Acute allergic reactions in the emergency department: characteristics and management practices

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Objective **The objective of this study is to determine the incidence of emergency department (ED) visits for acute allergic reactions, identify the triggers, assess the severity, evaluate the management practices, and examine patient outcomes at a single-center ED in Lebanon.**

Patients and methods **A retrospective review of all patient charts presenting with a final diagnosis of acute allergic reaction to a single ED within a 6-month period (July–December 2009) was carried out. Age, sex, triggers, management in the ED and at discharge, disposition, and return visit were determined.**

Results **Two hundred and forty-five patients were identified (82.4% mild, 15.1% moderate, and 2.6% severe, respectively). This accounted for 0.96% of all ED visits. Drugs were the most commonly identified trigger (23.7%). In the ED, 72.7% of patients received H1-antihistamines, 51.8% received corticosteroids, 7.3% received H2-antihistamines, and 7.3% received inhaled B2 agonists. Only 15.9% of anaphylaxis cases received epinephrine in the ED. Similarly, the majority of patients were discharged on H1-antihistamines (93.9%), with only 4.5% of patients with anaphylaxis receiving prescriptions for epinephrine injections. All patients except one were discharged home. No fatalities were noted and the return visit rate within 1 week was 9.8%.**

Conclusion **The incidence of ED visits for acute allergic reaction was high compared with other studies, although the majority of cases were mild. Deviations from published guidelines on the treatment of anaphylaxis are common, with rare use of epinephrine and heavy reliance on H1-antihistamines both in the ED and at discharge. This did not seem to result in any measurable impact on mortality.** ***European Journal of Emergency Medicine*** **00:000–000 © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Acute allergic reaction presentations account for ~1/128 [1] to 1/2300 emergency department (ED) visits [2]. The incidence of anaphylaxis is difficult to estimate because of a lack of consensus on an accepted definition [1,3] and epidemiologic trends may be impacted by improvements in disease recognition with time. Nevertheless, studies indicate that allergic reaction presentations are on the rise [4], particularly in Western and developing countries [5]. Increasing hospitalization rates for allergic reactions have been reported [6,7]; in some countries, such as the UK, hospitalization rates have increased by 700% for anaphylaxis, 500% for food allergy, and 100% for urticaria since 1990 [8]. Similar findings were reported in an Australian study, where the rate of admissions for angioedema, urticaria, and anaphylaxis over a decade increased by 3.0%, 5.7%, and 8.8% per year, respectively [9]. In New York, there was a progressive increase in angioedema hospitalizations from 293 in 1990 to 636 in 2003 [10].

Historically, anaphylaxis has been defined on a physiologic basis as an immunoglobulin E (IgE)-mediated hypersensitivity reaction, whereas anaphylactoid reactions are non-IgE or often nonimmune mediated [11]. Recognizing the challenge of making these distinctions clinically and the similarity in treatment, the mechanistic definitions have been largely replaced by more clinical definitions, with a mild allergic reaction in the form of isolated urticaria on the one end and severe anaphylaxis with cardiovascular collapse on the other. ED presentations run the continuum of this spectrum, with the majority being mild [1,12].

There are multiple peer-reviewed guidelines for the management of anaphylaxis in the general healthcare and community setting [3,13–15], with separate guidelines for urticaria and angioedema [14,16]. The cornerstone of anaphylaxis management is the use of epinephrine as a first-line treatment while reserving H1-antihistamines and corticosteroids as second-line agents [3,13–15]. Studies that have examined existing ED management practices for anaphylaxis have shown considerable deviation from these guidelines, with low rates of epinephrine administration ranging from 10.5 to 57% [1,12,17].

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The aim of this study is to determine the incidence of acute allergic reaction presentations at a single-center ED in Beirut, Lebanon, describe the common causative agents in this population, and evaluate thoroughly all aspects of ED management including administration of medication, disposition, return visits, discharge medications, and follow-up instructions.

