

Prevalence of anaphylaxis among adults admitted to critical care for severe asthma exacerbation

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ABSTRACT

Background In asthmatics, making a diagnosis of anaphylaxis could be challenging as respiratory symptoms are a common feature of both conditions. Identifying anaphylaxis is important to providing appropriate care. A prior study showed that anaphylaxis is sometimes misdiagnosed as acute asthma in children. We sought to identify the percentage of adults admitted to the intensive care unit (ICU) with asthma exacerbations who met criteria for anaphylaxis.

Methods Retrospective chart review of adults admitted with acute asthma to the ICU at Jacobi Medical Center, a Level 1 trauma centre in Bronx, New York. Study period was January 2012 to December 2014. Using the criteria outlined in the World Allergy Organization's Anaphylaxis Guidelines, we identified patients who met criteria for anaphylaxis.

Results 105 patients were identified: 17 were excluded because their main reason(s) for admission was not asthma. 7 (8%) of the 88 cases eligible for the study met diagnostic criteria for anaphylaxis while 3 (3.4%) were highly likely to have had anaphylaxis. The baseline characteristics of the seven patients were similar to that of the overall population studied. They however had shorter onset of symptoms (median (IQR): 3.5 (2–6) vs 24 hours (12–72), $p<0.001$), were more likely to have been intubated (71%vs31%, $p=0.04$), received intramuscular epinephrine by the emergency medical services or in the emergency room (86%vs42%, $p=0.04$) and received antihistamines (28.6%vs1.2%, $p=0.02$). None of these seven patients died. Only one of the seven patients was prescribed an epinephrine pen injector and referred to an allergist at discharge.

Conclusion In this single-centre retrospective review, 3.4% of adults admitted to the ICU for acute severe asthma also met criteria for anaphylaxis.

INTRODUCTION

Anaphylaxis is a potentially life-threatening multi-systemic reaction to an allergen.^{1 2} Early identification of anaphylaxis and prompt institution of appropriate therapy is crucial to the avoidance of adverse outcomes. However, cases are often not recognised and managed appropriately.^{1 3} The non-specific nature of the signs and symptoms of anaphylaxis pose a challenge to diagnosis. Prior studies have shown, for instance, that skin symptoms—the most common symptom of allergic reactions—are often absent in severe anaphylaxis.⁴ Furthermore, although symptoms of anaphylaxis commonly appear within minutes of exposure, some anaphylactic reactions, such as that to galactose-alpha-1,3-galactose in red meat, could present hours after initial exposure.⁵ A high index of

suspicion is therefore important in making the appropriate diagnosis of anaphylaxis.

In patients with underlying asthma, an episode of anaphylaxis could present like a simple asthma exacerbation.⁶ In these patients, fatality could be increased,⁶ making prompt diagnosis and early administration of epinephrine crucial. In a recent study, up to 18% of children admitted to the intensive care unit (ICU) for acute asthma met criteria for anaphylaxis.⁷ This study's objective was to identify the percentage of adult patients admitted to the ICU with acute asthma who met criteria for anaphylaxis.

METHODS

We conducted a retrospective study of patients >18 years of age admitted with a diagnosis of acute asthma to the ICU at Jacobi Medical Center, a Level 1 trauma centre in the Bronx, New York between January 2012 and December 2014. We defined acute severe asthma as a physician diagnosis of asthma exacerbation considered to warrant admission to the ICU. We included only patients whose primary reason for admission was for asthma exacerbation (International Classification of Diseases, Ninth Revision, codes of 493.xx). Using the criteria outlined in the World Allergy Organization's (WAO) Anaphylaxis Guidelines (box 1),⁸ we identified patients who, *at presentation*, met criteria for anaphylaxis. Two of the authors initially reviewed the patient's charts independently to determine if patients met these diagnostic criteria. We extracted details as per the WAO guidelines, such as time to onset of symptoms, exposure to a known or likely allergen, and presence of features such as hypotension. Concurrently, the lead author reviewed these cases and in cases of discrepancies, final adjudication occurred at a meeting of all the authors. Summary statistics were calculated, and t-test was used for the continuous variables and Fisher's exact test for the categorical variables. Analyses were conducted in STATA (STATA Release 14. StataCorp College Station, TX).

RESULTS

A total of 105 patients were identified: 17 were excluded because their main reason(s) for admission was not asthma. Seven (8%) of the 88 cases met diagnostic criteria for anaphylaxis. These patients were similar to the overall population studied in demographic variables (race/ethnicity were excluded due to the high proportion of missingness), smoking status, presence of chronic lung disease, prior history of anaphylaxis, presence of pre-existing medication and/or food allergy, and haematological indices (table 1). However, these seven patients were more likely to



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Box 1 World Allergy Organization's Anaphylaxis Guidelines

