

# Original Article



# Anaphylaxis diagnosis and management in the Emergency Department of a tertiary hospital in the Philippines

Michelle Joy De Vera (D), 1,2,\* and Iris Conela Tagaro (D)

<sup>1</sup>The Medical City Hospital, Pasig, the Philippines <sup>2</sup>Ateneo De Manila University School of Medicine and Public Health, Pasig, the Philippines



Received: Jul 22, 2019 Accepted: Jan 9, 2020

#### \*Correspondence to

#### Michelle Joy De Vera

The Medical City Hospital, Medical Arts Tower 1119, Ortigas Ave., Pasig City, the Philippines. Tel: +63-920-950-2029,

E-mail: mbdevera@themedicalcity.com deveramj@gmail.com

Copyright © 2020. Asia Pacific Association of Allergy, Asthma and Clinical Immunology. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ORCID iDs

Michelle Joy De Vera https://orcid.org/0000-0002-3247-6690 Iris Conela Tagaro https://orcid.org/0000-0002-5685-9354

#### **Conflict of Interest**

The authors have no financial conflicts of interest.

#### **Author Contributions**

Conceptualization: Michelle Joy De Vera. Data curation: Iris Conela Tagaro. Formal analysis: Iris Conela Tagaro. Methodology: Michelle Joy De Vera. Project administration: Iris Conela Tagaro. Supervision: Michelle Joy De Vera. Visualization: Michelle Joy De Vera. Writing - original draft: Iris Conela Tagaro. Writing - review & editing: Michelle Joy De Vera.

# **ABSTRACT**

**Background:** In the Emergency Department (ED), diagnosis and management of anaphylaxis are challenging with at least 50% of anaphylaxis episodes misdiagnosed when the diagnostic criteria of current guidelines are not used.

**Objective:** Objective of our study was to assess anaphylaxis diagnosis and management in patients presenting to the ED.

**Methods:** Retrospective chart review conducted on patients presenting to The Medical City Hospital ED, the Philippines from 2013–2015 was done. Cases were identified based on International Statistical Classification of Diseases, 10th revision coding for either anaphylaxis or other allergic related diagnosis. Cases fitting the definition of anaphylaxis as identified by the National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network (NIAID/FAAN) were included. Data collected included demographics, signs and symptoms, triggers and management.

**Results:** A total of 105 cases were evaluated. Incidence of anaphylaxis for the 3-year study period was 0.03%. Of the 105 cases, 35 (33%) were diagnosed as "urticaria" or "hypersensitivity reaction" despite fulfilling the NIAID/FAAN anaphylaxis criteria. There was a significant difference in epinephrine administration between those given the diagnosis of anaphylaxis versus misdiagnosed cases (61 [87%] vs. 12 [34%],  $\chi^2 = 30.77$ , p < 0.01); and a significant difference in time interval from arrival at the ED to epinephrine administration, with those diagnosed as anaphylaxis (48%) receiving epinephrine within 10 minutes, versus  $\geq$  60 minutes for most of the misdiagnosed group ( $\chi^2 = 52.97$ , p < 0.01).

**Conclusion:** Despite current guidelines, anaphylaxis is still misdiagnosed in the ED. Having an ED diagnosis of anaphylaxis significantly increases the likelihood of epinephrine administration, and at a shorter time interval.

Keywords: Anaphylaxis; Epinephrine; Emergency Department

https://apallergy.org



# INTRODUCTION

Anaphylaxis is now universally defined as a serious allergic reaction that is rapid in onset and can cause death [1]. It is a medical emergency affecting more people in different parts of the world, with overall mortality risk estimated at 1%. In the 2015 updates on epidemiology of anaphylaxis, the Word Allergy Organization (WAO) reported that hospitalizations due to anaphylaxis have been increasing [1-3].

Several studies have attempted to establish the true incidence of anaphylaxis in the Emergency Department (ED). Previously, the absence of a universal definition of anaphylaxis leading to variations in the interpretation and then underreporting and miscoding, made research on this disease difficult and inaccurate. In July 2005, the National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network (NIAID/FAAN) created a universally accepted definition and criteria for diagnosis and guidelines on the management of anaphylaxis [1]. These clinical criteria for the diagnosis of anaphylaxis have been validated in ED studies in children, teenagers, and adults as having high sensitivity (96.7%), reasonable specificity (82.4%), and a high negative predictive value (98%) [1, 4, 5].

In the ED, diagnosis and management of anaphylaxis remains challenging because symptoms are nonspecific, may resemble other conditions, and appears and progresses rapidly after exposure to a trigger [1]. There has been no known laboratory test which can confirm or rule out diagnosis of anaphylaxis, which could then promptly aid in the decision making on treatment upon arrival of a patient at the ED. The diagnosis of anaphylaxis thus largely relies upon the history and physical examination of the attending health professional [6]. It has been estimated that at least 50% of anaphylaxis episodes are misdiagnosed in the ED when the diagnostic criteria of current guidelines are not used [7].

The objective of the present study was to determine the incidence of anaphylaxis in the ED of a tertiary care hospital in the Philippines as identified by the NIAID/FAAN Criteria, and describe characteristics of these anaphylaxis cases, their management and outcomes.

## MATERIALS AND METHODS

## Study design

This study was a retrospective descriptive research, using chart review to identify and describe cases of anaphylaxis seen at the ED of The Medical City Hospital, a tertiary hospital in a major city in the Philippines.

