Asian Pacific Journal of
Allergy and Immunology
APJAI

ORIGINAL ARTICLE

Characteristics of anaphylaxis from tertiary-care hospital in lower northern Thailand: A ten-year retrospective cross-sectional study

Suwannee Uthaisangsook,[1] Nichayada Hirunwattana,[1,3] Chayanis Kajornrojanaruk,[1,2] Nadda Padsee[1]

Abstract

Background: The prevalence and etiology of anaphylaxis vary based on geographic regions, study design, and definition used. Anaphylaxis leading to emergency department visits and hospitalizations has increased worldwide.

Objective: To explore the causes, clinical manifestations, management, outcomes, and onset time of anaphylaxis correlated with age groups and severity risk factors in lower northern Thailand, including the time from onset to medical attention, with the ultimate goal of optimizing healthcare practices in the region.

Methods: A cross-sectional retrospective analysis of medical records from patients with ICD-10 confirmed anaphylaxis was performed at Naresuan University Hospital between March 2011 and February 2021.

Results: We identified 439 anaphylaxis episodes in 381 patients within 10 years. The average annual occurrence rates of anaphylactic episodes were 25.0 per 100,000 outpatient and emergency department visits and 11.2 per 100,000 inpatient visits. Both pediatric and adult anaphylaxis events increased annually, from 13.3 (children: 20.5, adults: 12.4) in 2012 to 46.6 (children: 52.6, adults: 46.1) episodes per 100,000 visits in 2021. Peak incidence was observed in adolescents and young adults. Food was the most common trigger, with shrimp and fried insects being predominant. Risk factors for severe anaphylaxis were underlying cardiovascular diseases, drug triggers, and wheezing. Epinephrine was administered in 98.4% of all episodes. Although, there were no fatalities, only 11.4% of patients received prescriptions for self-injectable epinephrine.

Conclusion: The study underscores an increasing trend of anaphylaxis affecting both children and adults in lower northern Thailand, with shrimp and fried insects as common triggers.

Key words: Anaphylaxis, Thailand, trigger, risk factors, epinephrine

Citation:
Uthaisangsook, S., Hirunwattana, N., Kajornrojanaruk, C., Padsee, N. (0000). Characteristics of anaphylaxis from tertiary-care hospital in lower northern Thailand: A ten-year retrospective cross-sectional study. *Asian Pac J Allergy Immunol*, 00(0), 000-000. https://doi.org/10.12932/ap-010424-1831

Affiliations:
1 Department of Pediatrics, Faculty of Medicine, Naresuan University, Phitsanulok, Thailand
2 Department of Pediatrics, Faculty of Medicine, King Chulalongkorn Memorial Hospital, Bangkok, Thailand
3 Wetchakarunrasm Hospital, Bangkok, Thailand

Corresponding author:
Suwannee Uthaisangsook
Department of Pediatrics, Faculty of Medicine, Naresuan University, 99 Tha Pho, Mueang Phitsanulok District, Phitsanulok 65000, Thailand
E-mail: suwannee_u@yahoo.com

Introduction

Anaphylaxis is an acute, potentially life-threatening systemic hypersensitivity reaction characterized by diverse clinical manifestations, necessitating immediate recognition and medical intervention. Previous studies indicate that variations in anaphylaxis prevalence result from factors including geographical location, study design, and diagnostic criteria used. The lifetime prevalence ranges from 0.3% to 5.1%.[1,2] Globally, the incidence is estimated between 50 and 112 episodes per 100,000 person-years, with a pediatric incidence ranging from 1 to 761 per 100,000 person-years.[1-3]

The triggers of anaphylaxis exhibit geographical and age-related disparities, highlighting the importance of identifying causative factors based on individual patient histories and local epidemiological data.[4] Predominantly, food, insect venom, and drugs emerge as the most frequent causative agents worldwide,[4,5] with children often experiencing food-induced reactions, while adults commonly encounter anaphylaxis triggered by insect stings and medications.[5] Specifically, in children, eggs, cow's milk, wheat, and peanuts constitute the primary culprits of food-induced anaphylaxis,[4] whereas in adults, peanuts and tree nuts predominate in North America and Australia, and shellfish in Asian adults.[4] In Central Europe, peanuts, tree nuts, sesame seeds, wheat, and shellfish rank among the leading triggers.[4]

In Thailand, most Bangkok-based studies report anaphylaxis rates ranging from 49 to 652 episodes per 100,000 emergency visits between 2008 and 2011,[6-9] and 9.2 to 451 episodes per 100,000 admitted patients per year between 1999 and 2013.[10-12] Common food-induced anaphylaxis identified in these studies include seafood, shrimp, shellfish, crab,[6-8,12,13] with additional reports of reactions to fried insects.[8,13] Peanuts and nuts are less frequent triggers compared to Western countries.

While the overall fatality rate of anaphylaxis remains relatively stable (estimated at 0.03-0.51 per million people/year), both hospitalizations due to anaphylaxis and drug-related anaphylaxis fatalities have increased over the recent years, particularly in the United States and Australia.[4,14,15] Moreover, a similar published study revealed a 3.2-fold increase in emergency department visits for anaphylaxis from 2008 to 2016,[16] prompting heightened public awareness regarding the severity and prevention of this condition. A large US study identified older age, medication triggers, concomitant cardiovascular diseases, ACE inhibitor use, and prior emergency department visits or hospitalizations as risk factors for severe anaphylaxis.[17]

To optimize anaphylaxis management and prevention in lower northern Thailand, a comprehensive understanding of the local context is required. Existing surveys in Thailand have predominantly focused on large medical centers in Bangkok, with limited study timeframes,[6,7,10] and only one study conducted in Chiang Mai, the second-largest city in northern Thailand.[13] Our university hospital in Phitsanulok serves as a tertiary care and referral medical center for the less urbanized regions of lower northern Thailand, characterized by greater agricultural activity compared to the more industrial and commercial settings of Bangkok and Chiang Mai. Therefore, this study aimed to analyze the prevalence, etiology, clinical presentation, time of onset, the time from onset to medical attention, management, and outcomes of anaphylaxis cases at Naresuan University Hospital over a ten-year period, with data stratified by age group. Additionally, risk factors for severe anaphylaxis were also explored.

Methods

This retrospective cross-sectional study was conducted at Naresuan University Hospital, Phitsanulok, one of the largest university hospitals in lower northern Thailand. Electronic medical records of patients diagnosed with anaphylaxis (ICD-10 codes: T78.0 – anaphylactic shock due to adverse food reaction, T78.2 – anaphylactic shock unspecified, T80.5 – anaphylactic shock due to serum, T88.6 – anaphylactic shock due to drug adverse effect) between March 2011 and February 2021 were reviewed. The diagnosis of anaphylaxis was confirmed using the clinical criteria proposed by the second US National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network (NIAID/FAAN).[18] Patients diagnosed with anaphylaxis in the emergency department (ED), outpatient department, and inpatient stays were included.

