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Construction and validation of a predictive model for allergic rhinitis complicating children with bronchial asthma

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Abstract
This study aimed to investigate the factors influencing the complication of allergic rhinitis in children with bronchial asthma and to construct a nomogram model to predict the occurrence of allergic rhinitis. A total of 190 children with bronchial asthma admitted to our hospital from August 2020 to August 2024 were retrospectively analyzed. The children were randomly divided into the training cohort (133 cases) and validation cohort (57 cases) in a ratio of 7:3. The children in the modeling set were divided into an allergic rhinitis group (n=44) and a non-allergic rhinitis group (n=89) depending on the presence or absence of concomitant allergic rhinitis. A total of 62 cases in 190 children with bronchial asthma had complications with allergic rhinitis, with an incidence of 32.63%. In the training cohort, compared with the children in the nonallergic rhinitis group, percentage of smokers in the household, C-reactive protein (CRP), white blood cell count (WBC), and neutrophils/lymphocytes (NLR) were significantly higher in the allergic rhinitis group ($P < 0.05$). Multivariable logistic regression analysis showed that smokers in the household; IgE; early use of antibiotics; and elevated CRP, WBC, and NLR were all risk factors for the complication of allergic rhinitis in children with bronchial asthma ($P < 0.05$). A nomogram prediction model was constructed based on the above risk factors. The C-index of the nomogram was 0.919 (95% CI: 0.742–0.934) and 0.841 (95% CI: 0.773–0.902) for the training cohort and validation cohort, respectively. The Hosmer–Lemeshow test results of the training and validation cohorts were both $P > 0.05$, suggesting a good model fit. The results of DCA showed that the training and validation cohorts had good threshold probability and clinical net benefit. Smokers in the household, IgE, CRP, WBC, and NLR levels were all risk factors for the complication of allergic rhinitis in children with bronchial asthma. A nomogram model based on these risk factors may be a valuable clinical tool for predicting allergic rhinitis in children with bronchial asthma.
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Introduction

Bronchial asthma is a chronic inflammatory disease of the airways involving multiple cells and cellular components. It is characterized by recurrent episodes of wheezing, shortness of breath, chest tightness, or coughing, and is easily exacerbated by environmental factors (cold air, allergens, respiratory infections, etc.).[1] Allergic rhinitis is a noninfectious inflammatory disease of the nasal mucosa mainly mediated by IgE after exposure of the organism to allergens, with clinical manifestations such as paroxysmal sneezing, clear watery nasal discharge, and nasal congestion.[2] Although bronchial asthma and allergic rhinitis have different sites of onset, they have similar pathogenesis. Studies have shown that nearly 40% of children with bronchial asthma have allergic rhinitis, and these two diseases affect each other and form a vicious circle, which has a serious impact on children's health and daily life.[3] Therefore, screening the factors influencing allergic rhinitis in children with bronchial asthma and constructing a prediction model is of great significance for optimizing comprehensive treatment and promoting the recovery of these children.

With the continuous progress of medical technology and the wide application of big data technology, the nomogram prediction model is being extensively applied in the medical field. The nomogram model can transform complex mathematical models into easy-to-understand prediction tools, providing doctors with more accurate and convenient means of predicting patients' conditions.[4] A nomogram model based on independent risk factors for poor prognosis in patients with smoking asthma can effectively predict the risk of poorly controlled treatment outcomes and provide a reference for early clinical identification of high-risk groups.[5] However, prediction models for predicting comorbid allergic rhinitis in children with bronchial asthma are still lacking. Therefore, this study aimed to construct a nomogram model of concurrent allergic rhinitis in children with bronchial asthma based on economical, effective, and easily accessible parameters. This study aims to provide some references for the clinical diagnosis and treatment of children with bronchial asthma complicated with allergic rhinitis.

