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ORIGINAL RESEARCH

Anaphylaxis in Chinese Children with Pollen Sensitization: Triggers, Clinical Presentation, and Acute Management

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Purpose: Pollen sensitization is increasing in children. However, there is little evidence regarding the characteristics of anaphylaxis in individuals with pollen sensitization.

Patients and Methods: We conducted a retrospective study of patients with anaphylaxis combined with pollen sensitization who attended an allergy department in a tertiary children's hospital from 2014 to 2021.

Results: A total of 157 anaphylaxis events in 108 patients were analyzed; the mean age at the reaction was 5.8 ± 4.17 years. A total of 99.1% (107/108) of the patients came from northern China. The most common sensitizing pollen was mugwort (93.5%,101/108), followed by ragweed (68.5%, 74/108) and birch (40.7%, 44/108). A total of 76.9% (83/108) of the patients showed polysensitization to pollen. Allergic rhinitis/conjunctivitis was the most common comorbidity (87.0%, 94/108). Children with severe anaphylaxis were more likely to have a history of recurrent urticaria (16.1% vs 3.9%, $p = 0.028$). The most frequently implicated foods were fruits/vegetables (22.3%, 35/157), followed by wheat (8.9%, 14/157) and milk (8.3%, 13/157), and the most common fruit allergen was peach ($n = 7$). Of 14% (22/157) exercise-induced reactions, 63.6% (14/22) occurred in pollen season. Skin symptoms were the most frequent (86.0%, 135/157) symptoms, followed by respiratory (73.9%, 116/157) and gastrointestinal (21%, 33/157) symptoms. Regarding acute management, only 7.4% of the patients were treated with epinephrine.

Conclusion: Our findings revealed the characteristics of anaphylaxis in children with pollen sensitization. Fruits/vegetables accounted for a substantial percentage of anaphylaxis triggers. The suboptimal use of epinephrine highlights the need for educational programs promoting the use of epinephrine.

Keywords: anaphylaxis, pollen, exercise, epinephrine

Introduction

Anaphylaxis is the most severe form of allergy and is characterized by an acute, potentially life-threatening systemic reaction of rapid onset.[1] Triggers and epidemiological factors associated with anaphylaxis vary with age, culture, and lifestyle.[2] Recent data from England have demonstrated that the level of certain specific pollen, including Fraxinus (Ash), Ambrosia (Ragweed), and Quercus (Oak), are associated with higher risk of seasonality in food-induced anaphylaxis hospital admissions[3] Similarly, one study in Sweden showed that the number of food-related anaphylaxis events among children allergic to pollen increased during tree pollen season;[4] the above-mentioned studies raise the possibility that sensitization to pollen cross-reactive foods may lead to an increased risk of anaphylaxis during the pollen season. Anaphylactic reactions may occur either because stable cross-reactive proteins (such as LTP), or augmentation factors (large amounts of food, exercise, and pollen season) that increase reaction severity and high-level pollen exposure may trigger anaphylaxis in very rare cases.[5–8]

Pollen-related foods (eg, fruits, vegetables, nuts, cereals, and legumes) are the main food triggers of anaphylaxis in older children, especially among individuals with pollen allergy or sensitized to pollen, which is also known as pollen-food

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allergy syndrome (PFAS).[2,9,10] About 9% of PFAS patients experience anaphylaxis.[11] Given that the etiology of PFAS is related to pollen sensitization, geographical distribution of pollen allergens and regional dietary habits influence pollen-related food trigger sensitization profiles and clinical symptoms. In northern China, birch and mugwort are common pollen that cause seasonal respiratory allergies in the spring and autumn, respectively.[12,13] Birch pollen has historically been considered the most common allergen among patients with pollen-related food allergy in Europe.[14] However, birch pollen sensitization and PFAS are now also common in China, especially in northern China.[12,15] Apples and hazelnuts are identified as the most frequent triggers in birch pollen-related food allergy.[16] Anaphylaxis is the primary sign of mugwort pollen-related food allergy in China, and peach is the most common culprit.[8]

Anaphylaxis in individuals with pollen sensitization may result from PFAS due to thermostable food allergens that cross-reactivity with pollen or an IgE allergy to the pollen protein independent of food allergens.[17] There is little evidence regarding the characteristics of anaphylaxis in individuals with pollen sensitization. The aim of this study was to identify the main elicitors of anaphylaxis in pediatric individuals with pollen sensitization, so as to help facilitate prompt recognition and management at an emergency department.

