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High level of initial *Aspergillus fumigatus*-specific IgE links increased risk of exacerbation in allergic bronchopulmonary aspergillosis patients

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Abstract

Background Elevated *Aspergillus fumigatus* (*A. fumigatus*)-specific Immunoglobulin E (IgE) is recognized as an essential diagnostic criterion for allergic bronchopulmonary aspergillosis (ABPA). However, it remains unknown whether initial *A. fumigatus*-specific IgE at acute stage has a role beyond diagnostic purposes.

Method This two-center retrospective study enrolled 149 acute ABPA patients. Risk factors for one-year exacerbation were analyzed using univariate and multivariate logistic regression. Participants were then divided into a discovery cohort ($n=93$) to determine the optimal initial *A. fumigatus*-specific IgE cut-off value via receiver operating characteristic (ROC) curve, and a validation cohort ($n=56$) to confirm exacerbation differences based on this cut-off value.

Result Multivariate logistic regression analysis revealed that female sex (odds ratio (OR) 2.44, 95% confidence interval (CI) 1.15–5.16, $P=0.020$), *A. fumigatus*-specific IgE (OR 1.05, 95% CI 1.02–1.08, $P=0.002$), and bronchiectasis (OR 3.61, 95% CI 1.07–12.21, $P=0.039$) were independent risk factors for ABPA exacerbation. In the discovery cohort, the optimal initial cut-off value for *A. fumigatus*-specific IgE was calculated to be 9.88 kUA/L. And, the validation cohort confirmed that patients with *A. fumigatus*-specific IgE > 9.88 kUA/L were at higher risk of exacerbation ($P=0.005$).

Conclusion This study highlighted the prognostic utility of initial *A. fumigatus*-specific IgE at acute stage and found that elevated levels, especially those exceeding 9.88 kUA/L, were associated with increased risks of exacerbation in ABPA patients.

Keywords Allergic bronchopulmonary aspergillosis, *Aspergillus fumigatus*-specific IgE, Exacerbation, Prognostic indicator

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Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a complex allergic disease caused by *Aspergillus fumigatus* (*A. fumigatus*), first systematically described in 1952 [1]. The chronic colonization of *A. fumigatus* in the airway and enhanced type 2 immune response are key pathogenic mechanisms of ABPA [2]. According to a global epidemiological survey conducted in 2023, the prevalence of ABPA is as high as 11.3% in adults with asthma [3] and 9.9% in children with asthma [4]. Given the possibility of underdiagnosis and misdiagnosis, the actual prevalence of ABPA may be underreported.

In 2013, the International Society for Human and Animal Mycology ABPA Working Group (ISHAM-AWG) proposed detailed diagnostic criteria for ABPA, which primarily included serum total Immunoglobulin E (IgE), *A. fumigatus*-specific IgE, peripheral blood eosinophil count, and imaging changes [5]. Among them, serum total IgE, peripheral blood eosinophil count and radiological abnormalities are all considered related to the prognosis of ABPA patients. Serum total IgE significantly decreases following treatment and rises again during exacerbation, making it a valid marker for monitoring treatment response and defining exacerbation [6, 7]. Peripheral blood eosinophils with counts exceeding 1000 cells/μL, along with more extensive bronchiectasis, were reported as independent risk factors for exacerbation in ABPA patients [7]. Previous studies suggested that *A. fumigatus*-specific IgE levels exceeding 0.35 kUA/L were a strong diagnostic indicator, with a sensitivity of up to 100% [8], but its fluctuations during follow-up were not significant [6]. Consequently, *A. fumigatus*-specific IgE is considered of limited value in monitoring ABPA patients, and is not currently recommended for follow-up [7]. However, whether initial *A. fumigatus*-specific IgE levels at acute stage are associated with exacerbation remains unclear.

This study enrolled 149 ABPA patients at acute stage treated with a combination of glucocorticoids and antifungals from two centers. The analyses aimed to explore the prognostic role of initial *A. fumigatus*-specific IgE in ABPA patients.

