Asian Journal of Clinical Pediatrics and Neonatology Original Article

Evaluation of Risk Factors for Occurrence of Bronchopulmonary Aspergillosis in Pediatric Patients with Cystic Fibrosis at a Tertiary Care Hospital

Yogesh Hareshbhai Bhadani
Assistant Professor, Department of Paediatrics, Index Medical College, Hospital and Research Centre, Indore, Madhya Pradesh, India.

Abstract

Background: Allergic bronchopulmonary aspergillosis (ABPA) represents a significant complication in individuals of all ages with cystic fibrosis (CF), with prevalence rates ranging from 6% to 25%. Hence; the present study was conducted to evaluate risk factors for occurrence of bronchopulmonary aspergillosis in pediatric patients with cystic fibrosis at a tertiary care hospital. **Materials & Methods:** A study was conducted on 50 pediatric patients with cystic fibrosis, gathering comprehensive demographic and clinical data. Patients underwent various evaluations, including clinical assessment, spirometry, chest radiography, sputum analysis, and tests for Aspergillus sensitization, such as IgE levels and skin prick testing. The results were recorded and analyzed to identify risk factors associated with Aspergillus sensitization in cystic fibrosis patients. **Results:** A study of 50 pediatric subjects with cystic fibrosis (CF) found that 80% had abnormal chest radiographic findings and 20% had allergic bronchopulmonary aspergillosis (ABPA). ABPA was more common in patients with low CF scores, age over 12, atopy, and eosinophilia. Patients with ABPA tended to have lower lung function, as measured by FEV1 and FVC. The study's mean subject age was 41.3 months, with 66% being boys and a mean BMI of 13.3 kg/m2. **Conclusion:** CF is an autosomal recessive life-limiting multisystem disorder. ABPA is a pulmonary disorder that often occurs in patients with asthma or CF. CF patients with ABPA should undergo regular follow-up.

Key Words: Bronchopulmonary Aspergillosis, Cystic fibrosis.

INTRODUCTION

Allergic bronchopulmonary aspergillosis (ABPA) represents a significant complication in individuals of all ages with cystic fibrosis (CF), with prevalence rates ranging from 6% to 25%. This condition arises from the colonization of the respiratory system by fungi from the Aspergillus genus, particularly Aspergillus fumigatus, leading to sensitization of the host to fungal antigens. This process triggers a Th2 CD4 type immune response characterized by the production of specific IgE.[1,2] The resulting inflammatory and obstructive damage to the bronchopulmonary system can advance to fibrosis. Early diagnosis is crucial for CF patients exhibiting symptoms such as wheezing, transient pulmonary infiltrates, and diminished lung function. However, establishing a definitive diagnosis can be challenging due to overlapping clinical and radiological features, especially the progression of bronchiectasis. To accurately diagnose ABPA in CF patients, specific criteria, such as those recommended by the Cystic Fibrosis Foundation, are essential. The assessment of specific IgE against recombinant antigens of A. fumigatus has significantly enhanced the early diagnosis of ABPA, demonstrating high sensitivity and specificity. This method also shows potential for monitoring patients post-steroid treatment and for the early identification of recurrences.[3,4] The treatment of patients with cystic fibrosis (CF) who also have allergic bronchopulmonary aspergillosis (ABPA) can be complicated by the overlapping clinical characteristics of ABPA and CF exacerbations caused by bacterial infections, asthma, or other factors. Consequently, in certain clinical scenarios, the choice to initiate treatment for ABPA in a CF patient may be ambiguous.[5,6] Hence; the present study was conducted to evaluate risk factors for occurrence of bronchopulmonary aspergillosis in pediatric patients with cystic fibrosis at a tertiary care hospital.

Address for correspondence*

Dr. Yogesh Hareshbhai Bhadani
Assistant Professor, Department of Paediatrics, Index Medical College, Hospital and Research Centre, Indore, Madhya Pradesh, India.
Email: ybhadani@gmail.com.