Materials and Methods

Patients

A retrospective analysis of 190 cases of children with bronchial asthma admitted to the Anhui Provincial Children's Hospital from August 2020 to August 2024 was performed. Inclusion criteria were: (1) meeting the relevant diagnostic criteria and clinically diagnosed with bronchial asthma[6]; (2) all aged less than 18 years. Exclusion criteria were: (1) those with a past history of sinusitis, nasal polyps, etc.; (2) those with a combination of other serious systemic diseases, such as congenital heart disease, malignant tumors, etc.; (3) those with cardiac, hepatic, renal, and other major organ insufficiencies; and (4) those with glucocorticosteroids or other immunosuppressant drugs in the past 3 months.

Data collection

Children aged between 5 and 11 years were selected for the study. This age range has high prevalence of bronchial asthma and allergic rhinitis, and a study involving them will have a strong relevance and application value. The researchers recruited the children through hospital channels. The guardians of the children were briefed in detail about the purpose of the study, its content, procedure, and possible benefits to the children at the outpatient clinic. The guardians of children willing to participate in the study were required to provide informed consent.

Before the inception of this study, a power analysis was conducted using G*Power software to scientifically determine the requisite sample size. By inputting the predicted effect size, the set significance level ($\alpha = 0.05$), and the statistical efficacy (Power = 0.8) into the statistical software for calculation, we arrived at the minimum sample size of 160 cases required for this study. In the actual recruitment process, we considered the possible loss of sample (some children dropped out of the study, missing data, etc.). At the same time, to make the sample more representative, the scope of recruitment was further expanded. The final number of participants was 190. This ensured that the actual sample size met the requisite minimum sample size for power analysis, thus providing sufficient statistical efficacy for the study.

Clinical data of the children were collected, including age, gender, body mass index (BMI), childcare experience, family history of asthma, history of allergies in the children, time spent outdoors, smokers in the household, neutrophils/lymphocytes (NLR), C-reactive protein (CRP), and white blood cell count (WBC). Peripheral fasting venous blood was drawn at 24 h of admission, and the supernatant was separated after centrifugation. Serum CRP levels were measured by the latex turbidimetric method using a Hitachi 7600 automatic biochemical analyzer and corresponding kits.

All staff involved in data collection have been given unified training to operate in accordance with standardized procedures, so as to avoid data bias arising from inconsistencies in the manner and standards of data collection by different personnel and to ensure that the data collected were true, accurate, and comparable.

Diagnostic criteria for allergic rhinitis[7]

The following are the diagnostic criteria for allergic rhinitis. (1) Accompanied by two or more symptoms, such as sneezing, clear watery runny nose, nasal itching, and nasal congestion, with symptoms lasting or accumulating for more than 1 h per day; (2) commonly pale and edematous nasal mucosa and watery nasal discharge; and (3) positive for at least one allergen test or serum-specific IgE.

Statistical analysis

The data of this study were analyzed using the SPSS 26.0 software. The children were randomly divided into the training cohort (133 cases) and validation cohort (57 cases) in the ratio of 7:3. Measurements were normally distributed, expressed as mean ± standard deviation, and compared using the *t*-test. Count data were compared using the χ^2 test. Multivariate logistic regression models were used to analyze the factors influencing the complication of allergic rhinitis in children with bronchial asthma. The related risk prediction model was constructed using the R software and internally validated using the Bootstrap method. The predictive efficacy, calibration, and clinical benefit of the nomogram model were assessed by C-index, calibration curve, and decision-making curve (DCA). $P < 0.05$ bit difference was statistically significant.

Results

Comparison of clinical data of children with the training cohort and validation cohort

A total of 62 of 190 children with bronchial asthma had allergic rhinitis, with an incidence of 32.63%.

Among them, 44 out of 133 (33.08%) children in the training cohort and 18 out of 57 (31.58%) children in the validation cohort had allergic rhinitis. There was no statistically significant difference between the clinical data of the training cohort and validation cohort ($P > 0.05$, Table 1).