Purposive sampling and complete enumeration of all cases of anaphylaxis identified through the hospital electronic records was done. All records of patients seen at ED from January, 2013 to December, 2015 with specific International Statistical Classification of Diseases, 10th revision (ICD-10) codes including (1) anaphylactic shock due to adverse food reaction T78.0, (2) anaphylactic shock, unspecified T78.2, (3) angioneurotic edema T78.3, (4) allergic reaction, not otherwise specified, hypersensitivity not otherwise specified T78.4, (5) anaphylactic shock due to adverse effect of correct drug or medicament properly administered T78.6, (6) allergic urticaria L50.0, (7) idiopathic urticaria L50.1, (8) urticaria unspecified L50.9, and (9) generalized skin eruption due to drug and medicaments L27.0, were reviewed.



The study was approved by the Institutional Review Board of The Medical City Hospital (approval number: GCS Ped 2016-013).

# Study population

The 2 authors reviewed together all the charts identified. Study population included all pediatric (age < 18 years) and adult (age  $\ge$  18 years) cases of anaphylaxis seen at the ED from January 2013 to December 2015, who satisfied the 2005 NIAID/FAAN clinical criteria for the diagnosis of anaphylaxis, regardless of the initial diagnosis assigned to them in the ED report. The 2005 NIAID/FAAN clinical criteria were used as this was the criteria included in the ED manual of the hospital at the time the study was done. These identified cases of anaphylaxis were divided into 2 groups: (1) diagnosed as anaphylaxis or (2) not diagnosed as anaphylaxis/other allergy-related diagnosis at ED.

We recorded demographic data, clinical symptoms, treatment received, triggers suspected by the patient and the ED physician, outcome of the anaphylactic episode, and the final diagnosis.

Patients who did not satisfy the NIAID/FAAN criteria for diagnosing anaphylaxis were excluded from the study.

The number of patients admitted daily to the ED was also recorded.

## Statistical analysis

Descriptive statistics used in this study were the following: frequency, percentage, mean and range. Chi-square was used to determine whether epinephrine administration and time interval of administration from time of arrival at ED were dependent on the diagnosis, and whether diagnosis was dependent on specific clinical features.

## RESULTS

# Incidence of anaphylaxis

Out of the 344,823 pediatric and adult patients seen at the ED from January 2013 to December 2015, a total of 105 cases of anaphylaxis were identified using the NIAID/FAAN criteria. There was only one readmitted patient due to anaphylaxis; the second episode occurring 1 year after. Thus, the study gathered 105 cases of anaphylaxis in 104 patients. Incidence rate for the 3-year study period was 0.03% or 0.34 episodes per 1,000 ED visit.

Out of 105 cases, 66.7% were diagnosed as anaphylaxis, while 33.3% were diagnosed as other allergy-related disease: "hypersensitivity reaction" (18.1%) or "urticaria" (15.2%). All patients diagnosed as anaphylaxis fit the criteria of NIAID/FAAN.

## Characteristic of the study population

Among anaphylaxis cases, 55.2% were females. There was an almost equal distribution of cases between pediatric (49.6%) and adult (50.4%) age groups. Among anaphylaxis cases, 11.4% had at least one previous episode of anaphylaxis. Majority (77.1%) had history of atopy, while 50.5% had family history of atopy (**Table 1**).

A previous history of anaphylaxis had no effect on whether the patients were eventually diagnosed with anaphylaxis or not (**Table 2**).



Table 1. Patient characteristics (n = 105)

Characteristic	No. of cases (%)	
Sex		
Male	47 (44.8)	
Female	58 (55.2)	
Age (yr)		
0-5	7 (6.7)	
6-9	9 (8.6)	
10-18	36 (34.3)	
19-29	18 (17.1)	
30-39	15 (14.3)	
40-59	14 (13.3)	
≥60	6 (5.7)	
With history of anaphylaxis	12 (11.4)	
History of atopic disease	81 (77.1)	
Asthma	32 (30.5)	
Food allergy	44 (41.9)	
Drug allergy	24 (22.9)	
Allergy aside from food and drugs	7 (6.7)	
Allergic rhinitis	8 (7.6)	
Atopic dermatitis	3 (2.9)	
Family history of atopy	53 (50.5)	
Intake of medications		
ACE inhibitors	5 (4.8)	
Beta blockers	4 (3.8)	
NSAID	1 (0.9)	
Medical comorbidity	17 (16.2)	
Hypertension	14 (13.3)	
Other cardiovascular disease	2 (1.9)	

ACE, angiotensin-converting-enzyme; NSAID, nonsteroidal anti-inflammatory drug.

**Table 2.** Diagnosis of anaphylaxis in relation to history of anaphylaxis

History of anaphylaxis	Anaphyla	Total	
	Diagnosed as anaphylaxis at ED	Not diagnosed as anaphylaxis at ED	
No	62 (66.7)	31 (33.3)	93 (88.6)
Yes	8 (66.7)	4 (33.3)	12 (11.4)
Total	70 (66.7)	35 (33.3)	105 (100)

Values are presented as number (%).

ED, Emergency Department.