Data extracted from medical records include patient demographics, underlying diseases, atopic status, previous allergic reactions, triggers, cofactors, anaphylaxis symptoms, time from allergen exposure to onset of symptoms, treatment, time to initiate epinephrine administration, outcomes, and allergy testing results. The severity of anaphylaxis was also evaluated, with criteria included any one of the following: hypotension, cardiovascular collapse, respiratory failure or cyanosis, and loss of consciousness.[13] Patients exhibiting severe symptoms group were categorized based on the presence of one or more of these characteristics. Hypotension was defined as systolic blood pressure < 70 mmHg in patients aged 1 month to 1 year; < 70 + (age in years × 2) mmHg in patients aged > 1 to 10 years; and < 90 mmHg in patients aged > 10 years. Cyanosis was considered if pulse oximetry saturation (SpO_2) was less than 95%. Patients under 16 years of age were classified as children.

This study was reviewed and approved by Naresuan University Institutional Review Board (NU-IRB), with NU-IRB ethics approval certification number P3-0097/2564. The NU-IRB Committee granted permission to conduct the study on patient medical records and waived the requirement of patient consent.

Statistics

We employed both descriptive and inferential statistics using the STATA software package, version 17.0, to analyze all data parameters. Categorical parameters were reported as frequency and percentage, while continuous parameters were expressed as median and interquartile range (IQR). To compare these data variables between children and adults, we utilized the t-test, chi-squared test, or Fisher's exact test as appropriate. To identify potential risk factors for severe anaphylaxis, a multivariable logistic regression analysis was conducted. Results are presented as odds ratio (OR) with 95% confidence interval (95% CI). A two-sided p-value < 0.05 was considered statistically significant.

Results

After reviewing electronic medical records coded with ICD-10 diagnoses for anaphylaxis at Naresuan University Hospital between March 2011 and February 2021, a total of 820 potential anaphylaxis episodes of all 715 consecutive patients were identified. Since the Hospital Medical Information System (MIS) was changed from fully paper-based medical documents to a partial electronic MIS containing both electronic and paper-based records, and due to a lack of medical document storage, some records of patients who had not visited the hospital for more than five years were removed. As a result, 264 medical documents (286 episodes, 36.9%), including seven inpatient episodes, could not be retrieved. Among 451 available medical documents (534 episodes), 50 medical records (75 episodes, 7.0%) had inadequate medical information, and 20 patients (20 episodes, 2.8%) were excluded for not meeting the clinical diagnostic criteria proposed by NIAID/FAAN.[18] The final analysis included 439 anaphylaxis episodes in 381 patients (including 8 inpatient episodes). The study flow diagram for medical records selection is presented in **figure 1**. Of these, 57 episodes (13%) involved children, and 382 (87%) involved adults.

During the 10-year study period, there were 3,273,779 combined outpatient, ED, and inpatient visits at Naresuan University Hospital. The average annual anaphylaxis occurrence rates were 24.4 episodes per 100,000 hospital visits, 25.0 episodes per 100,000 outpatient and ED visits, and 11.2 episodes per 100,000 inpatient visits. Both pediatric and adult anaphylaxis events increased annually, from a combined rate of 13.1 episodes (children 20.5, adults 12.4) per 100,000 in 2012 to 46.6 episodes (children 52.6, adults 46.1) per 100,000 in 2021 (**Figure 2**).

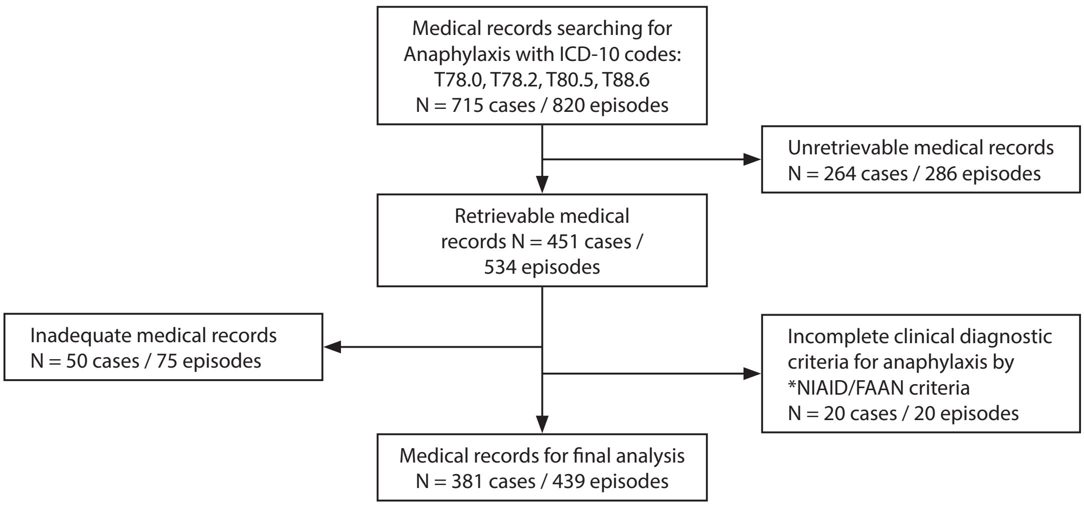

Figure 1. Study flow diagram for medical records selection.

*US National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network

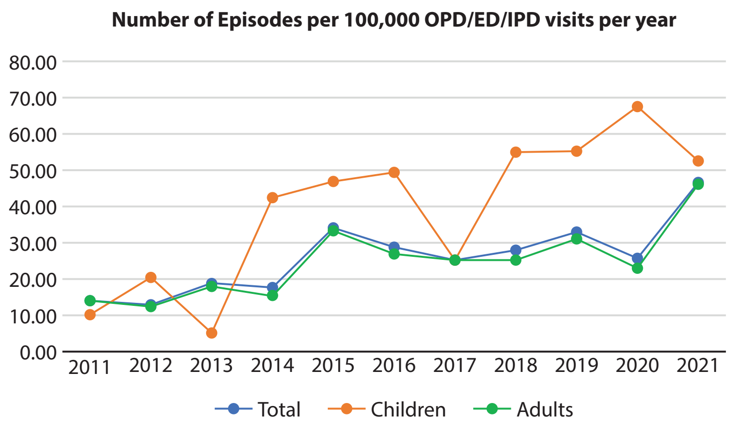

Figure 2. Number of anaphylaxis episodes per 100,000 outpatient, emergency, and inpatient visits per year from 2011–2021.