Methods

Study design and ethical approval

This study was a two-center retrospective study involving 149 ABPA patients at acute stage [9], including both newly diagnosed and exacerbation patients, conducted at Shanghai Pulmonary Hospital and Zhongshan Hospital between January 2018 and October 2023. The flowchart of patient inclusion and exclusion was shown in Fig. 1. The initial *A. fumigatus*-specific IgE referred to the levels of *A. fumigatus*-specific IgE measured in patients with acute-stage ABPA upon their visit to the two hospitals. Patients were then divided into a discovery cohort ($n=93$) and a validation cohort ($n=56$) based on the time point. The discovery cohort was used to obtain the cut-off value of initial *A. fumigatus*-specific IgE, while the validation cohort divided patients into two groups based on this cut-off value to compare one-year exacerbation rates. Ethical approval was obtained from the Ethics Committees of Shanghai Pulmonary Hospital, Tongji University (No. K18-153 and K18-167) and Zhongshan Hospital, Fudan University (No. B2019-020R and B2021-353).

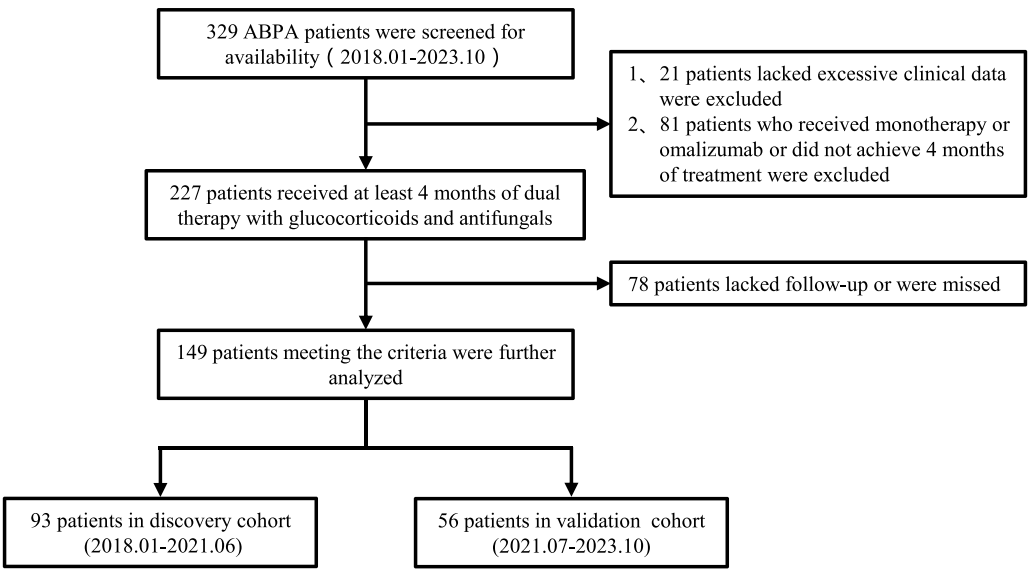

Fig. 1 Flowchart of recruitment and exclusion of participants in this study

Diagnostic and exclusion criteria for ABPA patients

The diagnosis of ABPA was based on the 2024 revised ISHAM-AWG consensus criteria [9]. The criteria included: (1) underlying disease: patients with susceptible diseases (asthma, cystic fibrosis, chronic obstructive pulmonary disease or bronchiectasis) or compatible clinicoradiologic manifestations; (2) two essential conditions: (a) *A. fumigatus*-specific IgE ≥ 0.35 kUA/L, (b) serum total IgE ≥ 500 IU/mL; (3) fulfillment of any two of the following: (a) positive *A. fumigatus*- IgG, (b) peripheral blood eosinophil count ≥ 500 cells/μL (could be historical) and (c) ABPA-compatible chest computed tomography (CT) images or transient opacities consistent with ABPA on chest radiographs. Serum total IgE and *A. fumigatus*-specific IgE levels in ABPA patients were measured using the ImmunoCAP 1000 from Thermo Fisher Scientific. The diagnosis was confirmed by three respiratory physicians, while CT images were evaluated by one radiologist and one respiratory physician.

Exclusion criteria included: (1) systemic corticosteroids use within 4 weeks prior to enrollment; (2) other immunosuppressive status including uncontrolled diabetes mellitus, chronic renal or hepatic failure, or immunosuppressive therapy; (3) pregnancy; (4) receipt of monotherapy or omalizumab; (5) dual therapy with glucocorticoids and antifungals for less than 4 months; (6) insufficient clinical data or lack of follow-up.