 $\chi^2 = 0.0, p > 0.05.$ 

In both age groups, majority had no identifiable obvious cause (38.1%) (**Table 3**). In those that had an identifiable trigger based on history alone, the most common were food (34.3%) and drugs (20%). The diagnosis of anaphylaxis was independent of the triggers identified

The most frequently involved organs were that of the skin and lungs. Difficulty of breathing was the most common chief complaint (48.6%) and overall symptom (90.5%). Pruritus was the most common skin symptom (85.7%) (**Table 4**). The diagnosis of anaphylaxis was shown to be dependent on the presence of specific symptoms such as wheezing, low oxygen saturation, hypotension, and abdominal pain (**Table 5**).

## Management of anaphylaxis

**Fig. 1** shows epinephrine administration between the cases diagnosed versus those not diagnosed as anaphylaxis. Seventy-three cases (69.5%) received epinephrine. Significantly more patients were given epinephrine when given the diagnosis of anaphylaxis as compared to those who were not (61,87.1% vs. 12, 34.3%,  $\chi^2$  = 30.767, p < 0.01).



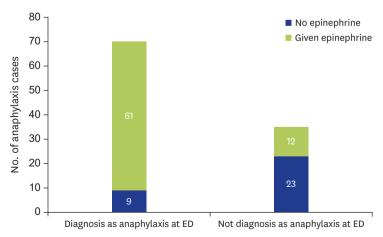
Table 3. Identified triggers of anaphylaxis

Trigger of anaphylaxis	Child (n = 52)	Adult (n = 53)	Total (n = 105)
Food	19 (18)	17 (16.1)	36 (34.3)
Crustacean	7 (6.6)	9 (8.6)	16 (15.2)
Fish	3 (2.8)	3 (2.8)	6 (5.7)
Peanut	5 (4.8)	0 (0)	5 (4.8)
Chicken	1 (1)	3 (2.8)	4 (3.8)
Sesame seed	0 (0)	1 (1)	1 (1)
Raisin	0 (0)	1 (1)	1 (1)
Fried rice	1 (1)	0 (0)	1 (1)
Chocolate	1 (1)	0 (0)	1 (1)
Noodles	1 (1)	0 (0)	1 (1)
Drugs	10 (9.5)	11 (10.5)	21 (20)
NSAID	5 (4.8)	6 (5.7)	11 (10.4)
Paracetamol	1 (1)	1 (1)	2 (1.9)
Amoxicillin	1 (1)	1 (1)	2 (1.9)
Coamoxiclav (amoxicillin + clavulanic acid)	2 (1.9)	1 (1)	3 (2.8)
Cefalexin	0 (0)	1 (1)	1 (1)
Probiotics	1 (1)	0 (0)	1 (1)
Hyoscine	0 (0)	1 (1)	1 (1)
Radiocontrast media	1 (1)	1 (1)	2 (1.9)
Rabies vaccine	0 (0)	1 (1)	1 (1)
Insect bite/sting	1 (1)	4 (3.8)	5 (4.8)
Unknown	21 (2)	19 (18.1)	40 (38.1)

Values are presented as number (%). NSAID, nonsteroidal anti-inflammatory drug.  $\chi^2 = 3.788$ , p > 0.05.

Most epinephrine doses were given via intramuscular route (87.6%). Other routes used include subcutaneous (5.5%), inhalation via nebulization (4.1%), intravenous bolus (1.4%), and continuous intravenous drip for a patient diagnoses with anaphylactic shock (1.4%). Majority of cases diagnosed as anaphylaxis (47.5%) received epinephrine within less than 10 minutes from time of arrival at ED. Of the patients who were not diagnosed as anaphylaxis, more than half (58.3%) eventually received epinephrine but only after 60 minutes (Fig. 2).

**Table 6** shows the rest of the management plans for the patients, including other medications given aside from epinephrine, referral to an allergist, and the disposition after being discharged from the ED. There was no difference in the referral rates whether the patients were initially diagnosed as anaphylaxis or not. The 14 patients who were admitted at the



**Fig. 1.** Epinephrine administration in anaphylaxis cases. ED, Emergency Department.  $\chi^2 = 30.767$ , p < 0.01.



Table 4. Chief complaint and signs and symptoms of anaphylaxis cases

riable No. of cases (n = 105)		
Chief complaints		
Difficulty of breathing	51 (48.6)	
Rashes	31 (29.5)	
Eye swelling	11 (10.5)	
Chest pain/tightness	3 (2.9)	
Throat discomfort	2 (1.9)	
Generalized body weakness	3 (2.9)	
Loss of consciousness	1 (1)	
Abdominal pain	1 (1)	
Nausea	1 (1)	
Dizziness	1 (1)	
Signs and symptoms		
Respiratory		
Difficulty of breathing	95 (90.5)	
Wheezing	68 (64.8)	
O <sub>2</sub> saturation < 95%	22 (21)	
Cough	14 (13.3)	
Rhinorrhea	11 (10.5)	
Choking	4 (3.8)	
Stridor	1 (1)	
Skin		
Pruritus	90 (85.7)	
Urticaria	61 (58.1)	
Flushing	43 (41)	
Periorbital edema	37 (35.2)	
Erythema	12 (11.4)	
Conjunctival redness	9 (8.6)	
Lip swelling	8 (7.6)	
Tearing	7 (6.7)	
Cardiovascular		
Tachycardia	55 (52.4)	
Hypotension	17 (16.2)	
Chest pain	17 (16.2)	
Syncope	6 (5.7)	
Arrhythmia	3 (2.9)	
Palpitation	4 (3.8)	
Gastrointestinal		
Abdominal pain	17 (16.2)	
Vomiting	15 (14.3)	
Diarrhea	4 (3.8)	
Nausea	2 (1.9)	
Central nervous system		
Dizziness	7 (6.7)	
Weakness	5 (4.8)	
Headache	1 (1)	

Values are presented as number (%).

intensive care unit (13.3%), all presented with hypotension at the ED. All admitted cases were discharged stable, mostly after 1 day of hospital stay. There were no cases of mortality among admitted patients.