Patients and methods

Study design

In this study, a retrospective medical records review of all patients presenting to a single ED in a 6-month period from 1 July to 31 December 2009 was performed, with the final International Classification of Diseases-9th revision-Clinical Modification discharge diagnostic codes listed under the following four major headings: allergy/allergic reaction, anaphylactic shock or reaction, urticaria, and angioedema (Table 1). Individual scanned patients' charts were retrieved from the hospital Electronic Medical Records and reviewed for demographic information, comorbidities, history of previous asthma or atopy, presenting symptoms and allergic reaction grade, causative agents, ED management, disposition, and return visit within 1 week. Research assistants (two medical doctorates) who were trained on the selection criteria and grading system completed all the reviews and data collection. This study was approved by the Institutional Review Board at American University of Beirut Medical Center.

Study setting

The facility is a tertiary care center in Beirut, Lebanon, a city with an estimated population of 361 000. The ED during that period saw a total of 25 613 number of patients, 5596 (*22%*) of whom were pediatrics. The distribution of triaged acuities at our institution by Emergency Severity Index (ESI) is 1, 10, 57, 28, and 4% for ESI 1, 2, 3, 4, and 5, respectively. The department is staffed with a mix of American Board-certified/eligible Emergency Medicine trained physicians and Internal Medicine trained physicians with extensive ED experience who cover 25 and 75% of clinical hours, respectively, along with house staff from internal medicine, pediatrics, and surgery. All the patients were self-referred and none were an interhospital transfer. Walk-in and ambulance transport to the ED is not documented consistently. Prehospital emergency care providers in Lebanon offer basic life support only and do not administer any medications.

Table 1 ICD-9-CM discharge codes included in the study

Major categories and subheadings
Allergy, allergic reaction (995.3)
Specified allergen (477.8)
Anaphylactic shock (999.4)
Angioneurotic edema (995.1)
Bee sting (989.5)
Drug, medicinal substance, and biological (995.2)
Food ingested (693.1)
Inhalant (477.9)
Serum (999.5)
Urticaria (708.0)
Anaphylactic shock or reaction (correct substance properly administered) (995.0)
Immunization (999.4)
Wrong substance given (977.9)
Following sting (989.5)
Following serum (999.4)
Angioedema, allergic, any site, with urticaria (995.1)
Hereditary (277.6)
Urticaria (708.9)
Angioneurotic edema (995.1)
Allergic (708.0)
Because of drugs (708.0)
Because of food (708.0)
Because of inhalants (708.0)
Because of plants (708.8)
Because of serum (999.5)
Idiopathic (708.1)
Larynx (995.1)

Definitions

Acute allergic reactions are hypersensitivity reactions that involve the response of the immunologic system to antigens and can range in severity from mild urticaria to severe anaphylaxis. Presentations were divided into two distinct groups (Table 2):

(1) Generalized allergic reaction (GAR), confined to cutaneous findings alone including urticaria, angioedema without respiratory or airway compromise, local edema, or generalized rash [17].
(2) Anaphylaxis, defined as a 'serious allergic reaction that is rapid in onset and might cause death' with clinical criteria in accordance with the World Allergy Organization guidelines (Table 2) [14,18].

All allergic reactions were then further categorized as mild, moderate, or severe according to the clinical severity grading system proposed by Brown [19] (Table 3), which was shown to correlate well with hypotension, hypoxia as well as epinephrine use. Return visit was defined as a patient returning to the ED within 1 week for a complaint related to the initial visit diagnosis.

Sample selection

A total of 293 charts were reviewed. Cases were included if the medical notes recorded findings consistent with the above definition of an allergic reaction or anaphylaxis. Individual charts with asthma, rash, or rhinitis and no clear trigger or no cutaneous or systemic allergic features were excluded. Forty-three charts were excluded as they did not meet the definition of allergic reaction. Five additional charts were missing and thus excluded. A total of 245 charts were included in the final analysis.

Data analysis

Descriptive statistics were calculated using the software package version 20.0 (SPSS Inc., Chicago, Illinois, USA). Results were expressed either as means ± SDs or ranges or as percentages. A Pearson χ^2 analysis was carried out

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Table 2 Clinical criteria for diagnosing anaphylaxis

