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Exploring the types of airway inflammation in hospitalized children with asthma

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Abstract

Background Asthma is a heterogeneous disease. Precise and personalized treatment is urgently needed to reduce the disease's burden. Thus, exploring the different types of airway inflammation in hospitalized children with asthma is beneficial for accurately managing childhood asthma.

Methods This retrospective study was conducted on children and adolescents with asthma who were hospitalized for asthma exacerbations. The classification cut-off values of blood eosinophil (EOS) were 150 (Standard 1), 300 (Standard 2), and 470/μL (Standard 3), respectively. Combined with specific IgE (sIgE, 0.7 kU/L), these individuals were divided into four airway inflammation types. We compared the proportion and characteristics of different airway inflammation. The *P* value < 0.05 indicated statistical significance.

Results A total of 351 children were enrolled in our study. Based on standard 1, 39.3% of the subjects were classified as Only-atopy group, 11.7% displayed Only-EOS group, 29.6% exhibited Type 2 (T2)-high group, and 19.4% exhibited T2-low group. Under standard 2, 51.3% of the subjects were classified as the Only-atopy group, 5.4% displayed the Only-EOS group, 17.7% exhibited the T2-high group, and 25.6% exhibited the T2-low group. In standard 3, 57.8% of the subjects were classified as the Only-atopy group, 2.9% displayed the Only-EOS group, 11.1% exhibited the T2-high group, and 28.2% exhibited the T2-low group. Furthermore, our findings indicate that patients with T2 low airway inflammation have a longer time from onset to admission, a longer hospitalization time, a lower proportion of atopic dermatitis, and a higher proportion of siblings.

Conclusion Regardless of the classification standard employed, the distribution of Only-atopy and Only-EOS was similar in different age periods. Moreover, the types of airway inflammation exhibited a consistent temporal pattern. The classification of airway inflammation in children based on peripheral blood and sIgE levels is a valuable tool for accurately treating asthma.

Trial registration The study was registered at https://clinicaltrials.gov/ with the number: NCT05800379 on 05/04/2023.

Keywords Children, Type 2 inflammation, Asthma, Hospitalization, Exploration

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Introduction

Bronchial asthma (asthma) is the most prevalent chronic respiratory disease during childhood [1]. The incidence of asthma among Chinese children and adolescents aged 0–14 years has been continuously increasing [2]. The asthma management objectives include maintaining symptom control, preventing exacerbations, and preventing asthma-related death [3, 4]. One study of almost 3,000 Chinese children with asthma in 29 cities revealed that 66.0% of children had experienced asthma attacks in the past year; 26.8% of children had visited the emergency department; and 16.2% of children were hospitalized due to asthma exacerbations [5]. Three hundred twenty-eight children and adolescents died of asthma reported in Chinese from 2016 to 2020 [6]. One of the risk factors for asthma-related mortality is hospitalization due to an acute asthma attack. An understanding of the clinical characteristics of hospitalized children with asthma is beneficial in reducing exacerbations.

Asthma is a heterogeneous disease characterized by chronic airway inflammation and hyperresponsiveness. In 2008, Anderson introduced the concept of endotypes of asthma and expounded upon the pathophysiological process and treatment characteristics of asthma [7]. As research into type 2 (T2) immune mechanisms has deepened, the crucial role of T2 inflammation in the pathogenesis of asthma has become increasingly evident. In 2019, the Global Initiative for Asthma (GINA) introduced a new classification system for asthma based on the presence of T2 inflammation. This system suggests that the most appropriate biological agents should be selected according to the type of inflammation [3]. The cut-off value of 150/μL is commonly used in GINA to identify patients with eosinophilic inflammation, which is a hallmark of T2-high asthma. Currently, there is no established evaluation standard for T2 inflammation in children with asthma under the age of twelve. Studies have shown that a blood EOS ≥ 300/μL is associated with a higher risk of asthma and better response to anti-inflammatory treatments [8, 9]. A study conducted in Europe utilized a threshold of 470/μL for the classification of blood EOS and combined it with specific IgE (SIgE, 0.7 kU/L) to classify airway inflammation in children with asthma of all ages [10]. The choice of 0.7 kU/L as a cut-off value is supported by studies that have shown its effectiveness in predicting clinical reactivity and allergic symptoms [10].

The definition of airway inflammation throughout the entire course of asthma in the aforementioned research provides a reference standard for evaluating type 2 inflammation in children [3, 8–10]. The precise prevention and personalized treatment are urgently needed to reduce the burden of childhood asthma worldwide. Thus, the exploration of the different types of airway inflammation in hospitalized children with asthma could be beneficial for the management of asthma and the reduction of the occurrence of exacerbations, hospitalizations, and related deaths.

