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Original Article

Serological markers, pulmonary function, and prognosis in pediatric asthma: predictive model development and validation

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Abstract: Background: Pediatric asthma is a chronic and heterogeneous respiratory disease that poses considerable challenges in predicting exacerbations and long-term outcomes. This study aimed to enhance prognostic prediction for pediatric asthma by integrating serological markers with pulmonary function parameters. Methods: A retrospective analysis was conducted involving 318 pediatric asthma patients from one hospital, with external validation performed on an additional cohort of 283 patients from another institution. Serological markers, including white blood cell (WBC) count, eosinophil percentage, interleukins, 14-3-3β protein, and total immunoglobulin E (IgE), were measured alongside pulmonary function indicators such as forced expiratory volume in one second (FEV1) and the FEV1/forced vital capacity (FVC) ratio. Statistical analyses included correlation testing, logistic regression analysis, and receiver operating characteristic (ROC) curve analysis to develop and validate the prognostic model. Results: Elevated WBC count, eosinophil percentage, 14-3-3β protein, and total IgE levels were significantly associated with poorer prognosis. Among interleukin profiles, increased interleukin-4 (IL-4) and interleukin-7 (IL-7) levels, along with reduced interleukin-10 (IL-10), were linked to unfavorable outcomes. In contrast, higher FEV1 and FVC values correlated with better outcomes. The integrated predictive model demonstrated strong predictive performance, with an area under the curve (AUC) of 0.818 in the modeling cohort and 0.874 in the validation cohort. Conclusion: The integration of serological biomarkers and pulmonary function indices provides a robust framework for predicting prognosis in pediatric asthma, supporting the development of individualized management strategies.

Keywords: Pediatric asthma, serological markers, pulmonary function, prognosis, predictive model, personalized treatment

Introduction

Asthma is a chronic respiratory disease characterized by airway inflammation, bronchial hyperresponsiveness, and reversible airflow obstruction. It affects millions of children worldwide and remains a leading cause of pediatric morbidity, imposing a significant burden on the quality of life and healthcare systems globally. Despite advances in the understanding of its underlying pathophysiology, accurately predicting disease exacerbations and long-term outcomes in pediatric asthma remains a major clinical challenge, largely due to its heterogeneous presentation [1-3]. Pediatric asthma is distinguished from adult asthma by its distinct pathogenesis, clinical manifestations, and response to treatment. Children with asthma often present with wheezing, shortness of breath, chest tightness, and chronic cough - symptoms frequently triggered by respiratory infections, environmental allergens, physical activity, and air pollutants [4]. Previous studies have identified a range of biomarkers associated with asthma prognosis in children. Serological markers such as white blood cell (WBC) count, eosinophil percentage, total immunoglobulin E (IgE), and various interleukins have been implicated in disease severity and progression. Additionally, pulmonary function parameters including forced expiratory volume in one second (FEV1), forced vital capacity (FVC), the FEV1/FVC ratio, peak expiratory flow (PEF), and the residual volume to total lung capacity

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ratio (RV/TLV) - have been utilized to evaluate airway obstruction and lung function impairment [5].

In recent years, the integration of serological markers into asthma management has gained increasing attention, as these biomarkers offer potential insights into underlying inflammatory pathways and immune responses. Commonly studied serological markers in asthma include IgE, eosinophil counts, and various pro-inflammatory cytokines, which have shown varying degrees of correlation with disease severity and control. However, their prognostic utility - particularly in the pediatric population - remains insufficiently characterized and warrants further exploration to elucidate their role in disease prediction [6-9].

Pulmonary function assessment is another cornerstone of asthma diagnosis and management. Spirometry is frequently used to measure key indicators such as FEV1 and the FEV1/FVC ratio, both of which are essential in quantifying airflow limitation. Nevertheless, interpreting these indices in children can be challenging due to inconsistent symptom expression and age-dependent lung development. Despite these challenges, quantifiable measures of airway function remain pivotal in gauging disease severity and monitoring treatment efficacy [10-12].

Integrating serological markers with pulmonary function parameters offers a promising approach to refining prognostic models for pediatric asthma. However, few studies to date have developed and validated predictive models that integrate these variables specifically in children. The ability to predict asthma exacerbations and future pulmonary function through such integrated models may facilitate individualized management, optimize therapeutic strategies, and ultimately improve patient outcomes. Although numerous studies have analyzed prognostic factors in asthma, most have focused on adult populations. This study addresses this gap by investigating a pediatric cohort, aiming to identify prognostic factors specific to children with asthma. The primary objective is to analyze the relationship between serological markers, pulmonary function, and asthma prognosis in pediatric patients and to develop and validate a predictive model based on these variables.

Materials and methods

Ethics statement

This study was approved by the Institutional Review Board (IRB) and Ethics Committee of Zhejiang Hospital. Due to the retrospective design and the use of anonymized data, the requirement for informed consent was waived in accordance with regulatory and ethical standards. Patient confidentiality and data security were rigorously maintained throughout the study.

Study design

A retrospective analysis was conducted using clinical data from 318 pediatric patients with asthma at Zhejiang Hospital between June 2020 and June 2022. Patients were categorized into two groups based on their prognosis: 166 were classified as having a good prognosis, and 152 as having a poor prognosis. For external validation, an additional cohort comprising 283 pediatric asthma patients from another hospital was included, with 151 patients exhibiting a good prognosis and 132 with poor prognosis. The inclusion criteria for both cohorts were consistent.

Patients were followed up for one year after treatment. The prognostic classification was based on the Global Initiative for Asthma Guidelines (2024 Edition) [13]. A good prognosis was defined by: asthma symptoms occurring no more than twice per week, no limitation of daily activities, nighttime symptoms occurring no more than once per month, no need for quick-relief medications (e.g. short-acting beta2-agonists, SABA), and near-normal or stable pulmonary function. In contrast, a poor prognosis was defined as: frequent asthma symptoms significantly interfering with daily activities, regular nighttime symptoms, persistent need for quick-relief medications, and an increased risk of acute exacerbation.

Eligibility and grouping criteria

Inclusion criteria were as follows: patients under 18 years of age who met the diagnostic criteria established in the “Global Initiative for Asthma Guidelines (2024 Edition)” [13], had completed standardized pulmonary function testing, and possessed complete medical records.

Exclusion criteria included the presence of comorbid conditions known to affect pulmonary ventilation other than asthma; significant dysfunction of major organs such as the heart, liver, or kidneys; other allergic diseases; concurrent psychiatric disorders or cognitive impairments; recent use (within four weeks prior to consultation) of systemic corticosteroids; and loss to follow-up within one year.

Data collection

Clinical data of all study participants were obtained from the medical record system and included the following variables: (1) demographic information, such as gender, age, and body mass index (BMI); (2) laboratory parameters, including peripheral blood white cell count, neutrophil and eosinophil percentages, and total serum IgE levels; and (3) pulmonary function parameters and fractional exhaled nitric oxide (FeNO) levels.

