
Features of patients with anaphylaxis admitted to a university hospital

Orathai Jirapongsananuruk, MD*; Wicharn Bunsawansong, MD*; Nuntawan Piyaphanee, MD*; Nualanong Visitsunthorn, MD*; Torpong Thongngarm, MD†; and Pakit Vichyanond, MD*

Background: Anaphylaxis in hospitalized patients has been infrequently reviewed. There are few studies of anaphylaxis from Asian countries.

Objective: To describe the clinical characteristics of patients with anaphylaxis admitted to Siriraj Hospital.

Methods: The medical records of 101 patients admitted with clinical anaphylaxis between January 1, 1999, and December 31, 2004, were reviewed. Data were analyzed using the χ^2 test.

Results: The annual occurrence of anaphylaxis increased from 9.16 per 100,000 admitted persons in 1999 to 55.45 per 100,000 admitted persons in 2004. The case fatality rate was 0.19 per 100,000 admitted persons. The mean $\pm$ SD age was 23.73 ± 21.84 years. Males experienced more anaphylaxis than females in pediatric patients and vice versa in adult patients. Biphasic anaphylaxis was found in 7% of pediatric and 2% of adult patients. Anaphylaxis occurred in the hospital in 37% of patients. Involved systems were cutaneous (86%), respiratory (80%), cardiovascular (52%), and oral and gastrointestinal (36%). Identifiable causes were drugs (50%), foods (24%), idiopathic (15%), and insect stings/bites (11%). Epinephrine was given to 77% of the patients.

Conclusions: We report the clinical characteristics of patients with anaphylaxis admitted to a university hospital. Knowing the clinical features will raise physician awareness of this condition.

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INTRODUCTION

Characterizing anaphylaxis would increase physician awareness and lead to proper diagnosis and prompt management. Anaphylaxis in hospitalized patients, mostly from drugs and foods, is not an uncommon condition. However, most anaphylaxis studies reported anaphylaxis that occurred outside the hospital. Anaphylaxis remains poorly described internationally. Clinical data of anaphylaxis in Asian countries are rarely available. We sought to study the clinical characteristic of patients with anaphylaxis admitted to the inpatient department (IPD) of Siriraj Hospital, Mahidol University. The hospital is Thailand's biggest university hospital, with 3,000 beds and 80,000 admissions per year.

MATERIALS AND METHODS

Medical Record Review

Medical records of all IPD admissions between January 1, 1999, and December 31, 2004, were accessed using the *International Statistical Classification of Diseases, 10th Revision (ICD-10)*. The ICD-10 codes used to search the medical records were as follow: T78.0, anaphylactic shock due to adverse food reaction; T78.2, anaphylactic shock, unspecified; T78.3, angioneurotic edema, laryngeal edema, Quincke

edema, urticaria-larynx; T80.5, anaphylactic shock due to serum; T88.6, anaphylactic shock due to adverse effect of correct drug of medicament properly administered; T63.2, venom of scorpion; T63.4, venom of other arthropods, insect bite or sting, venomous; T38.3, angioedema; L50.0, allergic urticaria; L50.9, urticaria, unspecified; J38.4, edema of larynx exclude laryngitis, croup; J46 and R11, asthma and vomiting; J46 and R55, asthma and syncope; R06.2 and R11, wheezing and vomiting; R06.2 and R55, wheezing and syncope; T38.3 and R11, angioedema and vomiting; T38.3 and R55, angioedema and syncope; R06.2 and T38.3, wheezing and angioedema; and J46 and T38.3, asthma and angioedema. A total of 228 records were recruited using the previously listed ICD-10 codes. They were individually reviewed by 2 of us (W.B. and N.P.), and the definition of anaphylaxis was applied. One hundred one records met the criteria for anaphylaxis and were included in this study.

Definition of Anaphylaxis

In this study, the term *anaphylaxis* refers to a severe, life-threatening generalized or systemic hypersensitivity reaction as suggested by the World Allergy Organization.¹ Definition of anaphylaxis was identified by symptoms and signs of generalized mast cell–mediator release plus mucocutaneous, oral or gastrointestinal, respiratory, or cardiovascular system involvement.² To classify an event as anaphylaxis, we required 1 symptom of generalized mediator release, such as flushing; pruritus or paresthesia of the lips, axilla, hands, or feet; general pruritus; urticaria or angioedema; lip tingling or paresthesia; and conjunctivitis or chemosis. In addition to 1

* Division of Allergy and Immunology, Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.