# **DISCUSSION**

There are few data on the incidence of anaphylaxis. Incidence rate calculated in our study was 0.03%, which was comparable to studies done in hospitals in Bangkok, Pakistan and Spain of 0.01%–0.08% [6, 8, 9].



Table 5. Diagnosis of anaphylaxis in relation to presence of symptoms

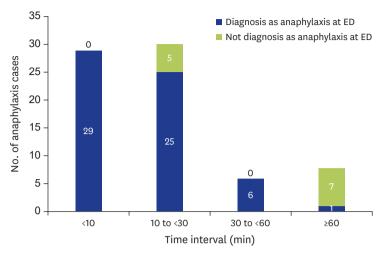
Symptom		Anaphylaxis cases		$\chi^2$ (p value)
	Diagnosed as anaphylaxis at ED	Not diagnosed as anaphylaxis at ED	Total	
Difficulty of breathing				1.382 (>0.05)
Absent	5 (50)	5 (50)	10 (9.5)	
Present	65 (68.4)	30 (31.6)	95 (90.5)	
Total	70 (66.7)	35 (33.3)	105 (100)	
Wheezing				4.090 (<0.05*)
Absent	20 (54.1)	17 (45.9)	37 (35.2)	
Present	50 (73.5)	18 (26.5)	68 (64.8)	
Total	70 (66.7)	35 (33.3)	105 (100)	
D <sub>2</sub> saturation < 95%	,	( )	,	4.859 (<0.05*)
Absent	51 (61.4)	32 (38.6)	83 (79)	,
Present	19 (86.4)	3 (13.6)	22 (21)	
Total	70 (66.7)	35 (33.3)	105 (100)	
Urticaria	70 (00.7)	33 (33.3)	103 (100)	2.367 (>0.05)
Absent	22 (7E)	11 (05)	44 (41 0)	2.307 (70.03)
	33 (75)	11 (25)	44 (41.9)	
Present	37 (60.7)	24 (39.3)	61 (58.1)	
Total	70 (66.7)	35 (33.3)	105 (100)	
lushing				0.020 (>0.05)
Absent	41 (66.1)	21 (33.9)	62 (59)	
Present	29 (67.4)	14 (32.6)	43 (41)	
Total	70 (66.7)	35 (33.3)	105 (100)	
Periorbital edema				1.022 (>0.05)
Absent	43 (63.2)	25 (36.8)	68 (64.8)	
Present	27 (73)	10 (27)	37 (35.2)	
Total	70 (66.7)	35 (33.3)	105 (100)	
Tachycardia Tachycardia				0.019 (>0.05)
Absent	33 (66)	17 (34)	50 (47.6)	
Present	37 (67.3)	18 (32.7)	55 (52.4)	
Total	70 (66.7)	35 (33.3)	105 (100)	
Hypotension	70 (00)	00 (0010)	.00 (.00)	4.246 (<0.05*)
Absent	55 (62.5)	33 (37.5)	88 (83.8)	11210 (10.00)
Present	15 (88.2)	2 (11.8)	17 (16.2)	
Total	` '	` '	` '	
	70 (66.7)	35 (33.3)	105 (100)	0 501 ( 0 05)
Chest pain	00 (00 0)	00 (01 0)	00 (00 0)	0.561 (>0.05)
Absent	60 (68.2)	28 (31.8)	88 (83.8)	
Present	10 (58.8)	7 (41.2)	17 (16.2)	
Total	70 (66.7)	35 (33.3)	105 (100)	
Abdominal pain				12.669 (<0.01*)
Absent	65 (73.9)	23 (26.1)	88 (83.8)	
Present	5 (29.4)	12 (70.6)	17 (16.2)	
Total	70 (66.7)	35 (33.3)	105 (100)	
/omiting				0.350 (>0.05)
Absent	59 (65.6)	31 (34.4)	90 (85.7)	
Present	11 (73.3)	4 (26.7)	15 (14.3)	
Total	70 (66.7)	35 (33.3)	105 (100)	

Values are presented as number (%).

ED, Emergency Department.

Studies on the epidemiology of anaphylaxis were hampered by a lack of consensus on the definition and criteria for its diagnosis. This was until recently when in 2005 the NIAID/FAAN established a consensus on the definition and diagnostic criteria to satisfy epidemiological, research, and clinical needs. Accurate diagnosis was also hindered by the lack of accurate diagnostic coding. Our study used the ICD-10 codes for anaphylaxis and allergy-related disorders to search for the charts that we reviewed. The ICD version used matter because reports show that anaphylaxis incidence varied between studies using the 9th or 10th ICD codes as selection criteria of cases using the NIAID/FAAN criteria [10]. Other studies have





**Fig. 2.** Time interval from arrival at Emergency Department (ED) to administration of epinephrine.  $\chi^2 = 2.969$ , p < 0.05.

likewise shown that the available codes were not very helpful when attempting to describe anaphylaxis [11-13], and there was also an insufficient number of codes available to document episodes of diagnosed anaphylaxis [14].