Serological marker testing

Upon admission, 5 mL of fasting venous blood was collected from each participant. Samples were centrifuged to separate the serum, which was then aliquoted and stored at -80°C until further analysis. Total IgE levels were measured using an automated analyzer (Beckman Coulter, Inc., USA). Neutrophil and eosinophil counts were determined using a hematology analyzer (Shenzhen Mindray Bio-Medical Electronics Co., Ltd.). Serum levels of 14-3-3β protein and selected interleukins - including interleukin-4 (IL-4), interleukin-7 (IL-7), interleukin-10 (IL-10), and interleukin-33 (IL-33) - were quantified using enzyme-linked immunosorbent assay (ELISA) kits provided by Shanghai Enzyme-Linked Biotechnology Co., Ltd. (catalog numbers: ml057767, ml105916, ml108599, ml063084). All assays were performed in accordance with the manufacturer's protocols.

Pulmonary function testing

Pulmonary function testing was performed using a high-precision spirometer (Jaeger GmbH, Germany). All assessments were performed with the patient seated and at rest, supervised by trained technicians in accordance with established protocols. The following parameters were recorded: FEV1, FVC, FEV1/FVC ratio, PEF, and the RV/TLV ratio. Testing procedures adhered to the guidelines of the American Thoracic Society [14] and the European Respiratory Society (ERS) [15]. Each participant completed a minimum of three acceptable maneuvers, and the highest value was used for analysis. Participants were instructed to avoid strenuous physical activity and caffeine intake prior to testing to ensure reliable results.

Statistical analysis

All continuous data were tested for normality using the Shapiro-Wilk test. Data conforming to a normal distribution are presented as mean ± standard deviation ($X \pm s$), while non-normally distributed data were analyzed using non-parametric methods, such as the Mann-Whitney U test. Statistical analyses were conducted using SPSS version 29.0 (SPSS Inc., Chicago, IL, USA).

Pearson correlation analysis was applied to continuous variables, including WBC count, eosinophil percentage, neutrophil percentage, 14-3-3β protein, total IgE, and interleukins (IL-4, IL-7, IL-10, and IL-33). Spearman correlation was used for categorical variables such as residence, income, and family smoking.

Variables with a univariate association at $P < 0.10$ were included in a multivariable logistic regression model to identify independent predictors of asthma prognosis. The following factors were considered in the model based on their clinical relevance and evidence from prior literature [16]: (1) Serological markers: WBC count, eosinophil percentage, 14-3-3β protein, total IgE, IL-4, IL-7, IL-10, and IL-33; (2) Pulmonary function indices: FEV1, FVC, FEV1/FVC, PEF, and RV/TLV ratio. Analyses were performed using SPSS 23.0 and GraphPad Prism 9, with significance set at $P < 0.05$. To evaluate multicollinearity, the variance inflation factor (VIF) was calculated, and all variables included in the final model had VIF values below 5, indicating an acceptable level of multicollinearity. A receiver operating characteristic (ROC) curve was plotted, and the area under the curve (AUC) was calculated to develop a prognostic prediction model. External validation was conducted using an independent patient cohort from another hospital to evaluate the generalizability of the prognostic model.

Results

Baseline characteristics of the study population

A total of 318 patients, including 166 in the good prognosis group and 152 in the poor prognosis group, were included (**Table 1**). The two groups showed balanced demographic characteristics, with no significant differences in gender, age, socioeconomic factors, or clinical management approaches (all P > 0.05) (**Table 1**). The incidence of respiratory infections was also comparable between the groups (82.5% in the good prognosis group vs 86.2% in the poor prognosis group; P = 0.61).

Distribution and comparison of key serological markers

Serological markers demonstrated significant associations with poor prognosis. Specifically, higher levels of WBC count (P = 0.003), eosinophil percentage (P = 0.002), 14-3-3β protein (P = 0.002), total IgE (P = 0.002), IL-4 (P = 0.001), IL-7 (P = 0.004), and IL-33 (P = 0.01) were observed in the poor prognosis group compared to the good prognosis group (**Figure 1**). Conversely, IL-10 levels were significantly lower in the poor prognosis group (P < 0.001). The neutrophil percentage did not differ significantly between the two groups (P = 0.128). These results indicate that specific serological markers, including WBC count, eosinophil percentage, 14-3-3β protein, total IgE, and certain interleukins, can serve as important prognostic indicators in pediatric asthma.

Assessment of pulmonary function indices

The FEV1 was significantly higher in the good prognosis group (89.37 ± 10.51 L) than in the poor prognosis group (85.36 ± 9.46 L; P < 0.001) (**Figure 2**). Similarly, FVC was greater in the good prognosis group (79.32 ± 11.05 L) compared to the poor prognosis group (76.07 ± 6.83 L; P = 0.002). The FEV1/FVC ratio was also higher among patients with a favorable prognosis (80.88 ± 7.62%) than those with a poor prognosis (78.24 ± 6.81%; P = 0.001). Peak expiratory flow (PEF) was significantly improved in the good prognosis group (82.19 ± 9.11 L/s) compared to the poor prognosis group (78.77 ± 8.92 L/s; P < 0.001). Additionally, the RV/TLV was lower in the good prognosis group (38.76 ± 8.84%) relative to the poor prognosis group (43.26 ± 14.58%; P = 0.001). These results suggest that higher FEV1, FVC, FEV1/FVC ratio, and PEF values - along with lower RV/TLV ratios - are associated with better clinical outcomes, highlighting the prognostic relevance of pulmonary function metrics in pediatric asthma management.

Correlation analysis of serological markers, pulmonary function, and asthma prognosis

Spearman correlation analysis was used to explore the relationships between serological markers, pulmonary function indices, and asthma prognosis. Positive correlations were observed between asthma prognosis and several serological markers, including WBC count (ρ = 0.169, P = 0.002), eosinophil percentage (ρ = 0.154, P = 0.006), 14-3-3β protein levels (ρ = 0.177, P = 0.002), total IgE (ρ = 0.155, P = 0.006), IL-4 (ρ = 0.169, P = 0.002), IL-7 (ρ = 0.149, P = 0.008), and IL-33 (ρ = 0.121, P = 0.031), indicating that these markers may serve as risk factors for poorer asthma outcomes (**Figure 3**). Conversely, IL-10 demonstrated a negative correlation with asthma prognosis (ρ = -0.187, P < 0.001), suggesting a protective role against disease progression. Among the pulmonary function indices, significant negative correlations were identified between poorer prognosis and FEV1 (ρ = -0.207, P < 0.001), FVC (ρ = -0.177, P = 0.001), FEV1/FVC (ρ = -0.183, P = 0.001), and PEF (ρ = -0.176, P = 0.002), while the RV/TLV showed a positive correlation with poorer prognosis (ρ = 0.200, P < 0.001). These findings suggest that higher levels of certain serological markers, coupled with impaired pulmonary function, are associated with unfavorable prognostic outcomes in pediatric asthma patients.