Methods

Ethics approval and trial registration

This study was a retrospective study using human data with identifiable information. The subjects cannot be found, and the research project did not involve personal privacy or commercial interests. This study has received approval to exempt participants from signing informed consent forms from the Ethics Committee of Beijing Children's Hospital affiliated with Capital Medical University (the ethical approval number: [2023]-E-078-Y). The study was registered at clinicaltrials.gov (NCT05800379) on 05/04/2023.

Study design

This was a retrospective study conducted on children and adolescents with asthma who were hospitalized for asthma exacerbations. The diagnosis of asthma and exacerbation of asthma was based on the diagnostic criteria of "Guidelines for Diagnosis and Prevention of Bronchial Asthma in Children (2016 Edition)" [4]. The diagnostic criteria for asthma were described as history of typical variable respiratory symptoms and/or confirmed variable expiratory airflow limitation: ① Recurrent wheezing, coughing, shortness of breath, and chest tightness, often triggered by exposure to allergens, cold air, physical or chemical irritants, respiratory infections, exercise, and hyperventilation (such as laughing or crying), which frequently occur or worsen at night or in the early morning; ② During an exacerbation, scattered or diffuse wheezing sounds, predominantly during expiration, can be heard in both lungs, with prolonged expiration and relief afterward; ③ The above symptoms and signs are effectively relieved by anti-asthma treatment or spontaneously relieved; ④Other diseases that can cause wheezing, coughing, shortness of breath, and chest tightness are ruled out; ⑤ If there is no obvious wheezing or stridor, at least one of the following criteria should be met: positive bronchodilator test (FEV_1 increases by > 12% within 15 min after inhaling 200–400 μg of salbutamol), improvement in FEV_1 by > 12% after 4–8 weeks of anti-inflammatory treatment with inhaled corticosteroids and/or anti-leukotriene agents, positive bronchial provocation test and diurnal variability of PEF > 13% (monitored for 2 weeks). The diagnosis of asthma can be made if a patient meets criteria ①-④ or criteria ④ and ⑤ [4]. The electronic case system includes cases diagnosed with bronchial asthma, namely cases coded as J45.0 ~ J45.9 and J46 in the International Statistical Classification of Diseases and Related Health Problems 10.

Selection and description of participants

The inclusion criteria for the study were age between 0 and 18 years and admission to Beijing Children's Hospital affiliated with Capital Medical University for asthma exacerbation from January 2016 to December 2021. Exclusion criteria: incomplete demographic information; lack of information on diagnosis and treatment after admission; hospital stay ≤ 1 day; with underlying diseases such as heart, liver, and kidney; suffering from primary or secondary immunodeficiency disease, hereditary metabolic disease, tumor, and organ or hematopoietic stem cell transplantation; suffering from active pulmonary tuberculosis and history of asthma and hospitalized for other reasons.

The included cases were retrieved and information on demographics, comorbidities, and case details were collected using a pre-designed case report form. The comorbidity of asthma in this study is defined as diseases with a higher prevalence rate than in healthy individuals that can affect the phenotype, treatment response, control level, or severity of asthma [11]. In this study, these include rhinitis, sinusitis, atopic dermatitis, and food allergy. Demographic information included gender, age, and siblings. Case details included first diagnosis during hospitalization, days from onset to admission, history of allergic diseases, family history of allergic diseases, and length of stay days.

Grouping standard

The children were classified into Only-atopy, Only-EOS, T2-high, and T2-low groups based on their blood EOS count and sIgE results before or after 3 days of admission, as shown in Table 1. Based on age, the participants were divided into four groups: infants (< 3 years old), preschoolers (3–5 years old), school-aged children (6–9 years old), and adolescents (≥ 10 years old).

Statistical analysis

All data were analyzed using SPSS 22.0 (IBM Corporation, Armonk, NY, USA). A P value < 0.05 indicated statistical significance (two-sided). Descriptive statistics were reported as means and standard deviations for normally distributed data and medians and interquartile ranges (IQR) for non-normally distributed data. Independent-sample t-tests were used to compare the means of two groups, while the Kruskal-Walli's test and rank sum test were used to analyze non-parametric data. Results for categorical data were presented as frequencies and proportions and analyzed with chi-square tests.