Comparison of clinical data between children in the allergic rhinitis group and the nonallergic rhinitis group in the training cohort

In the training cohort, there was no statistically significant difference between the children in the allergic rhinitis group and the nonallergic rhinitis group in terms of age, gender composition, BMI, daycare experience, family history of asthma, history of allergies in the children, and time spent outdoors ($P > 0.05$, Table 2). The proportion of smokers in the household, IgE, CRP, WBC, and NLR were significantly higher in the allergic rhinitis group compared to the children in the nonallergic rhinitis group ($P < 0.05$, Table 2).

Multivariate analysis of concurrent allergic rhinitis in children with bronchial asthma in the training cohort

In the training cohort, children with bronchial asthma were included in a multivariate logistic regression model with the presence of allergic rhinitis as the dependent variable, and smokers in the household, IgE, CRP, WBC, and NLR as the independent variables.

Table 1 Comparison of clinical data between the training and validation cohorts.

Parameters	Training cohort (n=133)	Validation cohort (n=57)	t/χ^2	*p*
Age (years)	7.49±1.42	7.58±1.44	0.399	0.690
Gender				
Male	71 (53.38)	33 (57.89)	0.328	0.567
Female	62 (46.62)	24 (42.11)		
BMI (kg/m²)	17.62±1.68	17.35±2.16	0.938	0.349
Nursery class experience				
Yes	68 (51.13)	34 (59.65)	1.165	0.280
No	65 (48.87)	23 (40.35)		
Family history of asthma				
Yes	30 (22.56)	18 (31.58)	1.720	0.190
No	103 (77.44)	39 (68.42)		
Child's allergy history				
Yes	31 (23.31)	19 (33.33)	2.068	0.150
No	102 (76.69)	38 (66.67)		
Outdoor activity time				
<5 h	32 (24.06)	14 (24.56)	0.005	0.941
≥5 h	101 (75.94)	43 (74.44)		
Smoking among family members				
Yes	40 (30.08)	18 (33.33)	0.043	0.837
No	93 (69.92)	39 (66.67)		
Identify allergens				
Yes	57 (42.86)	18 (31.58)	2.124	0.145
No	76 (57.14)	39 (68.42)		
Amenorrhea	32 (24.06)	17 (29.82)	0.693	0.405
PM2.5 air pollution	26 (19.55)	15 (26.32)	1.080	0.299
IgE (IU/mL)	168.51±26.32	162.72±25.18	1.407	0.161
Eosinophil (×10⁹/L)	0.73±0.17	0.69±0.14	1.563	0.120
CRP (mg/L)	46.88±7.40	45.31±6.34	1.396	0.164
WBC (×109/L)	11.26±1.89	11.39±2.22	0.384	0.701
NLR	3.59±0.82	3.34±1.10	1.741	0.083
Complicated allergic rhinitis	44 (33.08)	18 (31.58)	0.041	0.839

Table 2 Comparison of clinical data between children in the allergic rhinitis group and the nonallergic rhinitis group in the training cohort.

Parameter	Allergic rhinitis group (n=44)	Nonallergic rhinitis group (n=89)	t/χ^2	*p*
Age (years)	7.80±1.49	7.34±1.37	1.762	0.080
Sex				
Male	23 (52.27)	48 (53.93)	0.033	0.857
Female	21 (47.73)	41 (46.07)		
BMI (kg/m^2)	17.79±1.46	17.54±1.79	0.811	0.419
Nursery class experience				
Yes	26 (59.09)	42 (47.19)	1.669	0.196
No	18 (40.91)	47 (52.81)		
Family history of asthma				
Yes	14 (31.82)	16 (17.98)	3.229	0.072
No	30 (68.18)	73 (82.02)		
Child's allergy history				
Yes	12 (27.27)	19 (21.35)	0.578	0.447
No	32 (72.73)	70 (78.65)		
Outdoor activity time				
<5h	14 (31.82)	18 (20.22)	2.166	0.141
≥5h	30 (68.18)	71 (79.78)		
Smokers in the household				
Yes	22 (50.00)	18 (20.22)	12.413	<0.001
No	22 (50.00)	71 (79.78)		
Identify allergens				
Yes	16 (36.36)	41 (46.07)	1.132	0.287
No	28 (63.64)	48 (53.93)		
Amenorrhea	14 (31.82)	18 (20.22)	2.166	0.141
PM2.5 air pollution	12 (27.27)	14 (15.73)	2.494	0.114
IgE (IU/mL)	202.92±38.91	151.50±21.25	9.863	<0.001
Eosinophil (×10^9/L)	0.77±0.20	0.71±0.18	1.743	0.084
CRP (mg/L)	52.67±7.31	44.02±5.57	7.578	<0.001
WBC (×109/L)	12.24±1.96	10.78±1.67	4.494	<0.001
NLR	4.09±0.82	3.34±0.70	5.491	<0.001