Regarding patient demographics, the highest incidence rate occurred in adolescent and young adult groups (ages 16-20 and 21-30 years old), with females predominating the older age group (age ≥ 16) and males among the younger age group (age < 15), particularly those under 5 years old (**Figure 3A**).

Table 1 summarizes the characteristics of the subjects. Children had a higher proportion of males (54.4%) compared to adults (38.7%). The median age (IQR) was 8 (4-13) years for children and 23 (20-43) years for adults. Atopic diseases, allergic rhinitis, and asthma were more prevalent in children than adults (29.8%, 17.5%, 19.3% vs 17.5%, 12.3%. 5.0% respectively). Conversely, adults had a higher prevalence of drug allergy and cardiovascular diseases (19.1%, 11.8%) than children (8.8%, 1.8%).

The etiologies of anaphylaxis are presented in **Table 2**. Food emerged as the most common anaphylaxis trigger (49% of all episodes), with a higher prevalence in children (57.9%) compared to adults (47.6%). This was followed by drugs (13.9%), insect stings (10.0%), and miscellaneous causes (2.3%). Notably, a significant proportion of all anaphylaxis events 24.8% had unknown or idiopathic triggers. Among food-related triggers, shrimp ranked as the most frequent trigger, accounting for 19.4% of all episodes, with divergent rates in children (26.3%) and adults (18.3%). Other significant food allergens included fried insects (7.5%), a local delicacy comprising silkworms, bamboo worms, crickets, and grasshoppers, and clams/mussels (3.4%). Ant eggs, another local food, were implicated in 3 cases (0.7%).

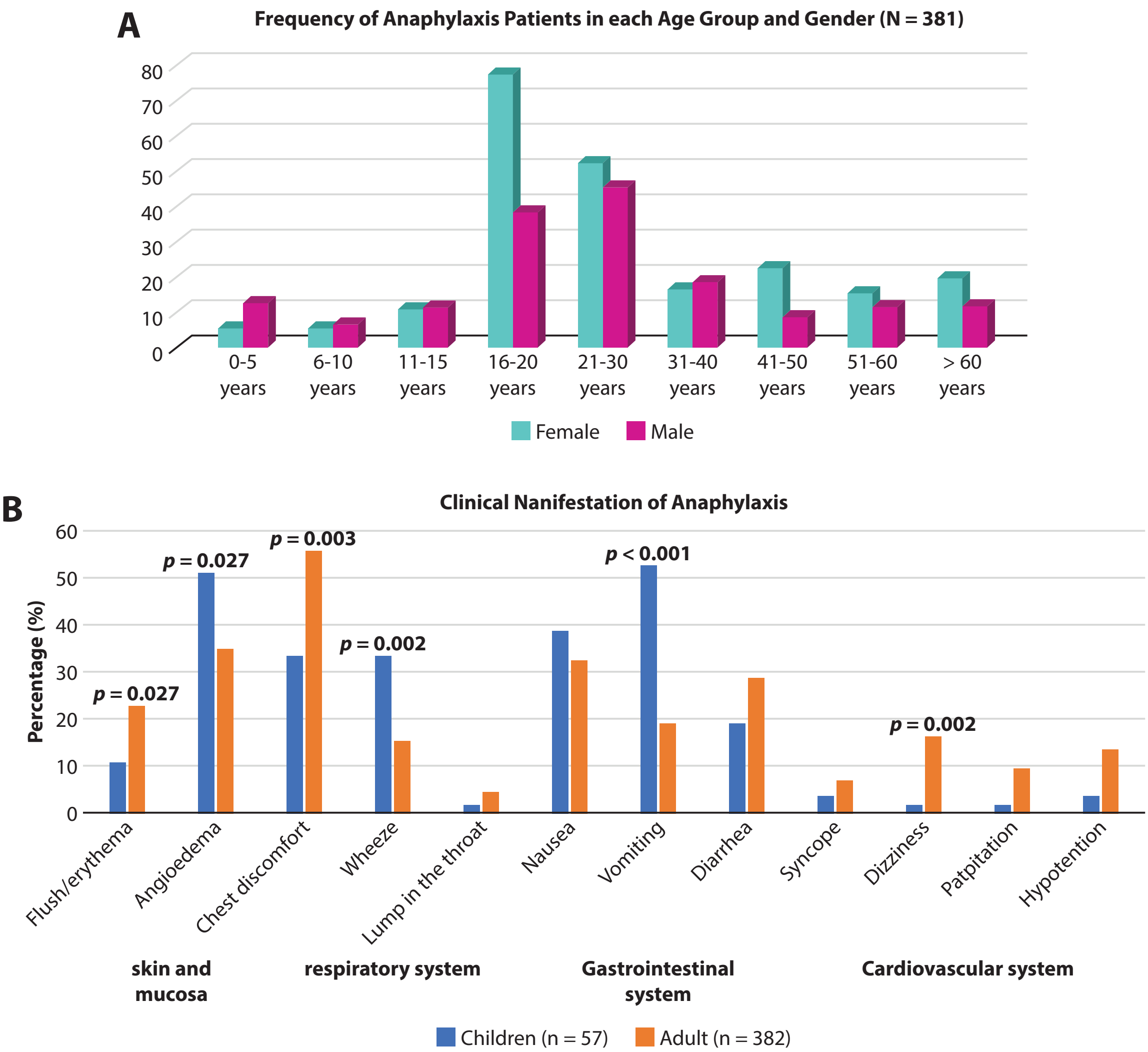

Figure 3. (A) Frequency of anaphylaxis patients in each age group and gender. (B) Differences in clinical manifestation of anaphylaxis between children and adults

Table 1. Characteristics of subjects; number of subjects (%).

	Total (n = 439)	Children (n = 57)	Adult (n = 382)
Sex: Male	179 (40.8)	31 (54.4)	148 (38.7)
Median age (year, IQR)	22 (19-37)	8 (4-13)	23 (20-43)
Atopic diseases	84 (19.1)	17 (29.8)	67 (17.5)
- Allergic rhinitis	57 (13.0)	10 (17.5)	47 (12.3)
- Allergic conjunctivitis	2 (0.5)	0	2 (0.5)
- Asthma	30 (6.8)	11 (19.3)	19 (5.0)
- Chronic urticaria	18 (4.1)	1 (1.75)	17 (4.5)
- Atopic dermatitis	7 (1.6)	2 (3.5)	5(1.3)
History of food allergy	137 (31.2)	20 (35.1)	117 (30.6)
History of insect sting allergy	15 (3.4)	2 (3.5)	13 (3.4)
History of drug allergy	78 (17.8)	5 (8.8)	73 (19.1)
Underlying cardiovascular disease	46 (10.5)	1 (1.8)	45 (11.8)
Previous history of anaphylaxis	86 (19.6)	11 (19.3)	75 (19.6)

Table 2. Causes of anaphylaxis; number of episodes (%).