Results

Demographic characteristics

In the electronic medical record system, 911 cases of children who met the inclusion criteria were retrieved. A total of 456 cases were included, as shown in Fig. 1. Finally, a total of 351 children could be classified as the known type of airway inflammation. There were 230 boys and 121 girls, with an age range of 0.42–17.08 years and a median age of 3.50 (IQR: 5.16) years. There were 148 (42.2%) cases identified in the infant group, 94 (26.8%) cases in the preschool group, 71 (20.2%) cases in the school-age group, and 38 (10.8%) cases in the adolescent group. Two hundred and eighty-one (80.1%) cases were first diagnosed with asthma by doctors during hospitalization.

The comparison of three classification results for airway inflammation

As illustrated in Fig. 2A, based on standard 1, 39.3% of the subjects were classified as the Only-atopy group, 11.7% displayed the Only-EOS group, 29.6% exhibited the T2-high group, and 19.4% exhibited the T2-low group. In standard 2, 51.3% of the subjects were classified as the Only-atopy group, 5.4% displayed the Only-EOS group, 17.7% exhibited the T2-high group, and 25.6% exhibited

Table 1 Classification standards of airway inflammation types in children with asthma

Airway inflammation groups		Classification details
Standard 1 (The cut-off value of blood EOS was 150/μL)	Only-atopy	Blood EOS < 150/μL, the sum of all sIgE ≥ 0.7 kU/L
	Only-EOS	Blood EOS ≥ 150/μL and the sum of all sIgE < 0.7 kU/L
	T2-high	Blood EOS ≥ 150/μL and the sum of all sIgE ≥ 0.7kU/L
	T2-low	Blood EOS < 150/μL and the sum of all sIgE < 0.7kU/L
Standard 2 (The cut-off value of blood EOS was 300/μL)	Only-atopy	Blood EOS < 300/μL, the sum of all sIgE ≥ 0.7 kU/L
	Only-EOS	Blood EOS ≥ 300/μL and the sum of all sIgE < 0.7 kU/L
	T2-high	Blood EOS ≥ 300/μL and the sum of all sIgE ≥ 0.7kU/L
	T2-low	Blood EOS < 300/μL and the sum of all sIgE < 0.7kU/L
Standard 3 (The cut-off value of blood EOS was 470/μL)	Only-atopy	Blood EOS < 470/μL, the sum of all sIgE ≥ 0.7 kU/L
	Only-EOS	Blood EOS ≥ 470/μL and the sum of all sIgE < 0.7 kU/L
	T2-high	Blood EOS ≥ 470/μL and the sum of all sIgE ≥ 0.7kU/L
	T2-low	Blood EOS < 470/μL and the sum of all sIgE < 0.7kU/L