Treatment of ABPA patients and definition of exacerbation

Previous studies have reported a trend toward lower exacerbation within one year in ABPA patients with the combination of glucocorticoids and antifungals compared to glucocorticoids monotherapy [10]. To eliminate treatment protocol variability, all included patients received a standardized two-drug regimen consisting of glucocorticoids and antifungals. Specifically, antifungal therapy with itraconazole or voriconazole 200 mg twice daily was administered for a minimum of 4 months. Glucocorticoids were initiated at a dose of 0.5 mg/kg/day for 4 weeks. Subsequent dose reductions of 5 mg every 2 to 4 weeks for a total duration of not less than 4 months were guided by a specialized clinician who assessed the patient's clinical presentation and total IgE fluctuations. After treatment was defined as at least 4 months of combined glucocorticoids and antifungals therapy and discontinuation of both glucocorticoids and antifungals. After treatment, the patients were followed up for one year to monitor exacerbation occurrence. Exacerbation of ABPA was defined by meeting all three of the following criteria: (1) an increase of ≥ 50% in serum total IgE compared to the last recorded value during clinical stabilization; (2) persistent (> 14 days) clinical deterioration or radiological deterioration; and (3) exclusion of other causes of deterioration [9]: Asthma exacerbation: worsening respiratory symptoms for at least 48 h without immunological or radiological deterioration of ABPA; Infective/ bronchiectasis exacerbation: clinical deterioration for at least 48 h with an increase in cough, breathlessness, sputum volume or consistency, sputum purulence, fatigue, malaise, fever, or hemoptysis, without immunological or radiological deterioration of ABPA.

Statistical analysis

Statistical analysis and data visualization were performed by *R* (version 4.2.1). Normally distributed continuous variables were reported as mean ± standard deviation (*sd*); while non-normal distributed continuous variables were reported as median (interquartile range, IQR). Discrete variables were expressed as number (percentage). Continuous variables were analyzed using either Student's t-test, Welch's t-test, or the Wilcoxon test, depending on normality and variance checks. Non-continuous variables were analyzed using the Chi-squared test or Yates' correction. The differences more than two groups were examined using Kruskal–Wallis Test followed by Dunn's test. Univariate and multivariate binary logistic regression were performed by the "rms" and "ResourceSelection" packages. The receiver operating characteristic (ROC) curve was generated using the "pROC" package and visualized with "ggplot2". Kaplan–Meier curve was plotted with the "survival" package. Statistical significance was defined as $P < 0.05$, $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

Results

Baseline characteristics of the study population

A total of 149 acute ABPA patients were included in this study, with a median age of 53.00, and the majority being male (52.3%). The duration of asthma varied widely with a median of 6.00 years. Table 1 summarized details of lung function, immunological tests, radiographic findings, and follow-up. The cohort had decreased forced expiratory volume in one second, percent of predicted value (FEV1%) and forced expiratory volume in one second/forced vital capacity (FEV1/FVC) ratios, indicating impaired lung function and airway obstruction. Elevated serum total IgE, peripheral blood eosinophil count and *A. fumigatus*-specific IgE were consistent with the allergic properties of ABPA. Most patients (83.9%) presented with bronchiectasis, and 24.2% exhibited high-attenuation mucus (HAM). Over the one-year follow-up period, exacerbation occurred in 72 patients (48.3%).

Table 1 Baseline characteristics of the study population ($n=149$)

Characteristics	Overall
Demographic features	
Age, years, median (IQR)	53.00 (40.00, 64.00)
Female sex, *n* (%)	71 (47.7%)
Body mass index, kg/m^2, median (IQR)	22.89 (21.27, 25.09)
Duration of asthma, years, median (IQR) ($n=96$)	6.00 (2.00, 20.00)
Smoking history, *n* (%)	33 (22.1%)
Spirometry	
FEV1, litres, median (IQR) ($n=142$)	1.92 (1.40, 2.42)
FVC, litres, median (IQR) ($n=142$)	2.85 (2.18, 3.37)
FEV1%, median (IQR) ($n=145$)	69.60 (54.20, 89.20)
FEV1/FVC, mean ± *sd* ($n=145$)	68.73 ± 12.00
Immunological tests	
Serum total IgE, IU/mL, median (IQR)	1894.00 (1304.00, 3720.00)
Peripheral blood eosinophil count, cells·10^9/L, median (IQR)	0.80 (0.53, 1.21)
A. fumigatus-specific IgE, kUA/L, median (IQR)	10.10 (3.38, 23.50)
Imaging	
Bronchiectasis, *n* (%)	125 (83.9%)
HAM, *n* (%)	36 (24.2%)
Follow-up	
Exacerbation, *n* (%)	72 (48.3%)