† Division of Allergy and Immunology, Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.

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symptom of generalized mediator release, we required at least 1 of the following additional symptoms: (1) involving the oral and gastrointestinal system: oral mucosal pruritus; intraoral angioedema of buccal mucosa, tongue, palate, or oropharynx; or nausea, emesis, dysphagia, abdominal cramps, or diarrhea; (2) involving the respiratory system: rhinitis, stridor, cough, hoarseness, aphonia, tightness in the throat, dyspnea, wheezing, hypopharyngeal or laryngeal edema, or cyanosis; or (3) involving the cardiovascular system: chest pain, arrhythmia, hypotension, presyncope, syncope, tachycardia, bradycardia, orthostasis, seizures, or shock.

Data Collection and Analysis

Data were collected on the case record form and were analyzed using χ^2 tests. Annual occurrence was calculated by using the number of episodes of anaphylaxis in the IPD that year in the numerator and the number of total patients in the IPD that year in the denominator, multiplied by 100,000. Annual incidence was calculated by using the number of new patients with anaphylaxis in the IPD that year in the numerator and the number of total patients in the IPD that year in the denominator, multiplied by 100,000. The case fatality rate was calculated by using the number of patients who died of anaphylaxis in the IPD between January 1, 1999, and December 31, 2004, in the numerator and the number of total patients in the IPD in the same period in the denominator, multiplied by 100,000. The χ^2 test for trend was used to analyze the trend of annual occurrence of anaphylaxis. Data analysis was performed using a software program (SPSS for Window version 11; SPSS Inc, Chicago, IL).

RESULTS

Characteristics of the Patients

One hundred one medical records of all IPD admissions met the criteria for the diagnosis of anaphylaxis. Annual episodes of anaphylaxis were calculated as rate of occurrence per 100,000 admitted persons (Fig 1). The annual occurrence of anaphylaxis increased from 9.16 per 100,000 admitted persons in 1999 to 55.45 per 100,000 admitted persons in 2004. Overall, there was a significant increasing trend of annual occurrence of anaphylaxis from 1999 to 2004 ($P = .04$). The annual incidence and occurrence of anaphylaxis were similar except in 2004. In that year, the occurrence of anaphylaxis was 55.45 per 100,000 admitted persons, and the incidence of anaphylaxis was 42.93 per 100,000 admitted persons because there was 1 patient with multiple drug allergies who had 8 episodes of anaphylaxis. Between 1999 and 2004, there was 1 fatal case, and the case fatality rate during the 6-year period was 0.19 per 100,000 admitted persons.

Fifty-three patients (52%) were males, with a male-female ratio of 1.1:1. Fifty-four patients were in the pediatric age range (≤ 15 years old) and 47 were in the adult age range (> 15 years old). The mean $\pm$ SD age was 23.7 ± 21.8 years (range, 2.8 months to 81.3 years). The distribution of sex in the pediatric and adult groups is shown in Figure 2. In the pediatric group, boys experienced more anaphylaxis than

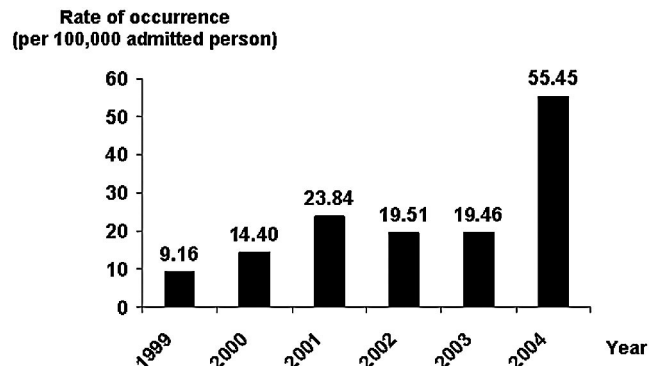


Figure 1. Annual occurrence of anaphylaxis per 100,000 admitted persons, which was calculated by using the number of episodes of anaphylaxis in the inpatient department of Siriraj Hospital that year in the numerator and the number of total patients in the same inpatient department that year in the denominator, multiplied by 100,000. Overall, there was a significant increasing trend of annual occurrence of anaphylaxis from 1999 to 2004 ($P = .04$).

