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Prevalence of allergic bronchopulmonary aspergillosis among patients with severe bronchial asthma in a tertiary care hospital in Northern India

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Abstract

Introduction: The link between fungi and asthma has been known for centuries. About one-third to one-half of severe asthmatics has history of atopic sensitization to filamentous fungi, most predominantly to *Aspergillus fumigatus*. Allergic bronchopulmonary aspergillosis (ABPA) is the one of the most documented fungal presentations among patients with asthma. This study was done on 50 patients with severe asthma who were consecutively enrolled from January 2016 to June 2017 to look for prevalence of ABPA. **Materials and Methods:** Blood samples were collected from 50 patients with severe asthma, and serum was separated to test for absolute eosinophil count, total IgE, and *Aspergillus fumigates*–specific IgE. **Results:** The prevalence of ABPA was found to be 70% (35/50). Of these, ABPA-B (ABPA with bronchiectasis) was less 31.4% (11/35) when compared with 68.5% (24/35) of patients with serological ABPA. Out of these 35 patients, there were 18 females and 17 were males. The mean age of the patients was 41.3 years. **Conclusion:** ABPA prevalence is high in patients with severe asthma, and there is a need to look for and evaluate this association further.

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Full Text

Introduction

Asthma is an inflammatory disease of the airways characterized by chronic airway inflammation, declining airway function, and tissue remodeling. It affects people of all age groups. When uncontrolled, it can lead to severe limitation on day-to-day activities and can even be fatal.[1] The prevalence of asthma has rapidly increased over the past few decades to epidemic proportions, and it is expected to rise dramatically over the next 15–20 years.[2]

Clinical presentation occurs as breathlessness, wheeze, and a variable airflow obstruction. Exposure to environmental fungal spores potentially causes worsening of asthma symptoms and lung function. Fungi can be associated with severe asthma in a number of ways, that is, (a) through inhalation of fungal spores, (b) through fungal sensitization which may or may not be associated with severe asthma and may present as immediate cutaneous hyperreactivity to fungal antigen or increase in specific IgE antibodies to a particular fungus, and (c) through causing allergic bronchopulmonary mycosis, a severe form of fungal sensitization with resultant irreversible bronchopulmonary damage. About 112 genera of fungi are thought to be a source of allergens. The four most common genera responsible for the development of allergy are Aspergillus, Alternaria, Cladosporium, and Penicillium.[3]

Aspergillus fumigatus is the most common allergen and there is colonization of the lower respiratory tract with Aspergillus species. The fungus acts as both a source of allergen and pathogen.[4] Clinically, fungal asthma can vary from fungal sensitization at one end, manifesting as A. fumigatus–associated asthma, to severe asthma with fungal sensitization and allergic bronchopulmonary aspergillosis (ABPA) at the most extreme end of the spectrum. ABPA presents itself by a range of clinical features including asthma exacerbation, recurrent pulmonary infiltrates, elevated total serum IgE, elevated A. fumigatus–specific IgE or IgG, central bronchiectasis, eosinophilia, and mucous plug production. As per latest guidelines,[5] ABPA is diagnosed by the presence of asthma, A. fumigates–specific IgE ≥0.35 kUA/L, total IgE >1000 IU/mL, and A. fumigates–specific IgG ≥27 mgA/L. Currently, ABPA is further classified as serological ABPA (ABPA-S) and ABPA with bronchiectasis depending on high-resolution computed tomography (HRCT) chest findings where they are normal (ABPA-S) or bronchiectasis is present (ABPA-B). There is a need to differentiate between these conditions as treatment varies. The patients with sensitization are kept under observation only, requiring no treatment, whereas ABPA patients require treatment.

Materials and Methods

This study was a prospective study, and a total of 150 patients with asthma were consecutively enrolled from January 2016 to June 2017. The patients were divided into 50 each of mild, moderate, and severe asthma as per Global Initiative for Asthma guidelines, 2014. After taking informed consent, patient's detailed case history, examination, and other relevant workup were done.

Collection of sample

Under aseptic conditions, venous blood sample was collected and serum was separated for further testing. Total eosinophil count and total IgE levels were tested in all 150 patients. ELISA-based test was performed using Genesis Diagnostics kit for total IgE. A. fumigates–specific IgE was noted in all those patients, in whom it was needed as per criteria for diagnosis. The results of all these tests were recorded and compiled.

