International Journal of Medicine

journal homepage: www.ijmjournal.org

Original Research Article

Special Issue: Respiratory Medicine

A Clinico-Serological Correlation with Radiologic Profile of Allergic Bronchopulmonary Aspergillosis (ABPA)

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HIGHLIGHTS

1. ABP shows distinct clinical symptom patterns.
2. Serological tests reveal specific antibody responses.
3. Radiologic profiles often indicate lung involvement.
4. Correlation aids in diagnosing ABPA accurately.
5. Integrated approach improves patient management outcomes

ARTICLE INFO

Handling Editor: Dr. Oliver Hastings

Key words:
ABPA
Clinico-serological correlation
Radiologic profile
Aspergillus
Diagnosis.

ABSTRACT

Background: Allergic bronchopulmonary aspergillosis (ABPA) is an inflammatory condition induced by immune responses to Aspergillus fumigatus, which colonizes the airways of people with asthma and cystic fibrosis. The most prevalent signs are treatment-resistant asthma, transitory and fleeting pulmonary opacities, and bronchiectasis. **Objective:** To assess clinical, immunological and radiology features of allergic bronchopulmonary aspergillosis (ABPA). **Materials and Methods:** The International Society for Human and Animal Mycology (ISHAM) criteria was applied. Patients in which Serum IgE levels >500 IU/ml, investigated for ABPA and classified as ABPA-S, ABPA-CB, ABPA-CB-HAM, ABPA-CB-ORF based on the high resolution CT findings. **Results:** Mean AEC was 1082.19 cells/µL,Mean,S.IgE level was 7466.91 IU/mL (range: 51.43-446331 IU/mL),Mean Asp. S. IgE was 19.86 kUA/L and Asp.S. IgG was 59.55 mgA/L. ABPA-CB was most common (55.33%), followed by ABPA-HAM (25.33%) and ABPA-S (19.33%). Significant association was seen between S.IGE (IU/mL) and CT features (p value=0.015). Significant association was seen between ASP. S.IGE (IU/mL) and CT features-Central bronchiectasis (p value=0.006). **Conclusion:** Asthmatic patients presenting to chest clinics should be routinely screened for ABPA with Total IgE Levels and A.*fumigatus* specific IgE levels. It is imperative that the diagnosis of ABPA is secured as early as possible, as untreated disease usually culminates in bronchiectasis and pulmonary fibrosis, all manifestations of end-stage lung disease.

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Received 21 September 2024; Received in revised form 25 October 2024; Accepted 02 December 2024