	Total (n =439)	Children (n =57)	Adult (n =382)	*p*-value
Foods	215 (49.0)	33 (57.9)	182 (47.6)	0.158
- Shellfish				
Shrimp	85 (19.4)	15 (26.3)	70 (18.3)	0.154
Clams/Mussels	15 (3.4)	0	15 (3.9)	0.236
Squid	11 (2.5)	3 (5.3)	8 (2.1)	0.161
Crab	9 (2.1)	3 (5.3)	6 (1.6)	0.099
- Fried insects	33 (7.5)	6 (10.5)	27 (7.1)	0.415
- Unidentified seafood	12 (2.7)	0	12 (3.1)	0.379
- Wheat	7 (1.6)	3 (5.3)	4 (1.1)	0.050
- Fish	7 (1.6)	1 (1.8)	6 (1.6)	1.000
- Milk	4 (0.91)	2 (3.51)	2 (0.52)	0.084
- Egg	4 (0.91)	1 (1.8)	3 (0.8)	0.428
- Ant eggs	3 (0.7)	0	3 (0.8)	1.000
- Soy	1 (0.2)	0	1 (0.3)	1.000
- Other food	43 (9.8)	2 (3.5)	41 (10.7)	0.097
Insect sting	44 (10.0)	6 (10.5)	38 (10.0)	0.816
- Bees	16 (3.6)	1 (1.8)	15 (3.9)	0.706
- Vespid	5 (1.1)	2 (3.5)	3 (0.8)	0.128
- Wasp	3 (0.7)	1 (1.8)	2 (0.5)	0.342
- Ant	3 (0.7)	1 (1.8)	2 (0.5)	0.342
- Other insect sting	4 (0.9)	1 (1.8)	3 (0.8)	0.428
- Unknown insect sting	13 (3.0)	0	13 (3.4)	0.391

Table 2. (Continued)

	Total (n =439)	Children (n =57)	Adult (n =382)	*p*-value
Medication	61 (13.9)	4 (7.0)	57 (14.9)	0.149
- Antibiotic	19 (4.3)	0	19 (5.0)	0.153
- NSAIDS	16 (3.6)	0	16 (4.2)	0.244
- Radio contrast Media	7 (1.6)	1 (1.8)	6 (1.6)	1.000
- Acetaminophen	2 (0.5)	0	2 (0.5)	1.000
- Antiepileptic drug	1 (0.2)	0	1 (0.3)	1.000
- Other medicines	20 (4.6)	3 (5.3)	17 (4.5)	0.734
Other triggers	10 (2.3)	3 (5.3)	7 (1.8)	0.128
Idiopathic/Unknown trigger	109 (24.8)	11 (19.3)	98 (25.7)	0.329
Cofactor	39 (8.9)	2 (3.5)	37 (9.7)	0.207

Antibiotics were the most frequent medication trigger for anaphylaxis (4.3% of all episodes), followed by NSAIDs (3.6%) and radiocontrast media (RCM) (1.6%). Bee stings were the most common insect trigger (3.6%), followed by unidentified insect stings (3.0%) and vespid stings (1.1%). Exercise was the most prevalent cofactor (3.4%). Overall, there were no significant differences in etiology between children and adults.

The clinical manifestations of anaphylaxis are illustrated in **Table 3**. Skin and mucosal symptoms were the predominant clinical features found in 97.3% of all 439 episodes. The second most common manifestation was respiratory symptoms (76.3%), followed by gastrointestinal symptoms (67.2%), cardiovascular symptoms (33.7%), ocular symptoms (5.0%), neurological symptoms (2.7%), and other symptoms (6.6%). Itching was the most frequent skin/mucosal symptom (60.8%), followed by urticaria (44.2%), angioedema (36.9%), maculopapular rash (30.1%), and flushing (21.2%). Skin flushing or erythema was significantly more prevalent in adults than in children, while angioedema was less predominant in adults compared to children (22.8% vs 10.5%, *p*-value 0.037; 34.8% vs 50.9%, *p*-value = 0.027, respectively).

Table 3. Clinical features, related time, management and outcome of anaphylaxis; number of episodes (%).

	Total (n = 439)	Children (n = 57)	Adult (n = 382)	*p*-value
1. Clinical manifestation				
- Skin and Mucosal symptoms	427(97.3)	54 (94.8)	373 (97.6)	0.195
- Itch	267 (60.8)	31 (54.4)	236 (61.8)	0.310
- Flush/erythema	93 (21.2)	6 (10.5)	87 (22.8)	0.037
- Urticaria	194 (44.2)	27 (47.4)	167 (43.7)	0.669
- Angioedema	162 (36.9)	29 (50.9)	133 (34.8)	0.027
- Maculopapular rash	132 (30.1)	14 (24.6)	118 (30.9)	0.358
- Respiratory symptoms	335 (76.3)	37 (64.9)	298 (78.0)	0.044
- Chest discomfort	231 (52.6)	19 (33.3)	212 (55.5)	0.003
- Dyspnea	156 (35.5)	14 (24.6)	142 (37.2)	0.075
- Wheeze	78 (17.8)	19 (33.3)	59 (15.5)	0.002
- Cough	16 (3.6)	2 (3.5)	14 (3.7)	1.000
- Rhinorrhea	35 (8.0)	8 (14.0)	27 (7.1)	0.109
- Nasal congestion	35 (8.0)	5 (8.8)	30 (7.9)	0.794
- Cyanosis (SpO_2 < 92%)	29 (6.6)	3 (5.3)	26 (6.8)	1.000
- Lump in the throat	18 (4.1)	1 (1.8)	17 (4.5)	0.490

Table 3. (Continued)