Identification of independent predictors using multivariate logistic regression

Univariate logistic regression analysis identified significant associations between serological markers, pulmonary function indices, and asthma prognosis in pediatric patients (**Table 2**). Elevated WBC count (OR = 1.258, P = 0.003), eosinophil percentage (OR = 1.539, P = 0.002), 14-3-3β protein (OR = 1.052, P = 0.002), total IgE (OR = 1.030, P = 0.002), IL-4 (OR = 1.083, P = 0.001), and IL-7 (OR = 1.195, P = 0.004) were associated with a poor progno-

Table 1. Demographic data

Parameters	Good prognosis (n = 166)	Poor prognosis (n = 152)	t/χ^2	P
Male/Female	97 (58.43%)/69 (41.57%)	91 (59.87%)/61 (40.13%)	0.068	0.795
Age (years)	10.93 ± 1.35	10.64 ± 1.58	1.748	0.081
BMI (kg/m^2)	19.03 ± 2.08	18.94 ± 2.16	0.372	0.71
Residence Location			0.522	0.77
City	96 (57.83%)	90 (59.21%)		
Suburb	47 (28.31%)	45 (29.61%)		
Rural Area	23 (13.86%)	17 (11.18%)		
Monthly Household Income Level			0.183	0.912
< 4000 yuan	55 (33.13%)	52 (34.21%)		
4000-8000 yuan	66 (39.76%)	62 (40.79%)		
> 8000 yuan	45 (27.11%)	38 (25%)		
Parental Educational Level			0.736	0.692
Junior High School or Below	51 (30.72%)	49 (32.24%)		
High School	71 (42.77%)	69 (45.39%)		
College or Above	44 (26.51%)	34 (22.37%)		
Family Members Smoking	50 (30.12%)	51 (33.55%)	0.431	0.511
Custodian Situation			0.404	0.817
Single-Parent Family	18 (10.84%)	20 (13.16%)		
Dual-Parent Family	139 (83.73%)	124 (81.58%)		
Other	9 (5.42%)	8 (5.26%)		
Family History of Asthma	42 (25.3%)	43 (28.29%)	0.362	0.548
Triggers			0.99	0.609
Sudden Temperature Drop	10 (6.02%)	6 (3.95%)		
Exposure to Allergens	19 (11.45%)	15 (9.87%)		
Respiratory Infections	137 (82.53%)	131 (86.18%)		
Classification of Acute Exacerbations			1.732	0.421
Mild Exacerbation	84 (50.6%)	66 (43.42%)		
Moderate Exacerbation	58 (34.94%)	59 (38.82%)		
Severe Exacerbation	24 (14.46%)	27 (17.76%)		
Treatment Methods			1.779	0.411
Rapid-Acting β2-Agonist Inhalers	106 (63.86%)	91 (59.87%)		
Nebulized Inhalation Therapy	51 (30.72%)	47 (30.92%)		
Intravenous Corticosteroids	9 (5.42%)	14 (9.21%)		
Time Patterns of Asthma Exacerbations			1.318	0.725
Morning	43 (25.9%)	41 (26.97%)		
Daytime	29 (17.47%)	23 (15.13%)		
Nighttime	53 (31.93%)	56 (36.84%)		
Irregular	41 (24.7%)	32 (21.05%)		

BMI: Body Mass Index.

sis. In contrast, IL-10 showed a protective effect (OR = 0.913, P = 0.001). Higher FEV1 (OR = 0.961, P < 0.001), FVC (OR = 0.963, P = 0.002), FEV1/FVC (OR = 0.951, P = 0.002), and PEF (OR = 0.959, P = 0.001) were protective, while an increased RV/TLV ratio was correlated with poorer outcomes (OR = 1.032, P = 0.001).

Multivariate analysis confirmed these associations. WBC count (OR = 1.240, P = 0.019), eosinophil percentage (OR = 1.441, P = 0.028), 14-3-3β protein (OR = 1.048, P = 0.018), total IgE (OR = 1.025, P = 0.031), IL-4 (OR = 1.100, P = 0.001), and IL-33 (OR = 1.023, P = 0.020) independently predicted poor prognosis (**Table**