FEV1 forced expiratory volume in one second, *FVC* forced vital capacity, *FEV1%* forced expiratory volume in one second percent of predicted value, *IgE* Immunoglobulin E, *A. fumigatus Aspergillus fumigatus*, *HAM* High-attenuation mucus

Exacerbation predictors in patients with ABPA

To investigate the risk factors associated with exacerbation in ABPA patients, univariate and multivariate logistic regression were performed. Univariate analysis identified female sex, serum total IgE, *A. fumigatus*-specific IgE and bronchiectasis as risk factors (Fig. 2). The above four variables, as well as key variables reported in previous studies [7], were jointly included for consideration in the multivariate analysis. These included age, female sex, serum total IgE, peripheral blood eosinophil count, bronchiectasis, HAM and *A. fumigatus*-specific IgE. In subsequent analyses adjusting for potential confounders, multivariate logistic regression analysis determined several independent factors of exacerbation (Fig. 3). Female sex was significantly associated with a higher risk of exacerbation (odds ratio (OR) 2.44, 95% confidence interval (CI) 1.15–5.16, $P=0.020$). Notably, elevated levels of initial *A. fumigatus*-specific IgE were identified as an essential independent risk factor (OR 1.05, 95% CI 1.02–1.08, $P=0.002$). The presence of bronchiectasis also emerged as a strong predictor (OR 3.61, 95% CI 1.07–12.21, $P=0.039$), underscoring the impact of this radiographic feature on disease prognosis. Other variables, such as age, peripheral blood eosinophil count, serum total IgE and HAM did not show significant correlations with exacerbation risk.

Predictive value of initial *A. fumigatus*-specific IgE for exacerbation in ABPA patients

Multivariate logistic regression suggested that elevated levels of initial *A. fumigatus*-specific IgE have the potential to indicate ABPA exacerbation. The total population was then divided into a discovery cohort ($n=93$) and a validation cohort ($n=56$) based on the time point. In the discovery cohort, the characteristics of the exacerbation ($n=42$) and non-exacerbation groups ($n=51$) were compared (Table 2). A key focus was that patients in the exacerbation group exhibited significantly higher levels of initial *A. fumigatus*-specific IgE, with a median of 18.40 kUA/L compared with 8.22 kUA/L in the non-exacerbation group ($P<0.001$). The exacerbation group also had a higher proportion of females (57.1% vs. 35.3%, $P=0.035$) and bronchiectasis (95.2% vs. 76.5%, $P=0.012$), as well as a higher tendency of peripheral blood eosinophil count (0.84 vs. 0.69, $P=0.056$) compared to the non-exacerbation group.

To further validate the clinical utility of *A. fumigatus*-specific IgE as an exacerbation predictive biomarker, ROC curves were applied to determine concrete thresholds. The results showed that the optimal cut-off value for initial *A. fumigatus*-specific IgE was 9.88 kUA/L, which has the maximum Yoden index (Fig. 4). The validation cohort was then used to assess this threshold.