Anaphylaxis is highly likely when any one of the following three criteria is fulfilled:
1. Acute onset of an illness (minutes–several hours) AND
At least one of the following:
A. Respiratory compromise
B. Reduced BP or associated symptoms of end-organ dysfunction
OR
2. Two or more of the following (occur rapidly after exposure to a likely allergen)
A. Involvement of the skin-mucosal tissue (urticaria, tongue-lip-uvula swelling, itch-flush)
B. Respiratory compromise (e.g. dyspnea, stridor, wheeze-bronchospasm)
C. Reduced BP or associated symptoms (hypotonia, syncope, incontinence)
D. Persistent GI symptoms
OR
3. Reduced BP after exposure to known allergen
A. Infants and children: low SBP (age-specific or >30% decrease in SBP)
B. Adults: SBP < 90 mmHg (or >30% of the patient's baseline)

Anaphylaxis criteria adapted from Simons *et al.* [18].
BP, blood pressure; GI, gastrointestinal tract; SBP, systolic blood pressure.

Table 3 Grading system for generalized hypersensitivity reactions

Grades	Defined by
1: Mild: skin and subcutaneous tissues only	Generalized erythema, urticaria, periorbital edema, or angioedema
2: Moderate: features suggesting respiratory, cardiovascular, or gastrointestinal involvement	Dyspnea, stridor, wheeze, nausea, vomiting, dizziness (presyncope), diaphoresis, chest or throat tightness, or abdominal pain
3: Severe: hypoxia, hypotension, or neurologic compromise	Cyanosis or $SpO_2 \leq 92\%$ at any stage, hypotension (SBP < 90 mmHg in adults), confusion, collapse, LOC, or incontinence

Grading system adapted from Brown [19].
LOC, loss of consciousness; SBP, systolic blood pressure.

using treatments received in the ED, discharge treatments with severity of hypersensitivity reaction, and return visit to determine whether there was an association. An unadjusted regression model was performed using the Enter method to determine whether increasing age was a predictor of increased severity of hypersensitivity reaction. Two multivariate analyses were carried out using logistic regression: the first to determine whether discharge treatment from the ED could predict a return visit to the ED and the second to determine other predictors of severity of hypersensitivity reaction. A backward (Wald) selection procedure, with significance level for removal from the model set at 0.1, was used. The first model was adjusted for age, sex, history of previous allergy, asthma or atopy, and the various discharge treatments and the second model was adjusted for age and sex. In models that were significant ($P < 0.05$), the magnitude of association was reported as the odds ratio with the corresponding 95% confidence intervals (CIs).

Results

A total of 245 patients were evaluated for an acute allergic reaction. Fifty-eight percent of the patients were men and 42% were women. The majority of patients presented with GAR (201) whereas only 44 had anaphylaxis of which only seven were severe (Table 4). The mean age was 31.8 years (SD: 19.2, range: 28 days–83 years). In an unadjusted

Table 4 Severity of hypersensitivity reactions according to age group

	GAR [*n* (%)]	Anaphylaxis [*n* (%)]	
Age groups (years)	Mild	Moderate	Severe
0–2	9 (100)	0	0
3–17	46 (88.5)	6 (11.5)	0
≥ 18	146 (79.3)	31 (16.87)	7 (3.8)
All ages	201 (82.0)	37 (15.1)	7 (2.9)

GAR, generalized allergic reactions.

regression model, increasing age was a predictor of increased severity of hypersensitivity reaction (odds ratio 2.38; 95% CI 1.02–5.53, $P = 0.045$). Acute allergic reactions constituted 0.96 and 0.72% of ED visits for all ages and pediatric population, respectively, with a presentation incidence of one in 105 ED visits.

Causative agents

Overall, the causative agent was not identified in 130 (53.1%) cases. No trigger was identified in 110 (54.7%) of GAR and 20 (45.5%) of the anaphylaxis cases. Drugs accounted for the majority of cases (23.7%), followed by food and cosmetic products, which accounted for 13.8 and 4.9% of the cases, respectively (Table 5).

Comorbidity

In our series, 96 (39.2%) had a history of allergy, asthma, or atopy – with a preponderance in the anaphylactic group compared with the GAR group (54.5 vs. 35.8%). Adjusting for age and sex, the odds of having a severe allergic reaction were two times greater if patients had a history of previous allergy, asthma, or atopy than if they did not (95% CI: 1.08–4.08, $P = 0.028$).