Patients and Methods

Ethics Statement

This study was performed in accordance with the principles stated in the Declaration of Helsinki, and the study protocol was approved by the Research and Ethics Board of Beijing Children's Hospital (Approval number:2022-E-023-R).

Patients and Study Design

This was a retrospective study of children with symptoms and signs of anaphylaxis who were referred to a specialized allergy department in a tertiary children's hospital. Medical records were retrospectively analyzed to identify the patients who were diagnosed with "anaphylactic shock" (ICD code T78.201), "anaphylaxis" (ICD code T78.402), and "severe allergic reactions" (ICD code T78.402) from January 2014 to December 2021. The patients' records were manually reviewed by a pediatric allergy specialist to confirm whether the World Allergy Organization (WAO) 2020 diagnostic criteria were met, and then we selected the patients with pollen sensitization according to the report of allergen testing (Serum levels of sIgE testing and/or skin prick testing). A total of 108 patients with anaphylaxis who met the criteria were enrolled in this study. A detailed history was collected by allergists and included a combined allergic disease. Factors evaluated in our analysis included demographic data (eg, age and sex); clinical characteristics of the reaction (possible triggers and severity); comorbidities (prior history of anaphylaxis, asthma, allergic rhinitis, atopic dermatitis); acute management. The flowchart is shown in Figure 1.

Clinical Diagnostic Criteria and Severity Grading

Assessment of the outpatients with anaphylaxis was based on the WAO 2020 criteria. Based on the current diagnostic criteria, anaphylaxis was defined as an acute allergic reaction involving more than two organ systems or life-threatening compromise in breathing and/or circulation alone. A modified grading system described by Muraro et al was used to classify the severity of anaphylaxis.[18] Severe reactions were defined as loss of bowel control, cyanosis, respiratory arrest, hypotension (SBP <70 mm Hg in infants [1 month–1 year old], <70+[2×age] mm Hg in children aged 1–10 years), and <90 mmHg in patients aged >10 years) and/or circulatory collapse, arrhythmia, severe tachycardia and/or cardiac arrest, confusion, and loss of consciousness.

Identification of Triggers

Identification of a food as the trigger for anaphylaxis was based on an acute allergic reaction in which the onset was related to a known or suspected food allergen exposure. Serum levels of specific IgE testing (Phadia AB Uppsala, Sweden) and/or skin prick testing were performed to determine aeroallergen and food allergens. The detection limit was defined as 0.35 kUA/L, in accordance with the manufacturer's recommendations. Skin tests were regarded as positive if the mean wheal diameter was ≥3 mm in the prick test. The skin testing was performed using standardized allergen