EOS: eosinophils; sIgE: specific IgE

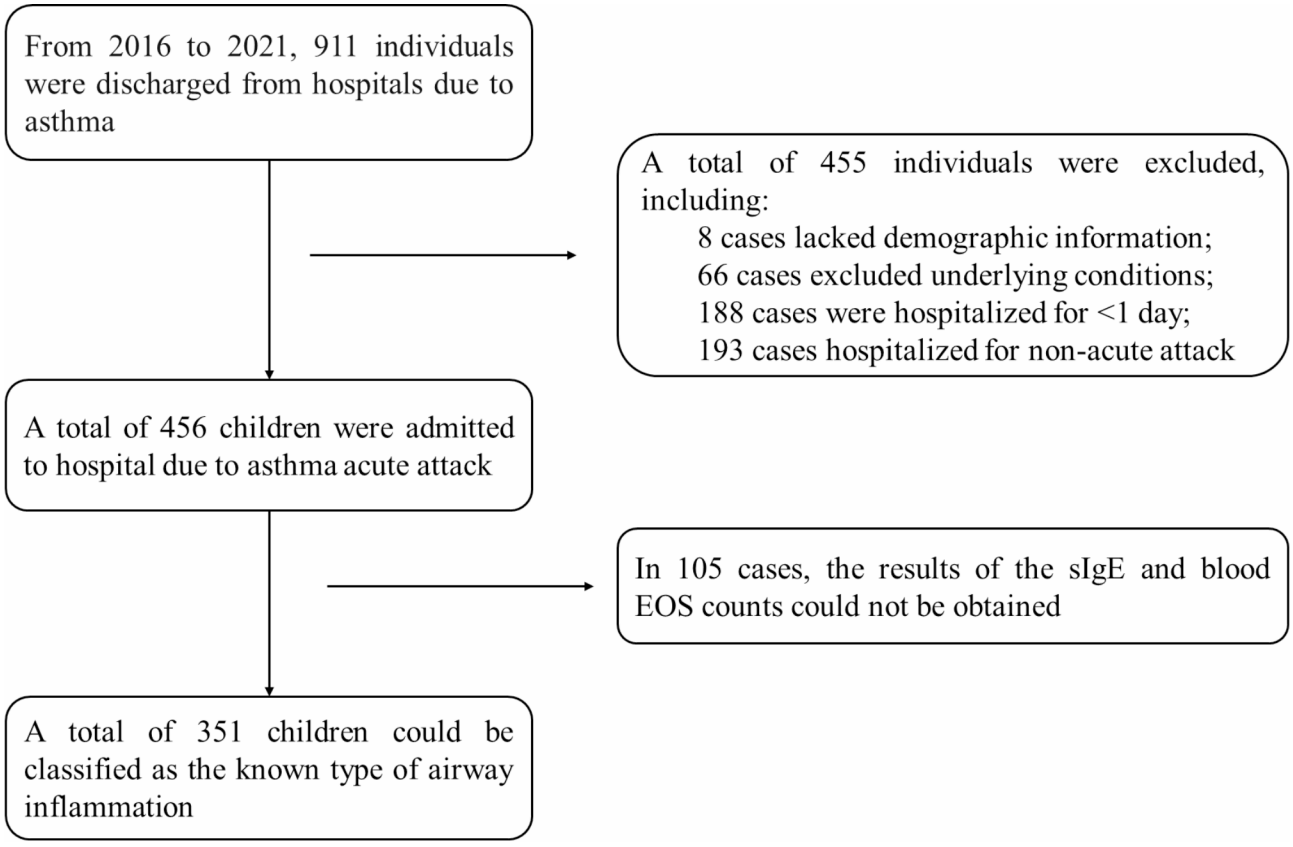

Fig. 1 Enrolment and exclusion of research individuals. This depicts the main workflow of the enrolment and exclusion of subjects. A total of 911 subjects had the diagnosis of asthma. Among them, 455 subjects met exclusion criteria, including 8 subjects who lacked demographic information; 66 subjects suffered from basic diseases; 188 subjects were hospitalized for ≤ 1 day; 193 subjects were hospitalized for non-exacerbations. A total of 456 children were admitted to the hospital due to asthma exacerbations. In 105 cases, the results of the sIgE and blood EOS counts before or after 3 days of admission could not be obtained. Finally, a total of 357 children could be classified as the known type of airway inflammation

the T2-low group. In standard 3, 57.8% of the subjects were classified as the Only-atopy group, 2.9% displayed the Only-EOS group, 11.1% exhibited the T2-high group, and 28.2% exhibited the T2-low group. Following the three classification standards, the proportion of Only-atopy airway inflammation in hospitalized children with asthma was the highest, while the proportion of Only-EOS was the lowest.

The description of individuals' characteristics based on the standard 1

Figure 2B displayed the distribution of airway inflammation types among hospitalized children stratified by age. Based on classification standard 1, the proportion of individuals in the Only-atopy group and the Only-EOS group did not differ significantly when comparing the four age periods. However, the proportion of T2-high in adolescents (57.9%) was greater than that in infants (16.2%, $P<0.001$) and preschoolers (30.9%, $P<0.05$). Moreover, the proportion of T2-low in infants (28.4%) was greater than that in school-aged children (8.5%, $P< 0.05$) and adolescents (5.3%, $P < 0.05$).

In comparison to the T2-high group, the interval between the onset of symptoms and admission to the hospital was longer (5.00 vs. 9.00 and 7.50, $P<0.05$), the proportion of having siblings was higher (37.5% vs. 63.4% and 61.8%, $P<0.05$), and length of stay days were longer (7.00 vs. 8.00 and 8.00, $P<0.05$) in Only-EOS group and T2-low group. The proportion of patients with atopic dermatitis was higher in the Only-atopy group than in the T2 low group (72.0% vs. 23.5%, $P=0.001$). As shown in Table 2, there was no statistically significant difference in the proportion of allergic history, family history of allergic diseases, allergic rhinitis, sinusitis, and food allergy among the four types of airway inflammation.

The description of individuals' characteristics based on the standard 2

Based on the classification standard 2, the proportion of individuals in the Only-atopy group and the Only-EOS group did not differ significantly when comparing the four age periods. As shown in Fig. 2C, the proportion of T2-high in adolescents (44.7%) was greater than that in infants (8.1%, $P<0.001$) and preschoolers (14.9%, $P<$