	Total (n = 439)	Children (n = 57)	Adult (n = 382)	*p*-value
- Eye symptoms	22 (5.0)	3 (5.3)	19 (5.0)	1.000
- Itchy eye	5 (1.1)	2 (3.5)	3 (0.8)	0.128
- Tearing	5 (1.1)	2 (3.5)	3 (0.8)	0.128
- Injected conjunctiva	16 (3.6)	2 (3.5)	14 (3.7)	1.000
- Gastrointestinal symptoms	295 (67.2)	40 (70.2)	255 (66.8)	0.653
- Nausea	145 (33.0)	22 (38.6)	123 (32.2)	0.366
- Vomiting	102 (23.2)	30 (52.6)	72 (18.9)	<0.001
- Diarrhea	121 (27.6)	11 (19.3)	110 (28.8)	0.154
- Abdominal pain	179 (40.8)	22 (38.6)	157 (41.1)	0.774
- Cardiovascular symptoms	148 (33.7)	8 (14.0)	140 (36.7)	<0.001
- Syncope	29 (6.6)	2 (3.5)	27 (7.0)	0.404
- Dizziness	63 (14.4)	1 (1.8)	62 (16.2)	0.002
- Palpitation	37 (8.4)	1 (1.8)	36 (9.4)	0.069
- Arrhythmia	6 (1.4)	2 (3.5)	4 (1.1)	0.176
- Hypotension	53(12.1)	2 (3.5)	51 (13.4)	0.300
- Tachycardia	31 (7.1)	3 (5.3)	28 (7.3)	0.783
- Neurological symptoms	12 (2.7)	0	12 (3.1)	0.379
- Anxiety	3 (0.7)	0	3 (0.8)	1.000
- Drowsiness/Stupor	2 (0.5)	0	2 (0.5)	1.000
- Unconsciousness	6 (1.4)	0	6 (1.6)	1.000
- Other symptoms	29 (6.6)	2 (3.5)	27 (7.0)	0.404
2. Related time				
- Time from exposure to onset of symptoms				
- < 5 min	110 (33.3)	7 (16.3)	103 (35.9)	0.014
- 6-30 min	72 (21.8)	16 (37.2)	56 (19.5)	0.016
- 31-60 min	52 (15.8)	7 (16.3)	45 (15.7)	1.000
- > 60 min	96 (29.1)	13 (30.2)	83 (28.9)	0.858
-Time from onset of symptoms to first dose of epinephrine (minutes, median (IQR))	70 (35-186)	95 (45-189)	70 (34-186)	0.227
- Time from ER arrival to first dose of epinephrine (minutes, median (IQR))	10 (5-15)	10.5 (5-24)	9 (5-15)	0.223
3. Management				
- Epinephrine used prior to hospital arrival	10 (2.3)	4 (7.0)	6 (1.6)	0.030
- Epinephrine treatment	432 (98.4)	54 (94.7)	378 (99.0)	0.050
- IM	432 (100)	54 (100)	378 (100)	
- 1 dose	418 (96.8)	51 (94.4)	367 (97.1)	0.399
- > 1 dose	14 (3.3)	3 (5.7)	11 (2.9)	0.396

Table 3. (Continued)

	Total (n = 439)	Children (n = 57)	Adult (n = 382)	*p*-value
- Antihistamine	438 (99.8)	57 (100)	381 (99.7)	1.000
- Systemic corticosteroid	432 (98.4)	55 (96.5)	377 (98.7)	0.227
- Nebulized beta-agonist	69 (15.7)	18 (31.6)	51 (13.4)	0.001
- Oxygen supplement	55 (12.5)	4 (7.0)	51 (13.4)	0.205
- IV fluid	75 (17.1)	15 (26.3)	60 (15.7)	0.058
- Intubation	1 (0.2)	0	1 (0.3)	1.000
- CPR	1 (0.2)	0	1 (0.3)	1.000
4. Outcome				
- Biphasic reaction	4 (0.9)	1 (1.8)	3 (0.8)	0.432
- Admitted in hospital	101 (23.0)	47 (82.5)	54 (14.1)	<0.001
- Discharged from ER	334 (76.1)	10 (17.5)	324 (84.8)	<0.001
- Death	0	0	0	-
- prescription of epinephrine after discharge	50 (11.4)	29 (50.9)	21 (5.5)	<0.001
5. Severe anaphylaxis	123 (28.0)	12 (21.1)	111 (29.1)	0.268
6. Recurrent anaphylaxis	58 (13.2)	8 (14.0)	50 (13.1)	0.834

Among respiratory symptoms, the most prevalent symptoms were chest discomfort (52.6%), dyspnea (35.5%), wheeze (17.8%), rhinorrhea (8.0%), nasal congestion (8.0%), cyanosis (6.6%), lump in the throat (4.1%), and cough (3.6%). Adults experienced significantly more chest discomfort but less wheezing than children (55.5% vs 33.3%, *p*-value 0.003; 15.5% vs 33.3%, *p*-value 0.002 respectively). Conjunctival injection (3.6%) was the most common ocular symptom.

Abdominal pain (40.8%) was the most prominent gastrointestinal symptom, followed by nausea (33.0%), diarrhea (27.6%), and vomiting (23.2%). Children experienced significantly more vomiting than adults (52.6%, 18.9%, *p*-value < 0.005). Dizziness and hypotension were frequent cardiovascular symptoms (14.4%, 12.1%), both significantly more noticeable in adults than in children. Subsequent cardiovascular symptoms were palpitation (8.4%), tachycardia (7.1%), and syncope (6.6%).

Onset of symptoms after exposure to suspected triggers occurred within 5 minutes in most adults (35.9%, 103/287 episodes) and between 6-30 minutes in most children (37.2%, 16/43 episodes). Overall, symptoms commenced within 30 minutes in 182 of 330 anaphylactic episodes (55.1%). The median time (IQR) of epinephrine injection after ED arrival was 10 (5-15) minutes, with no delay observed. However, the median time (IQR) lapse between onset of symptoms and epinephrine injection was 70 (35-186) minutes. Notably, there was no significant difference in these time periods between children and adults (**Table 3**).

Almost all anaphylactic episodes were treated with intramuscular epinephrine injection (98.2%). Antihistamines and systemic glucocorticoids were also administered in almost all cases (99.8%, 98.4% respectively). Other notable interventions included intravenous fluids (17.1%), oxygen supplementation (12.5%), and nebulized beta-agonists (15.7%), which were given more frequently in children than in adults. Only one patient required intubation and cardiopulmonary resuscitation.

In this survey, the prevalence of biphasic reaction was low (0.9%), and the hospitalization rate was 23%, with children exhibiting a significantly higher rate than adults (82.5%, 14.1%, *p*-value < 0.001). Although no fatalities were recorded, severe anaphylaxis and recurrent anaphylaxis were observed in 28% and 13.2% of all episodes respectively (**Table 3**). Among 381 patients, 46 (12.1%) underwent allergy tests, including skin prick tests (39, 10.2%), specific IgE tests (11, 2.9%), serum tryptase tests (4, 1.1%), and oral drug challenge tests (1, 0.003%). Among these, suspected allergens were identified in 34 patients (8.9% of all anaphylactic patients) through skin prick tests (30), specific IgE tests (5), or oral food challenge tests (1). Only 11.4% of all anaphylaxis cases were prescribed prophylactic self-injectable epinephrine, with 98% receiving pre-filled syringe epinephrine and one patient receiving auto-injected epinephrine.