INTRODUCTION

Allergic bronchopulmonary aspergillosis (ABPA) is a complex immune condition caused by an exaggerated response to Aspergillus fungi in the airways, affecting individuals with asthma or cystic fibrosis. The prevalence of allergic bronchopulmonary aspergillosis (ABPA) in asthmatics is estimated to be 2.5% globally and around 5% in India, with higher rates (39%) seen in severe asthma patients, and bronchiectasis.It involves a Type I hypersensitivity reaction marked by elevated IgE levels and eosinophilia. Immune response to Aspergillus fungi, with airway epithelial dysfunction and lung microbiome dysbiosis playing key roles in its pathogenesis. The involvement of altered cytokine signaling and epigenetic modifications further complicates the disease. ABPA patients often exhibit mucus plugging, airway inflammation, and reduced lung function due to bronchiectasis. Emerging therapies, including biologics targeting cytokines and strategies to restore epithelial integrity and antifungal defenses, highlight the need for personalized treatment approaches. Identifying Aspergillus sensitization is crucial, as it may indicate undiagnosed ABPA in asthma patients. Although Aspergillus conidia are common and easily enter airways, not all asthmatics develop ABPA, suggesting a role for fungal persistence and host susceptibility. In ABPA, A. fumigatus conidia germinate into hyphae in susceptible individuals, triggering a predominant Th2 immune response, marked by IL-4, IL-5, and IL-13 production. Geographical variations in ABPA prevalence are influenced by factors like humidity, air pollution, and occupational exposure(ABPA) presents grossly with cystically dilated bronchi and bronchioles filled with brownish mucus, often characteristic of the disease. Microscopically, allergic mucin fills dilated bronchial lumens, containing eosinophils, eosinophilic debris, Charcot crystals, and fungal hyphae. Special stains like PAS and Grocott's highlight dispersed fungal hyphae within the mucin. Epidemiologically, ABPA occurs across all age groups, with a strong association with poorly controlled asthma, though it can also be asymptomatic or present in non-asthmatic individuals. Clinical features include hemoptysis, brownish mucus plug expectoration, and rarely, clubbing. Immunological diagnostics, particularly elevated Aspergillus fumigatus-specific IgE, are crucial for diagnosis. HRCT of the chest is the gold standard for diagnosing bronchiectasis in ABPA, showing superior sensitivity compared to conventional radiography. HRCT preferred for detailed assessment, classifying patients into serologic ABPA (ABPA-S) or ABPA with central bronchiectasis (ABPA-CB). Key HRCT features are "finger in glove" opacities, tramline shadows, and "toothpaste shadows," with classifications like ABPA-B for bronchiectasis and ABPA-HAM for high attenuation mucus. Diagnosis relies on a combination of clinical, serological, and radiological assessments, but ABPA remains underdiagnosed, particularly in regions like India where asthma prevalence is rising. Emerging research highlights the need for a deeper understanding of ABPA's evolving clinical and radiological features.

MATERIALS AND METHODS

The study aimed to gather comprehensive demographic, clinical, laboratory, and radiological data from patients diagnosed with allergic bronchopulmonary aspergillosis (ABPA) at AIMSR, Bathinda. Information was collected through a pre-designed proforma, which included patient demographics, medical and exposure history, comorbidities, symptoms, signs, laboratory findings, chest CT scans, and treatment regimens (glucocorticoids, antifungals). Missing data were retrieved from patient records or through follow-ups with patients or relatives, with permission obtained from hospital administration.

ABPA diagnosis followed the ISHAM 2013 criteria, requiring both obligatory criteria (a positive Aspergillus skin test or elevated IgE against Aspergillus and total IgE > 1000 IU/ml) and at least two out of three additional criteria (IgG antibodies against Aspergillus, radiographic pulmonary opacities, eosinophil count > 500 cells/μL in steroid-naïve patients).

Inclusion criteria:

include patients aged 18-65 with frequent asthma exacerbations or difficulty tapering inhalational steroids, regardless of sex. Exclusion criteria encompass severely ill patients with other respiratory diseases, disoriented patients unable to participate, and those not consenting to the study. Each case will be thoroughly examined, and observations will be systematically recorded.

RESULTS

The study conducted at AIMSR, Bathinda, included 150 patients with frequent asthma exacerbations and difficulties in tapering inhalational steroids. The participants had a mean age of 39.83 years, with the most common age group being 31-40 years. The sample was predominantly female (56%). The mean duration of bronchial asthma among the patients was 14.81 years. Additionally, hypertension was present in 12.67% of the cases, while type II diabetes mellitus was reported in 12%. Immunological assessments revealed a mean absolute eosinophil count of 1082.19 cells/μL and a mean serum IgE level of 8245.43 IU/mL. Specifically, the mean Aspergillus-specific IgE level was noted

to be 5056.89 IU/mL. Radiologically, 55.33% of patients exhibited ABPA with central bronchiectasis (ABPA-CB), 25.33% had ABPA with high attenuation mucous (ABPA-HAM), and 19.33% presented with ABPA-S. The study found no significant associations between age, gender, and duration of asthma with CT features (Figure 1). However, a significant correlation was observed between type II diabetes and CT findings, particularly with ABPA-HAM, which showed no diabetic cases. Additionally, serum IgE (Figure 2)and allergen-specific IgE levels (Figure 2) demonstrated significant associations with CT features, particularly higher levels in ABPA-CB compared to ABPA-HAM and ABPA-S. Overall, the study emphasizes the importance of immunological variations among patients with different ABPA types, suggesting that these findings may guide the development of more tailored treatment strategies for asthma patients struggling with exacerbations and steroid tapering.