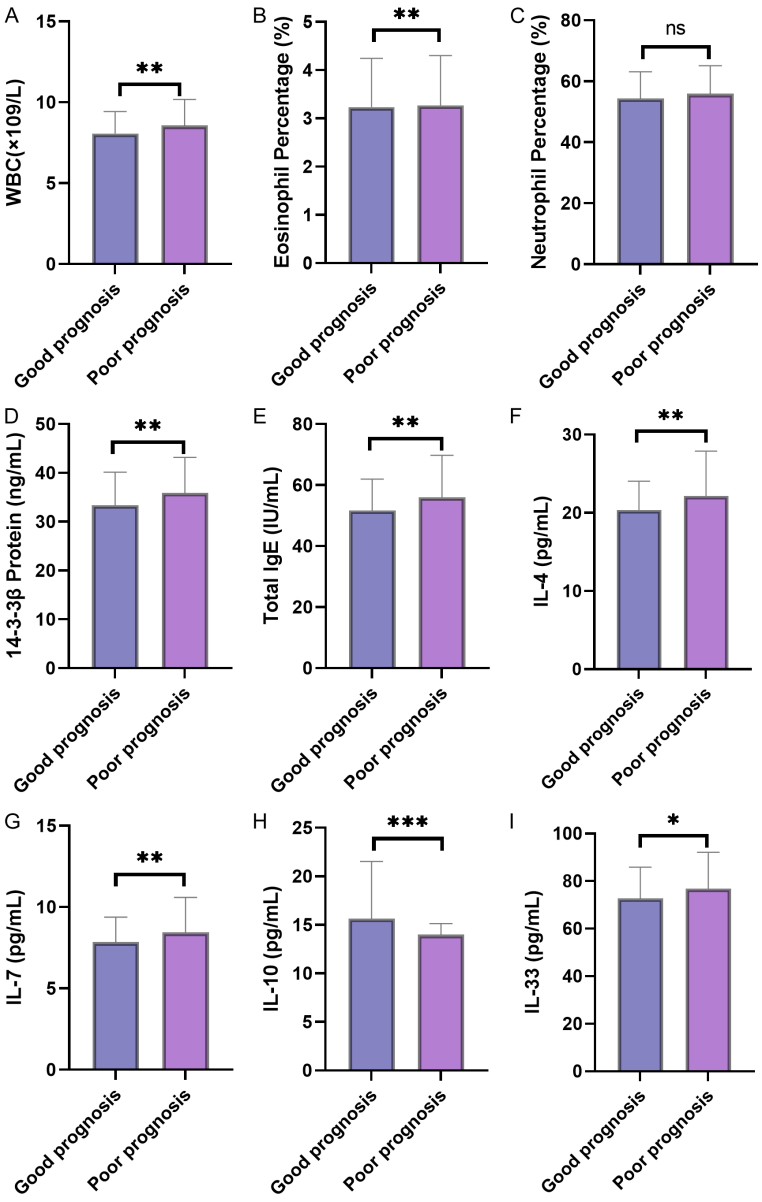

Figure 1. Comparison of serological markers between the two groups. A. WBC: White Blood Cell Count; B. Eosinophil Percentage; C. Neutrophil Percentage; D. 14-3-3β Protein; E. Total IgE: Total Immunoglobulin E; F. IL-4: Interleukin-4; G. IL-7: Interleukin-7; H. IL-10: Interleukin-10; I. IL-33: Interleukin-33. WBC: White Blood Cell Count; Total IgE: Total Immunoglobulin E; IL: Interleukin. ns: No statistically significant difference; *: P < 0.05; **: P < 0.01; ***: P < 0.001.

3). IL-10 remained protective (OR = 0.906, P = 0.003), and pulmonary function indices (FEV1, FVC, FEV1/FVC, PEF) consistently correlated with better outcomes (all P < 0.05).

Multifactorial predictive model for pediatric asthma prognosis

This study integrates various independent risk factors to develop a combined predictive model for assessing the prognosis of pediatric asthma. The formula for the model is as follows: Prognosis score = β1 * WBC + β2 * Eosinophil percentage + β3 * 14-3-3β protein + β4 * Total IgE + β5 * IL-4 + β6 * IL-7 + β7 * IL-33 - β8 * IL-10 + β9 * FEV1 + β10 * FVC + β11 * FEV1/FVC + β12 * PEF - β13 * RV/TLV, where β1 - β13 are coefficients derived from logistic regression analysis. Decision curve analysis (DCA) was employed to assess the clinical utility of this predictive model. The AUC was 0.818, indicating that the model provides a significant prognostic value (**Figure 4**).

External validation of prognostic model performance

The demographic and clinical characteristics were well-balanced between the good and poor prognosis groups in the external validation cohort (n = 283). No significant differences were observed in gender distribution, mean age, BMI, residence location, monthly household income, parental educational levels, family sm oking status, custodial situation, or family history of asthma (all P > 0.05) (**Table 4**). Common asthma triggers, such as respiratory infections, were prevalent in both groups, with no significant differences observed (good prognosis: 82.78%, poor prognosis: 84.85%). These results support the robustness of the prognostic model.

When comparing the modeling dataset (n = 318) with the external validation cohort (n = 283), no significant differences were noted in demographic data (**Table 5**). This further affirms the high comparability of the two datasets and validates the use of the modeling dataset to develop predictive models for asthma exacerbation. Patients with poor prognosis exhibited significantly higher WBC counts (P = 0.001) and

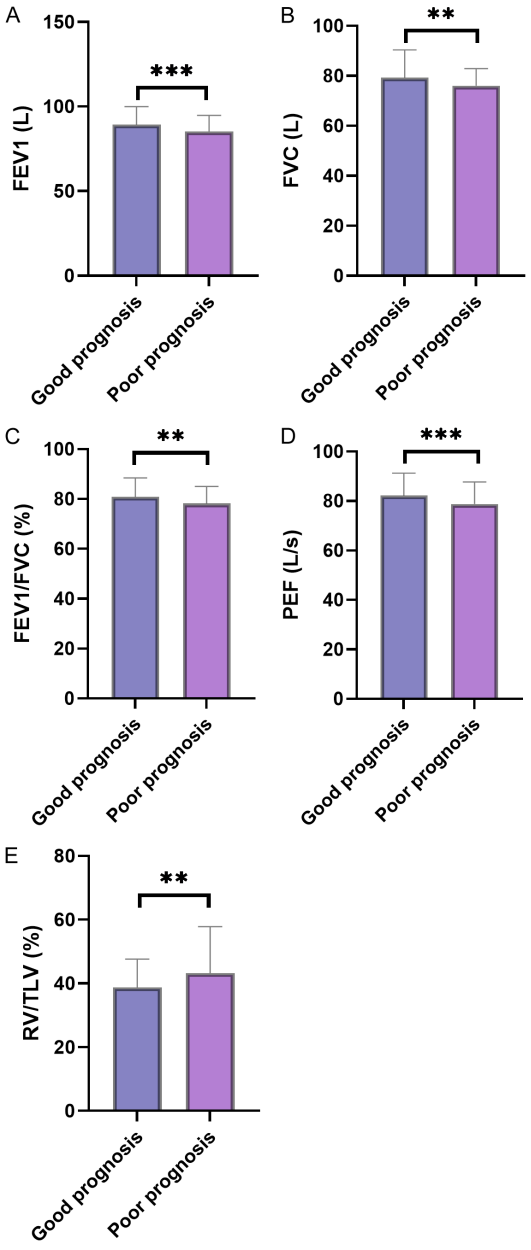

Figure 2. Comparison of pulmonary function indices between the two groups. A. FEV1: Forced Expiratory Volume in 1 second; B. FVC: Forced Vital Capacity; C. FEV1/FVC Ratio; D. PEF: Peak Expiratory Flow; E. RV/TLV. FEV1: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; PEF: Peak Expiratory Flow; RV/TLV: Ratio of Residual Volume to Total Lung Capacity. **: P < 0.01; ***: P < 0.001.

eosinophil percentages (P = 0.002), elevated levels of 14-3-3β protein (P = 0.002) and total IgE (P = 0.003), and increased IL-4 (P = 0.003) and IL-7 (P = 0.017) levels compared to those with a good prognosis. Conversely, IL-10 levels were higher in the good prognosis group (P = 0.004). IL-33 levels were also significantly elevated in the poor prognosis group (P < 0.001). Regarding pulmonary function, patients in the poor prognosis group had significantly lower FEV1 (P < 0.001), FVC (P = 0.007), FEV1/FVC ratio (P = 0.001), and PEF (P = 0.001), while their RV/TLV was significantly higher (P < 0.001). These findings highlight the association between specific biomarkers and pulmonary function indices with asthma prognosis in pediatric patients (**Table 6**).

In the external validation phase, the comprehensive predictive model developed in the primary cohort was successfully validated. Calibration curve analysis revealed a strong agreement between predicted probabilities and observed outcomes in both the training and test sets. Decision curve analysis further confirmed the clinical utility of the model. The model yielded an AUC of 0.874, demonstrating its excellent predictive value (**Figure 5**).