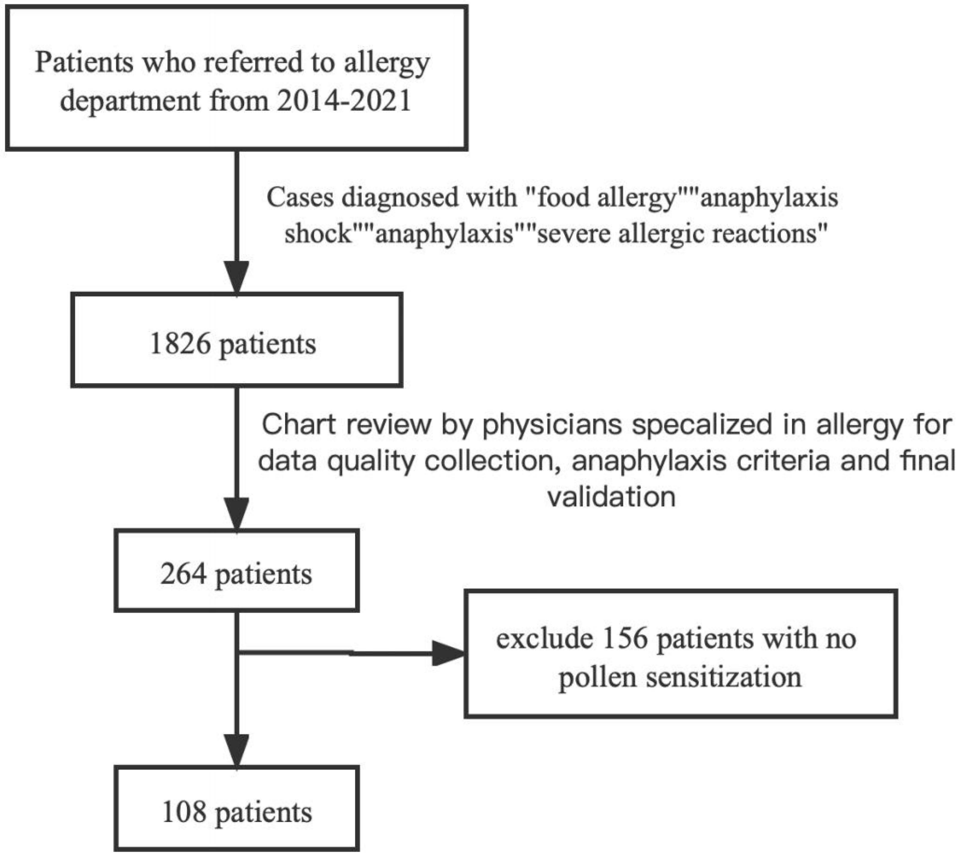

Figure 1 Study review flow chart.

extracts (Macro-Union Pharmaceutical Lim, Beijing, China). The diluent was administered as a negative control, and histamine hydrochloride (1 mg/mL) as a positive control. In addition, a positive score based on the wheal size was recorded as follows: Class 1, a wheal diameter between 3 and 5 mm; Class 2, a wheal diameter between 5 and 10 mm; Class 3, a wheal diameter between 1 and 2 cm; and Class 4, a wheal diameter ≥2 cm and the presence of pseudopods. Drug-induced anaphylactic episodes were mainly diagnosed based on medical history. If the medical records did not suggest a potential trigger and allergen-specific tests were negative, the episode was diagnosed as idiopathic.

Statistical Analysis

All statistical analyses were performed using SPSS 20.0 (IBM Inc., Chicago, IL). A descriptive analysis was used for characterization of the study population. The patient's demographic and clinical characteristics were described as a percentage for categorical data and as mean ± standard deviation for continuous data. To compare frequencies of categorical variables, comparisons between different groups were performed using Pearson's chi-squared test, or Fisher's exact test, while *t*-tests were used to compare continuous variables. *P*-values lower than 0.05 were considered statistically significant.

Results

General Characteristics of the Patients

There were 108 children meeting the inclusion criteria after manual review using the WAO anaphylaxis criteria. These enrolled children were stratified into two groups based on the severity of anaphylaxis (Table 1). The mean age at the reaction was 5.8±4.17 years, and it was significantly older in severe anaphylaxis than in mild-to-moderate anaphylaxis (6.6 ± 4.94 years vs 5.6 ± 3.88 years, $p = 0.01$). When analyzing the allergic comorbidities, allergic rhinitis/conjunctivitis was the most common

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Table 1 General Characteristics of 108 Patients

	Total Patients (n = 108)	Mild to Moderate Anaphylaxis (n = 77)	Severe Anaphylaxis (n = 31)	P value (Mild to Moderate vs Severe Anaphylaxis)
Characteristics				
Age at reaction, y (mean±SD)	5.8±4.17	5.6±3.88	6.6±4.94	0.01[a]
Gender, no (%)				
Male	66 (61.1)	48 (62.3)	18 (58.1)	0.68
Allergic comorbidities, no (%)				
AR/AC	94 (87.0)	6 (85.7)	28 (90.3)	0.519
Asthma /recurrent wheezing	48 (44.4)	35 (45.5)	13 (41.9)	0.739
Food allergy	33 (30.6)	21 (27.3)	12 (38.7)	0.243
Atopic dermatitis	31 (28.7)	20 (26.0)	11 (35.5)	0.323
Recurrent urticaria	8 (7.4)	3 (3.9)	5 (16.1)	0.028[b]
Family history of allergic diseases, no (%)	41 (38.0)	28 (36.4)	13 (41.9)	0.589
Episodes before referral				
1	65 (60.2)	46 (59.7)	19 (61.3)	0.882
2	28 (25.9)	20 (26.0)	8 (25.8)	0.986
Recurrent anaphylaxis (≥3)	15 (13.9)	11 (14.3)	4 (12.9)	0.851
Rate of pollen sIgE positive (≥0.35KUA/L), no (%)				
Mugwort	101 (93.5)	74 (96.1)	27 (87.1)	0.085
Ragweed	74 (68.5)	53 (68.8)	21 (67.7)	0.912
Birch	44 (40.7)	25 (32.5)	19 (61.2)	0.006[c]
Pollen sensitization individual profile, no (%)				
Mugwort (monosensitization)	20 (18.5)	19 (24.7)	1 (3.2)	0.009[d]
Ragweed (monosensitization)	3 (2.8)	3 (3.9)	0 (0)	0.265
Birch (monosensitization)	2 (1.9)	0 (0)	2 (6.5)	0.024[e]
Mugwort+ragweed	41 (38.0)	30 (39.0)	11 (35.5)	0.736
Mugwort+birch	11 (10.2)	5 (6.5)	6 (19.4)	0.046[f]
Mugwort+ragweed+birch	29 (26.9)	20 (26.0)	9 (29)	0.746
Ragweed+birch	2 (1.9%)	0 (0)	2 (6.5)	0.024[g]
sIgE level of pollen (KUA/L)				
Mugwort, mean±SD	32.9±36.2	30.8±35.2	38.6±39.1	0.381
Ragweed, mean±SD	7.3±15.0	8.4±17.3	4.9±6.5	0.378
Birch, mean±SD	7.79±15.4	11.1±18.8	2.3±2.2	0.132