Immediate recognition and accurate diagnosis of anaphylaxis at the point of care, especially in the setting of an ED, is crucial for initiation of urgent and appropriate care. It was estimated that 57% of anaphylaxis cases in the ED are misdiagnosed [6]. In our study, anaphylaxis was diagnosed by ED physicians in a little more than half (66.7%) of cases, despite fulfilling the criteria of the NIAID/FAAN consensus. Kastner et al. [15] even suggested that there appears to be excessive caution in using the term anaphylaxis by physicians.

Labelling a case as anaphylaxis matters because it was shown in our study that there were significantly more patients given epinephrine versus those diagnosed as "hypersensitivity reaction" or "urticaria." This observation is consistent with other studies showing that patients labelled as anaphylaxis at the ED received epinephrine more often, regardless of the severity of their symptoms than patients diagnosed with other allergy-related diagnoses [6, 16]. All in all, only about 70% of patients seen in our ED received epinephrine despite

Table 6. Management care plan

Variable	Diagnosed as	Not diagnosed as	Total
	Anaphylaxis at ED (n = 70)	Anaphylaxis at ED (n = 35)	(n = 105)
Other drugs administered aside from e	pinephrine		
Corticosteroid	66 (94.3)	34 (97.1)	100 (95.2)
Antihistamine	64 (91.4)	34 (97.1)	98 (93.3)
Bronchodilator	48 (68.6)	18 (51.4)	66 (62.8)
H <sub>2</sub> blocker/proton pump inhibitor	27 (38.6)	25 (71.4)	52 (49.5)
Referral to an allergist			
With referral	32 (45.7)	17 (48.6)	49 (46.7)
Without referral	38 (54.3)	18 (51.4)	56 (53.3)
Disposition			
Admitted to regular room	56 (80)	24 (68.6)	80 (76.2)
Admitted to ICU	13 (18.6)	1 (2.9)	14 (13.3)
Discharged from ED	1 (1.4)	9 (25.7)	10 (9.5)
DAMA from ED	0 (0)	1 (2.9)	1 (1)

Values are presented as number (%).

ED, Emergency Department; ICU, intensive care unit; DAMA, discharged against medical advice.



fulfilling the criteria of the NIAID/FAAN consensus. Epinephrine was also given in a timelier manner when anaphylaxis was the diagnosis.

These findings are not unique to our study. Several studies have demonstrated inconsistent anaphylaxis management in the ED showing even less frequent epinephrine use [17-22], and significant delay in epinephrine administration [23-27].

In our study, other medications were also given more often than epinephrine. Even with the lack of evidence that antihistamines and corticosteroids are life-saving in the acute management of anaphylaxis [28], these were given to more anaphylaxis cases than epinephrine (93% and 95% respectively).

The route of administration of epinephrine is also part of the current recommendation for anaphylaxis management. In some studies, lack of knowledge of the correct route of epinephrine administration was an identified gap, with physicians administering via the subcutaneous or intravenous route rather than the recommended intramuscular route [20, 21, 23, 29-31]. It was encouraging to see that in our study, the majority of ED physicians gave epinephrine intramuscularly.

Evidence has shown that delayed epinephrine injection is associated with higher morbidity and mortality [32]. It was fortunate in our study that despite not receiving epinephrine, or a significant delay in epinephrine administration, there were no mortalities. This might be partly due to that fact that these patients were the ones with milder symptoms. Patients who had a higher risk for mortality and morbidity (respiratory compromise, low oxygen saturation, and hypotension) were appropriately diagnosed as anaphylaxis and given epinephrine in a well-timed manner. Data from our study showed that diagnosis of anaphylaxis at the ED was found to be dependent on the signs and symptoms of wheezing, oxygen saturation of <95%, abdominal pain, and hypotension. It appears therefore that patients need to present with moderate to severe signs and symptoms for anaphylaxis to be consistently diagnosed. The systematic review done by Kastner et al. [15] noted that some practitioners still think that "shock" needs to be present for anaphylaxis to be diagnosed even though this has been eliminated from new definitions. Therefore, insufficient knowledge by medical practitioners to identify the signs and symptoms of anaphylaxis or to correctly diagnose anaphylaxis is a major gap that needs to be addressed.

As in literature, our study showed that a large percentage of anaphylaxis cases had unknown triggers. Among those cases with identified triggers from history, the most common agents found in this study were food and drugs. Unfortunately, we failed to include specific ICD coding for anaphylaxis secondary to insect sting during the chart review, which could have affected our results showing only 5 cases triggered by insect stings. Among food triggers, crustaceans, fish, and peanut were the most common. NSAIDs were the most frequent among drugs. All these agents are also indicated by WAO to be significant triggers of anaphylaxis globally [10]. Recent studies have demonstrated that food-induced anaphylaxis have shown increasing trend not just in pediatric patients but also in all age groups [33, 34]. However, we need to consider possible overestimation of food allergy as a trigger. Currently, the majority of available data based on self-reporting generally overestimates food allergy prevalence by a factor of 3 to 4 [35-37]. The study done by Alvarez-Perea et al. [6] confirmed that after an allergy workup, the trigger differed in many cases from that reported by the patient or that proposed by the physician in the ED. And in those patients who did not know



the cause of their reaction, the work up revealed the real trigger. The possible disconnect between the suspected culprit and real cause of the anaphylaxis, therefore, highlights the need for improved follow-up care for the patients after the acute event.