Table 4. Risk factors for severe anaphylaxis.

	Univariable Odds ratio (95%CI)	Multivariable Odds ratio (95%CI)	*p*-value
Gender	0.99 (0.65-1.52)	0.96 (0.57-1.60)	0.864
History of allergic diseases	0.77 (0.44-1.33)	0.79 (0.36-1.75)	0.564
History of asthma	0.77 (0.32-1.84)	0.81 (0.23-2.91)	0.747
Underlying cardiovascular disease	2.93 (1.58-5.45)	2.38 (1.14-4.96)	0.021
Age ≥ 16 years of age	1.54 (0.78-3.01)	1.64 (0.69-3.88)	0.259
Trigger/cause			
- Insect sting	1	1	
- Food	1.20 (0.56-2.58)	1.77 (0.74-4.23)	0.202
- Drug	2.7 (1.13-6.43)	3.04 (1.14-8.09)	0.026
Symptoms: wheezing	1.46 (0.87-2.46)	1.94 (1.01-3.72)	0.047
Time from exposure to onset ≤ 30 minutes	1.38 (0.85-2.26)	1.45 (0.86-2.43)	0.161

Out of 439 episodes, 123 were classified as severe anaphylaxis, with 12 episodes (21.1%) occurring in children and 111 episodes in adults (29.1%). Multivariable logistic regression analysis identified the following significant predisposing factors for severe anaphylaxis (**Table 4**): underlying cardiovascular disease (OR 2.38, 95%CI 1.14-4.96, p = 0.021), drug trigger (OR 3.04, 95% CI 1.14-8.09, p = 0.026), and wheezing (OR 1.94, 95% CI 1.01-3.72, p = 0.047). History of allergic diseases, asthma and rapid onset within 30 minutes were not statistically significant risk factors in our study.

Discussion

This study described the prevalence, etiology, clinical features, treatment, and outcomes of anaphylaxis at Naresuan University Hospital in lower northern Thailand over a 10-year period, a region for which such data had not been previously reported. The average anaphylaxis rate in our hospital within this period (2011 - 2021) was 25.0 episodes per 100,000 outpatient and ED visits per year, and 11.2 per 100,000 admissions per year, which were lower than the global incidence rates and those reported in Bangkok University Hospitals.[6-12] However, our study demonstrated a higher anaphylaxis rate than that reported in Chiang Mai University Hospital, the largest hospital in northern Thailand, with a rate of 3.9 episodes per 100,000 outpatient and emergency visits per year from 2007 to 2016.[13] This discrepancy may indicate a higher prevalence of anaphylaxis in lower northern Thailand compared to northern Thailand, although it is lower than in Bangkok and globally. These variations align with previous studies suggesting geographic and methodological influences on anaphylaxis prevalence.[4] The rising anaphylaxis trend in our population mirrors global increases in both ED visits and hospitalizations.[14-16] Similar to northern Thailand survey,[19] we observed male predominance in younger age groups and female predominance over the age of 16. For diagnosing anaphylaxis, Thai medical practitioners including our study utilize the clinical diagnostic criteria recommended by the 2006 NIAID/FAAN criteria[18] and the Thai clinical practice guideline for anaphylaxis.[20] The NIAID/FAAN criteria which has been widely adopted and validated, demonstrated high sensitivity (95%) as established by the EAACI guideline[21] and the Joint Task Force on the 2023 Practice Parameters update from the American Academy of Allergy, Asthma & Immunology (AAAAI) and the American College of Allergy, Asthma, and Immunology (ACAAI).[22] The high sensitivity of this clinical criteria probably lead to early detection of anaphylaxis and early epinephrine treatment in our study. Recently, the World Allergy Organization (WAO) 2020 guideline has modified the 3 clinical criteria from 2006 NIAID/FAAN to 2 diagnostic criteria to simplify the criteria.[4] The updated 2023 Anaphylaxis Practice Parameters discussed some notable differences between these two diagnostic criteria, mostly related to the timing, associated exposure, or the specific organ systems involved.[22] For example, WAO 2020 criteria 2 includes isolated respiratory symptoms (bronchospasm or laryngeal involvement) after exposure to a known or highly probable allergen in addition to isolated hypotension with no typical skin involvement.[22] Australasian Society of Clinical Immunology and Allergy (ASCIA) also has implemented WAO 2020 criteria in ASCIA 2023 guideline.[23] Further validation of the WAO 2020 criteria to determine the clinical utility will be beneficial.[22] Our study identified merely 4 patients (1.1%) who had a blood test for tryptase, which is understandable because, in our hospital setting, the serum tryptase must be sent to an external laboratory, and clinical diagnosis for patients with anaphylaxis is critical. On the other hand, the most recent updated 2023 anaphylaxis practice parameter has recommended that patients with a history of recurrent, idiopathic, or severe anaphylaxis should be measured for baseline serum tryptase, and suggest obtaining an acute-phase tryptase level ideally within 2 hours after the symptoms with a second tryptase measurement later as baseline for comparison.[22]

Consistent with global[3] and Thai studies,[6-8,13] food was the most common causative allergen in our anaphylaxis survey, with shrimp as the primary trigger in both Thai children and adults.[6,7,13] Unlike the global data,[3] we did not observe cow's milk predominance in younger children, likely due to small sample size of infants (4/49 cases) in our study. Interestingly, among identified food triggers, consumption of fried insects ranked as the second most prevalent trigger, exceeding rates in most Thai surveys[6,10,12,13] and are not reported in global studies.[2,3] This may reflect the popularity of this local food in our region, suggesting increased risks of exposure and allergic sensitization. Our findings and others in northern[13] and suburban Bangkok[7,8] highlight the growing significance of this trend in our region and some other regions of Thailand.

Surprisingly, drug-induced anaphylaxis was lower in our survey (13.9%) compared to global data[2,3] and other regions of Thailand.[6-8,13] This lower prevalence may be attributed to the limited number of inpatients in our study (8 patients), which could impact drug-related anaphylaxis rates. These rates are typically higher in inpatient settings (32-48%).[10-12] Antibiotics and NSAIDs were the two most common drug triggers, aligning with other studies.[2,3,8,12,13]

The incidence of anaphylaxis triggered by insect stings in lower northern Thailand (10%) from our survey confirmed that insect sting induced anaphylaxis in Thailand is less common than in many other countries worldwide.[3,5,24] Nonetheless, our result was much lower than expected and lower than that reported in northern Thailand (23.1%), possibly indicating genetic variation within the population.