(*Continued*)

Table 1 (Continued).

	Total Patients (n = 108)	Mild to Moderate Anaphylaxis (n = 77)	Severe Anaphylaxis (n = 31)	P value (Mild to Moderate vs Severe Anaphylaxis)
Other aeroallergen sensitization, no (%)				
Mold	46 (42.6)	30 (39.0)	16 (51.6)	0.229
Dust mite	31 (28.7)	22 (28.6)	9 (29.0)	0.962
Cat dander	35 (32.4)	27 (35.1)	8 (25.8)	0.352
Dog dander	31 (28.7)	22 (28.6)	9 (29.0)	0.962
Cockroach	2 (1.9)	1 (1.3)	1 (3.2)	0.502

Notes: [a]The mean age at severe reaction w was significantly older in severe anaphylaxis than in mild to moderate anaphylaxis (6.6±4.94 vs.5.6±3.88, p = 0.01). [b]Children with severe anaphylaxis were more likely to have a history of chronic urticaria (16.1% vs 3.9%, p = 0.028). [c]Birch sensitization rate was much higher in severe anaphylaxis patients (61.2% vs 32.5%, p=0.006); [d]monosensitization to mugwort was more common in the mild-to-moderate group (24.7% vs 3.1, p = 0.009); [e]monosensitization to birch was more common in the severe group (6.5% vs 0%, p=0.024); [f]patients co-sensitized to birch and mugwort tended to experience severe anaphylaxis (19.4% vs 6.5%, p = 0.046); [g]patients co-sensitized to birch and ragweed tended to experience severe anaphylaxis (6.5% vs 0%, p=0.024).

comorbidity (87.0%, 94/108). Children with severe anaphylaxis were more likely to have a history of chronic urticaria (16.1% vs 3.9%, p = 0.028). In terms of the pollen sensitization rate, the most common sensitized pollen was mugwort (93.5%,101/108), followed by ragweed (68.5%, 74/108) and birch (40.7%, 44/108). A total of 76.9% (83/108) of the patients showed polysensitization to pollen. A total of 99.1% (107/108) of the patients came from northern China. The geographic distribution of the patients is shown in Supplement Table 1. Birch sensitization rate was much higher in severe anaphylaxis patients (61.2% vs 32.5%, p = 0.006), while monosensitization to mugwort was more common in the mild-to-moderate group (24.7% vs 3.1, p = 0.009); however, patients co-sensitized to birch and mugwort tended to experience severe anaphylaxis (19.4% vs 6.5%, p = 0.046). Recurrence of anaphylaxis was observed in 43 patients (39.8%).

Triggers of Anaphylaxis

The triggers for 157 anaphylactic events are shown in Table 2 and Figure 2. Foods were the most common causative agents (80.3%, 126/157), followed by food+exercise/exercise (14%, 22/157) and drugs (2.5%, 4/157). The triggers were not determined in 3.2% (5/157) of all reactions, which were classified as idiopathic. Overall, the most frequently implicated foods were fruits/vegetables (22.3%, 35/157), wheat (8.9%, 14/157), and milk (8.3%, 13/157). The most common fruit trigger was peach (n = 7), followed by mango (n = 5) and pitaya (n = 5), and the most common nuts trigger was walnut (n = 4), followed by almond (n = 2) and hazelnut (n = 2). There was no difference in the trigger profile between the mild-to-moderate and severe anaphylaxis group.

