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ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS (ABPA) AMONG ADULT PATIENTS PRESENTING WITH ASTHMA

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ABSTRACT

Background: Allergic bronchopulmonary aspergillosis (ABPA) is an immune reaction in the lungs to Aspergillus species, particularly Aspergillus fumigatus.

Objective: To establish the incidence of allergic bronchopulmonary aspergillosis (ABPA) in adult bronchial asthma patients among tertiary care hospital in Karachi, Pakistan.

Methods: This Descriptive cross-sectional study was undertaken in Department of Pulmonology, Aga Khan University Hospital, Karachi for six months. The number of adult patients who have bronchial asthma is 101 obtained by non-probability consecutive sampling. Data pertaining to demographic and clinical characteristics were gathered on a pre-designed proforma. The serum total Immunoglobulin E (IgE) level was quantified by chemiluminescence immunoassay and Aspergillus fumigatus sensitization was determined by skin prick testing. The analysis of data was done using SPSS version 25 and expressed in frequencies, percentages and Mean ±SD.

Results: The mean age of patients was 52.3 ± 12.1 years and the mean duration of asthma was 5.8 ± 3.5 years. Out of 101 patients, 44 (43.6%) were male and 57 (56.4%) were female. A history of smoking was found in 34 (33.7%) of them. 17/100 patients were diagnosed with ABPA (16.8%). 27.7% of patients were positive for Aspergillus skin test. There was no significant correlation of ABPA with age, sex, smoking status, duration of asthma and skin test positivity.

Conclusion: ABPA is a relatively common condition, affecting 16.8% of adult asthma patients in this study. The diagnosis and regular assessment of ABPA in asthmatics is very important, to enhance disease control and to avoid long-term lung damage.

KEYWORDS: Allergic bronchopulmonary aspergillosis, asthma, *Aspergillus fumigatus*, hypersensitivity, frequency.

INTRODUCTION

An important immunological complication of asthma is allergic bronchopulmonary aspergillosis (ABPA) resulting from hypersensitivity reactions to the fungus Aspergillus species, usually Aspergillus fumigatus. It is a complex interplay of fungal colonisation of the airways, type 2 immune reactions, bronchial inflammation, mucous plugging and chronic damage to the airways. [1]. The importance of ABPA in adult bronchial asthma has been growing in the field of respiratory medicine. A systematic review of data from around the world found that Aspergillus sensitization and ABPA were not uncommon in adults with asthma; therefore, fungal allergy should be suspected in subjects with asthma who continue to be symptomatic despite optimal asthma care [2].

There has been population level evidence supporting the public health importance of ABPA in asthma. An epidemiological study in North India with 43261 participants provided valuable information on the prevalence of ABPA among the population with asthma and also suggested that ABPA is not exclusive to the tertiary-care referral population [3]. Biological and clinical relevance of the association between Aspergillus and asthma. Exposure to aspergillus can lead to a spectrum of airway reaction from sensitization to definite ABPA. However, if the individual is susceptible, chronic exposure to the fungus and colonisation of the airways can exacerbate airway inflammation, the severity of asthma and lead to repeated exacerbations [4].

Recent evidence based on treatment also revealed that asthma associated with ABPA requires a more specific therapeutic approach than asthma alone. Treatment includes systemic steroids, antifungal agents, in selected cases, biological agents and monitoring the clinical, immunological, and radiological response [5]. With these advances in treatment, early detection is even more critical, as ABPA may be identified and properly treated early in the course of the disease before it is too late. In adults with asthma, the failure to recognize ABPA can cause repeated inappropriate treatment of asthma as an uncontrolled asthma without considering the fungal allergic aspects of asthma.

The prevalence of ABPA may be particularly high among patients with severe asthma. In evaluating the prevalence of ABPA in severe asthma, evidence suggested that the severe asthma population warranted more careful evaluation since persistent symptoms, frequent exacerbations and higher treatment levels could be indicative of ABPA and not just severe asthma alone [6].

Screening strategies are crucial as the diagnosis of ABPA depends on clinical, immunological and radiological criteria. A decision tree analysis was conducted to determine the best method to screen ABPA in asthmatic patients and indicated that there is a need for working diagnostic pathways to assist in identifying patients who should be further investigated [7]. The quality of diagnosis has also been enhanced by optimization of the Aspergillus-specific IgE thresholds. Studies on the optimal cut-off point of ImmunoCAP Aspergillus fumigatus-specific IgE and its diagnostic accuracy for the diagnosis of ABPA in adult asthmatic patients showed that the determination of optimal cut-off points can lead to better detection of the cases and less misclassification [8].