Anaphylaxis management guidelines recommend that patients who had previous anaphylaxis episode be prescribed with epinephrine and referred to an allergist for the long-term management and prevention of anaphylaxis [38]. In our study, less than half of anaphylaxis cases were referred to an allergist. Only 1 patient was given a prescription of epinephrine upon discharge from the ED. Because the onset of anaphylaxis symptoms often occurs in the community setting [39], at-risk patients should have epinephrine auto-injectors to provide rapid intramuscular administration of epinephrine [40-42]. There are numerous evidences demonstrating that delayed medication administration leads to increased risk of progression to severe anaphylaxis [27, 28, 43, 44]. The dearth of prescription of epinephrine in our study can be due to the fact that self-injectable epinephrine is actually not available in the Philippines. This lack of access to self-injectable epinephrine for patients in the Philippines is a crucial point as this is a cornerstone for long-term management of anaphylaxis. Some allergists, therefore, instruct caregivers and patients to draw up the dose from a 1-mL ampule. Others have tried to use unsealed syringes prefilled by the physician with the appropriate epinephrine dose. Studies have shown however that dose preparation by a lay person from an ampule can be delayed as much as 3-4 minutes and can be inaccurate [45], and epinephrine in a prefilled syringe typically degrades within a few months from air exposure [46]. Clearly, these make-shift solutions are nowhere near adequate.

The limitations of our study are inherent in all studies that use a retrospective method, with only medical records as the sole source for data. Chart reviews could be lacking in vital information regarding the clinical assessments during the ED visit including exposure to allergens, progression of the symptoms, or other parts of the history that could help differentiate from other diseases including laryngeal or bowel angioedema with concomitant urticarial for instance. There was no way for us to verify the accuracy of the data in the medical records, or interact with the patients to probe more on their history.

The incidence of anaphylaxis in this study is 0.03%, comparable to studies in other centers. Despite available clinical practice guidelines, diagnosis and management of anaphylaxis continue to be inconsistent. Our study shows that there appears to be a lack of clarity among ED physicians on how to diagnose anaphylaxis consistently. The labelling of anaphylaxis is critical as these patients were more likely to receive epinephrine in a timely manner than those who were given other allergy-related diagnoses. The lack of recognition of anaphylaxis meant that patients often do not receive first-line epinephrine treatment. Although epinephrine was given more often to anaphylaxis cases by ED physicians in our institution as compared to previous studies, the situation still leaves a lot to be desired. Especially considering that epinephrine administration is the single most important determinant of outcomes of anaphylaxis. The role of the ED physician cannot be overly emphasized in the management of anaphylaxis. Discharge from the ED represents the transition from acute stabilization of the patient to transition to long-term management. They play a pivotal role in correctly identifying anaphylaxis, and then initiate longterm management during discharge including referral to an allergist and the provision of epinephrine in an out-patient setting. Further education and quality improvement programs, and then prospective methods to assess quality of diagnosis and management of anaphylaxis in the ED are imperative.



# **REFERENCES**

Sampson HA, Muñoz-Furlong A, Campbell RL, Adkinson NF Jr, Bock SA, Branum A, Brown SG, Camargo CA Jr, Cydulka R, Galli SJ, Gidudu J, Gruchalla RS, Harlor AD Jr, Hepner DL, Lewis LM, Lieberman PL, Metcalfe DD, O'Connor R, Muraro A, Rudman A, Schmitt C, Scherrer D, Simons FE, Thomas S, Wood JP, Decker WW. 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. Ann Emerg Med 2006;47:373-80.

#### PUBMED | CROSSREF

 Neugut AI, Ghatak AT, Miller RL. Anaphylaxis in the United States: an investigation into its epidemiology. Arch Intern Med 2001;161:15-21.

#### PUBMED | CROSSREF

3. Simons FE, Ebisawa M, Sanchez-Borges M, Thong BY, Worm M, Tanno LK, Lockey RF, El-Gamal YM, Brown SG, Park HS, Sheikh A. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. World Allergy Organ J 2015;8:32.

#### PUBMED I CROSSREF

- Campbell RL, Hagan JB, Manivannan V, Decker WW, Kanthala AR, Bellolio MF, Smith VD, Li JT. Evaluation
  of national institute of allergy and infectious diseases/food allergy and anaphylaxis network criteria for the
  diagnosis of anaphylaxis in emergency department patients. J Allergy Clin Immunol 2012;129:748-52.
- Sicherer SH, Simons FE; Section on Allergy and Immunology, American Academy of Pediatrics. Selfinjectable epinephrine for first-aid management of anaphylaxis. Pediatrics 2007;119:638-46.
- Alvarez-Perea A, Tomás-Pérez M, Martínez-Lezcano P, Marco G, Pérez D, Zubeldia JM, Baeza ML.
   Anaphylaxis in adolescent/adult patients treated in the Emergency Department: differences between initial impressions and the definitive diagnosis. J Investig Allergol Clin Immunol 2015;25:288-94.
- Russell WS, Farrar JR, Nowak R, Hays DP, Schmitz N, Wood J, Miller J. Evaluating the management of anaphylaxis in US emergency departments: Guidelines vs. practice. World J Emerg Med 2013;4:98-106.
   PUBMED | CROSSREF
- 8. Khan NU, Shakeel N, Makda A, Mallick AS, Ali Memon M, Hashmi SH, Khan UR, Razzak JA. Anaphylaxis: incidence, presentation, causes and outcome in patients in a tertiary-care hospital in Karachi, Pakistan. QJM 2013;106:1095-101.