Among the 157 anaphylactic reactions, 14% (22/157) occurred during exercise. Supplement Table 3 shows the detailed clinical characteristics of 16 patients who experienced anaphylaxis during exercise. The mean age at the reaction was 10.1 ± 3.56 years, range (3–17 years); 63.6% (14/22) occurred in pollen season (10 episodes in the autumn, 4 episodes in the spring). A total of 90.9% (20/22) of the episodes occurred during outdoor exercise (running, n = 11; jogging, n = 3; playing basketball, n = 3; quick walking, n = 2; playing golf, n = 1). When analyzing food triggers before exercise, food triggers were not recorded in the chart (n = 11); mix foods (n = 3); wheat (n = 2); banana (n = 2); apple (n = 1), cherry (n = 1); pitaya (n = 1), cauliflower (n = 1); allergic comorbidities in 16 patients, included allergic rhinitis in 75% (12/16), asthma in 37.5% (6/16), food allergy in 18.5% (3/16), and recurrent urticaria in 12.5% (2/16) of the patients.

Symptoms of Anaphylaxis

Supplement Table 2 summarizes the symptoms of anaphylaxis. Skin and mucocutaneous symptoms were the most frequent (86.0%, 135/157), followed by respiratory (73.9%, 116/157), gastrointestinal (21%, 33/157), oropharyngeal (15.9%, 25/157), neurological (6.4%, 10/157), and cardiovascular (8.9%, 14/157) symptoms. Thirty-eight reactions (22.8%,38/157) were classified as severe anaphylaxis.

Table 2 Triggers of 157 Anaphylactic Reactions

	Total n = 157, n (%)	Mild to Moderate Anaphylaxis (n = 119)	Severe Anaphylaxis (n = 38)	P value (Mild to Moderate vs Severe Anaphylaxis)
Suspect triggers, **n (%)**				
Foods	126 (80.3)	97 (81.5)	29 (76.3)	0.484
Fruit /vegetables	35 (22.3)	28 (23.5)	7 (18.4)	0.727
Peach	7 (4.5)	6 (5.0)	1 (2.6)	0.531
Mango	5 (3.2)	3 (2.5)	2 (5.3)	0.402
Pitaya	5 (3.2)	4 (3.4)	1 (2.6)	0.824
Lychee	4 (2.5)	3 (2.5)	1 (2.6)	0.97
Other fruit/ vegetables[a]	14 (8.9)	12 (10.1)	2 (5.3)	0.595
Wheat	14 (8.9)	12 (10.1)	2 (5.3)	0.364
Milk	13 (8.3)	12 (10.1)	1 (2.6)	0.147
Egg	10 (6.4)	6 (5.0)	4 (10.5)	0.228
Nuts/seeds	12 (7.6)	11 (9.2)	1 (2.6)	0.182
Walnut	4 (2.5)	4 (3.4)	0 (0)	0.252
Almond	2 (1.3)	2 (1.7)	0 (0)	0.421
Hazelnut	2 (1.3)	2 (1.7)	0 (0)	0.421
Pistachio nuts	1 (0.6)	1 (0.8)	0 (0)	0.571
Cashew nut	1 (0.6)	1 (0.8)	0 (0)	0.571
Nuts not specified	2 (1.3)	1 (0.8)	1 (2.6)	0.391
Peanut	5 (3.2)	3 (2.5)	2 (5.3)	0.402
Seafoods	5 (3.2)	4 (3.4)	1 (2.6)	0.824
Soybean	4 (2.5)	4 (3.4)	0 (0)	0.252
Mix foods[b]	10 (6.4)	7 (5.9)	3 (7.9)	0.658
Foods unclear[c]	9 (5.7)	5 (4.2)	4 (10.5)	0.144
Foods+exercise / exercise	22 (14.0)	15 (12.6)	7 (18.4)	0.369
Drug	4 (2.5)	2 (1.7)	2 (5.3)	0.222
Idiopathic	5 (3.2)	5 (4.2)	0 (0)	0.199

Notes: [a]Other fruits/vegetables include: pear (n=1), physalis peruviana L (n=2), longan (n=2), apple (n=2), rambutan (n= 1), pineapple (n=1), melon (n=1), orange (n= 1), grape (n=1), sea buckthorn (n=1), watermelon (n=1); [b]mix foods represented that the offending foods may contain multiple potential allergens several food allergens, such as cake, cookies, pizza; [c]food unclear represented the food triggers were not determined during chart review, such as the reactions occur just after a meal that may ingest several foods.