Discussion

Our study identifies two synergistic pathways that drive the progression of pediatric asthma: the inflammatory axis (elevated WBC, eosinophils, IL-4/33) and the allergic-remodeling axis (14-3-3β, IgE). Asthma-related inflammation is primarily driven by immune cells, such as eosinophils, neutrophils, and various cytokines, which contribute to airway hyperreactivity and remodeling [17]. Increased WBC counts are often indicative of an underlying inflammatory response, which is a hallmark of asthma [18]. Eosinophils release cytotoxic granules and pro-inflammatory mediators that exacerbate airway hyperresponsiveness and mucus production, contributing to asthma exacerbations [19, 20]. Recent studies have highlighted the role of eosinophil extracellular traps (EETs) in promoting airway remodeling, further underscoring their contribution to disease severity [21]. The 14-3-3β protein modulates cellular stress responses and inflammatory pathways, including NF-κB and MAPK signaling, both of which are critical in asthma pathogenesis [22]. Overexpression of 14-3-3β amplifies NF-κB/MAPK signaling [23], which, in synergy with total IgE-mediated mast cell degranulation [24], perpetuates bronchoconstriction. Advances in anti-IgE therapies, such as omalizumab, have demonstrated efficacy in reducing asthma exacerbations, particularly in patients with

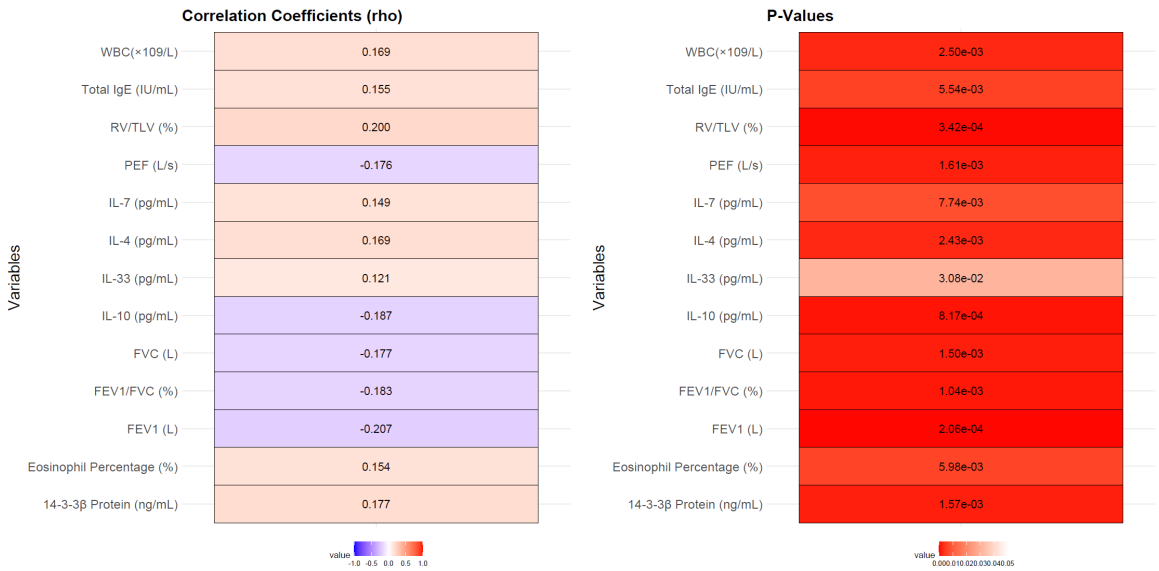

Figure 3. Correlation analysis between serological markers, pulmonary function, and asthma.

Table 2. Univariate logistic regression analysis examining the relationship between serological markers, pulmonary function, and asthma prognosis

Influencing Factors	Coefficient	Std Error	Wald	P	OR	95% CI
WBC (×10^9/L)	0.230	0.078	2.952	0.003	1.258	1.083-1.470
Eosinophil Percentage (%)	0.431	0.136	3.159	0.002	1.539	1.183-2.024
14-3-3β Protein (ng/mL)	0.051	0.016	3.075	0.002	1.052	1.019-1.087
Total IgE (IU/mL)	0.030	0.010	3.107	0.002	1.030	1.011-1.051
IL-4 (pg/mL)	0.08	0.024	3.251	0.001	1.083	1.033-1.137
IL-7 (pg/mL)	0.178	0.062	2.852	0.004	1.195	1.059-1.354
IL-10 (pg/mL)	-0.091	0.028	3.232	0.001	0.913	0.863-0.963
IL-33 (pg/mL)	0.021	0.008	2.547	0.011	1.021	1.005-1.037
FEV1 (L)	-0.040	0.012	3.448	< 0.001	0.961	0.939-0.983
FVC (L)	-0.038	0.013	3.031	0.002	0.963	0.939-0.986
FEV1/FVC (%)	-0.051	0.016	3.157	0.002	0.951	0.921-0.981
PEF (L/s)	-0.042	0.013	3.271	0.001	0.959	0.934-0.983
RV/TLV (%)	0.032	0.01	3.246	0.001	1.032	1.013-1.053

WBC: White Blood Cell Count; FEV1: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; PEF: Peak Expiratory Flow; RV/TLV: Ratio of Residual Volume to Total Lung Capacity.

elevated IgE levels [25]. Elevated levels of IL-4 and IL-7 in asthma patients with poor outcomes indicate a shift towards a Th2 phenotype, characterized by increased IgE production and eosinophilic inflammation. IL-4 drives B cell class switching to IgE, while IL-7 promotes T cell proliferation and survival, both of which contribute to chronic inflammation [14, 26, 27]. In contrast, lower levels of IL-10 in these patients suggest deficiencies in regulatory mechanisms that typically suppress excessive immune responses. IL-10 plays a crucial role in inhibiting Th2 cytokine production and promoting Treg activity [28]. Additionally, elevated IL-33 levels in severe asthma cases amplify allergic inflammation and airway remodeling via activation of ILC2s and mast cells [29, 30]. This suggests the importance of epithelial-derived cytokines in determining disease severity and highlights IL-33 as a potential therapeutic target for severe pediatric asthma [31-33].