Overall, our findings on clinical manifestations largely align with previous studies,[6,7,13] but there were some manifestations that were significantly different between adults and children in the present study. Angioedema, wheezing, and vomiting were significantly more prevalent in children, whereas flushing, chest discomfort, dizziness, and hypotension were more frequently reported in adults. The higher prevalence of underlying asthma among children compared to adults likely contributed to the prominence of wheezing in this group. Similarly, the elevated incidence of cardiovascular diseases in adults may explain the increased occurrence of hypotension in adult cases of anaphylaxis compared to children.

The high rate of intramuscular epinephrine use (98.4%) aligns with treatment guidelines[5,21] and exceeds reported rates in China (25%),[25] Korea (30%),[26] Iran (10.8%),[27] and Turkey (51%),[28] likely due to physician awareness in academic university hospitals.[9,11-13] However, the low frequency of anaphylactic subjects (11.4%) receiving prophylactic self-injectable epinephrine after discharge, compared to studies in the USA,[29-31] may account for the high recurrence rates of anaphylaxis observed in our study (13.2%). This highlights the need for improved management in post anaphylaxis follow-up care, including greater involvement of allergists, as only 12.1% of our patients received allergy testing. Moreover, healthcare providers and patients/guardians need to establish plans to prevent the recurrent events, and prescribe self-injectable epinephrine.

Several potential risk factors for severe anaphylaxis identified in previous studies, including cardiovascular comorbidities, lung disease, asthma, drug and venom triggers, older age (≥ 65 years), male sex,[17,32,33] and rapid onset of symptoms[19,34] were corroborated by our findings. However, coexistent asthma, venom allergy, older age, male sex, or rapid onset were not found to be significant risk factors in our study. Remarkably, wheezing symptoms were revealed as a risk factor in our observed severe episodes.

The 2020 anaphylaxis practice parameter has identified a more severe anaphylaxis and/or the need for repeated doses of epinephrine to treat anaphylaxis as risk factors for biphasic anaphylaxis.[5] Although 28.2% of all episodes were severe, no deaths were reported, and only 0.9% developed biphasic reactions in our study. Few episodes (3.3%) required repeated dose of epinephrine in our study, which probably explained our low biphasic reaction, supporting the report from 2020 practice parameters.[5] In addition, the low rate of biphasic anaphylaxis likely correlated with the high rate of epinephrine injection (98.4%), and early administration of epinephrine in the emergency room, with a median time (IQR) of 10 (5-15) minutes. Furthermore, high rates of systemic glucocorticoid and antihistamine treatment in our study could prevent biphasic reaction nonetheless the updated systemic review in 2020 practice parameters recommended against administering glucocorticoid or antihistamine to prevent biphasic anaphylaxis.[5] The high frequency of hospitalization in our pediatric patients (82.5%) was due to available inpatient capacity at the hospital and for close observation of biphasic reactions.

The limitations of this study include incomplete medical records and unretrievable medical documents due to the retrospective design used to acquire 10-year hospital medical records and storage issues of both electronic and paper-based medical documents. These limitations could influence the interpretation of the results. Furthermore, the screening of patients' medical records using ICD-10 codes for anaphylaxis may exclude few patients who had anaphylaxis but were diagnosed with ICD-10 codes: L50 – urticaria, T38.3 – angioedema, and T45 – drug poisoning. Another study limitation is that the medical records included in this study covers the 10-year period from March 2011 to February 2021 because of the prior ethics approval in 2021, which could have an impact on the most recent results. Nonetheless, our study encompassed a relatively large population compared to other studies in Thailand, making the outcome still beneficial. Future epidemiological surveys may benefit from cohort or prospective study designs to improve data collection.

Conclusion

This study reveals an increasing trend of anaphylaxis affecting both children and adults in lower northern Thailand, with shrimp and fried insects as common triggers. Drug triggers, underlying cardiovascular diseases, and wheezing were significant risk factors for severe anaphylaxis. Improvements in post-anaphylaxis follow-up care are needed, including involvement of allergists, increased allergy testing, collaboration between healthcare providers and patients/guardians, and expanded self-injectable epinephrine prescription.

Acknowledgements

The authors express their sincere gratitude to Professor Dr. Jayanton Patumanond, M.D., M.P.H., D.Sc. and the Clinical Epidemiology Unit of the Faculty of Medicine, Naresuan University, Phitsanulok, Thailand for their valuable guidance in statistical analysis.

The study was financially supported by the Faculty of Medicine, Naresuan University, Phitsanulok, Thailand.

Conflict of Interest

The authors have no conflict of interest to disclose.

Contributors

- Concept and Design: Suwannee Uthaisangsook, Chayanis Kajornrojanaruk
- Data collection: Suwannee Uthaisangsook, Chayanis Kajornrojanaruk, Nichayada Hirunwattana, Nadda Padsee
- Analysis and Interpretation: Suwannee Uthaisangsook, Nadda Padsee
- Writing the Article: Suwannee Uthaisangsook.
- All authors have read and approved the final manuscript.

