B (Bronchiectasis ABPA)	5	3
ABPA-HAM	14	8.5
ABPA-CPF	10	6.1
Total	165	100

According to a study by Kumar R, and Gaur SN where chest CT of 31 patients showed central bronchiectasis in 24 cases, labelling these patients as ABPA-CB (ABPA with Central Bronchiectasis) and another 7 as ABPA-S (serological positive) while in our present study, 13 had ABPA-S (Serological ABPA) and 5 had ABPA-B (Bronchiectasis ABPA) out of total 165 cases. This major variation in the result is due to the availability of more advanced machines, better diagnostic criteria and more patient orientation and alertness towards themselves compared to the era of the year 2000.

In a study done by Bhankhur et al. reported prevalence of ABPA was found to be 70% (35/50). Out of these 35 patients, there were 18 females and 17 were males while in our present study, out of 165 (100%) patients, 43% were males and 57% were females, so the results of both studies are in alignment.

Maleki et al. reported a frequency of positive for *A. fumigatus* specific IgE, total IgE as 9 (10.5%) and 47 (54.6%) respectively while in the present study, positive for *A. fumigatus* specific IgE, total IgE>1000 IU/ml were 20 (12.2%) and 33 (20%), respectively.

As the number of fungal infections is increasing day by day, not only the *Aspergillus* species but also the role of various fungi in complicating bronchial asthma should be explored in detail. This study highlights a high prevalence of ABPA in patients with severe asthma. Hence, evaluating all such patients for the presence of ABPA using standard guidelines seems pertinent. This study's main strength is the quantity and caliber of instances. However, the limitation of the study was that the study sample size was small and conducted at a single center. However, studies with larger sample sizes are required

Table 4: Overall prevalence of age.

Age (Years)	N	%
18-30	4	12.4
31-45	7	21.2
46-60	11	33.3
>61	11	33.3

Table 5: Overall prevalence according to gender.

Gender	N	%
Male	15	45.4
Female	18	54.5

to clarify the picture in mild to moderate grades of asthmatic patients. Results may variate from population-based studies and it might be higher in the asthma patients attending our institute which is a tertiary care center.

Conclusion

There are no age or gender-specific preferences for ABPA. To exclude the potential of ABPA, *Aspergillus* skin testing and/or serum total IgE screening should always be performed on any patient with long-standing, poorly managed bronchial asthma who also has noticeably high peripheral eosinophil counts. Because total serum IgE has a wide range of levels depending on the stage of ABPA, a diagnosis of ABPA should not be ruled out based solely on these cutoff values. Due to the radiological resemblance, ABPA is frequently misdiagnosed as pulmonary tuberculosis in India, delaying the diagnosis of ABPA. High suspicion and early investigation should be used to avoid this situation and prevent lung tissue damage.

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