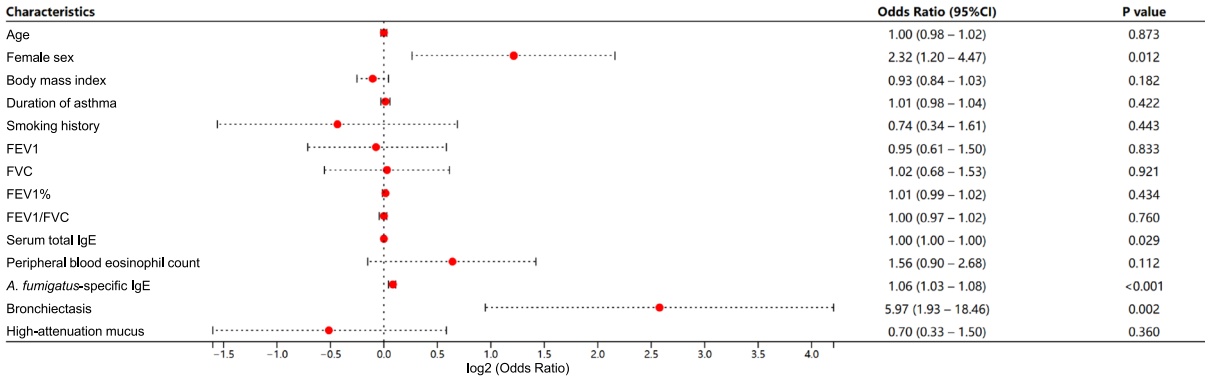

Fig. 2 Univariate logistic regression showing predictive factors for exacerbation in ABPA patients

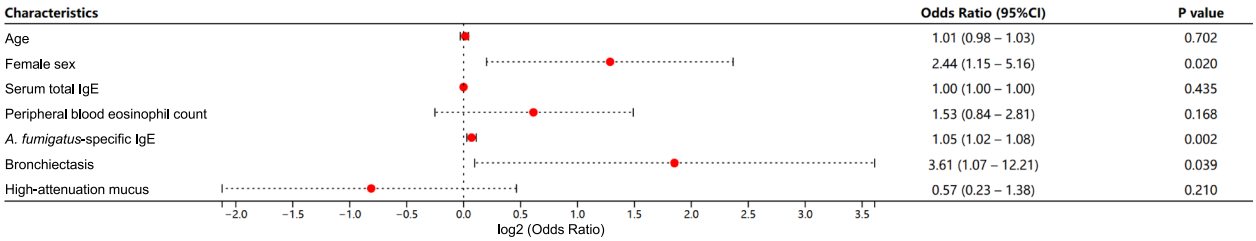

Fig. 3 Multivariate logistic regression showing predictive factors for exacerbation in ABPA patients

Table 2 Characteristic differences of ABPA patients in discovery cohort stratified by prognosis ($n=93$)

Characteristics	Non-exacerbation ($n=51$)	Exacerbation ($n=42$)	*P* value
Demographic features			
Age, years, mean ± *sd*	49.06 ± 17.38	49.71 ± 17.10	0.856
Female sex, *n* (%)	18 (35.3%)	24 (57.1%)	**0.035**
Body mass index, kg/m^2, median (IQR)	23.71 (21.73, 25.15)	22.26 (21.29, 23.71)	0.137
Duration of asthma, years, median (IQR)	6.00 (2.50, 20.00)[a]	10.00 (3.00, 26.00)[b]	0.594
Smoking history, *n* (%)	12 (23.5%)	8 (19.0%)	0.601
Spirometry			
FEV1, litres, mean ± *sd*	2.03 ± 0.76[c]	2.00 ± 0.75[d]	0.856
FVC, litres, median (IQR)	2.90 (2.29, 3.44)[c]	2.82 (2.17, 3.51)[d]	0.742
FEV1%, mean ± *sd*	69.35 ± 18.32[e]	71.78 ± 22.51[d]	0.576
FEV1/FVC, mean ± *sd*	68.91 ± 12.76[e]	68.82 ± 13.91[d]	0.976
Immunological tests			
Serum total IgE, IU/mL, median (IQR)	1814.00 (1120.50,3137.50)	2045.50 (1432.20, 5097.50)	0.183
Peripheral blood eosinophil count, cells·10^9/L, median (IQR)	0.69 (0.41, 0.94)	0.84 (0.55, 1.31)	0.056
A. fumigatus-specific IgE, kUA/L, median (IQR)	8.22 (2.33, 16.60)	18.40 (9.96, 37.83)	**<0.001**
Imaging			
Bronchiectasis, *n* (%)	39 (76.5%)	40 (95.2%)	**0.012**
HAM, *n* (%)	19 (37.3%)	10 (23.8%)	0.164

[a] $n=31$ in non-exacerbation group; [b] $n=33$ in exacerbation group; [c] $n=46$ in non-exacerbation group; [d] $n=40$ in exacerbation group; [e] $n=49$ in non-exacerbation group