References

1. Wang Y, Allen KJ, Suaini NHA, McWilliam V, Peters RL, Koplin JJ. The global incidence and prevalence of anaphylaxis in children in the general population: A systematic review. Allergy. 2019;74:1063-80.
2. Tejedor Alonso MA, Moro Moro M, Mugica Garcia MV. Epidemiology of anaphylaxis. Clin Exp Allergy. 2015;45:1027-39.
3. Motosue MS, Li JT, Campbell RL. Anaphylaxis: Epidemiology and Differential Diagnosis. Immunol Allergy Clin North Am. 2022;42:13-25.
4. Cardona V, Ansotegui IJ, Ebisawa M, El-Gamal Y, Fernandez Rivas M, Fineman S, et al. World allergy organization anaphylaxis guidance 2020. World Allergy Organ J. 2020;13:100472.
5. Shaker MS, Wallace DV, Golden DBK, Oppenheimer J, Bernstein JA, Campbell RL, et al. Anaphylaxis-a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis. J Allergy Clin Immun. 2020;145:1082-123.
6. Poachanukoon O, Paopairochanakorn C. Incidence of anaphylaxis in the emergency department: A 1-year study in a University Hospital. Asian Pac J Allergy. 2006;24:111-6.
7. Piromrat K, Chinratanapisit S, Trathong S. Anaphylaxis in an Emergency Department: A 2-Year Study in a Tertiary-Care Hospital. Asian Pac J Allergy. 2008;26:121-8.
8. Lertnawapan R, Maek-a-nantawat W. Anaphylaxis and biphasic phase in Thailand: 4-year observation. Allergol Int. 2011;60:283-9.
9. Sricharoen P, Sittichanbuncha Y, Wibulpolprasert A, Srabongkosh E, Sawanyawisuth K. What clinical factors are associated with biphasic anaphylaxis in Thai adult patients? Asian Pac J Allergy Immunol. 2015; 33:8-13.
10. Jirapongsananuruk O, Bunsawansong W, Piyaphanee N, Visitsunthorn N, Thongngarm T, Vichyanond P. Features of patients with anaphylaxis admitted to a university hospital. Ann Allerg Asthma Im. 2007;98:157-62.
11. Manuyakorn W, Benjaponpitak S, Kamchaisatian W, Vilaiyuk S, Sasisakulporn C, Jotikasthira W. Pediatric anaphylaxis: triggers, clinical features, and treatment in a tertiary-care hospital. Asian Pac J Allergy Immunol. 2015;33:281-8.
12. Techapornroong M, Akrawinthawong K, Cheungpasitporn W, Ruxrungtham K. Anaphylaxis: a ten years inpatient retrospective study. Asian Pac J Allergy. 2010;28:262-9.
13. Lao-Araya M, Rangkakulnuwat P. Anaphylaxis: A ten years retrospective data from Northern Thailand. Allergy. 2018;73:280-.
14. Turner PJ, Campbell DE, Motosue MS, Campbell RL. Global Trends in Anaphylaxis Epidemiology and Clinical Implications. J Aller Cl Imm-Pract. 2020;8:1169-76.
15. Motosue MS, Bellolio MF, Van Houten HK, Shah ND, Campbell RL. Increasing Emergency Department Visits for Anaphylaxis, 2005-2014. J Allergy Clin Immunol Pract. 2017;5:171-5.e3.
16. Michelson KA, Dribin TE, Vyles D, Neuman MI. Trends in emergency care for anaphylaxis. J Allergy Clin Immunol Pract. 2020;8:767-8.e2.
17. Clark S, Wei W, Rudders SA, Camargo CA Jr. Risk factors for severe anaphylaxis in patients receiving anaphylaxis treatment in US emergency departments and hospitals. J Allergy Clin Immunol. 2014;134:1125-30.
18. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF Jr, Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol. 2006;117:391-7.
19. Rangkakulnuwat P, Sutham K, Lao-Araya M. Anaphylaxis: Ten-year retrospective study from a tertiary-care hospital in Asia. Asian Pac J Allergy Immunol. 2020;38:31-9.
20. The Allergy, Asthma, And Immunology Association of Thailand [Internet]. Bangkok: The Allergy, Asthma, And Immunology Association of Thailand; c2015-2019 [cited 2024 May 24].Clinical Practice Guidelines for Anaphylaxis 2017. Available from: https://www.allergy.or.th/2016/pdf/Thai_CPG_Anaphylaxis_2017_Full_version.pdf.
21. Muraro A, Worm M, Alviani C, Cardona V, DunnGalvin A, Garvey LH, et al. EAACI guidelines: Anaphylaxis (2021 update). Allergy. 2022;77: 357-77.
22. Golden DBK, Wang J, Waserman S, Akin C, Campbell RL, Ellis AK, et al. Anaphylaxis: A 2023 practice parameter update. Ann Allergy Asthma Immunol. 2024;132:124-76.
23. ASCIA [Internet]. New South Wales: Australasian society of clinical immunology and allergy; c2024 [cited 2024 May 22]. ASCIA Guidelines: Acute Management of Anaphylaxis. Available from: https://www.allergy.org.au/images/ASCIA_HP_Guidelines_Acute_Management_Anaphylaxis_2023.pdf.
24. Wood RA, Camargo CA Jr, Lieberman P, Sampson HA, Schwartz LB, Zitt M, et al. Anaphylaxis in America: the prevalence and characteristics of anaphylaxis in the United States. J Allergy Clin Immunol. 2014;133: 461-7.
25. Jiang N, Yin J, Wen L, Li H. Characteristics of Anaphylaxis in 907 Chinese Patients Referred to a Tertiary Allergy Center: A Retrospective Study of 1,952 Episodes. Allergy Asthma Immunol Res. 2016;8:353-61.
26. Yoon L, Kim BR, Lee JY, Kim K, Kim YM, Kim SH, et al. Clinical features of anaphylaxis according to age in a single university hospital in Korea. Asian Pac J Allergy Immunol. 2017;35:96-101.
27. Nabavi M, Lavavpour M, Arshi S, Bemanian MH, Esmaeilzadeh H, Molatefi R, et al. Characteristics, Etiology and Treatment of Pediatric and Adult Anaphylaxis in Iran. Iran J Allergy Asthma Immunol. 2017;16: 480-7.
28. Orhan F, Canitez Y, Bakirtas A, Yilmaz O, Boz AB, Can D, et al. Anaphylaxis in Turkish children: a multi-centre, retrospective, case study. Clin Exp Allergy. 2011;41:1767-76.
29. Robinson M, Greenhawt M, Stukus DR. Factors associated with epinephrine administration for anaphylaxis in children before arrival to the emergency department. Ann Allergy Asthma Immunol. 2017;119: 164-9.
30. Curtis C, Stukus D, Scherzer R. Epinephrine preparedness in pediatric patients with food allergy: an ideal time for change. Ann Allergy Asthma Immunol. 2014;112:560-2.

31. Prince BT, Mikhail I, Stukus DR. Underuse of epinephrine for the treatment of anaphylaxis: missed opportunities. J Asthma Allergy. 2018;11:143-51.
32. Worm M, Francuzik W, Renaudin JM, Bilo MB, Cardona V, Scherer Hofmeier K, et al. Factors increasing the risk for a severe reaction in anaphylaxis: An analysis of data from The European Anaphylaxis Registry. Allergy. 2018;73:1322-30.
33. Motosue MS, Bellolio MF, Van Houten HK, Shah ND, Campbell RL. Risk factors for severe anaphylaxis in the United States. Ann Allergy Asthma Immunol. 2017;119:356-61.e2.
34. Olabarri M, Vazquez P, Gonzalez-Posada A, Sanz N, Gonzalez-Peris S, Diez N, et al. Risk Factors for Severe Anaphylaxis in Children. J Pediatr. 2020;225:193-7.e5.