METHODS

A total of 50 patients pediatric patients with presence of cystic fibrosis were enrolled. Complete demographic and clinical details of all the patients were obtained. Clinical evaluation, spirometry, chest radiograph, sputum, total IgE, specific IgE for Aspergillus fumigatus, IgG precipitins and skin prick test (SPT) were done. ImmunoCAP test was used for estimation of total IgE, A. fumigatus specific IgE and common aeroallergen. IgG precipitins were assayed by agar gel double diffusion method. SPT was done using A. fumigatus extracts. The diagnosis of ABPA was based on the criteria suggested by the Cystic Fibrosis Foundation.[8] Aspergillus colonization was defined as the presence of Aspergillus species in sputum from two samples collected on two consecutive days. Aspergillus sensitization was defined as positive specific IgE (>3.5 KU) in serum against A. fumigatus or immediate cutaneous reactivity. Various risk factors were evaluated. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

RESULTS

A total of 50 pediatric subjects with CF were enrolled. The mean age of the subjects was 41.3 months. Among these 50 subjects, 66 percent were boys while the remaining were girls. The mean BMI was 13.3 kg/m^2. While evaluating the chest radiographic findings, abnormality was detected in 80 percent of the subjects. ABPA was seen in 20 percent of the subjects. ABPA was more often seen in patients with low CF score, age >12 years, atopy, and eosinophilia. Patients with ABPA had a

trend towards lower FEV1 and FVC. ABPA was observed in 20 percent of the participants. It was more frequently identified in individuals with a low CF score, those older than 12 years, as well as in patients with atopy and eosinophilia. Patients diagnosed with ABPA exhibited a tendency towards reduced FEV1 and FVC values.

Table 1: Prevalence of ABPA

ABPA	Number	Percentage
Present	10	20
Absent	40	80
Total	50	100

Table 2: Risk factors

Risk factors	With ABPA	Without ABPA	p-value
Mean age (months)	63.3	32.8	0.09
Males (n)	4	29	0.15
Mean CF score	55.9	81.3	0.01*
Reversibility on PFT	3	8	0.72
Presence of AC	2	5	0.64
Atopy	10	3	0.01*

DISCUSSION

Aspergillus species are widely distributed saprophytic fungi that inhabit various environments, including water, soil, decaying organic matter, and indoor settings. The species most frequently linked to respiratory illnesses in humans is Aspergillus fumigatus. Although Aspergillus spores are typically inhaled daily without adverse effects, individuals with pre-existing pulmonary conditions, such as cystic fibrosis (CF), may experience colonization of the lungs by Aspergillus conidia, leading to allergic bronchopulmonary aspergillosis (ABPA). ABPA is a Th2-mediated pulmonary condition resulting from hypersensitivity to Aspergillus hyphae, which significantly impacts the health of CF patients and can lead to complications such as bronchiectasis and pulmonary fibrosis. While the detrimental effects of bacterial infections, particularly those caused by Pseudomonas aeruginosa, on CF lung disease are well-documented, the consequences of fungal infections are less understood. Nevertheless, early identification of ABPA appears to be clinically important to prevent further decline in lung function.[7,8] Hence; the present study was conducted to evaluate risk factors for occurrence of bronchopulmonary aspergillosis in pediatric patients with cystic fibrosis at a tertiary care hospital.