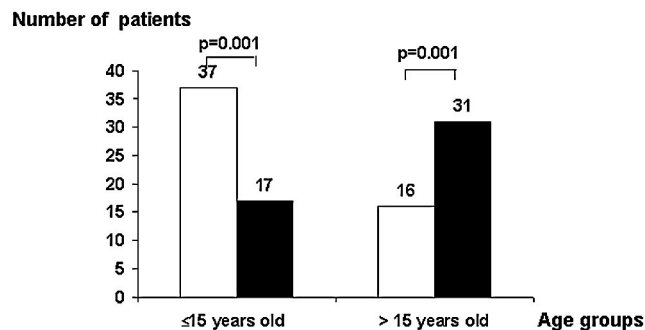


Figure 2. Distribution of sex in the pediatric and adult groups. White bars represent males; black bars, females. In the pediatric group, boys experienced more anaphylaxis than girls. In contrast, males experienced less anaphylaxis than females in the adult group ($P = .001$).

girls (odds ratio [OR], 1.917, 95% confidence interval [CI], 1.294–3.003; $P = .001$). In contrast, males experienced less anaphylaxis than females in the adult group (OR, 0.467; 95% CI, 0.295–0.740; $P = .001$). Eighty-two (81%), 10 (10%), and 9 (9%) patients were admitted on their first, second, and more than second episodes, respectively. Biphasic anaphylaxis was found in 4 children (7% of pediatric patients) and 1 adult (2% of adult patients).

Symptoms and Signs of Anaphylaxis

The presenting symptoms and signs of anaphylaxis are given in Table 1. The most commonly involved system was cutaneous (86%), followed by respiratory (80%), cardiovascular (52%), and oral and gastrointestinal (36%). Presenting symptoms were not different between adult and pediatric patients (data not shown). Initial symptoms and signs were most commonly found in the cutaneous system (63%), followed by the respiratory (18%), cardiovascular (12%), and oral and gastrointestinal (7%) systems. Fourteen patients had no cutaneous symptoms, and these patients had significantly more

Table 1. Symptoms and Signs of Anaphylaxis in 101 Study Patients

Symptom or sign	Patients, No.
Cutaneous system	87
Urticaria/angioedema	79
Conjunctivitis/chemosis	22
General pruritus	22
Flushing	12
Pruritus or paresthesia of the lips, axilla, hand, or feet	10
Respiratory system	81
Wheezing	43
Dyspnea	41
Cough	18
Cyanosis	12
Rhinitis	11
Throat tightness	10
Stridor	9
Hoarseness	2
Hypopharyngeal or laryngeal edema	2
Aphonia	1
Cardiovascular system	53
Hypotension	38
Presyncope	16
Chest pain	11
Syncope	11
Tachycardia	10
Shock	3
Orthostasis	2
Seizures	1
Bradycardia	0
Arrhythmia	0
Oral and gastrointestinal system	36
Emesis	25
Nausea	14
Abdominal cramps	12
Intraoral angioedema of buccal mucosa, tongue, palate, or oropharynx	7
Diarrhea	6
Dysphagia	2
Oral mucosal pruritus	1

cardiovascular system involvement (13/14, 93%) than the group with cutaneous symptoms (40/87, 46%; OR, 2.020; 95% CI, 1.542–2.646; $P = .003$).

Time of Onset and Place of Exposure

The most common time of onset after exposure to inciting agents was less than 30 minutes (50%), followed by more than 60 minutes (32%), 30 to 60 minutes (10%), and unknown time of onset (9%). Time of onset was not related to symptoms and outcome of treatment (data not shown). The occurrence of anaphylaxis in each month or season of the year did not differ significantly (data not shown).

Overall, 37% of the patients developed anaphylaxis in the hospital. The places outside the hospital where anaphylaxis occurred were homes (53%), schools and offices (4%), gardens (2%), restaurants (1%), and others (3%).

History of Atopy and Other Diseases

Fifty-three patients (52%) had a previous history of atopy, and some patients had more than 1 allergic disease. The most common allergic disease was asthma (26%), followed by allergic rhinitis (20%), food allergy (16%), drug allergy (16%), insect allergy (11%), atopic dermatitis (3%), and allergic conjunctivitis (3%). There were 40% of patients who were nonatopic and 8% of unknown atopic history.