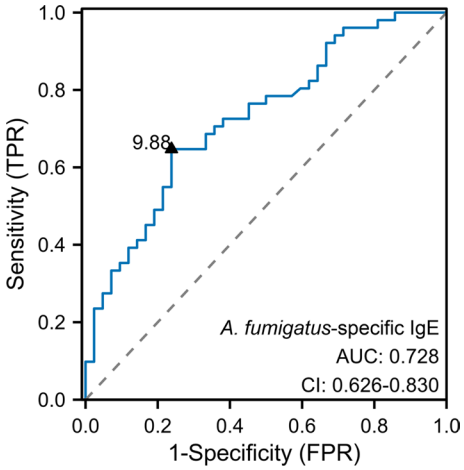

Fig. 4 ROC curves for *A. fumigatus*-specific IgE of ABPA patients in the discovery cohort

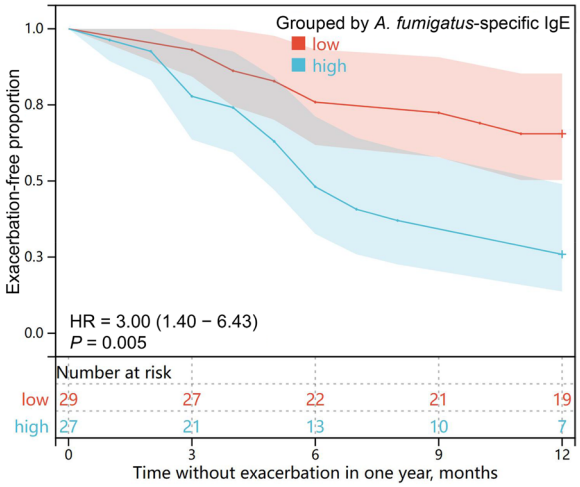

Fig. 5 Kaplan–Meier curve for two groups of ABPA patients in the validation cohort

Based on this cut-off value, patients were stratified into low *A. fumigatus*-specific IgE group and high *A. fumigatus*-specific IgE group. Kaplan–Meier curves demonstrated that the high *A. fumigatus*-specific IgE group had a significantly higher risk of exacerbation during the one-year follow-up ($P=0.005$) (Fig. 5). Detailed characteristic differences between the two groups were presented in Table 3. In contrast to the low *A. fumigatus*-specific IgE group, the high *A. fumigatus*-specific IgE group had a higher serum total IgE levels (3240.00 vs. 1549.00, $P=0.006$). As for radiology, the high *A. fumigatus*-specific IgE group had the higher percentage of bronchiectasis (100% vs. 65.5%, $P=0.003$).

Finally, three immunologic tests, namely serum total IgE, peripheral blood eosinophil count, and *A. fumigatus*-specific IgE were tracked. Data were collected at three time points: acute stage, after treatment, and exacerbation. The dynamic changes of these markers were illustrated in Figure.S1.

Discussion

This study preliminarily identified female, *A. fumigatus*-specific IgE, and bronchiectasis as independent risk factors for exacerbation in ABPA patients. Moreover, it was found that the cut-off value of 9.88 kUA/L for initial *A. fumigatus*-specific IgE at acute stage could effectively predict the one-year exacerbation of ABPA patients.

Few studies had explored the risk factors for ABPA exacerbation. Several large-scale studies from India have provided some insights. For instance, a study by Ritesh Agarwal's team involving 155 ABPA patients with asthma identified HAM and bronchiectasis as exacerbation risk factor [11]. In a follow-up study of 179 ABPA patients in 2012, HAM and aspergilloma were linked to exacerbations [12]. In 2023, they included 188 patients with ABPA and showed that peripheral blood eosinophil count ≥ 1000 cells/μL, the extent of bronchiectasis, age, and female sex were risk factors for exacerbation [7]. The above studies mainly focused on the population of ABPA combined with asthma, and the diagnostic values of IgE were all more than 1000 IU/mL. Besides, the treatment regimen was limited to glucocorticoids monotherapy. In 2022, a Chinese team conducted a study involving 154 ABPA patients, and found that duration of asthma history, duration of misdiagnosis, mucus plugs, and poor pulmonary function were associated with exacerbation. However, the treatment regimen for patients in this study differed significantly [13]. It was worth noting that a randomized controlled trial revealed that combination therapy (glucocorticoids with antifungals) reduced exacerbation rates in ABPA patients with extensive bronchiectasis and elevated eosinophil counts (> 1000 cells/μL) compared to monotherapy [10]. Nevertheless, risk factors for exacerbation under combination therapy remain underexplored. In 2024, ISHAM-AWG revised diagnostic criteria for ABPA, broadening the underlying conditions of ABPA to include asthma, cystic fibrosis, chronic obstructive pulmonary disease, bronchiectasis, or similar clinical radiological manifestations. And the IgE diagnostic threshold was reduced to 500 IU/mL [9]. Therefore, this study was the first to apply the updated diagnostic criteria, involving 149 acute ABPA patients treated with a combination of glucocorticoids and antifungals from two clinical centers. Our multivariate logistic regression analysis revealed female sex,