# PUBMED | CROSSREF

- Techapornroong M, Akrawinthawong K, Cheungpasitporn W, Ruxrungtham K. Anaphylaxis: a ten years inpatient retrospective study. Asian Pac J Allergy Immunol 2010;28:262-9.
   PUBMED
- Simons FE, Ardusso LR, Bilò MB, El-Gamal YM, Ledford DK, Ring J, Sanchez-Borges M, Senna GE, Sheikh A, Thong BY; World Allergy Organization. World Allergy Organization anaphylaxis guidelines: summary. J Allergy Clin Immunol 2011;127:587-93.
   PUBMED | CROSSREF
- 11. Klein JS, Yocum MW. Underreporting of anaphylaxis in a community emergency room. J Allergy Clin Immunol 1995;95:637-8.

## PUBMED | CROSSREF

12. Tanno LK, Ganem F, Demoly P, Toscano CM, Bierrenbach AL. Undernotification of anaphylaxis deaths in Brazil due to difficult coding under the ICD-10. Allergy 2012;67:783-9.

#### PUBMED | CROSSRE

- Trojan T, Ma Y, Khan DA. Anaphylaxis identification using direct and combined ICD-9 methods. J Allergy Clin Immunol 2013;131(2 Suppl):AB224. https://www.jacionline.org/article/S0091-6749(12)03466-5/abstract CROSSREF
- Lieberman P. Epidemiology of anaphylaxis. Curr Opin Allergy Clin Immunol 2008;8:316-20.
   PUBMED | CROSSREF
- 15. Kastner M, Harada L, Waserman S. Gaps in anaphylaxis management at the level of physicians, patients, and the community: a systematic review of the literature. Allergy 2010;65:435-44.
- Campbell RL, Li JT, Nicklas RA, Sadosty AT; Members of the Joint Task Force; Practice Parameter Workgroup. Emergency department diagnosis and treatment of anaphylaxis: a practice parameter. Ann Allergy Asthma Immunol 2014;113:599-608.
   PUBMED | CROSSREF



 Bansal PJ, Marsh R, Patel B, Tobin MC. Recognition, evaluation, and treatment of anaphylaxis in the child care setting. Ann Allergy Asthma Immunol 2005;94:55-9.

PUBMED | CROSSREF

 Clark S, Bock SA, Gaeta TJ, Brenner BE, Cydulka RK, Camargo CA; Multicenter Airway Research Collaboration-8 Investigators. Multicenter study of emergency department visits for food allergies. J Allergy Clin Immunol 2004;113:347-52.

PUBMED | CROSSREF

 Gaeta TJ, Clark S, Pelletier AJ, Camargo CA. National study of US emergency department visits for acute allergic reactions, 1993 to 2004. Ann Allergy Asthma Immunol 2007;98:360-5.

PUBMED | CROSSREF

 Gompels LL, Bethune C, Johnston SL, Gompels MM. Proposed use of adrenaline (epinephrine) in anaphylaxis and related conditions: a study of senior house officers starting accident and emergency posts. Postgrad Med J 2002;78:416-8.

PUBMED | CROSSREF

21. Haymore BR, Carr WW, Frank WT. Anaphylaxis and epinephrine prescribing patterns in a military hospital: underutilization of the intramuscular route. Allergy Asthma Proc 2005;26:361-5.

22. Krugman SD, Chiaramonte DR, Matsui EC. Diagnosis and management of food-induced anaphylaxis: a national survey of pediatricians. Pediatrics 2006;118:e554-60.

PUBMED | CROSSREF

 Bernstein DI, Wanner M, Borish L, Liss GM; Immunotherapy Committee, American Academy of Allergy, Asthma and Immunology. Twelve-year survey of fatal reactions to allergen injections and skin testing: 1990-2001. J Allergy Clin Immunol 2004;113:1129-36.

PUBMED I CROSSREF

24. Bock SA, Muñoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. J Allergy Clin Immunol 2001;107:191-3.

PUBMED | CROSSREF

 de Silva IL, Mehr SS, Tey D, Tang ML. Paediatric anaphylaxis: a 5 year retrospective review. Allergy 2008;63:1071-6.

PUBMED | CROSSREF

26. Lee JM, Greenes DS. Biphasic anaphylactic reactions in pediatrics. Pediatrics 2000;106:762-6. PUBMED | CROSSREF

27. Pumphrey RS. Lessons for management of anaphylaxis from a study of fatal reactions. Clin Exp Allergy 2000;30:1144-50.

PUBMED | CROSSREF

 Wood RA, Camargo CA Jr, Lieberman P, Sampson HA, Schwartz LB, Zitt M, Collins C, Tringale M, Wilkinson M, Boyle J, Simons FE. Anaphylaxis in America: the prevalence and characteristics of anaphylaxis in the United States. J Allergy Clin Immunol 2014;133:461-7.
 PUBMED | CROSSREF

29. Jose R, Clesham GJ. Survey of the use of epinephrine (adrenaline) for anaphylaxis by junior hospital doctors. Postgrad Med J 2007;83:610-1.