Thirty-one patients (31%) had underlying diseases other than atopic diseases, and some patients had more than 1 underlying disease. Some of these patients were admitted to the hospital for their underlying diseases before the onset of anaphylaxis. The most common underlying diseases were malignancy (11%), followed by cardiovascular diseases (7%), neuromuscular diseases (6%), urinary tract diseases (6%), endocrine and metabolic diseases (5%), chronic respiratory diseases (2%), hematologic diseases (2%), chronic hepatobiliary diseases (1%), acquired immunodeficiency diseases (1%), Down syndrome (1%), and systemic lupus erythematosus (1%).

Causes of Anaphylaxis

The causes of anaphylaxis are given in Table 2. The most common causes of anaphylaxis were drugs, followed by foods, unidentified causes, and insect stings/bites. The most common drugs causing anaphylaxis were antibiotics, which were mainly penicillins and cephalosporins. The most common foods causing anaphylaxis were seafood, followed by wheat. The most common insect stings/bites causing anaphylaxis were fire ants, followed by wasps. Causes of anaphylaxis in pediatric and adult patients are shown in Figure 3. Adult patients had significantly more drug-induced anaphylaxis than pediatric patients (OR, 6.927; 95% CI, 2.879–16.669; $P = .001$). In contrast, adult patients had significantly less idiopathic anaphylaxis than pediatric patients (OR, 0.140; 95% CI, 0.030–0.659; $P = .01$). Causes of biphasic anaphylaxis were drugs in 2 patients, unidentified causes in 2 patients, and seafood in 1 patient.

Drugs were found to be significantly more common causes of in-hospital than out-of-hospital anaphylaxis (32% vs 19%; OR, 15.158; 95% CI, 5.125–44.831; $P = .001$). In contrast, foods, insect stings/bites, and unidentified causes were found to be significantly less common causes of in-hospital than out-of-hospital anaphylaxis (foods: 4% vs 20%; OR, 0.267; 95% CI, 0.083–0.855; $P = .04$; insect stings/bites: 0% vs 11%; OR, 0.589; 95% CI, 0.496–0.700; $P = .02$; and unidentified causes: 1% vs 14%; OR, 0.099; 95% CI, 0.012–0.789; $P = .02$). The causes of anaphylaxis in atopic and nonatopic patients were compared, and there was no significant difference (data not shown).

Treatment of Anaphylaxis and Outcomes

The medications used to treat anaphylaxis are given in Table 3. The most commonly used medications were antihistamines, followed by corticosteroids. Epinephrine was given to 78 patients (77%). There was no report of epinephrine self-

Table 2. Causes of Anaphylaxis in 101 Study Patients

Cause of anaphylaxis	Patients, No.
Drugs	51
Antibiotics	21
Penicillin groups	9
Amoxicillin	5
Penicillin	4
Cephalosporin groups	7
Ceftriaxone	4
Cefotaxime	1
Ceftazidime	1
Cefazolin	1
Sulfa groups	2
Quinolone groups	2
Erythromycin	1
Radiocontrast media	7
Allergen immunotherapy	7
Chemotherapy	5
Nonsteroidal anti-inflammatory drugs	4
Intravenous immunoglobulin	1
Hydrochlorothiazide	1
10% Cocaine	1
Iron-sucrose	1
Amifostine	1
Unidentified drugs	2
Foods	24
Seafood	11
Shrimp	6
Crab	3
Mollusk	1
Squid	1
Wheat	2
Wheat-dependent exercise-induced anaphylaxis	1
Milk	1
Fried insects	1
Freshwater prawn	1
Freshwater fished bread	1
Freshwater fish maw	1
Unidentified foods	5
Unidentified causes	15
Insect stings/bites	11
Fire ants	6
Wasps	3
Centipedes	1
Rasps	1

injection. Most patients received epinephrine more than 30 minutes after the onset of anaphylaxis (49%), followed by within 30 minutes (27%) and unknown timing (1%). Twenty-three patients (23%) did not receive epinephrine. Five of these patients had hypotension and received dopamine infusion. Eighteen patients (18%) did not receive either epinephrine or dopamine owing to mild symptoms. Four patients received both epinephrine and dopamine because of severe hypotension or shock.