Anaphylaxis is *highly likely* when any of the following three criteria is met:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue or both (eg, generalised hives, pruritus or flushing, swollen lips–tongue–uvula) *and* at least one of the following:
 - A. Sudden respiratory compromise (eg, dyspnoea, wheeze–bronchospasm, stridor, hypoxaemia).
 - B. Sudden reduced blood pressure or associated symptoms of end-organ dysfunction (eg, hypotonia, collapse, syncope, incontinence).
2. Two or more of the following that occur rapidly after exposure to a *likely* allergen or other trigger for that patient (minutes to several hours):
 - A. Sudden involvement of the skin–mucosal tissue (eg, generalised hives, itch-flush, swollen lips–tongue–uvula).
 - B. Sudden respiratory compromise (eg, dyspnoea, wheeze–bronchospasm, stridor, hypoxaemia).
 - C. Sudden decrease in blood pressure or associated symptoms (eg, hypotonia, collapse, syncope, incontinence).
 - D. Sudden gastrointestinal symptoms (eg, crampy abdominal pain, vomiting).
3. Reduced blood pressure after exposure to a *known* allergen for that patient (minutes to several hours):
In adults, systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline.

have had shorter onset of symptoms (median (IQR): 3.5 (2–6) vs 24 (12–72) hours, $p<0.001$), been intubated (71% vs 31%, $p=0.04$), received intramuscular epinephrine by the emergency medical services or in the emergency room (86% vs 42%, $p=0.04$) and received antihistamines (28.6% vs 1.2%, $p=0.02$). None of these seven patients died while 3 of the 81 patients who did not meet criteria for anaphylaxis died (3.4%). This difference was not statistically significant.

All the seven patients who met criteria for anaphylaxis had respiratory symptoms, four of them had hypotension and circulatory collapse with a patient having gone unconscious, while another had required cardiopulmonary resuscitation (table 2). Cutaneous/mucosal symptoms (urticaria, angioedema) were present in two of the patients and two had gastrointestinal symptoms. Three of these seven patients (3.4% of entire cohort) were highly likely to have had anaphylaxis due to rapid onset of symptoms, exposure to potential allergen (food-induced symptoms in one of the patients with known peanut allergy; circulatory collapse following ambulatory surgery; stridor and rapid deterioration to unconsciousness in another patient) and presence of dermatological features. The three of them had received intramuscular epinephrine and were intubated. One patient was discharged with an epinephrine injector and referred to an allergist. None of the patients returned to the index hospital within 30 days of discharge.

DISCUSSION

In this study, 8.0% of adults admitted to the ICU with acute asthma met criteria for anaphylaxis, with 3.4% having a clinical picture

Table 1 Demographic and clinical characteristics of participants and features of index admission

	Met criteria for anaphylaxis	Other participants	P values
N	7	81	
Age in years (mean, SD)	41.6±18.0	51.2±13.8	0.09
Female gender (n, %)	5 (71)	56 (69)	1.00
Smoker (n, %)	0 (0)	25 (31.3)	0.19
Presence of other chronic lung disease	1 (14.3)	29 (35.8)	0.42
History of:			
Allergic rhinitis	2 (28.6)	17 (21.0)	0.64
Anaphylaxis	1 (14.3)	9 (11.1)	0.58
Any medication allergy	4 (57.1)	34 (42.5)	0.69
Any food allergy	4 (57.1)	29 (36.2)	0.42
Duration of symptoms prior to presentation, in hours (median, IQR)	3.5 (2–6)	24 (12–72)	<0.001
Therapies* received			
Intramuscular epinephrine administration prior to or on arrival to emergency room	6 (85.7)	34 (42.0)	0.04
Magnesium sulfate	5 (71.4)	60 (74.1)	1.00
Antihistamines	2 (28.6)	1 (1.2)	0.02
Haematological indices			
Immunoglobulin E, median (IQR)	100 (77–116)	252 (66–638)	0.27
Total eosinophil count at admission, median (IQR)	110 (100–1210)	190 (90–500)	0.87
Significant increase in eosinophils from baseline, n (%)	2 (28.6)	24 (30)	1.00
ICU LOS in days (median, IQR)	3 (1–8)	2 (1–4)	0.78
Hospital LOS in days (median, IQR)	9 (3–10)	4 (3–8)	0.28
Endotracheal intubation	5 (71.4)	25 (30.9)	0.04
Mortality rate	0 (0)	3 (3.7)	1.00

Significant increase in eosinophils from baseline: increase from a normal level at baseline to >500 cells/mm³.

*All patients received inhaled albuterol.

ICU, intensive care unit; LOS, length of stay.