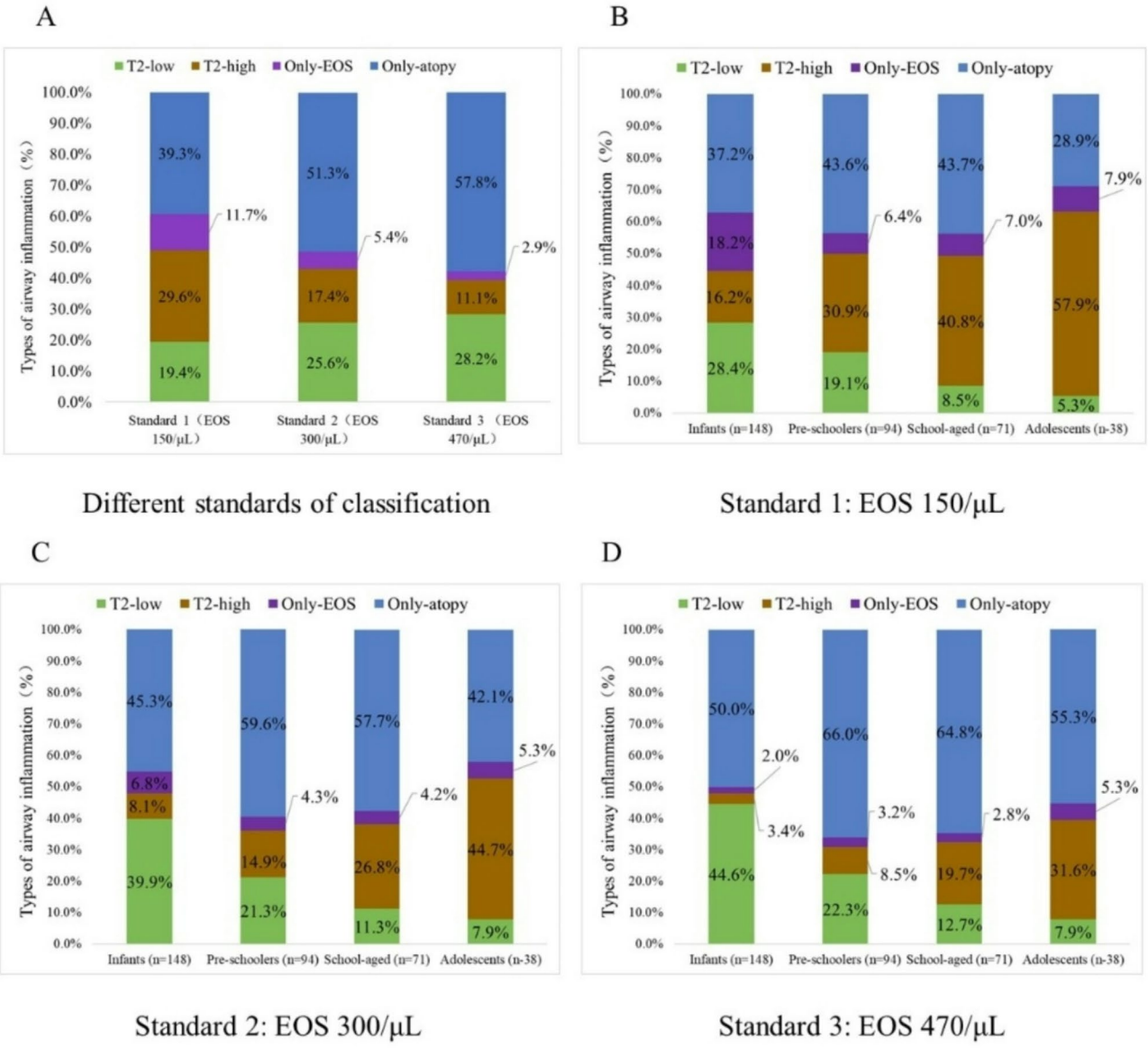

Fig. 2 Distribution of airway inflammation types in enrolled children and different age periods based on the different classification standards. **A** showed the distribution of airway inflammation types in enrolled children. The classification cut-off values of blood EOS were 150 (Standard 1; **B**), 300 (Standard 2; **C**), and 470/μL (Standard 3; **D**), respectively. Combined with serum sIgE (0.7 kU/L), these individuals were divided into four airway inflammation types: Only-atopy (blue), Only-EOS (orange), T2-high (grey), and T2-low (yellow)

0.05). Similar to classification standard 1, the proportion of T2-low in infants (39.9%) was greater than that in preschoolers (21.3%, $P < 0.05$), school-aged children (11.3%, $P < 0.001$) and adolescents (7.9%, $P = 0.001$).