Treatment in the emergency department

In our series, 20.8% of patients did not receive any intervention in the ED. Of these patients, 92.2% cases were GAR and 7.8% cases were anaphylactic reactions. The most commonly administered medication in the hospital for both GAR and anaphylaxis was an H1 blocker, followed by corticosteroids (Table 6). Only 15.9% of anaphylactic patients (three moderate and four severe) received epinephrine: six (0.3–0.5 mg) intramuscularly and one subcutaneously.

Discharge management

Upon discharge from the ED, 4.5% of all patients were discharged with no medication. The majority of patients were discharged on H1-antihistamines (93.9%). Only two patients were prescribed epinephrine injections (Table 7). Out of all patients, 28 (11.4%) were instructed to follow-up with their primary care physician whereas 35 (14.3%) were referred to an allergy specialist, of whom 31 (15.4%) and four (9.1%) were GAR and anaphylaxis, respectively.

Disposition of patients with acute allergic reactions

All the patients survived. Only one patient was admitted to the general medical floor; the rest were discharged

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Table 5 Suspected triggers for acute allergic reactions

Categories	Frequency [*n* (%)]	Details
Not identified	130 (53.1)	
Food	34 (13.8)	
Nuts and seeds	6 (2.4)	4 Nuts, 1 almond, 1 sesame
Seafood	15 (6.1)	12 Fish, 3 shellfish
Dairy products	3 (1.2)	2 Milk, 1 cheese
Fruits	2 (0.82)	1 Peach, 1 strawberry
Miscellaneous food	8 (3.3)	5 Spicy food, 2 mushroom, 1 mayonnaise
Drugs	58 (23.7)	
Antibiotics	20 (8.2)	8 Amoxicillin, 5 fluoroquinolone, 3 cephalosporin, 1 nitrofurantoin, 1 TMP-SMX, 1 spiramycin, 1 clarithromycin
NSAID	12 (4.9)	
Miscellaneous drugs	26 (10.6)	3 Fluconazole, 3 antitussive medication, 2 iodinated contrast, 2 pregabalin, 1 carbocisteine, 1 carnitine, 1 cetrorelix, 1 chemotherapy (unspecified), 1 codeine, 1 eosine, 1 fenofibrate, 1 fluoxetine, 1 loratadine, 1 minoxidil, 1 nicotinic acid, 1 oseltamavir, 1 pamidronate injection, 1 perfilgastrim, 1 peptoprazole, 1 radioactive iodine
Outdoor allergen	4.10%	
	10 (4.1)	8 Insect bite, 1 flower (unknown), 1 bird dropping
Cosmetic products	12 (4.9)	
Body creams	7 (2.9)	3 Facial cream, 3 cream, 1 vitamin E cream
Hair products	3 (1.2)	3 Henna
Soaps and perfume	2 (0.8)	1 Soap, 1 perfume
Others	0.40%	
	1 (0.4)	1 Gunpowder

Table 6 Medications administered in the hospital by severity

	n (%)			
Treatment	GAR (*n*=201)	Anaphylaxis (*n*=44)	Total (*N*=245)	*P*-value*
No medications or intervention	47 (23.4)	4 (9.1)	51 (20.8)	0.034
H1 antihistamine	141 (70.1)	37 (84.1)	178 (72.7)	0.000
Corticosteroids	96 (47.8)	31 (70.5)	127 (51.8	0.006
Epinephrine	0	7 (15.9)	7 (2.9)	0.000
H2 antihistamine	12 (6.0)	6 (13.6)	18 (7.3)	0.770
Inhaled B2 adrenergic agonist	4 (2.0)	14 (31.8)	18 (7.3)	0.000
Fluid bolus	4 (2.0)	12 (2.3)	16 (6.5)	0.000
Oxygen	1 (0.5)	5 (11.4)	6 (2.4)	0.000

GAR, generalized allergic reaction.
*Pearson χ^2 analysis, significance set at $P<0.05$.