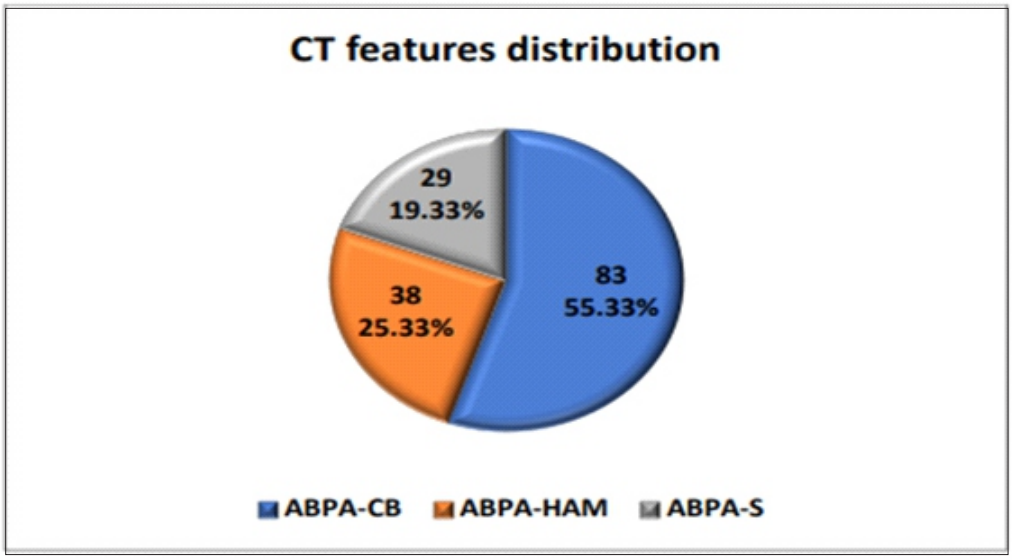

Figure 1: CT features distribution. CT features were ABPA-CB in 83 (55.33%) cases, ABPA-HAM in 38 (25.33%) cases, and ABPA-S in 29 (19.33%) cases.

Table 18:-Association of S.IGE (IU/mL) with CT features.

S.IGE (IU/mL)	ABPA-CB(n=82)	ABPA-HAM(n=38)	ABPA-S(n=29)	P value
Mean ± SD	6047.94 ± 4109.39	5096.66 ± 5522.41	18585.01 ± 82297.87	0.015§ ABPA-CB vs ABPA-HAM:0.044 ABPA-CB vs ABPA-S:0.01 ABPA-HAM vs ABPA-S:0.523
Median(25th-75th percentile)	5961 (2160.25-8757)	3076 (1285.75-7105.75)	3006 (1792-5360)	
Range	510-17094	351-27752	51.43-446331	

§ **Kruskal Wallis test**

Table 1: Association of S.IGE (IU/mL) with CT features. (non-parametric variable) Significant association was seen between S.IGE (IU/mL) and CT features (p value=0.015). Median (25th-75th percenti-le) of S.IGE (IU/mL) in and in ABPA-CB was 5961(2160.25-8757) which was significantly higher as compared to ABPA-HAM (3076(1285.75-7105.75); p=0.044) and ABPA-S (3006(1792-5360); p=0.01).

Table 19:-Association of ASP. S. IGE (kUA/L) with CT features.