In comparison to the T2-low group, the interval between the onset of symptoms and admission to the hospital was shorter (8.00 vs. 4.00 and 5.00, $P < 0.05$) in Only-atopy group and T2-high group. The proportion of patients with allergic diseases history (37.3% vs. 21.1%, $P < 0.05$) and the proportion of patients with atopic dermatitis (69.5% vs. 36.0%, $P < 0.05$) was higher in Only-atopy group than in T2-low group. However, the proportion of having siblings (41.7% vs. 61.0%, $P < 0.05$) was lower in the Only-atopy group than in the T2-low group. In comparison to the T2-high group, the length of stay days was longer (7.00 vs. 8.00 and 8.00, $P < 0.05$) in Only-EOS group and T2-low group. As shown in Table 3, there was no statistically significant difference in the proportion of family history of allergic diseases, allergic rhinitis, sinusitis, and food allergy among the four types of airway inflammation.

The description of individuals' characteristics under the standard 3

Shown in Fig. 2D, the results of the proportion of Only-atopy and Only-EOS in four periods under the

Table 2 The description of characteristics between four airway inflammation types under the standard 1

	Only-atopy (*n* = 138)	Only-EOS (*n* = 41)	T2-high (*n* = 104)	T2-low (*n* = 68)
First diagnosis during hospitalization	113(81.9%)	33(80.5%)	83(79.2%)	52(76.5%)
Days from onset to admission (median, IQR)	4.00(8.00)*	9.00(26.00)#	5.00(12.50)*	7.50(27.00)
History of allergic diseases	87(63.0%)	33(80.5%)	65(62.5%)	52(76.5%)
Family history of allergic diseases	70(50.7%)	27(65.9%)	52(50.0%)	40(59.7%)
Siblings ≥ 1	62(44.9%)	26(63.4%)#	39(37.5%)	42(61.8%)#
Allergic rhinitis&	40(53.3%)	7(46.7%)	46(62.2%)	9(52.9%)
Sinusitis&	8(10.7%)	2(13.3%)	9(12.2%)	4(23.5%)
Atopic dermatitis&	54(72.0%)*	9(60.0%)	39(52.7%)	4(23.5%)
Food allergy&	6(8.0%)	1(6.7%)	2(2.7%)	2(11.8%)
Length of stay days (median, IQR)	7.00(4.00)	8.00(4.00)#	7.00(3.00)*	8.00(4.00)

& A total of 181 children were able to obtain detailed information about whether they had comorbidity. Among them, there were 75 cases in the Only-atopy group, 15 cases in the Only-EOS group, 74 cases in the T2-high group, and 17 cases in the T2-low group. *Compared with T2-low group, *P* value< 0.05. # Compared with T2-high group, *P* value< 0.05

Table 3 The description of characteristic between four airway inflammation types under the standard 2

	Only-atopy (*n* = 180)	Only-EOS (*n* = 19)	T2-high (*n* = 62)	T2-low (*n* = 90)
First diagnosis during hospitalization	145(80.6%)	16(84.2%)	51(82.3%)	69(76.7%)
Days from onset to admission (median, IQR)	4.00(9.00)*	7.00(26.00)	5.00(12.00)*	8.00(27.00)
History of allergic diseases	66(37.3%)*	5(26.3%)	21(33.9%)	19(21.1%)
Family history of allergic diseases	95(52.8%)	9(47.4%)	25(40.3%)	32(36.0%)
Siblings ≥ 1	75(41.7%)*	13(68.4%)	26(41.9%)	55(61.0%)
Allergic rhinitis&	55(52.4%)	3(42.9%)	31(70.5%)	13(50.2%)
Sinusitis&	13(12.4%)	2(28.6%)	4(9.1%)	4(16.0%)
Atopic dermatitis&	73(69.5%)*#	4(57.1%)	20(45.5%)	9(36.0%)
Food allergy&	6(5.7%)	1(14.3%)	2(4.5%)	2(8.0%)
Length of stay days (median, IQR)	7.00(3.00)	8.00(4.00)#	7.00(3.00)*	8.00(4.00)

& A total of 181 children were able to obtain detailed information about whether they had comorbidity. Among them, there were 105 cases in the Only-atopy group, 7 cases in the Only-EOS group, 44 cases in the T2-high group, and 25 cases in the T2-low group. *Compared with T2-low group, *P* value < 0.05. # Compared with T2-high group, *P* value < 0.05

classification standard 3 were similar to standard 1 and standard 2. Furthermore, the proportion of T2-high in adolescents (31.6%) was also higher than that in infants (3.4%, $P = 0.001$) and preschoolers (8.5%, $P < 0.05$). Similar to the classification standard 2, the proportion of T2-low in infants (44.6%) was higher than that in preschoolers (22.3%, $P < 0.05$), school-aged children (12.7%, $P < 0.001$) and adolescents (7.9%, $P < 0.001$).