Higher FEV1, FVC, FEV1/FVC ratios, and PEF were found to be protective against poor prog-

Table 3. Multivariate logistic regression analysis examining the relationship between serological markers, pulmonary function, and asthma prognosis

Influencing Factors	Coefficient	Std Error	Wald Stat	P	OR	OR CI Lower	OR CI Upper
WBC (×10^9/L)	0.215	0.092	2.345	0.019	1.240	1.036	1.484
Eosinophil Percentage (%)	0.365	0.166	2.201	0.028	1.441	1.041	1.995
14-3-3β Protein (ng/mL)	0.046	0.020	2.365	0.018	1.048	1.008	1.089
Total IgE (IU/mL)	0.024	0.011	2.158	0.031	1.025	1.002	1.048
IL-4 (pg/mL)	0.095	0.030	3.197	0.001	1.100	1.038	1.166
IL-7 (pg/mL)	0.145	0.075	1.914	0.056	1.155	0.997	1.340
IL-10 (pg/mL)	-0.099	0.033	-2.957	0.003	0.906	0.848	0.967
IL-33 (pg/mL)	0.023	0.010	2.331	0.020	1.023	1.004	1.043
FEV1 (L)	-0.041	0.014	-2.931	0.003	0.959	0.933	0.986
FVC (L)	-0.038	0.015	-2.573	0.010	0.963	0.935	0.991
FEV1/FVC (%)	-0.046	0.019	-2.434	0.015	0.955	0.920	0.991
PEF (L/s)	-0.050	0.016	-3.121	0.002	0.951	0.921	0.981
RV/TLV (%)	0.034	0.012	2.890	0.004	1.035	1.011	1.059

WBC: White Blood Cell Count; FEV1: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; PEF: Peak Expiratory Flow; RV/TLV: Ratio of Residual Volume to Total Lung Capacity.

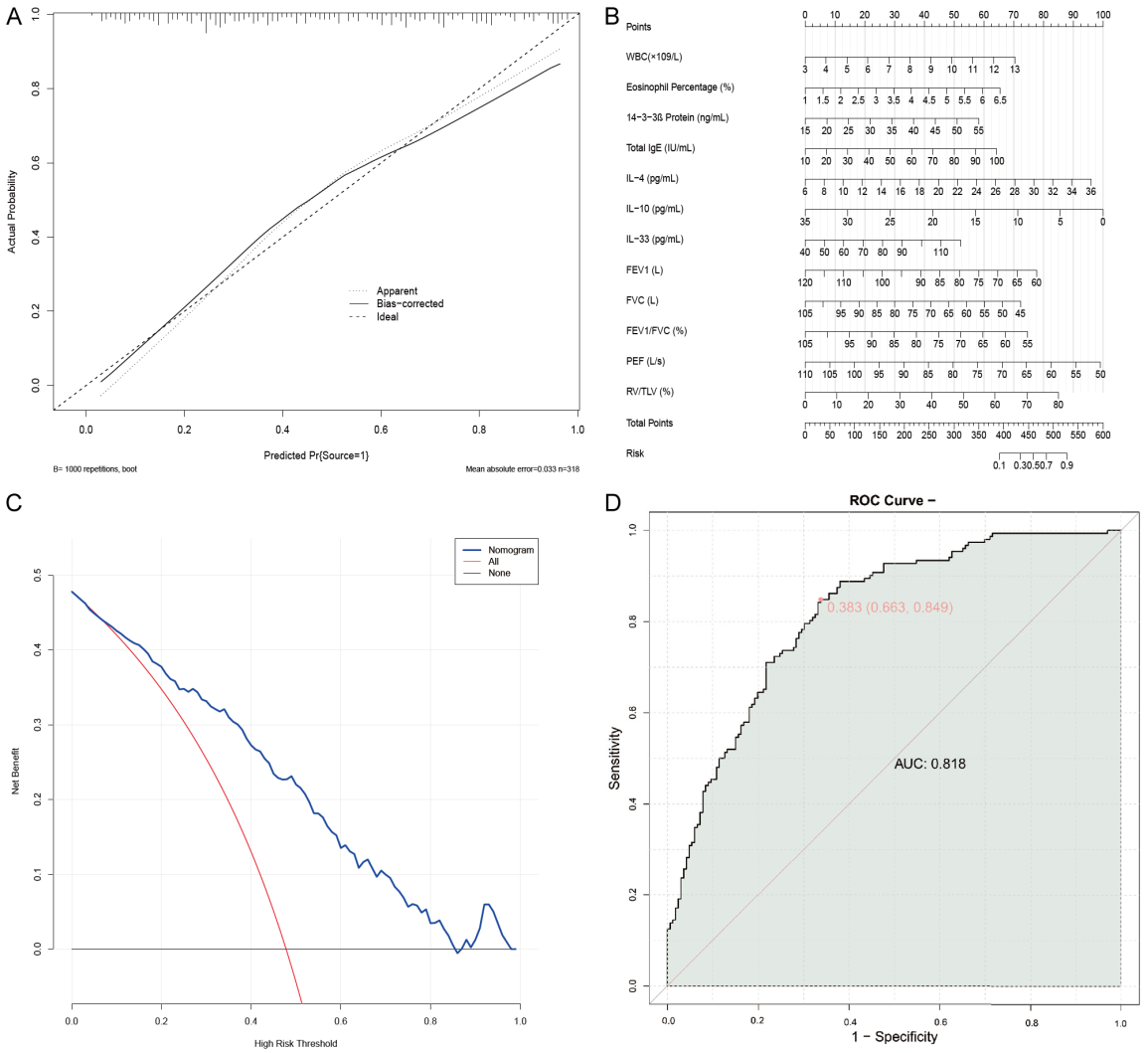

Figure 4. Combined predictive model of the prognosis of children with asthma. A. Calibration Curve; B. Nomogram; C. Decision Curve; D. Combined Receiver Operating Characteristic (ROC) Curve.

Table 4. Demographic data for external validation cohort

Parameters	Good Prognosis (n = 151)	Poor Prognosis (n = 132)	t/χ^2	P
Male/Female	90 (59.6%)/61 (40.4%)	83 (62.88%)/49 (37.12%)	0.318	0.573
Age (years)	10.12 ± 1.23	10.21 ± 1.44	0.576	0.565
BMI (kg/m^2)	18.97 ± 1.93	18.97 ± 2.02	0.017	0.987
Residence Location			0.034	0.983
City	92 (60.93%)	79 (59.85%)		
Suburb	39 (25.83%)	35 (26.52%)		
Rural Area	20 (13.25%)	18 (13.64%)		
Monthly Household Income Level			0.764	0.683
< 4000 yuan	56 (37.09%)	47 (35.61%)		
4000-8000 yuan	67 (44.37%)	55 (41.67%)		
> 8000 yuan	28 (18.54%)	30 (22.73%)		
Parental Educational Level			0.352	0.838
Junior High School or Below	43 (28.48%)	41 (31.06%)		
High School	71 (47.02%)	62 (46.97%)		
College or Above	37 (24.5%)	29 (21.97%)		
Family Members Smoking:	43 (28.48%)	42 (31.82%)	0.374	0.541
Custodian Situation			1.647	0.439
Single-Parent Family	18 (11.92%)	16 (12.12%)		
Dual-Parent Family	126 (83.44%)	105 (79.55%)		
Other	7 (4.64%)	11 (8.33%)		
Family History of Asthma	41 (27.15%)	39 (29.55%)	0.199	0.656
Triggers			0.709	0.702
Sudden Temperature Drop	9 (5.96%)	5 (3.79%)		
Exposure to Allergens	17 (11.26%)	15 (11.36%)		
Respiratory Infections	125 (82.78%)	112 (84.85%)		
Classification of Acute Exacerbations			2.313	0.315
Mild Exacerbation	74 (49.01%)	53 (40.15%)		
Moderate Exacerbation	51 (33.77%)	54 (40.91%)		
Severe Exacerbation	26 (17.22%)	25 (18.94%)		
Treatment Methods			2.833	0.243
Rapid-Acting β2-Agonist Inhalers	98 (64.9%)	76 (57.58%)		
Nebulized Inhalation Therapy	41 (27.15%)	38 (28.79%)		
Intravenous Corticosteroids	12 (7.95%)	18 (13.64%)		
Time Patterns of Asthma Exacerbations			1.397	0.706
Morning	41 (27.15%)	36 (27.27%)		
Daytime	25 (16.56%)	21 (15.91%)		
Nighttime	49 (32.45%)	50 (37.88%)		
Irregular	36 (23.84%)	25 (18.94%)		