Different IgE based tests have also been studied in comparative diagnostic studies to determine their usefulness in the diagnosis of ABPA. Knowledge of the comparisons between mx4-IgE and species-specific IgE revealed that the type of diagnostic test could affect the detection of ABPA among asthma patients [9]. Clinical and immunological studies of Aspergillus fumigatus-sensitized asthma and ABPA have also contributed to the differentiation between fungal sensitization and the presence of ABPA. These patients with ABPA may show greater immunologic responses, greater allergic load, and more intense clinical manifestations than the patients with sensitization alone [10].

Since allergic bronchopulmonary aspergillosis was frequently masked by the term difficult-to-treat or uncontrolled asthma, a rationale for studying ABPA in adults with asthma was based on the clinical problem. Frequently, many adult patients would have recurrent respiratory symptoms, frequent exacerbations, persistent cough, wheezing, and poor asthma control, but the fungal-allergic nature of this was not always explored. This may have led to missed diagnosis of ABPA, delayed diagnosis and treatment, and repeated asthma therapy without focusing on ABPA.

METHODS

This study was performed as a descriptive cross-sectional study in the department of Pulmonology, Aga Khan University Hospital (AKUH), Karachi, Pakistan for a period of six months after the synopsis was approved. The study population consisted of bronchial asthma patients (adults) attending the tertiary care hospital during the study period who met the inclusion criteria.

Non-probability consecutive sampling was used to enroll a total of 101 patients. All participants provided informed consent after being informed about the purpose, procedures, risks, and benefits of the study. Demographic and clinical variables were documented on a structured proforma specially created for the study.

A chemiluminescence immunoassay (CLIA) was used to quantify serum total Immunoglobulin E (IgE) and an IgE level less than 1000 IU/mL was regarded as normal. Sensitisation to Aspergillus fumigatus (AF) was determined by skin prick tests, which was the major diagnostic indicator for allergic bronchopulmonary aspergillosis (ABPA) based on the study operational criteria.

The patients' demographic data such as age, gender, smoking status and duration of asthma were recorded. SPSS version 25 was used to enter and analyze the data. The continuous variables like age and duration of asthma were expressed as mean ± standard deviation and categorical variables like gender, smoking status, and ABPA status were expressed as frequencies and percentages. Effect modifiers were determined by stratifying age group, duration of asthma, gender, smoking status and Aspergillus skin test.

RESULTS

A total of 101 adult bronchial asthma patients were included in the study. **Table 1** shows that the mean age was 52.3 ± 12.1 years and mean duration of asthma was 5.8 ± 3.5 years. Males were 44 (43.6%) and females were 57 (56.4%). Smoking history was present in 34 (33.7%) patients and absent in 67 (66.3%). No significant association was observed between ABPA and gender ($p = 0.393$) or smoking status ($p = 0.459$).

Table 2 shows that ABPA was found in 17 patients (16.8%), while 84 (83.2%) were negative.

As shown in **Table 3**, no significant association was observed between ABPA and age ($p = 0.538$) or duration of asthma ($p = 0.451$).

Table 4 shows Aspergillus skin test was positive in 28 (27.7%) patients and negative in 73 (72.3%), with no significant association with ABPA ($p = 0.444$).

Table 1: Baseline Demographic and Clinical Characteristics (n = 101)

Variable	n (%) / Mean ± SD	p-value
Age (years)	52.3 ± 12.1	—
Duration of asthma (years)	5.8 ± 3.5	—
Gender		0.393
• Male	44 (43.6%)	
• Female	57 (56.4%)	
Smoking status		0.459
• Yes	34 (33.7%)	
• No	67 (66.3%)	

Table 2: Frequency of Allergic Bronchopulmonary Aspergillosis (ABPA)

Outcome	n (%)	p-value
ABPA Positive	17 (16.8%)	—
ABPA Negative	84 (83.2%)	—
Total	101 (100%)	—

Table 3: Association of Age and Duration of Asthma with ABPA

Variable	n (%) / Mean ± SD	p-value
Age (years)	52.3 ± 12.1	0.538
Duration of asthma (years)	5.8 ± 3.5	0.451

Table 4: Association of Aspergillus Skin Test with ABPA

Aspergillus Skin Test	n (%)	p-value
Positive	28 (27.7%)	0.444
Negative	73 (72.3%)	
ABPA Positive cases	17 (16.8%)	

DISCUSSION

The aim of the present study was to determine the prevalence of allergic bronchopulmonary aspergillosis (ABPA) in bronchial asthma (BA) patients in a tertiary care hospital. ABPA was present in 16.8% in this study showing that a substantial number of patients with asthma may harbor allergic fungal sensitization as a potential cause of suboptimal control of asthma. This finding is clinically important as ABPA is frequently underdiagnosed and often mistaken for uncontrolled asthma. Agarwal et al. showed that simpler diagnostic criteria would not compromise the diagnostic performance and there would be an improvement in the clinical applicability, particularly in resource-limited settings [11]. Likewise, diagnostic algorithm comparisons have revealed differences in how ABPA was detected, with under or over-estimation of the prevalence of disease using different diagnostic approaches [12]. This variation might contribute to the differences in prevalence reported in various studies, including the present one.