Acute Management of Anaphylaxis

Table 3 shows the treatment of the 121 anaphylactic episodes. Acute management was not accessible for 36 anaphylactic events. Among the 121 anaphylactic events with detailed management records, 9.9% (12/121) self-resolved and 38.8% (47/121) were home-treated. A total of 59.5% (72/121) of the anaphylactic events were treated in the emergency department; 22.3% (27/121) received with glucocorticoids; and only 7.4% (9/121) were treated with epinephrine.

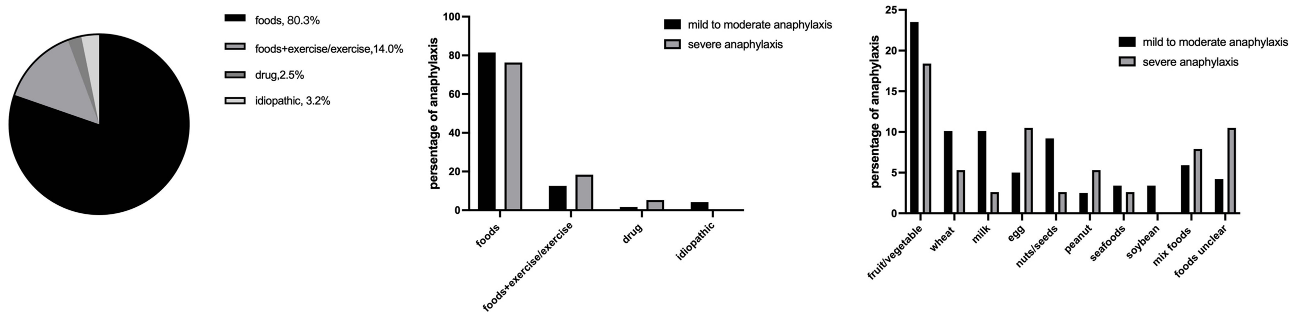

Figure 2 Triggers and food triggers of 158 anaphylactic reaction.

Discussion

The findings of this study revealed the characteristics of anaphylaxis in children with pollen sensitization, which demonstrated different profiles from our recently published age-dependent profiles of anaphylaxis in children.[2]

The present study showed that mugwort was the most common culprit. This may be because almost all children in our cohort were from northern China, and mugwort pollen is the most allergenic pollen in late summer and autumn in northern China.[13,19,20] This finding is consistent with our previously published data, where we reported that mugwort sensitization was common in patients with specific food-induced anaphylaxis, especially in fruit/vegetables (67%) and spices (75%).[9] Furthermore, compared with oropharyngeal symptoms, systemic reactions are the main manifestation of mugwort pollen-related food allergy in Chinese population.[2] Ragweed was the second most common pollen sensitization in our study. Ragweed is one of the major allergen sources causing allergy in North America and Europe.[21] However, it has spread and has also become a serious problem in China. One study summarized 215,210 tests with the ImmunoCAP system from 2008 to 2010, and suggested that ragweed sensitization rate in Chinese population was 48%.[20] Our study

Table 3 Acute Management of 121 Anaphylactic Reactions (Unrecorded N = 36)

Acute Management	Total n = 121, n (%)	Mild to Moderate Anaphylaxis (n = 92)	Severe Anaphylaxis (n = 29)	P value (Mild to Moderate vs Severe Anaphylaxis)
Treatment at home	47 (38.8)	41 (44.6)	6 (20.7)	0.021[a]
Self-relief	12 (9.9)	9 (9.8)	3 (10.3)	0.930
Oral antihistamines	3 2 (26.4)	29 (31.5)	3 (10.3)	0.024[b]
Nebulized β-agonist	3 (2.5)	3 (3.3)	0 (0)	0.325
Oral montelukast	1 (0.8)	1 (1.1)	0 (0)	0.573
Treatment in ED	72 (59.5)	50 (54.3)	22 (75.9)	0.04
Epinephrine	9 (7.4)	5 (5.4)	4 (13.8)	0.135
Corticosteroid	27 (22.3)	20 (21.7)	7 (24.1)	0.787
Antihistamines	16 (13.2)	8 (8.7)	8 (27.6)	0.009[c]
Nebulized β-Agonist	14 (11.6)	10 (10.9)	4 (13.8)	0.668
Oxygen supplement	2 (1.7)	2 (2.2)	0 (0)	0.423
Unclear	15 (12.4)	11 (12.0)	4 (13.8)	0.794
Hospitalization	3 (2.5)	2 (2.2)	1 (3.4)	0.700