Results

Of 50 severe asthma patients, 35(70%) were diagnosed as ABPA according to its criteria which are total IgE >1000 IU/mL and A. fumigates–specific IgE ≥0.35 kUA/L. Of these 35 patients, there were 18 females and 17 males. Twenty-four patients were diagnosed as ABPA-S and 11 patients as ABPA-B. The mean age was 41.3 years. The mean absolute eosinophil count (AEC) in our patients was 417 ± 405.8 cells/μL. The difference in mean AEC was statistically significant between both severe and mild asthma (P = 0.004) and severe and moderate asthma group (P = 0.042) [Table 1]. The total IgE values were significantly high in patients with severe asthma in comparison to those of mild and moderate asthma [Table 1].{Table 1}

Discussion

Allergy to fungi is associated with increased asthma symptoms and severity with increased asthma admissions and even death sometimes.[1]Aspergillus is one of the most common environmental molds present in both indoor and outdoor air. Prevention to exposure of such airborne allergens is difficult.[1] Establishing a cause and effect between fungi and asthma is still a challenge. A number of patients develop sensitization before development of lung changes. Patients with severe asthma with recurrent attacks and persistent asthma with irreversible lung changes are at higher risk of fungal colonization and sensitization.

In the current study group, there were 37 patients who had total IgE more than 1000 IU/mL with a mean value of 1407.7 ± 1062.8 IU/mL. Sarkar et al. reported higher serum total IgE level in 8 out of 10 patients with ABPA.[6] Nath et al. reported mean total serum IgE levels as 1970.5 IU/mL.[7] Our study had 35 patients with A. fumigates–specific IgE ≥0.35 kUA/L. The study by Prasad et al. observed high serum titers for specific IgE in 30 of 37 (81.1%) patients.[8] Sarkar et al. reported that 9 of 10 ABPM patients had raised specific IgE against A. fumigatus.[6]

Therefore, considering that 35 patients had asthma, raised total IgE, and raised A. fumigates–specific IgE, the overall prevalence of ABPA among patients with severe asthma was found to be 70% (35 of 50 patients) in our study. A meta-analysis done by Agarwal et al.[9] reported the prevalence of ABPA in bronchial asthma as ranging from 2% to 32%, with a pooled prevalence of 12.9% [95% confidence interval (CI) 7.9–18.9] by the random effects model. The prevalence of ABPA reported from industrialized countries (25.6%) was higher than in developing countries (12.7%) and the difference was statistically significant (P = 0.0001). The prevalence of ABPA in Aspergillus-sensitized bronchial asthma varied from 6% to 68%, with a pooled prevalence of 40% (95% CI 27–53). Previously, ABPA prevalence was reported to be 16%, 7.5%, and 27.5% in patients with asthma by Kumar and Gaur, Maurya et al., and Agarwal et al. respectively.[10],[11],[12]

The mean age in our study was 41 years which was slightly higher than that reported previously. In most of the Indian studies, the mean age of ABPA varies. Kumar and Gaur reported it to be 34 years,[10] Agarwal et al. as 34.4 years,[12] and Sarkar et al. as 33.1 years.[6] In our study, females were more than males. There were 18 females and 17 males. The study by Nath et al.[7] reported no significant gender prediction toward ABPA.

The mean AEC in our patients was 417 ± 405.8 cells/μL. In an Indian study done on ABPA patients, there was no significant relationship observed between AEC and severity of asthma (P = 0.63). Only 2% of patients with raised AEC were explainable clinically. Fungal sensitization was also not significantly different between patients with low AEC to high AEC.[13]

There is a need to identify clinical presentations as the treatment may vary. On the basis of HRCT chest finding in ABPA-diagnosed patients, a high prevalence of ABPA-S (68.5%) was seen compared with ABPA-B which was 31.4%. ABPA-S is an immunologically active disease which has all the features of ABPA but without bronchiectasis. It can be speculated that ABPA-S is a condition with predilection to ABPA-B in future. However, Agarwal et al.[14] have reported that if these patients are closely monitored and diligently followed, they may not necessarily progress to ABPA-B. Is antifungal treatment necessary? It has been seen that therapy to reduce the amount of fungus within the airway by giving antifungal agents (mostly itraconazole) can improve ABPA control and may help in reducing the dependency on corticosteroid treatment and dose. However, the duration of therapy with an antifungal agent needs to be individualized.

As the numbers of fungal infections are 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, it seems pertinent to evaluate all such patients for the presence of ABPA using standard guidelines. However, studies with bigger sample size are required to clarify the picture in patients with mild to moderate grades of asthma.

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Conflicts of interest

There are no conflicts of interest.[16]

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