PUBMED | CROSSREF

30. Mehl A, Wahn U, Niggemann B. Anaphylactic reactions in children--a questionnaire-based survey in Germany. Allergy 2005;60:1440-5.

PUBMED | CROSSREF

31. Thain S, Rubython J. Treatment of anaphylaxis in adults: results of a survey of doctors at Dunedin Hospital, New Zealand. N Z Med J 2007;120:U2492.

PUBMED

32. Sheikh A, Shehata YA, Brown SG, Simons FE. Adrenaline for the treatment of anaphylaxis: cochrane systematic review. Allergy 2009;64:204-12.

PUBMED | CROSSREF

33. Ben-Shoshan M, Clarke AE. Anaphylaxis: past, present and future. Allergy 2011;66:1-14. PUBMED | CROSSREF

 Ma L, Danoff TM, Borish L. Case fatality and population mortality associated with anaphylaxis in the United States. J Allergy Clin Immunol 2014;133:1075-83.
 PUBMED | CROSSREF

35. McBride D, Keil T, Grabenhenrich L, Dubakiene R, Drasutiene G, Fiocchi A, Dahdah L, Sprikkelman AB, Schoemaker AA, Roberts G, Grimshaw K, Kowalski ML, Stanczyk-Przyluska A, Sigurdardottir S, Clausen M, Papadopoulos NG, Mitsias D, Rosenfeld L, Reche M, Pascual C, Reich A, Hourihane J, Wahn U, Mills EN, Mackie A, Beyer K. The EuroPrevall birth cohort study on food allergy: baseline characteristics of 12,000



newborns and their families from nine European countries. Pediatr Allergy Immunol 2012;23:230-9.

- Roehr CC, Edenharter G, Reimann S, Ehlers I, Worm M, Zuberbier T, Niggemann B. Food allergy and non-allergic food hypersensitivity in children and adolescents. Clin Exp Allergy 2004;34:1534-41.
   PUBMED | CROSSREF
- 37. Woods RK, Stoney RM, Raven J, Walters EH, Abramson M, Thien FC. Reported adverse food reactions overestimate true food allergy in the community. Eur J Clin Nutr 2002;56:31-6.
- 38. Nurmatov U, Worth A, Sheikh A. Anaphylaxis management plans for the acute and long-term management of anaphylaxis: a systematic review. J Allergy Clin Immunol 2008;122:353-61.

  PUBMED | CROSSREF
- Kemp SF, Lockey RF, Simons FE; World Allergy Organization ad hoc Committee on Epinephrine in Anaphylaxis. Epinephrine: the drug of choice for anaphylaxis. A statement of the World Allergy Organization. Allergy 2008;63:1061-70.
   PUBMED | CROSSREF
- 40. NIAID-Sponsored Expert Panel, Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, Plaut M, Cooper SF, Fenton MJ, Arshad SH, Bahna SL, Beck LA, Byrd-Bredbenner C, Camargo CA Jr, Eichenfield L, Furuta GT, Hanifin JM, Jones C, Kraft M, Levy BD, Lieberman P, Luccioli S, McCall KM, Schneider LC, Simon RA, Simons FE, Teach SJ, Yawn BP, Schwaninger JM. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol 2010;126(6 Supp):S1-58.
  PUBMED | CROSSREF
- 41. Lieberman P, Nicklas RA, Randolph C, Oppenheimer J, Bernstein D, Bernstein J, Ellis A, Golden DB, Greenberger P, Kemp S, Khan D, Ledford D, Lieberman J, Metcalfe D, Nowak-Wegrzyn A, Sicherer S, Wallace D, Blessing-Moore J, Lang D, Portnoy JM, Schuller D, Spector S, Tilles SA. Anaphylaxis--a practice parameter update 2015. Ann Allergy Asthma Immunol 2015;115:341-84.

  PUBMED | CROSSREF
- Simons FE, Ardusso LR, Bilò MB, Cardona V, Ebisawa M, El-Gamal YM, Lieberman P, Lockey RF, Muraro A, Roberts G, Sanchez-Borges M, Sheikh A, Shek LP, Wallace DV, Worm M. International consensus on (ICON) anaphylaxis. World Allergy Organ J 2014;7:9.

  PUBMED I CROSSREF
- Kaplan MS, Jung SY, Chiang ML. Epinephrine autoinjector refill history in an HMO. Curr Allergy Asthma Rep 2011;11:65-70.
   PUBMED | CROSSREF
- 44. Song TT, Worm M, Lieberman P. Anaphylaxis treatment: current barriers to adrenaline auto-injector use. Allergy 2014;69:983-91.
  - PUBMED | CROSSREF
- 45. Simons FE, Chan ES, Gu X, Simons KJ. Epinephrine for the out-of-hospital (first-aid) treatment of anaphylaxis in infants: is the ampule/syringe/needle method practical? J Allergy Clin Immunol 2001;108:1040-4.
  - PUBMED | CROSSREF
- Rawas-Qalaji M, Simons FE, Collins D, Simons KJ. Long-term stability of epinephrine dispensed in unsealed syringes for the first-aid treatment of anaphylaxis. Ann Allergy Asthma Immunol 2009;102:500-3.
   PUBMED | CROSSREF