Notes: [a]Home-treated rate was significantly higher in mild to moderate anaphylaxis (44.6% vs.20.7%, p=0.021); [b]oral histamine was more common in mild to moderate anaphylaxis among home treated reactions (31.5% vs.10.3%, p=0.024); [c]oral histamine was more common in severe anaphylaxis among ED treated reactions.(27.6% vs.8.7%, p=0.009).

showed that birch pollen sensitization was more common in severe anaphylaxis, we speculate was that the majority of patients (73%) with birch pollen allergy are likely to experience pollen-related food allergy,[14] and thus there may be a higher risk of anaphylaxis episodes triggered by a food allergen.

Based on the present study, recurrent urticaria was more common in children with severe anaphylaxis. According to the new grading system, allergic reaction is classified into five grades, from generalized urticaria, to hypotension, collapse, and loss of consciousness (ie, anaphylaxis).[22] It has been reported that wheat-induced anaphylaxis could manifest as a mild reaction, such as urticaria and angioedema.[23] Thus, recurrent urticaria and anaphylaxis may be two different degrees or phases of food allergy. Severe allergic reactions occur when potentially exacerbating co-factors exist, such as physical activity, use of aspirin and nonsteroidal anti-inflammatory drugs, and alcohol consumption. Certain co-factors are well documented to aggravate or precipitate wheat-induced anaphylaxis (WIA)/wheat-dependent exercise induced anaphylaxis (WDEIA).[24] Hence, the clinical progression of recurrent urticaria may be relevant for evaluating the risk of anaphylaxis among patients with pollen sensitization.

Foods were confirmed to be the most frequent trigger for anaphylaxis in the current study, which is consistent with other studies of anaphylaxis in children.[2] The most common food triggers were fruits/vegetables, which is in accordance with our previous study that demonstrated that fruits/vegetables were the most common food allergens in preschool-age children (35.9%) and school-age children (31.6%),[2] and other published data in China suggested that fruit/vegetables were the most common food triggers in children aged 4–9 years (59%).[9] In contrast, relatively lower rates of fruits/vegetables-induced anaphylaxis have been reported in studies from European countries. Alvarez-Perea et al[25] reported that 7% of Spanish children attending hospital for reported anaphylaxis had a confirmed allergy to fruits, and data from the European Anaphylaxis Registry also show that fruits are responsible for 5% of all causes of anaphylaxis to foods in children and adolescents.[26] Fruits/vegetable-induced anaphylaxis may result from PFAS due to cross-reactivity with a heat stable pollen allergen component.[27] In the current cohort, the most common fruit allergen causing anaphylaxis was peach, which is in line with a previous study from China,[15] and a nationwide survey conducted in Korea that showed that peach was the top pollen-related food trigger.[11] Nevertheless, kiwi is the top fruit trigger in the North America.[7] Sensitization patterns of cross-reactive allergens are related to pollen sensitization; thus, geographical distribution of pollen allergens and regional dietary habits influence plant-derived food trigger sensitization profiles and clinical symptoms. Severe or anaphylactic reactions to fruits and vegetables are more likely to occur due to lipid transfer proteins (LTP), originally described only in southern Mediterranean countries but more recently also recognized in Chinese population where it is related to sensitization to peach, tree nuts, peanuts, and also to pollens, such as plane tree and mugwort.[8,15,28]