Table 7 Medications prescribed upon discharge from emergency department

	n (%)			
Discharge treatment	GAR (*n*=201)	Anaphylaxis (*n*=44)	Total	*P*-value*
No medications or intervention	11 (5.5)	0	11 (4.5)	0.112
H1 antihistamine	188 (93.5)	42 (95.5)	230 (93.9)	0.630
Corticosteroids (PO)	68 (33.8)	26 (59.1)	94 (38.4)	**0.002**
Epinephrine injection	0	2 (4.5)	2 (0.8)	**0.002**
H2 antihistamine	3 (1.5)	3 (6.8)	6 (2.4)	**0.038**
B2 adrenergic agonist	1 (0.50)	2 (4.5)	3 (1.2)	**0.027**
Corticosteroids cream	8 (4.0)	0	8 (3.3)	0.178
Antihistamine cream	2 (1.0)	0	2 (0.8)	0.506

GAR, generalized allergic reaction.
*Pearson χ^2 analysis, significance set at $P<0.05$ and listed in bold.

from the ED. The mean length of stay (LOS) was 1.88 h (±2.27 SD) and 4.05 h (±4.07 SD) for GAR and anaphylaxis, respectively.

Return visit

Out of all cases, 24 patients (9.8%) returned to the ED within 1 week of the initial visit for the same chief complaint. Of those who returned, only one patient had a moderate allergic reaction on the second visit whereas the rest had mild symptoms. Multivariate logistic regression was used to examine various discharge treatments and the risk of return visit. After adjusting for age, sex, severity of hypersensitivity reaction, and history of previous allergy, asthma, or atopy, no significant model predicting return visit could be generated.

Discussion

This is the first study to examine acute allergic reaction ED presentations in the Lebanese setting and is aimed

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at expanding the currently limited data on the global epidemiology of acute allergic reactions as well as adding to the existing literature on ED management practices. Compared with single-center studies in adult Australian and the UK EDs, where incidence was found to be 1 in 439 ED visits and 1 in 277 ED visits, respectively [12,17], our incidence of one in 105 ED visits is relatively high, but comparable with those found in a national study of ED visits for acute allergic reactions in the USA, where acute allergic reactions comprised 1% of all ED visits [20]. The median age in our study was 31 years (28 days–83 years), which was similar to what was reported in other studies. Men outnumbered women by $\sim$1.4 : 1. This was in contrast to other studies where women more commonly presented with acute allergic reactions than men [12,17,20]. Both age and history of asthma, atopy, or allergies were predictive of severity of allergic reaction as has been reported in previous studies [1,7,17].

The majority of patients (82%) in our study presented with GAR whereas only 18% of patients fulfilled the criteria for anaphylaxis, of which only seven were severe. Differences in the definitions and grading systems used in the literature make comparative analysis a challenge. Braganza *et al.* [7] used similar definitions as those in our study and found that the majority of patients presented with GAR (90%) whereas only 10% fulfilled the criteria for anaphylaxis. Another study with similar definitions looked at patients presenting to an Australian ED and found that 142 of 304 patients presented with anaphylaxis – a much higher rate than that reported in our study [17]. A US national study found that only 1% of charts were coded for anaphylaxis although documented clinical criteria were not analyzed for categorization [20], and this may under-represent actual incidence as coding for anaphylaxis is generally underused [21,22].

The fatality rate was 0 for our study. This could be related to the generally mild severity of presentations as well as the small sample size. In general, however, reported mortality for anaphylaxis is low. Australian studies report a fatality rate between zero and 0.7% [7,17]. In Italy, studies that have looked at ED presentations for anaphylaxis found a fatality rate of 0.2 and 0.1% [1,23]. UK studies suggest a fatality rate of less than 1% [24,25], with similarly low rates reported from the USA (0.65%) [26]. Although other ED-based studies have reported admission rates between 4 and 67 [12,17,20], the admission rate in our ED was only 0.4%. This, however, may reflect inpatient bed availability rather than ED physician's decision to admit.

The reported causative agent was not identified in 52% of the cases. Medications accounted for 23.7% of the triggers, with antibiotics (8.2%) and NSAIDs (4.9%) being the most common. In contrast to other studies [1,2,7,17,27], where food is considered to account for most allergic reactions, especially in the pediatric age group, food causes accounted for only 13.8% of all cases and 11.5% of the pediatric cases, with nuts accounting for only six cases (2.4%). This is similar to the Brown study, where only four out of 304 cases were related to nut allergy. Although one study detected specific IgE to sesame seed in around 3.79, 2.65, and 1.91% of Lebanese infants, children, and adults, respectively [28], sesame seed was the suspected trigger in only one patient in our study. The retrospective review and reliance on physician documentation is a major limitation in identifying possible causative agents in our study.