The standards of diagnosis have also been further refined with the adoption of new clinical criteria. Asano et al. developed new diagnostic criteria based on clinical, radiological and immunological markers which increased the accuracy of diagnosis for ABPA and allergic mycosis [13]. Moreover, with the help of latent class analysis, the optimal composition of the diagnostics has been identified indicating that none of the diagnostics is enough and multidimensional diagnostics strategies are necessary for accurate case identification [14]. These developments confirm the need to adopt comprehensive diagnostic strategies in asthmatics, especially in tertiary care.

Diagnostic immunology is also important in the identification of ABPA. The diagnostic accuracy of immunoprecipitation and immunoassay techniques has been found to be different in the detection of Aspergillus fumigatus-specific IgG, a useful biomarker in the evaluation of ABPA, as reported by Sehgal et al. [15]. Furthermore, new technologies like lateral flow assays have shown good sensitivity and specificity and could be used for rapid and cheap ABPA screening in clinical practice [16]. Given these advances, greater access to diagnosis could result in an earlier diagnosis of ABPA in the asthma population.

From a clinical point of view, ABPA continues to be a serious complication of asthma, with recurrent exacerbations, eosinophilic inflammation, progressive airway damage and mucus plugging. Agarwal et al. stressed the importance of considering ABPA a separate entity which may present with mild asthma like symptoms to severe bronchiectasis and fibrosis [17]. Likewise, extensive reviews have underscored the wide spectrum of ABPA, the need for early diagnosis and treatment to prevent permanent lung damage [18].

Corticosteroids continue to be the primary therapy and, in select cases, are given with antifungal therapy. Combined therapy of prednisolone and itraconazole might yield superior control of disease activity over corticosteroid alone in acute ABPA, according to a randomized, controlled trial [19]. Based on these findings, this could aid in individualized treatment strategies based on disease severity and patient response.

Epidemiological evidence too suggests that ABPA is not unusual in asthma populations. A large population-based study in the United States suggested that ABPA is likely a measurable prevalence among asthma patients, further supporting the importance of ABPA as a clinically relevant comorbidity of asthma and not a rare disorder [20]. The frequency of observed in the present study is comparable with the data published worldwide which indicates the need for routine assessment of ABPA in asthmatic patients especially those with poor disease control.

Limitations Of Study: This study has certain limitations. First, it was performed in a single tertiary care hospital; thus, these results may not be applicable to the general population. Second, the sample size was relatively small (n = 101) and this may impact the precision of prevalence estimates. Third, the study used only available diagnostic tools such as serum IgE levels and skin prick tests, and the sensitivity of these tests is not always the same; this may result in under-diagnosis of ABPA. Also, the use of advanced diagnostic testing methods like high-resolution imaging patterns and molecular assays was not included, which could have further enhanced the accuracy of diagnostics. There are important strengths in the study despite the limitations. It offers regionally relevant data about incidence of ABPA in adults with asthma, where there is scarce regional literature. Standardized diagnostic procedures were employed, and sample characteristics and various clinical and demographic factors were systematically analyzed. Further, stratified analysis was performed which enabled the checking of possible confounding factors and thus enhanced the reliability of the findings. This provides additional data from a tertiary care centre in Pakistan and increases the overall understanding of the burden of ABPA. From the results, it is recommended that all adult patient with uncontrolled or long-standing asthma should be routinely assessed for ABPA. Immunological testing (including total IgE and aspergillus-specific testing) should be considered for early screening in high-risk patients. Standardised diagnostic procedures in local health care facilities are needed as well, to facilitate early diagnosis.

CONCLUSION

This study suggests that allergic bronchopulmonary aspergillosis is common in adult asthma population, occurring in 16.8% of the patients. There was no significant correlation between ABPA and age, gender, smoking, duration of asthma or positivity of Aspergillus skin test. From these findings, it is important to note that ABPA can manifest itself without the classical demographic and clinical features. To prevent progression of disease and achieve the best long-term respiratory outcomes, it is important to recognise ABPA early in the asthma population and make timely diagnosis.

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