Exercise was the most common factor for aggravating or triggering anaphylaxis in our study. This finding is consistent with that from a previous study on anaphylaxis in children and teenagers in Europe.[29] In our study, about 64% of exercise-induced anaphylaxis occurred during pollen season, especially in the autumn. In contrast, Gabrielli et al[7] revealed that severe anaphylactic reactions to fruits in a Canadian population were more likely to occur during the spring; the authors concluded that the increased risk in the spring may be related to higher pollen counts that would sensitize the immune system and reduce the reaction threshold. Given these data and the recognized cofactors of anaphylaxis, it would be worthwhile to advise patients with pollen allergy who have a known fruit/vegetable allergy to avoid exercise in association with food consumption. Previously described food-dependent exercise-induced anaphylaxis (FDEIA) is a rare subtype of anaphylaxis occurring after exposure to an offending food followed by physical activity, while both the implicated food and exercise, isolated, are tolerated independently.[30] Our present study showed that pollen-related fruits are the most common food triggers before exercise, which may be due to the cross-reactive allergen components such as LTP, which are thermostable and less susceptible to enzymatic degradation due to their compact, folded structure.[31] As mentioned above, allergic reactions to LTP tend to be more severe.[32] Moreover, according to Romano et al.[33] LTPs were the most frequent primary allergen (78%) in a group of Italian patients with FDEIA. However, wheat is the most commonly reported allergen; as the best-studied subtype of FDEIA,[34] recently published data have demonstrated that wheat anaphylaxis is highly dependent on the presence of co-factors (eg, exercise) and is less frequently associated with atopic diseases compared with other food allergies.[35] Unfortunately, although we speculated that the FDEIA cases in our study may be induced by LTPs, we did not conduct a component allergen test.

The risk factors for severe anaphylactic reactions in pollen sensitization individuals have not been reported to date. In our study, sensitization to birch and recurrent urticaria were more common in patients with severe anaphylaxis, indicating that these may be risk factors for severe reactions. A nationwide study in South Korea demonstrated that the sensitization to specific pollen (hazel, timothy and ragweed) and the presence of atopic dermatitis (AD) were the risk factors for anaphylaxis in PFAS.[36] Furthermore, the current study indicated that exercise, especially exercise during pollen season, was a co-factor or augmenting factor that triggered anaphylactic reactions dependently or independently of food allergens. Thus, if pollinosis patients have pollen-related food allergies, sIgE positive to birch and the presence of recurrent urticaria may be related to the development of severe anaphylaxis, and other risk factors, such as augmentation factors (pollen sensitization profile, exercise, pollen season, and atopy status), may increase the reaction severity.

In this cohort, there was under-use of epinephrine in the treatment, considering that only 7.4% of the patients received epinephrine in the emergency department. The finding is consistent with previously published studies in China,[2,9,37] and the low use of epinephrine demonstrates the need for education promoting the use of epinephrine in all cases of anaphylaxis. However, there is controversy regarding the need to prescribe epinephrine to patients with PFAS because it has been reported that only a minority of PFAS progress to anaphylaxis.[11] Although guidelines on epinephrine auto-injector (EAI) prescription remain controversial,[28] we suggest that children with a history of anaphylaxis should be prescribed EAI even if the diagnosis is PFAS.

This study had several limitations. The study was performed in a single center in north China; hence, our findings may not apply to the general population of China. A major limitation of the study was the lack of information about skin prick testing or specific IgE measurements to fruit and vegetable allergens to support assumptions about pollen cross-reactivity, and due to the limitation of allergen-specific IgE panel, in our cohort, sIgE level of only three common pollen (mugwort, ragweed and birch) were quantified by Phadia system (immunoCAP) in our cohort. Furthermore, the diagnosis of anaphylaxis was established on the basis of reported information, rather than laboratory testing and challenge tests.

Conclusion

Fruits/vegetables account for a substantial percentage of anaphylaxis cases in children with pollen sensitization. Exercise is the most common factor that aggravates or triggers anaphylaxis.

The suboptimal use of epinephrine highlights the need for educational programs promoting the use of epinephrine. Because severe anaphylaxis to plant-derived food could result from cross-reactivity to pollen, it is important to promote awareness among parents and caregivers regarding this increased risk in children with pollen sensitization.

Abbreviations

FDEIA, food-dependent exercise-induced anaphylaxis; LTP, lipid transfer proteins; EAI, epinephrine auto-injector; PFAS, pollen-food allergy syndrome; IgE, immunoglobulin E.

Data Sharing Statement

The data and materials are available from the corresponding authors based on reasonable requirement.

Ethics Approval and Informed Consent

This study has been performed in accordance with the principles stated in the Declaration of Helsinki, and the study protocol was approved by the Research and Ethics Board of Beijing Children's Hospital. (Approval number:2022-E-023-R) Because this study was based on the retrospective analysis of medical electronic record, the informed consent was deemed exempt by the Research and Ethics Board.

Consent for Publication

All authors have approved the manuscript and agree with its submission to the Journal of Asthma and Allergy.

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Disclosure

The authors report no conflicts of interest in this work.

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