Studies have repeatedly shown that H1 blockers and corticosteroids are the most commonly used medications in the ED management of acute allergic reactions including anaphylaxis despite multiple anaphylaxis guidelines recommending them only as second-line treatment [14,15,29]. In our study, 70.1% of GAR patients and 84.1% of anaphylactic patients received H1 blockers and 47.8 and 70.5% received steroids, respectively. The WAO anaphylaxis guidelines recommend epinephrine as the first-line treatment of anaphylaxis irrespective of severity. Epinephrine was administered in only 15.9% of anaphylactic cases in our study. Under-utilization of epinephrine in the ED for anaphylaxis has been reported in multiple studies [7,17,20]. Deviations from practice guidelines could be related to the challenge that ED physicians face in differentiating between early anaphylaxis and GAR presenting as isolated urticaria or angioedema, where the cornerstone for treating the latter is H1-antihistamines and corticosteroids – not epinephrine [7]. Moreover, studies suggest that ED physicians have a tendency to lump these presentations all within the diagnosis of allergic reaction even in the presence of multisystem organ involvement [20], whereas most existing guidelines approach anaphylaxis separately. Controversies over epinephrine's dosing requirements, concentration, and route of administration may also hinder physicians from using it [30]. One study that looked at junior physician knowledge of epinephrine dosing for anaphylaxis found that 28.4% of physicians would administer it intravenously and, of those who would administer it intramuscularly, 32.7% would administer 1 mg, and 30.9% did not know what dose to administer [31,32]. This is supported by studies that looked at the incidence of iatrogenic errors related to epinephrine use in anaphylactic cases, which was reported to be 2.4% in one study [33], and 15% (7/46) in another [34]. Although no iatrogenic adverse effects related to medication errors were noted in our study, such errors are potentially life-threatening, with reported complications including myocardial angina or infarcts, dysrhythmias, and intracerebral bleeds [30]. Given the low fatality rate of anaphylaxis in the ED and the low incidence of severe anaphylaxis, these iatrogenic risks need to be considered carefully in the application of anaphylaxis guidelines in the ED setting where the availability of multiple concentration of epinephrine for different

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indications, frequent interruptions, and the pressure of time-sensitive conditions all make it an error-prone environment [34,35].

The majority of patients with GAR in our study were discharged on H1-antihistamine (93.5%), with 33.8% receiving corticosteroids. For patients with anaphylaxis, 95.5% received H1-antihistamine prescriptions on discharge, 59% received corticosteroid prescription, and only 16% received a prescription for epinephrine. Prescribing antihistamines and steroids at discharge is a common practice despite the lack of existing evidence supporting any protective value against recurrence of symptoms [3]. Although published guidelines on anaphylaxis recommend discharging patients on epinephrine injections [13–15], under-prescribing at discharge has been reported in multiple studies [7,17]. In Lebanon, epinephrine autoinjectors are not commonly available on the market. The only way to provide self-administered epinephrine to the patient with a history of anaphylaxis is to prescribe a vial of epinephrine and a syringe, with instructions on drawing up and administering the appropriate dose. The complexity and risk of this method may deter the Lebanese physician from using it and contribute toward under-prescribing. Our return visit rate was 9.8%, but multilinear regression failed to show any particular significant discharge medication that was protective. This could be because of the small sample size, with only 24 return visits. Noble *et al.* [12] reported a 5% return visit rate, but defined return visit within 72 h as opposed to 1 week. The return visit rate may be an underestimate of true rates, given that we did not look at return visits to other EDs or surrounding clinics.

Conclusion

The incidence of acute allergic reaction presentations to the ED was relatively high in our setting, with the majority being mild. No fatalities were recorded and the return visit to the ED within 1 week was 9.8%. Given the predominance of GAR presentations over anaphylaxis in the ED, ED-specific management guidelines for acute allergic reactions should take into consideration the spectrum of severities that present to the ED and carefully weigh the risks of a treatment that is error prone in the ED setting against the morbidity and mortality risks of each severity category. Further studies are needed to evaluate contributors to ED physician under-utilization of epinephrine in anaphylaxis as well as the impact of discharge medications on outcomes and return visits.

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Conflicts of interest

There are no conflicts of interest.

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