The results showed that smokers in the household, IgE, CRP, WBC, and NLR were all risk factors for the complication of allergic rhinitis in children with bronchial asthma ($P < 0.05$, Table 3).

Construction of the nomogram prediction model

The nomogram prediction model was constructed based on the influencing factors screened by the training cohort (Figure 1). The weight of each parameter on allergic rhinitis is expressed in the form of a specific score, which can be summed up to obtain a total score. Based on the total score, the corresponding probability value can be matched on the risk axis, and the predicted probability value of allergic rhinitis complication for an individual child can be inferred.

Validation of the nomogram prediction model

The C-index of the nomogram model in the training cohort and validation cohort for predicting concurrent allergic rhinitis in children were 0.919 (95% CI: 0.742-0.934) and 0.841 (95% CI: 0.773-0.902), respectively. The Hosmer-Lemeshow test and results for the training cohort and validation

Table 3 Multivariate analysis of concomitant allergic rhinitis in children with training cohort bronchial asthma.

Factors	B	S.E.	Wald	OR	95%CI	P
Smokers in the household	1.407	0. 708	3.955	4.086	1.021-16.356	0.047
IgE	0.065	0.017	15.040	1.067	1.033-1.102	<0.001
CRP	0.124	0.059	4.447	1.1323	1.009-1.270	0.035
WBC	0.413	0.177	5.439	1.511	1.068-2.138	0.020
NLR	1.824	0.604	9.102	6.195	1.894-20.257	0.003