In comparison to the T2-low group, the interval between the onset of symptoms and admission to the hospital was shorter (8.00 vs. 4.00, $P < 0.001$) in the Only-atopy group. The proportion of patients with an allergic history (38.0% vs. 20.2%, $P < 0.05$), family history of allergic diseases (52.2% vs. 35.7%, $P < 0.05$), and atopic dermatitis (66.4% vs. 37.9%, $P < 0.05$) in only atopy group were higher than that in T2-low group. In comparison to the Only atopy group and T2-high group, the proportion of having siblings (42.9%, 35.9% vs. 61.6%, $P < 0.05$) was higher and the length of stay days was longer (7.00, 7.00 vs. 8.00, $P < 0.05$) in T2-low group. As shown in Table 4, there was no statistically significant difference in the proportion of allergic rhinitis, sinusitis, and food allergy among the four types of airway inflammation.

Discussion

Despite the existence of numerous studies conducted across different age groups, there is still no consensus regarding the standard for judging type 2 inflammation. A comprehensive understanding of type 2 immunity has gradually elucidated the pathogenesis of asthma [10, 12]. The identification of the specific types of airway inflammation associated with asthma is a crucial step in the development of more effective asthma management strategies. Biomarkers of childhood asthma can be measured in a variety of samples, including sputum, bronchoalveolar lavage fluid, exhaled condensate, urine, and blood [13]. Among children with asthma, the sputum inflammatory phenotype exhibits unstable characteristics [14]. This indicates that the inflammatory phenotype in pediatric asthma patients is likely to change over time and in response to various factors, including therapeutic interventions [15]. In clinical practice, the invasive procedure of inducing sputum or obtaining airway samples

Table 4 The description of characteristics between four airway inflammation types under the standard 3

	Only-atopy (*n* = 203)	Only-EOS (*n* = 10)	T2-high (*n* = 39)	T2-low (*n* = 99)
First diagnosis during hospitalization	165(81.3%)	8(80.0%)	31(79.5%)	77(77.8%)
Days from onset to admission (median, IQR)	4.00(9.00)*	7.00(10.00)	7.00(12.00)	8.00(27.00)
History of allergic diseases	76(38.0%)*	4(40.0%)	11(28.2%)	20(20.2%)
Family history of allergic diseases	106(52.2%)*	6(60.0%)	14(35.9%)	35(35.7%)
Siblings ≥ 1	87(42.9%)*	7(70.0%)	14(35.9%)*	61(61.6%)
Allergic rhinitis&	68(55.7%)	1(33.3%)	18(66.7%)	15(51.7%)
Sinusitis&	14(11.5%)	2(66.7%)	3(11.1%)	4(13.8%)
Atopic dermatitis&	81(66.4%)*	2(66.7%)	12(44.4%)	11(37.9%)
Food allergy&	7(5.7%)	1(33.3%)	1(3.7%)	2(6.9%)
Length of stay days (median, IQR)	7.00(3.00)*	8.50(7.00)	7.00(3.00)*	8.00(4.00)

& A total of 181 children were able to obtain detailed information about whether they had comorbidity. Among them, there were 122 cases in the Only-atopy group, 3 cases in the Only-EOS group, 27 cases in the T2-high group, and 29 cases in the T2-low group. *Compared with T2-low group, *P* value< 0.05. # Compared with T2-high group, *P* value< 0.05

is challenging, particularly in young children. It is recommended that more accessible measurement indexes be utilized to evaluate the types of airway inflammation in children with asthma.

Currently, EOS, sIgE, and fractional exhaled nitric oxide (FeNO) were recommended by GINA for the evaluation of airway inflammation types in children over 12 years old with severe asthma [3]. In a study by Nicole Maison and colleagues, it was demonstrated that the blood EOS and sIgE results can be utilized to classify the types of airway inflammation in children of all ages. Furthermore, the study confirmed the feasibility and stability of this classification standard [8]. Thus, in our study, the classification threshold for blood EOS was set at 150, 300, and 470/μL, and the children were divided into groups of airway inflammation types in conjunction with sIgE (0.7 kU/L).

In our study, the majority of hospitalized children with asthma were found to be in the Only-atopy group, with the lowest proportion of Only-EOS. With increasing age, there was a downward trend in airway inflammation of T2-low and Only-EOS. Only-EOS airway inflammation tended to decrease with age, and there was no child with Only-EOS airway inflammation in the adolescent group, which was consistent with findings from other research [16, 17]. However, in another study, it was found that T2-low airway inflammation was the main cause of childhood asthma in infants (64.8%) and preschool children (36.9%), T2-high airway inflammation was the main cause in school-age children (47.6-48.7%), and Only-atopy was the most common in adolescents (52.3-63.0%) [10]. This result was not observed in our study. The discrepancy in the findings can be attributed to the fact that the children enrolled in this study were hospitalized for exacerbations.