ASP. S. IGE (kUA/L)	ABPA-CB(n=83)	ABPA-HAM(n=38)	ABPA-S(n=29)	P value
Mean ± SD	26.67 ± 30.7	13.06 ± 12.21	24.19 ± 40.47	0.006§ ABPA-CB vs ABPA-HAM:0.002 ABPA-CB vs ABPA-S:0.106 ABPA-HAM vs ABPA-S:0.302
Median(25th-75th percentile)	17.2 (8.02-32.9)	7.38 (3.8-21.1)	11.7 (3.8-27)	
Range	0.7-195	0.46-39.9	1.8-195	

§ Kruskal Wallis test

Table 2:

Association of ASP. S. IGE (KUA/L) with CT features. (non-parametric variable) Significant association was seen between ASP. S.IGE (IU/mL) and CT features (p value=0.006). Median (25th-75th percentile) of ASP. S. IGE (kUA/L) in ABPA-CB was 17.2(8.02-32.9) which was significantly higher as compared to ABPA-HAM (7.38(3.8- 21.1); p=0.002) and was comparable with ABPA-S (11.7(3.8-27); p=0.106). (Table 19, figure 19) Table 20: Association of ASP.S. IGG (mgA/L) with CT features. ASP.S. IGG(mgA/L) ABPACB(n=77) ABPAHAM(n=38) ABPA-S(n=28) P value Mean ± SD 55.67 ± 47.75 76.42 ± 155.98 47.36 ± 46.55 0.514§ ABPA-CB vs ABPA-HAM:0.822 ABPA-CB vs ABPA-S:0.251 Median (25th75th percentile) 49 (20.7-74.5) 58.4 (14.325-72.625) 43.35 (12.875-67.225).

The correlation between elevated Aspergillus-specific IgE and IgG levels emphasizes their significance in diagnosing allergic bronchopulmonary aspergillosis (ABPA) and assessing disease progression and severity. While the study found no significant association between absolute eosinophil count (AEC) and ABPA, the elevated serum IgE (S. IgE) levels and Aspergillus-specific antibodies are critical diagnostic markers. This aligns with findings from previous studies by Zhang et al. (2020), Shankar et al. (2023), and Neyaz et al. (2020), underscoring their relevance in clinical practice. Assessing these immunological markers can facilitate early diagnosis, evaluate disease severity, and guide treatment strategies for ABPA patients. In terms of imaging findings, the study revealed that the most common CT feature was Allergic Bronchopulmonary Aspergillosis with central bronchiectasis (ABPA-CB), observed in 55.33% of cases. This aligns with Ünal et al. (2019), who also identified ABPA-CB as the predominant high-resolution computed tomography (HRCT) feature in ABPA patients, where central bronchiectasis serves as a key diagnostic indicator. Following ABPA-CB, the next most common CT feature was ABPA with high-attenuation mucus (ABPA-HAM), present in 25.33% of cases. ABPA-HAM is characterized by dense mucus plugs within the bronchial tree, identifiable on CT scans as high-attenuation areas. Lastly, ABPA with serologic criteria only (ABPA-S) was seen in 19.33% of cases, typically diagnosed based on serologic tests rather than distinct imaging characteristics.The study also noted the presence of the tree-in-bud pattern in 40% of cases, a radiologic sign indicating small airway inflammation or infection. This pattern is characterized by small centrilobular nodules and branching linear structures that resemble budding trees on CT images.

CONCLUSION

A high degree of suspicion for ABPA should be entertained while treating a patient with bronchial asthma, particularly in specialized clinics. The result of this study reinforces the need for routine screening of asthmatics to diagnose ABPA before the onset of bronchiectasis as diagnosis and treatment can prevent progression of ABPA-S to ABPA-CB Careful screening should therefore be performed in all patients with bronchial asthma The combination of serological testing of total and Aspergillus-specific IgE, in concert with radiology (hrct chest), appears promising.

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How to cite: Ravishek Jindal, Arsh Kumar, Avneet Garg, Sweta Gupta,Shivam Salaria, Roohpreet, Pulkit Sharma, Preetinder Singh, Deepak Chawdhary, Rohit Bhagat,Vishal Goyal, Abhinav Uppal. A Clinico-Serological Correlation with Radiologic Profile of Allergic BronchopulmonaryAspergillosis (ABPA). *International Journal of Medicine*, 2024;8(2):1-5.