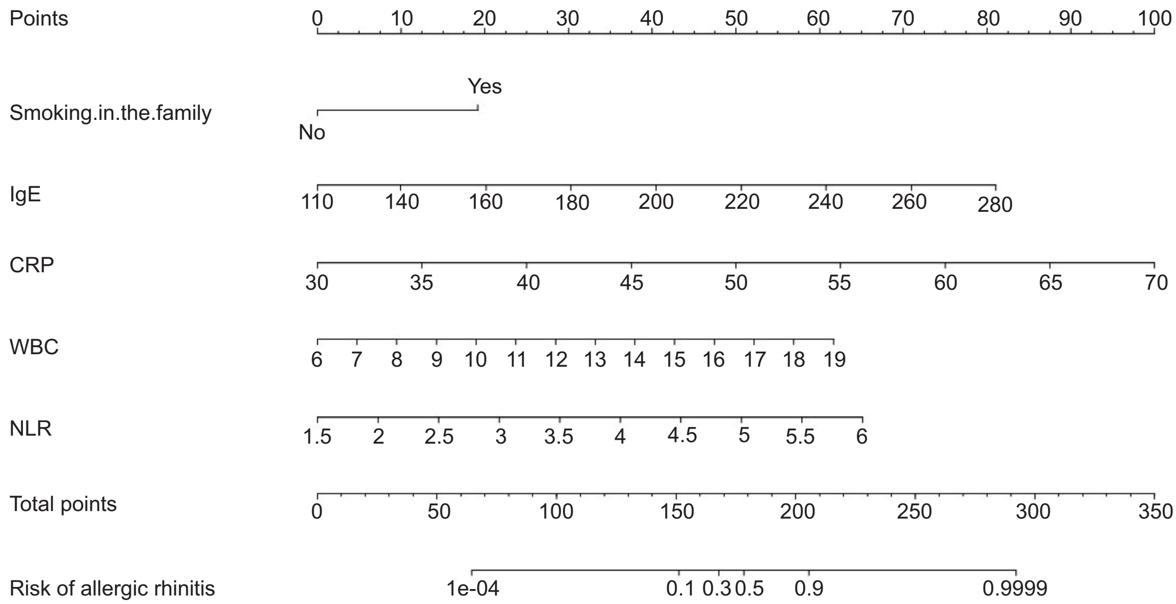

Figure 1 The nomogram prediction model for children with bronchial asthma complicated by allergic rhinitis.

cohort were χ^2 = 3.234 (P = 0.919) and χ^2 = 4.257 (P = 0.763), respectively. The calibration curves were basically consistent with the ideal curves, indicating that the column-line diagram model had good consistency and accuracy (Figure 2). The results of DCA (Figure 3) showed that the training cohort and validation cohort had good threshold probabilities and net clinical benefit.

Discussion

The incidence of bronchial asthma has been increasing in recent years, especially in the pediatric population, and it is considered that it may be related to factors such as lifestyle and environmental changes.[8] Allergic rhinitis is a common clinical inflammatory disease, and patients mostly present with itchy nose, sneezing, and itchy eyes.[9] When children with bronchial asthma have complications with allergic rhinitis, the clinical manifestations often become more complex and diverse. Persistent nasal discomfort not only affects children's quality of life but even further aggravates asthma symptoms, causes airway remodeling, and affects lung function.[10] Therefore, screening risk factors for allergic rhinitis in children with bronchial asthma is of considerable clinical value for clinical assessment and treatment.

The upper and lower respiratory tracts are closely linked in terms of anatomical structure and physiological function, and the inflammatory process also has mutual influence.[11,12] As the first line of defense of the respiratory tract, inflammation of the nasal cavity can directly affect the lower respiratory tract, leading to asthma attacks or exacerbations; conversely, poor asthma control can increase the frequency and severity of allergic

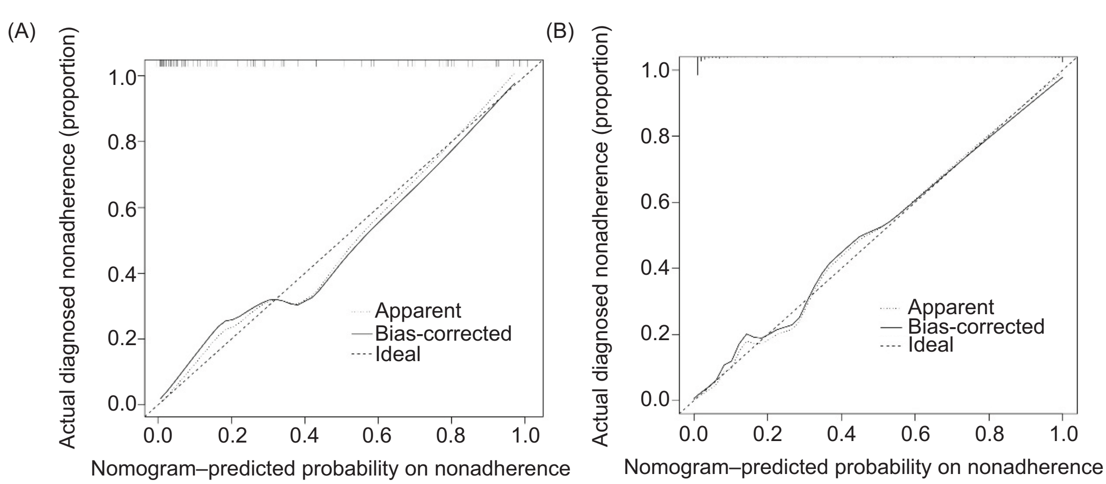

Figure 2 Calibration curve of the nomogram model for predicting comorbid allergic rhinitis in children. (A) Training cohort, (B) Validation cohort.