Mean $\pm$ SD length of hospital stay was 2.64 ± 1.17 days. Most patients who required more than 3 days in the hospital had underlying diseases and had been treated in the hospital

Number of patients

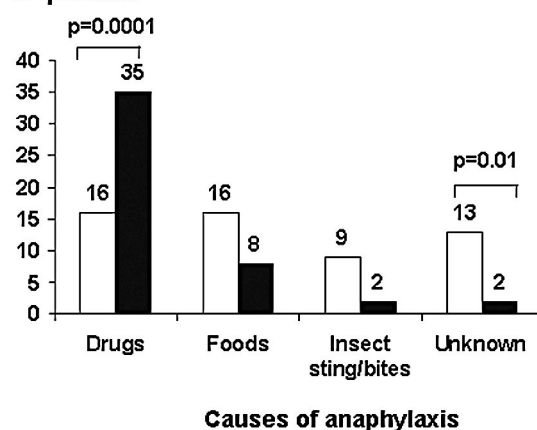


Figure 3. Causes of anaphylaxis in the pediatric and adult groups. White bars represent the pediatric group (≤ 15 years of age); black bars, the adult group (> 15 years of age). Adult patients had significantly more drug-induced anaphylaxis than pediatric patients ($P = .001$). In contrast, adult patients had significantly less idiopathic anaphylaxis than pediatric patients ($P = .01$).

Table 3. Medications Used to Treat Anaphylaxis

Medications	Patients, No.
Antihistamine (H_1 and/or H_2 blocker)	93
Corticosteroids	83
Intravenous fluid	81
Epinephrine	78
Inhaled β_2 -agonist	39
Dopamine	9
Oxygen therapy	5
Sodium bicarbonate	1

before the occurrence of anaphylaxis. Mean length of stay did not differ significantly in the groups with different symptoms and signs, places of exposure, or timing of epinephrine injection (data not shown). Twelve patients (12%) were admitted to the intensive care unit. Seven patients were intubated. Timing of epinephrine injection did not significantly relate to intensive care unit admission (data not shown). One patient died. He was a 42-year-old man with an unknown atopic or other underlying disease history. He developed anaphylactic shock after receiving a nonsteroidal anti-inflammatory drug for arthralgia. The epinephrine was given at unknown timing. He was intubated and died within 24 hours.

DISCUSSION

Awareness of anaphylaxis features and causative triggers is important for prompt diagnosis and management. Data regarding anaphylaxis in the admitted patients were infrequently reported despite frequent exposure to antigens such as drugs and foods in the hospital. Limited information regarding anaphylaxis is available from Asian countries, which might have unique features owing to distinct culture. The

World Allergy Organization reported the occurrence of anaphylaxis in different countries in Asia. The prevalence of anaphylaxis ranged from 300 to 350 episodes per annum for a population of 100 million in Japan, 3,000 episodes per annum for a population of 1.2 billion in China, and 0.1% of the population in Korea.³ Despite these numbers, the clinical characteristics of anaphylaxis in these countries are rarely available.

We studied the clinical characteristic of patients with anaphylaxis admitted to the IPD, Siriraj Hospital, which is the largest university hospital in Thailand. The mean number of IPD admissions ranged from 76,000 in 1999 to 96,000 in 2004. Overall, the annual occurrence of anaphylaxis significantly increased from 1999 to 2004, ranging from 9.16 per 100,000 admitted persons in 1999 to 55.45 per 100,000 admitted persons in 2004 (Fig 1). The rising trend of anaphylaxis occurrence followed a rising trend of other allergic diseases, such as asthma and allergic rhinitis, in Thailand.⁴ In the United Kingdom, the rising trend in admissions for anaphylaxis, along with other allergic diseases, was also observed from 1990 to 2001.⁵ Another explanation for the increasing occurrence of anaphylaxis in this study is the increasing reports of anaphylaxis. Most epidemiologic studies of anaphylaxis demonstrated that the occurrence of anaphylaxis was underreported and that by increasing physician awareness, the number might be close to the real occurrence. In recent years, there have been increasing publications of anaphylaxis in the medical literature and anaphylaxis education at Mahidol University, which might have affected physician awareness at Siriraj Hospital. The case fatality rate during the 6-year study was 0.19 per 100,000 admitted persons, which was lower than the number reported in a previous study,² which showed that the fatality rate during the 5-year period was 0.65%. The case fatality rate might be underreported because we did not include patients in the emergency department (ED) or outpatient department (OPD) who died before admission.