Table 3 Characteristic differences of ABPA patients in validation cohort stratified by Serum *A. fumigatus*-specific IgE ($n=56$)

Characteristics	Low *A. fumigatus*-specific IgE group ($n=29$)	High *A. fumigatus*-specific IgE group ($n=27$)	*P* value
Demographic features			
Age, years, mean ± *sd*	54.38 ± 13.46	54.59 ± 14.32	0.954
Female sex, *n* (%)	16 (55.2%)	13 (48.1%)	0.599
Body mass index, kg/m^2, mean ± *sd*	23.88 ± 3.61	22.71 ± 3.53	0.224
Duration of asthma, years, median (IQR)	1.50 (1.00, 9.25)[a]	4.50 (1.00, 9.50)[b]	0.372
Smoking history, *n* (%)	6 (20.7%)	7 (25.9%)	0.643
Spirometry			
FEV1, litres, mean ± *sd*	1.89 ± 0.69	1.93 ± 0.72	0.829
FVC, litres, mean ± *sd*	2.74 ± 0.78	2.77 ± 0.86	0.883
FEV1%, mean ± *sd*	72.90 ± 27.82	69.74 ± 16.20	0.604
FEV1/FVC, mean ± *sd*	68.13 ± 9.21	68.93 ± 10.71	0.765
Immunological tests			
Serum total IgE, IU/mL, median (IQR)	1549.00 (1250.00, 2407.00)	3240.00 (1624.00, 4703.50)	**0.006**
Peripheral blood eosinophil count, cells·10^9/L, median (IQR)	0.69 (0.53, 1.08)	0.97 (0.70, 1.38)	0.140
A. fumigatus-specific IgE, kUA/L, median (IQR)	1.62 (1.07, 6.12)	22.7 (13.15, 33.45)	**< 0.001**
Imaging			
Bronchiectasis, *n* (%)	19 (65.5%)	27 (100%)	**0.003**
HAM, *n* (%)	2 (6.9%)	5 (18.5%)	0.363

[a] $n=18$ in low *A. fumigatus*-specific IgE group; [b] $n=14$ in high *A. fumigatus*-specific IgE group

bronchiectasis, and *A. fumigatus*-specific IgE as independent exacerbation risk factors.

Female sex has been linked to a higher incidence, prevalence, and severity of asthma, potentially due to genetic or glucocorticoid-related factors [14]. ABPA is considered a genetically related disease [15, 16]. The higher exacerbation risk among females observed in our study aligns with previous research, including the research results from India in 2023 [7]. Bronchiectasis develops at sites of previous infiltrates, and chronic colonization by *A. fumigatus* may lead to continuing bronchial wall damage [7]. Our research also found that bronchiectasis was a risk factor for ABPA exacerbation. Consistent with the findings of Ritesh Agarwal's team, this study did not identify serum total IgE and HAM as significant risk factors for ABPA exacerbation [7]. This may be partly due to the adoption of updated diagnostic criteria, variations in treatment regimens, and the use of thin-layer CT.