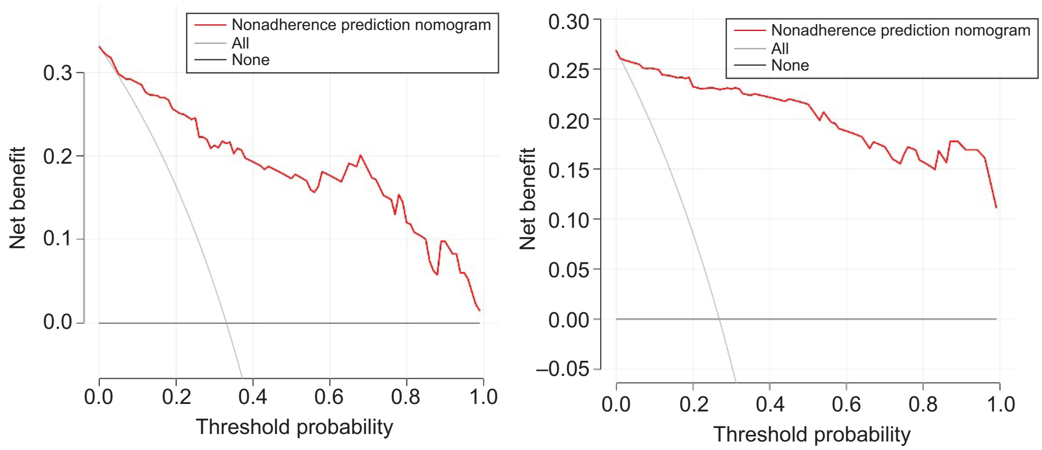

Figure 3 DCA curve of the nomogram model to predict the complication of allergic rhinitis in children. (A) Training cohort, (B) Validation cohort.

rhinitis attacks.[13] This continuity of inflammation in the upper and lower airways provides an important pathologic basis for the complication of both. A total of 62 of the 190 children with bronchial asthma selected for this study had concurrent allergic rhinitis, with an incidence of 32.63%. After multivariate logistic regression analysis, the results showed that smoking by family members, IgE, and elevated CRP, WBC, PCT, and NLR were risk factors for the complication of allergic rhinitis in children with bronchial asthma. Cigarette smoke contains many harmful substances such as nicotine and tar. These components can activate immune cells as well as epithelial cells in the respiratory tract, prompting them to release a large number of inflammatory mediators. These mediators can lead to local inflammatory reactions, such as redness, swelling, and itching, and simultaneously attract more immune cells to gather at the site of inflammation, which further exacerbates the inflammatory cascade and weakens immune defenses. Long-term exposure of children to secondhand smoke increases the risk of complication of allergic rhinitis due to irritation of respiratory mucosa and impaired immune function.[14] IgE is an important antibody type in the human immune system that plays a central role in mediating allergic reactions. Bronchial asthma itself is a heterogeneous disease characterized by chronic airway inflammation and airway hyperresponsiveness, and elevated IgE is a common phenomenon in such children. Allergic rhinitis is also a chronic inflammatory disease of the nasal mucosa mediated by IgE. Elevated IgE increases the activation of mast cells in the nasal mucosa, which degranulate and release inflammatory mediators, leading to symptoms of allergic rhinitis and a significant increase in the risk of allergic rhinitis.[15,16] The level of CRP, as an acute temporal response protein, increases rapidly when the body encounters infection, inflammation, or tissue damage.[17] In children with bronchial asthma, persistent airway inflammation is a central feature of the disease. Allergic rhinitis, as an inflammatory response in the upper airways, is often closely associated with bronchial asthma in the lower airways. When CRP levels are elevated, it not only reflects the widespread inflammatory response present in children with bronchial asthma but also signals that this inflammation may spread to the upper airways, increasing the risk of allergic rhinitis.[18] Inflammation was more pronounced in patients with asthma combined with allergic rhinitis than in bronchial asthma patients, and CRP levels were significantly higher than those in the bronchial asthma group.[19] The results of this study also found that elevated CRP levels may affect the progression of children with bronchial asthma and increase the likelihood of allergic rhinitis. Therefore, monitoring CRP levels is important for early identification of and intervention in allergic rhinitis complications in children with bronchial asthma. WBC is an important component of the body's immune response. When WBC counts are elevated, they are often accompanied by the activation and migration of immune cells, and the aggregation of these cells in the respiratory mucosa can exacerbate the local inflammatory response and promote the development of allergic rhinitis.[20] NLR is the ratio of neutrophils to lymphocytes and reflects the dynamic balance between immune cells.[21] In children with bronchial asthma, an elevated NLR often implies a relative increase in neutrophils and a relative decrease in lymphocytes. This change is closely related to the increased inflammatory response and imbalance of immune regulation in the body. A state of high NLR not only exacerbates the local inflammatory response in the airways but may also affect the body's immune response to allergens, thereby increasing susceptibility to allergic rhinitis.[22]