In this study, the proportion of atopic dermatitis in the Only-atopy and T2-high groups was higher than that of the T2-low group. This was related to T2 inflammation, which is the main pathophysiological mechanism of asthma. A variety of T2 inflammatory diseases can coexist, with the respiratory system, digestive system, and skin being the most commonly involved. In this study, it was observed that the interval between the onset of symptoms to admission and the duration of hospitalization was longer in the T2-low airway inflammation group. This may be related to the involvement of neutrophils in the pathogenesis of asthma and the insensitivity of glucocorticoid therapy [18].

Biologics can effectively target and inhibit the key pathways involved in T2 inflammation. At present, it has been demonstrated that Omalizumab, Mepolizumab, Benralizumab, Dupilumab, and Tezepelumab can be employed for the treatment of childhood asthma [3, 19]. In the context of biologics, it is imperative that clinicians possess a comprehensive understanding of airway inflammation in children with asthma and enhance their comprehension of biological treatment for asthma. The enhancement of the precision of airway inflammation categorization is beneficial for the rationality and accuracy of biological preparation prescriptions. Consequently, the treatment of childhood asthma can be tailored to the individual, resulting in improved control of the disease and a reduction in exacerbations and related deaths.

Strengths and limitations

Our study represents the inaugural effort to categorize airway inflammation in hospitalized children with asthma aged 0–18 in China. It served as a foundation for subsequent research endeavors. Our study also had some limitations. Firstly, this study was retrospective, which may introduce a degree of selection bias. Furthermore, detailed information (such as residence, pet exposure, and dietary factors), treatment information, and some results of examination of children before admission cannot be obtained. The external environmental factors can significantly influence asthma pathogenesis and

exacerbations. We would conduct targeted experiments or cohort studies to systematically evaluate the independent effects of specific factors. It was acknowledged that glucocorticoid therapy nonmatter inhaled or systematic administration might affect the EOS count, which may affect the classification results of airway inflammation types of asthma [20, 21]. However, in our study, among the 351 participants included in our study, 281 were diagnosed with asthma for the first time, accounting for 80%. Different thresholds of EOS were selected to describe the classification results of airway inflammation, which mitigated the influence of glucocorticoid before admission on the results to some extent. Future studies should prioritize comprehensive data collection on prior treatments to provide more reliable and interpretable results. This study represented an important attempt to classify airway inflammation in children by using sIgE and EOS count in peripheral blood. Different age groups may have varying responses to treatments and different underlying pathophysiological mechanisms. The modest sample size may restrict our ability to identify statistically significant differences in certain age groups, especially in subgroup analyses, potentially limiting the generalizability of our findings. Additionally, the broad age range introduces substantial heterogeneity, complicating result interpretation. Further research is required to elucidate the classification standard for airway inflammation in children aged 0–18 in China, to enable the accurate treatment of childhood asthma.

Conclusion

Regardless of the classification standard employed, the proportion of Only-atopy airway inflammation in hospitalized children with asthma was the highest, while the proportion of Only-EOS was the lowest. Moreover, the types of airway inflammation exhibited a consistent temporal pattern. As age increased, there was a downward trend in the T2-low group, while the T2-high group exhibited an upward trend. Furthermore, our findings indicated that patients with T2-low airway inflammation could have a longer time from symptoms onset to admission, a longer time for hospitalization, a lower proportion of atopic dermatitis, and a higher proportion of siblings. The classification of airway inflammation in children based on peripheral blood EOS and sIgE is a valuable tool for the accurate treatment of asthma. Further study is warranted.

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Author contributions
KLS and PH: Conceived the study. PH: Data collection, analyzed the data, drafted and revised the manuscript. KLS, JY, AXJ, HMZ, YLL: Data collection, case analysis, and manuscript revision. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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Data availability
All data generated or analyzed during this study were included in this published article.

Declarations

Ethics approval and consent to participate
This study was reviewed and approved by the Ethics Committee of Beijing Children's Hospital affiliated with Capital Medical University (Ethical Approval Number: [2023]-E-078-Y). The study could not recontact the original subjects as a retrospective analysis utilizing human data with identifiable information. The research did not involve personal privacy concerns or commercial interests. Given these considerations, the Ethics Committee approved the waiver of informed consent, as the study posed no risk to participants and did not involve sensitive personal information. This study followed the Declaration of Helsinki, relevant guidelines, and regulations.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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