Table 2 Demographic, clinical features and comorbidities of the patients who met criteria for anaphylaxis

Case	Age (years)	Sex	Time to onset (hours)	Likely allergen	Skin/mucosa	Airway	Circulatory collapse	Gastrointestinal symptoms	WAO Criteria met	Presenting complaints	Comorbid condition
1*	71	F	<0.5	Food, likely peanut	(+)	(+)	(+)		1	Dyspnoea, wheezing, facial swelling immediately after eating, syncope	Asthma, hypertension, diabetes
2	34	F	2	Unknown	(+)	(+)			1	Dyspnoea, wheezing, pruritus, tongue swelling	Asthma, angioedema, allergic rhinitis, diabetes
3	43	F	Unclear	Unknown, possibly NSAID		(+)	(+)		2	Dyspnoea, wheezing, non-productive cough	Samter's triad
4	22	F	4	Unknown		(+)		(+)	2	Dyspnoea, stridor	Asthma, diabetes, chronic renal failure
5*	47	M	0.5–1	Anaesthetic agent or antibiotic		(+)	(+)		2	Dyspnoea, wheezing, hypoxia, vomiting postambulatory surgery	Hypertension, renal failure
6	52	F	4	Food, likely peanut		(+)		(+)	2	Dyspnoea, wheezing	Asthma, vocal cord dysfunction, allergic rhinitis
7*†	20	M	6	Food, likely peanut or shellfish		(+)	(+)		2	Dyspnoea, stridor, syncope	Asthma, hypertension, diabetes

*Highly likely to have had anaphylaxis.

†Needed cardiopulmonary resuscitation.

NSAID, non-steroidal anti-inflammatory drug; WAO, World Allergy Organization.

highly suggestive of anaphylaxis. This is similar to a study in children⁷ in which 18% of children admitted to the ICU for acute asthma met criteria for anaphylaxis with 4.1% highly likely to have had anaphylaxis.

The diagnosis of anaphylaxis could be challenging to make, particularly in asthmatics in whom respiratory symptoms may be mistakenly attributed to an exacerbation. While skin and respiratory symptoms are common in patients with anaphylaxis, over-reliance on these as critical elements to making the diagnosis of anaphylaxis could be misleading as these may be absent.¹ Despite these challenges in the diagnosis of anaphylaxis, fatality is stable due to improved awareness around early administration of intramuscular epinephrine.⁹ In this study, we found that a significant proportion (45%) of patients who arrived by ambulance had received intramuscular epinephrine. Although this is a positive as early administration of epinephrine is important in the management of anaphylaxis,^{2,8} it might contribute to incomplete evaluation of patients particularly if patients are assumed to have improved due to the management of 'acute asthma'.

A thorough work-up to detect possible triggers, education of patients and the development of an emergency treatment plan is essential to preventing future hospitalisations. Prior studies have shown that evaluation by an allergist after an anaphylactic episode increases the likelihood that the trigger will be identified.² Only one of the seven patients who met anaphylaxis criteria was prescribed an epinephrine injector and referred to an allergist for evaluation. Increased attention to concomitant symptoms and details of exposure may allow to establish the diagnosis of anaphylaxis in this subset of patients.

Limitations to this study include the retrospective nature. The data collection was limited by the details included by providers during the initial visit. Skin findings, in particular, were frequently absent. Although one could argue that if skin findings were present, providers would most likely have documented those. Despite these limitations, this study suggests that some of the patients presenting

with acute severe asthma may meet clinical criteria for anaphylaxis. Maintaining a high index of suspicion for anaphylaxis when taking care of asthmatics may be helpful in identifying such patients and formulating appropriate acute and postacute care plans.

Contributors GSdV conceived the project and supervised the work in its entirety. ATA collated the initial data and developed the data extraction instrument. ATA, AA and EA-N were involved in the chart reviews. ATA conducted the data analysis. ATA, AA, EA-N and GSdV were all involved in the interpretation of the data. ATA put together the initial draft of the manuscript, and all the authors were involved in editing the manuscript. All authors approve this final version.

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REFERENCES

- Commins SP. Outpatient emergencies: anaphylaxis. *Med Clin North Am* 2017;101:521–36.
- Simons FE, Ebisawa M, Sanchez-Borges M, et al. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. *World Allergy Organ J* 2015;8:32.
- Wood RA, Camargo CA, Lieberman P, et al. Anaphylaxis in America: the prevalence and characteristics of anaphylaxis in the United States. *J Allergy Clin Immunol* 2014;133:461–7.
- Simons FE, Sheikh A. Anaphylaxis: the acute episode and beyond. *BMJ* 2013;346:f602.
- Commins SP, Satinover SM, Hosen J, et al. Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose-alpha-1,3-galactose. *J Allergy Clin Immunol* 2009;123:426–33.
- Rainbow J, Browne GJ. Fatal asthma or anaphylaxis? *Emerg Med J* 2002;19:415–7.
- Sargent N, Erlewyn-Lajeunesse M, Bengier J. Does anaphylaxis masquerade as asthma in children? *Emerg Med J* 2015;32:83–4.
- Simons FE, Arduoso LR, Bilò MB, et al. World Allergy Organization guidelines for the assessment and management of anaphylaxis. *World Allergy Organ J* 2011;4:13–36.
- Turner PJ, Gowland MH, Sharma V, et al. Increase in anaphylaxis-related hospitalizations but no increase in fatalities: an analysis of United Kingdom national anaphylaxis data, 1992–2012. *J Allergy Clin Immunol* 2015;135:956–63.