The nomogram can convert complex regression equations into clear and concise graphs, enabling clinicians to visualize the trend of patients' conditions and identify high-risk groups early.[23] In this study, a prediction model was established based on six influencing factors derived from multivariate analysis. Based on the sum of the risk factor scores of each influencing factor, the risk probability of children with allergic rhinitis can be derived, which is intuitive and easy to understand. In addition, the model was internally and externally validated to have good predictive efficacy. The calibration and standard curves for both the training and validation sets were fitted, demonstrating that the model's accuracy in predicting the risk of concurrency was more stable across probability intervals. Furthermore, the DCA results also showed that the net clinical benefit of the prediction model was good, indicating that the model has high clinical applicability.

This study also has some limitations. This study used a single-center retrospective analysis method and included a relatively limited sample size. This may lead to some limitations in generalizing the model to a wider population and may also affect the accuracy and reliability of the model's prediction results. The prevalence and distribution of pathogens in different regions differ significantly, which means that populations in different regions have been exposed to different pathogenic microorganisms for a long period of time, and their immune systems have gradually developed their own unique adaptive response patterns in response to different pathogens. Therefore, the results on immune response and risk of disease occurrence involved in this study may be affected by the different types of major pathogens faced by populations in different regions, which poses a challenge to the generalizability of the results of this study. Future studies should aim to expand the sample size and adopt a multicenter, prospective study design in order to more comprehensively validate and optimize the prediction model. In addition, with the in-depth study of the comorbid mechanisms of bronchial asthma and allergic rhinitis, new risk factors and intervention targets are emerging, and future studies still need to pay attention to these new findings, with a view to continuously updating and improving the relevant prediction models.

In conclusion, smoking by family members, IgE, CRP, WBC, and NLR are all risk factors for the complication of allergic rhinitis in children with bronchial asthma. A nomogram model based on these risk factors may be a valuable clinical tool for predicting allergic rhinitis in children with bronchial asthma.

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Not applicable.

Authors Contribution

Qi Zhang designed the study and carried them out; Qi Zhang, Fengqin Xu, and Fuzhe Chen supervised the data collection; Qi Zhang, Fengqin Xu, and Fuzhe Chen analyzed the data; Qi Zhang, Fengqin Xu, and Fuzhe Chen interpreted the data; Qi Zhang prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the final manuscript.

Conflict of Interest

The authors state that there are no conflicts of interest to disclose.

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Ethics Approval

Ethical approval was obtained from the Ethics Committee of Anhui Provincial Children's Hospital.

Consent to Participate Statement

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

Data Availability

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

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