nosis, likely reflecting less severe airway obstruction and better respiratory muscle function. Spirometric indices are critical in assessing the mechanical properties of the lungs and airways, and they correlate directly with disease severity and control [34]. Recent pediatric imaging studies have shown that a decrease in the FEV1/FVC ratio is closely related to the volume of air trapping regions observed on high-resolution CT scans, suggesting that this index may serve as a non-invasive surrogate marker for small airway remodeling [35]. The lower RV/TLV ratio observed in the good prognosis group indicates more efficient lung ventilation and reduced air trapping, both of which are crucial for effective asthma management [36-38]. We

Table 5. Comparison of demographic data between the modeling dataset and the external validation dataset

Parameters	Modeling Dataset (n = 318)	External Validation (n = 283)	t/χ^2	P
Male/Female	188 (59.12%)/130 (40.88%)	173 (61.13%)/110 (38.87%)	0.253	0.615
Age (years)	10.33 ± 1.45	10.15 ± 1.34	1.546	0.123
BMI (kg/m)	19.01 ± 2.03	18.97 ± 1.99	0.242	0.809
Residence Location				
City	186 (58.49%)	171 (60.42%)		
Suburb	92 (28.93%)	74 (26.15%)		
Rural area	40 (12.58%)	38 (13.43%)		
Monthly Household Income Level			2.623	0.269
< 4000 yuan	107 (33.65%)	103 (36.4%)		
4000-8000 yuan	128 (40.25%)	122 (43.11%)		
> 8000 yuan	83 (26.1%)	58 (20.49%)		
Parental Educational Level			0.534	0.766
Junior High School or Below	100 (31.45%)	84 (29.68%)		
High School	140 (44.03%)	133 (47%)		
College or Above	78 (24.53%)	66 (47%)		
Family Members Smoking	101 (31.76%)	85 (30.04%)	0.209	0.648
Custodian Situation			0.286	0.867
Single-Parent family	38 (11.95%)	34 (12.01%)		
Dual-Parent family	263 (11.95%)	231 (81.63%)		
Other	17 (5.35%)	18 (6.36%)		
Family History of Asthma	85 (6.36%)	80 (28.27%)	0.178	0.673
Triggers			0.059	0.971
Sudden Temperature Drop	16 (5.03%)	14 (4.95%)		
Exposure to Allergens	34 (10.69%)	32 (11.31%)		
Respiratory Infections	268 (84.28%)	237 (83.75%)		
Classification of Acute Exacerbations			0.522	0.770
Mild Exacerbation	150 (47.17%)	127 (44.88%)		
Moderate Exacerbation	117 (36.79%)	105 (37.1%)		
Severe Exacerbation	51 (36.79%)	51 (18.02%)		
Treatment Methods			2.36	0.307
Rapid-Acting β2-Agonist Inhalers	197 (61.95%)	174 (61.48%)		
Nebulized Inhalation Therapy	98 (30.82%)	79 (27.92%)		
Intravenous Corticosteroids	23 (7.23%)	30 (10.6%)		
Time Patterns of Asthma Exacerbations			0.189	0.979
Morning	84 (26.42%)	77 (27.21%)		
Daytime	52 (16.35%)	46 (16.25%)		
Nighttime	109 (34.28%)	99 (34.98%)		
Irregular	73 (22.96%)	61 (21.55%)		

speculate that patients with an elevated RV/TLV ratio may benefit from respiratory muscle training. This hypothesis is consistent with the significant efficacy of pulmonary rehabilitation observed in children with high RV/TLV in recent randomized trials [39]. These pulmonary function indices not only serve as diagnostic tools but also provide valuable prognostic information. They allow clinicians to identify patients at higher risk for severe exacerbations and adjust treatment strategies accordingly. For instance, early identification of a decline in FEV1 or an

Table 6. Correlational indices for external validation cohort

Parameters	Good Prognosis (n = 151)	Poor Prognosis (n = 132)	t/χ^2	P
WBC ($\times 10^9$/L)	7.72 ± 1.29	8.21 ± 1.31	3.216	0.001
Eosinophil Percentage (%)	2.71 ± 0.71	3.06 ± 1.12	3.115	0.002
14-3-3β Protein (ng/mL)	32.17 ± 6.88	34.85 ± 7.19	3.192	0.002
Total IgE (IU/mL)	55.51 ± 9.37	59.38 ± 12.02	2.989	0.003
IL-4 (pg/mL)	28.33 ± 3.79	30.22 ± 6.14	3.052	0.003
IL-7 (pg/mL)	8.75 ± 1.41	9.26 ± 2.09	2.4	0.017
IL-10 (pg/mL)	10.26 ± 5.42	8.89 ± 1.74	2.936	0.004
IL-33 (pg/mL)	81.63 ± 12.06	91.84 ± 14.26	6.452	< 0.001
FEV1 (L)	84.08 ± 10.22	76.62 ± 9.61	6.299	< 0.001
FVC (L)	73.06 ± 10.27	69.98 ± 8.64	2.738	0.007
FEV1/FVC (%)	76.94 ± 7.84	73.85 ± 7.95	3.288	0.001
PEF (L/s)	77.08 ± 7.16	73.92 ± 8.62	3.325	0.001
RV/TLV (%)	41.32 ± 8.04	47.03 ± 12.16	4.585	< 0.001

WBC: White Blood Cell Count; FEV1: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; PEF: Peak Expiratory Flow; RV/TLV: Ratio of Residual Volume to Total Lung Capacity.