A total of 50 pediatric subjects with CF were enrolled. The mean age of the subjects was 41.3 months. Among these 50 subjects, 66 percent were boys while the remaining were girls. The mean BMI was 13.3 kg/m^2. While evaluating the chest radiographic findings, abnormality was detected in 80 percent of the subjects. ABPA was seen in 20 percent of the subjects. ABPA was more often seen in patients with low CF score, age >12 years, atopy, and eosinophilia. Patients with ABPA had a trend towards lower FEV1 and FVC. ABPA was observed in 20 percent of the participants. It was more frequently identified in individuals with a low CF score, those older than 12 years, as well as in patients with atopy and eosinophilia. Patients diagnosed with ABPA exhibited a tendency towards reduced FEV1 and FVC values. The prevalence of ABPA changes according to the population (child/adult), geographic region, or diagnostic criteria that have been used. At the same time, ABPA is believed to be underdiagnosed, especially in developing countries, because its clinical features are much the same as cystic fibrosis (CF). In asthmatic patients the prevalence is reported to be about 1 to 2% and is more common in adults than in children. The prevalence is higher in CF patients than in asthmatic patients and thought to be 8.9% (ranged from 3 to 25%) with a significantly higher occurrence among adults.[9- 11]

Sharma VK et al determined the prevalence and risk factors for ABPA in Indian children with cystic fibrosis. Clinical evaluation, spirometry, chest radiograph, sputum, total IgE, specific IgE for Aspergillus fumigatus, IgG precipitins and skin prick tests were done in 33 CF patients. Prevalence of allergic bronchopulmonary aspergillosis was 18.2% (95% CI 6.9% - 35.4%): allergic bronchopulmonary aspergillosis was higher in patients with low cystic fibrosis score, age >12 years, atopy, and eosinophilia. Prevalence of ABPA is higher in Indian children with cystic fibrosis.[5]

CONCLUSION

CF is an autosomal recessive life-limiting multisystem disorder. ABPA is a pulmonary disorder that often occurs in patients with asthma or CF. CF patients with ABPA should undergo regular follow-up.

REFERENCES

1. Banerjee B, Greenberger PA, Fink JN, Kurup VP. Immunological characterization of Asp f 2, a major allergen from Aspergillus fumigatus associated with allergic bronchopulmonary aspergillosis. Infect Immun. 1998;66:5175–82.
2. Chotirmall SH, McElvaney NG. Fungi in the cystic fibrosis lung: Bystanders or pathogens? Int J Biochem Cell Biol. 2014;52:161–73.
3. Chotirmall SH, Al-Alawi M, Mirkovic B, Lavelle G, Logan PM, Greene CM, et al. Aspergillus-associated airway disease, inflammation, and the innate immune response. Biomed Res Int. 2013;2013:723129.
4. Becker JW, Burke W, McDonald G, Greenberger PA, Henderson WR, Aitken ML. Prevalence of allergic bronchopulmonary aspergillosis and atopy in adult patients with cystic fibrosis. Chest. 1996;109:1536–40.
5. Sharma VK, Raj D, Xess I, Lodha R, Kabra SK. Prevalence and Risk Factors for Allergic Bronchopulmonary Aspergillosis in Indian Children with Cystic Fibrosis. Indian Pediatr 2014;51: 295-297.
6. Hemmann S, Nikolaizik WH, Schöni MH, Blaser K, Crameri R. Differential IgE recognition of recombinant Aspergillus fumigatus allergens by cystic fibrosis patients with allergic bronchopulmonary aspergillosis or Aspergillus allergy. Eur J Immunol. 1998;28:1155–60.
7. Mintzer RA, Rogers LF, Kruglik GD, Rosenberg M, Neiman HL, Patterson R. The spectrum of radiologic findings in allergic bronchopulmonary aspergillosis. Radiology. 1978;127:301–7.
8. Logan PM, Müller NL. High-attenuation mucous plugging in allergic bronchopulmonary aspergillosis. Can Assoc Radiol J. 1996;47:374–7.

9. Patterson R, Greenberger PA, Radin RC, Roberts M. Allergic bronchopulmonary aspergillosis: Staging as an aid to management. Ann Intern Med. 1982;96:286–91.
10. Maturu VN, Agarwal R. Prevalence of Aspergillus sensitization and allergic bronchopulmonary aspergillosis in cystic fibrosis: systematic review and meta-analysis. Clin Exp Allergy. (2015) 45:1765–78.
11. Agarwal R. Allergic bronchopulmonary aspergillosis. Chest. (2009) 135:805–26.