This study is the first to identify initial *A. fumigatus*-specific IgE as a risk factor for ABPA exacerbation. Previous research mainly focused on the value of *A. fumigatus*-specific IgE in the diagnosis of ABPA [17, 18]. Mechanistically, *A. fumigatus* could directly damage bronchial epithelial cells via proteases, and/or interact with surface pathogen recognition receptors [19]. Then, epithelium released cytokine thymic stromal lymphopoietin (TSLP), interleukin-25 (IL-25), interleukin-33 (IL-33), and group 2 innate lymphoid cells (ILC2) stimulation mediates a type 2 immune response in concert with dendritic cell -mediated T-helper 2 lymphocyte activation [2, 20]. In this type 2 cascade, the plasma cell recruitment led to a persistent production of both total IgE and *A. fumigatus*-specific IgE [21]. Moreover, *A. fumigatus* can persist and colonize the lungs for a long time, leading to recurrent and prolonged illness [22, 23]. A retrospective study involving 154 individuals in China found that *A. fumigatus*-specific IgE levels were significantly elevated in ABPA patients compared to *A. fumigatus*-positive asthma. Additionally, *A. fumigatus*-specific IgE levels were significantly negatively correlated with asthma control test scores and lung function, indicating that this biomarker played a crucial role in poor symptom control and reduced lung function in both asthma and ABPA patients [24]. A prospective study involving 106 ABPA patients in Japan demonstrated a positive correlation between *A. fumigatus*-specific IgE levels and both serum total IgE and house dust mite (HDM)-specific IgE levels. Similarly, the allergic components score (including *A. fumigatus*-specific, HDM-specific IgE and serum total

IgE) was significantly elevated in the group with poor prognosis [25]. These above studies all suggested that *A. fumigatus*-specific IgE may be a risk factor for ABPA exacerbation. Consistently, our results identified a cut-off value of 9.88 kUA/L for initial *A. fumigatus*-specific IgE as an effective predictor of ABPA exacerbation within one year. Meanwhile, *A. fumigatus*-specific IgE showed a decreased trend after treatment, and then increased again after exacerbation, which may be related to the decrease in fungal load caused by the use of antifungal drugs. Therefore, the results are inconsistent with the previous use of monotherapy corticosteroids [6]. However, due to its small fluctuations, its value for follow-up is still limited.

Our research has several limitations. Firstly, as a retrospective study, treatment regimens were not completely standardized. In spite of that, our enrolled subjects had similar treatment regimens, and they all reached more than 4 months of glucocorticoids and antifungals treatment. Secondly, the small sample size in the validation cohort may have limited the statistical significance of some findings. There is still need for expanding the number of patients. And, prospective studies are needed to further evaluate the role of *A. fumigatus*-specific IgE in ABPA exacerbation. Finally, the cut-off value of *A. fumigatus*-specific IgE in this study is applicable for predicting exacerbation within one year after treatment with glucocorticoids and antifungals. Therefore, it is unknown whether it would be applicable to other situations, like monotherapy and other follow-up times.

Conclusion

In conclusion, our study identified female, bronchiectasis, and *A. fumigatus*-specific IgE as independent risk factors for ABPA exacerbation. The cut-off value of 9.88 kUA/L for initial *A. fumigatus*-specific IgE at acute stage was found to predict the prognosis of ABPA patients treated with glucocorticoids and antifungals. This finding could be very useful as a predictive assessment tool for ABPA exacerbations and help physicians plan more appropriate treatments to prevent disease exacerbations in this group of patients.

Abbreviations

A. fumigatus	*Aspergillus fumigatus*
ABPA	Allergic bronchopulmonary aspergillosis
CT	Computed tomography
CI	Confidence interval
FEV1	Forced expiratory volume in one second
FVC	Forced vital capacity
FEV1%	Forced expiratory volume in one second, percent of predicted value
HAM	High-attenuation mucus
HDM	House dust mite
IgE	Immunoglobulin E
ISHAM-AWG	The International Society for Human and Animal Mycology ABPA Working Group
IQR	Interquartile range
IL-25	Interleukin-25
IL-33	Interleukin-33
ILC2	Group 2 innate lymphoid cells
OR	Odds ratio
ROC	Receiver operating characteristic
sd	Standard deviation
TSLP	Thymic stromal lymphopoietin

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12931-025-03171-3.

Supplementary Material 1. Figure S1 The levels of serum total IgE, peripheral blood eosinophil count, and *A. fumigatus*-specific IgEat acute stage, after treatment, and exacerbation.

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Author contributions

JFX and MLJ conceived and designed the study. HQ, JYX and RF performed the study and analyzed the data. HQ, JYX, RF, JS, HWL, LY, JWY, RJ, LSZ and YFW collected clinical data. HQ, JYX and RF wrote the manuscript. JFX, MLJ and HWL supervised the study and critically reviewed the manuscript. All authors read and approved the manuscript.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committees of Shanghai Pulmonary Hospital, Tongji University (No. K18-153 and K18-167) and Zhongshan Hospital, Fudan University (No. B2019-020R and B2021-353). Informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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