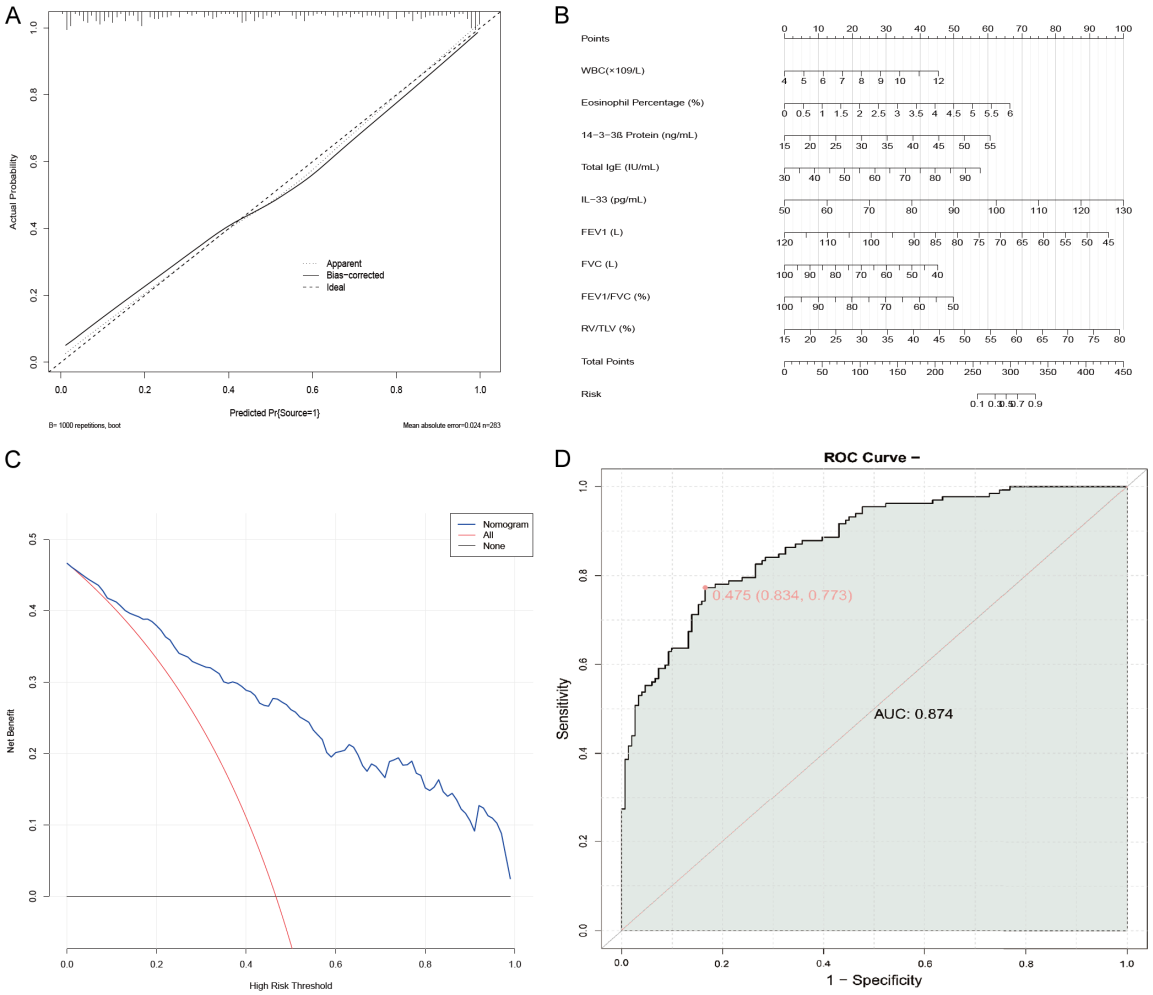

Figure 5. Combined predictive model of various factors for the prognosis of children with asthma (external validation cohort). A. Calibration Curve; B. Nomogram; C. Decision Curve; D. Combined Receiver Operating Characteristic (ROC) Curve. FEV1: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; RV: Residual Volume.

increase in RV/TLV could prompt more aggressive treatment strategies to prevent disease progression.

Our predictive model, which integrates key serological markers and pulmonary function indices, demonstrates significant prognostic value. The multifactorial predictive model developed in this study incorporates various independent risk factors, including WBC count, eosinophil percentage, 14-3-3β protein, total IgE, IL-4, IL-7, IL-33, IL-10, FEV1, FVC, FEV1/FVC, PEF, and RV/TLV. Each of these factors uniquely contributes to the overall prediction score, providing a comprehensive assessment of asthma prognosis. Identifying prominent biomarkers and functional indices that predict asthma progression can guide the development of personalized treatment plans, allowing healthcare providers to tailor interventions according to the individual risk profiles of pediatric patients. Furthermore, this study adds to the ongoing discourse on the complex mechanisms underlying asthma exacerbations and control. The interaction between systemic inflammation, immune dysregulation, and altered lung mechanics forms a multifaceted network that influences asthma outcomes. Future research could focus on longitudinal studies to track changes in these biomarkers over time, potentially uncovering causal relationships and temporal sequences in asthma pathophysiology. Compared to adult asthma, pediatric asthma has some differences in prognostic factors. For example, the impact of growth and development on pulmonary function is likely more significant in children. However, both populations exhibit similar inflammation - related biomarkers [40].

This study has some limitations that should be acknowledged. First, the retrospective design inherently introduces potential biases related to data completeness and accuracy. Additionally, the study was conducted at two medical institutions; while the external validation cohort supports the broader applicability of the findings, further validation across diverse populations and geographical regions would strengthen the generalizability of the model. Despite these limitations, our findings provide valuable insights into the prognostic indicators of pediatric asthma and lay the foundation for future studies aimed at refining and validating predictive models. We believe that directing future research toward several key areas will facilitate more comprehensive improvements. First, conducting multi-time point dynamic modeling by collecting fluctuating biomarker data from patients during acute exacerbations and remission phases could help build time-dependent predictive models. These models would more accurately capture disease progression and predict risks. Furthermore, developing point-of-care rapid testing tools that integrate key indicators such as 14-3-3β and IL-33 with portable spirometers could enable real-time risk assessment in outpatient settings, thereby enhancing the timeliness of clinical diagnosis and intervention. Additionally, exploring gene-environment interactions through genome-wide association studies (GWAS) in individuals with larger prediction errors in the model could identify potential modifying genetic loci. This would further elucidate the interaction mechanisms between genetic susceptibility and environmental factors in disease onset, providing a stronger theoretical foundation for precision medicine.

Conclusion

In conclusion, our study highlights the pivotal role of specific serological markers and pulmonary function indices in predicting the prognosis of pediatric asthma. The integration of multiple biological and functional parameters offers a comprehensive approach to risk stratification, with the potential to enhance asthma management and patient outcomes. Further research focusing on the mechanistic pathways and longitudinal validation of predictive models will be crucial in advancing personalized medicine for pediatric asthma.

Disclosure of conflict of interest

None.

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