In the present study, males and females experienced anaphylaxis equally, which was supported by a previous study.² Interestingly, the number of males with anaphylaxis was higher than that of females in the pediatric group and vice versa in the adult group (Fig 2). This finding was confirmed by the study by Mertes et al,⁶ which showed that patients with anaphylaxis aged 0 to 20 years were predominantly male and those aged 20 to 90 years were predominantly female. In the present study, most patients were admitted on their first episode of anaphylaxis. Biphasic anaphylaxis was found in 7% of the pediatric group, which was close to the number reported previously (6%).⁷ However, biphasic anaphylaxis was found in only 2% of the adult group. This is in contrast to a previous study,⁸ which showed that the rate of biphasic anaphylaxis was 20% in adults.

The most common symptoms and signs in the present study were in the cutaneous system, followed by the respiratory, cardiovascular, and oral and gastrointestinal systems. These findings are supported by a previous study,⁹ which

consisted of data from 1,865 patients from 14 studies. We found that patients without cutaneous symptoms were more likely to develop cardiovascular symptoms. This may be due to the lack of awareness of anaphylaxis in patients without cutaneous symptoms, leading to a delay in diagnosis and management.

Previous studies showed that drugs^{10–12} or foods^{13,14} were the leading causes of anaphylaxis. The present data demonstrate that drugs are the most common causes of anaphylaxis (50%) (Table 2). Antibiotics, in particular, penicillins and cephalosporins, were the leading drugs, causing 40% of the drug-induced anaphylaxis. This was supported by previous studies.^{15,16} Some patients with underlying diseases were admitted to the hospital before the onset of anaphylaxis. These patients developed anaphylaxis after receiving antibiotics, chemotherapy, or other drugs. Therefore, drugs were the major cause of anaphylaxis in hospital. The second most common cause of anaphylaxis in the present study was foods. Seafood was the most common cause of food-induced anaphylaxis (46%). This finding was supported by studies from Asia.^{14,17} Besides, we found 3 other patients who had anaphylaxis from freshwater prawn, freshwater fish bread, and fish maw. Fried insects, a native food of the northeastern part of Thailand, was the cause of anaphylaxis in 1 patient. This cause of anaphylaxis was rarely reported by other studies because it is not a common food in other areas of the world. In contrast, peanuts and nuts, the major causes of food-induced anaphylaxis in Western countries,^{13,16} were not found to be causes of anaphylaxis in these patients. We also did not identify any cases of allergy to bird's nest, which was the major cause of food-induced anaphylaxis in Singapore.¹⁸ Beside drugs and foods, insect stings/bites and idiopathic anaphylaxis were found in 11% and 15% of patients, respectively, comparable with a previous study.¹² In the present study, we postulated that adult patients had more drug-induced anaphylaxis than children owing to higher drug exposure (Fig 3). Adult patients had less idiopathic anaphylaxis than children owing to their ability to provide more detailed information of allergen exposure.

In the present study, 92% of patients received antihistamines, which was close to the study by Smit et al (95%).¹⁴ However, 77% of the present patients received epinephrine, which was slightly higher than the study from Singapore by Smit et al (67%).¹⁴ This difference was probably because one third of the anaphylaxis in the study occurred in the hospital. None of the patients reported epinephrine self-injection. However, overall they had favorable outcomes, with a mean $\pm$ SD length of stay of 2.64 ± 1.17 days. Adrenaline kits are not available in Thailand owing to their high cost. Most physicians draw the appropriate dose of adrenaline into a tuberculin syringe and teach the patient to use it when anaphylaxis occurs. The patient is instructed to come to the hospital to change the adrenaline every month.

In conclusion, we report the epidemiologic features of anaphylaxis in the IPD setting, which included patients who developed anaphylaxis while they were admitted to the hos-

pital for their underlying diseases and patients who were admitted from the ED or OPD owing to anaphylaxis. As previously mentioned, the case fatality rate might be under-reported because we did not include patients in the ED or OPD who died before admission. Also, patients in the ED or OPD who were discharged after a period of observation or treatment for anaphylaxis were not included. The retrospective medical record review may have limitation because of the data registry in the *ICD-10* system. The prospective study of epidemiologic features of anaphylaxis in the ED, OPD, and IPD in Asian countries needs to be explored in the future.

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Requests for reprints should be addressed to:
 Orathai Jirapongsananuruk, MD
 Division of Allergy and Immunology
 Department of Pediatrics
 Siriraj Hospital
 Mahidol University
 2 Prannok Rd
 Bangkoknoi
 Bangkok 10700, Thailand
 E-mail: siojr@mahidol.ac.th or jirapongo@yahoo.com