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Results: 44 (46%) trainees claimed they had not received training about how to treat anaphylaxis. There was a discrepancy between claimed knowledge of how to treat anaphylaxis 86 (90%) and actual knowledge as none of the trainees' level answered all the questions correctly. Moreover 41 (49%) were unaware that EpiPen® should be administered IM in the lateral part of the thigh and 24 (28%) did not know it should be used in case of anaphylaxis.

Conclusion: Deficient knowledge about Epinephrine injection site, concentration and mode of administration among pediatric trainees were the most concerning outcome. Overconfidence in anaphylaxis management in senior trainees was worrisome. Continuing medical education, coupled with training opportunities to apply knowledge and practice skills, is needed to improve trainees' knowledge.

I. INTRODUCTION

Anaphylaxis is a life-threatening event, which requires urgent and prompt medical attention. Its exact incidence in pediatric is unknown, because few epidemiologic studies to date have examined the incidence of anaphylaxis in the general pediatric population.¹ Available UK estimates suggest that approximately 1 in 1333 of the population of England has experienced anaphylaxis at some point in their lives.² Lifetime prevalence based on international studies is estimated at 0.05-2%.³ This translates to a

major impact on quality of life and healthcare costs. ⁴ Increase in diagnosis of anaphylaxis and hospitalizations were reported from multiple countries. ⁵⁻⁸ Pediatric trainees are at the frontline managing children at risk for anaphylaxis in the hospital and at community level. In many instances, they are the first medical responders. Their fundamental knowledge is crucial in all sorts of emergencies including anaphylaxis. Clinical diagnosis of anaphylaxis is based on consideration of the patient's presenting symptoms and signs and on ruling out other sudden-onset multisystem diseases.^{1 9 10} Epinephrine is the first-line and lifesaving medication of choice in anaphylaxis. Its use is recommended in guidelines issued by the World Allergy Organization.^{1 9} Epinephrine should be injected by the intramuscular route in the mid-anterolateral thigh as soon as anaphylaxis is diagnosed or strongly suspected, in a dose of 0.01 mg/kg of a 1:1,000 (1 mg/mL) solution, to a maximum dose of 0.3 mg in children and the patient should be placed on the back with the lower extremities elevated. Intravenous epinephrine is potentially hazardous and should be avoided except in an intensive care setting.¹

These guidelines advise that epinephrine via the intramuscular route should be given by first medical responders. ¹¹ Early administration of epinephrine effectively reduces morbidity and mortality in human anaphylaxis, whereas delayed administration of epinephrine is associated with increased mortality because epinephrine becomes progressively less effective in reversing anaphylaxis with the passage of time.^{12 13} Cardiovascular side effects and overdoses were significantly more likely with intravenous epinephrine compared to intramuscular administration. ¹⁴ Plumb and colleagues found that junior doctors today seem to be no better at correctly identifying the clinical need for, and correct dose and route for administration of, adrenaline than their predecessors a decade earlier.¹⁵ Deaths have been reported from the inappropriate use of epinephrine in the context of allergic reaction.^{16 17} The latest NICE guideline 2016 recommended sufficient and appropriate training of healthcare professionals in management of patients with anaphylaxis.¹⁸ Immunologists Pete Storey and Penny Fitzharris stated that the knowledge gap regarding anaphylaxis was not unique to the United Kingdom.

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1. "We need to rethink how we train doctors and nurses in the care of all aspects of the management of this life-threatening condition," they wrote,
2. "We know that some patients die because they are not given adrenaline soon enough, or at all, or are given it by the wrong route.
3. "This is a longstanding and international problem. Doctors, especially those in emergency departments need to be skilled and confident in the care of these patients."¹⁹

The primary objective of our study was to evaluate the level of knowledge regarding anaphylaxis and its management in our pediatric training program. The secondary objective was to compare knowledge between the most junior and most senior residents for any observed knowledge gap. Understanding key knowledge gaps and their underlying reasons are vital to optimizing the training at medical school and/or during the training program, thus ensuring that a fatal outcome to a reversible condition is avoided. This furthermore will give the chance to implement training interventions at the right time points of pediatric training.

II. METHODS

a) Study Design

This study was a two-phase cross-sectional study where verbal consent was taken from the trainees after explaining the objectives of the study. Questionnaires with pre-determined multiple-choice questions and one open ended question were handed out to the trainees. Phases one and two were 1 month apart. The reason for the two-phase study was to reinforce the accuracy of the responses. The study was

approved by the IRB and Hamad Medical Corporation Hospital Committee.

b) Setting

The study was conducted at Hamad Medical Center (HMC), the only tertiary hospital in the state of Qatar. In phase one, the participants were approached after the morning report and asked to fill a questionnaire. They were divided into six groups according to their training level. Each questionnaire took about 3 minutes to complete. Phase two questionnaire was started 1 month after completed Phase one. The surveys were collected immediately after they were completed. 12 trainees were reached via WhatsApp® only. Their responses were received electronically. Each round of surveys took around 7 days to complete

c) Participants

Our six trainee groups included interns, who rotate in all specialties one year prior to residency program, and pediatric residents divided into post-graduate year 1 (PGY1), post-graduate year 2 (PGY2), post-graduate year 3 (PGY3), post-graduate year 4 (PGY4), and pediatric fellows from all pediatric subspecialties. The study was done between February and March 2015.

d) Selection criteria

We selected all trainees in the pediatric department including interns, residents and fellows. We only excluded those who were not willing to participate. Sample Size

The questionnaires were distributed to 96 trainees. For sample size refer to Figure 1.

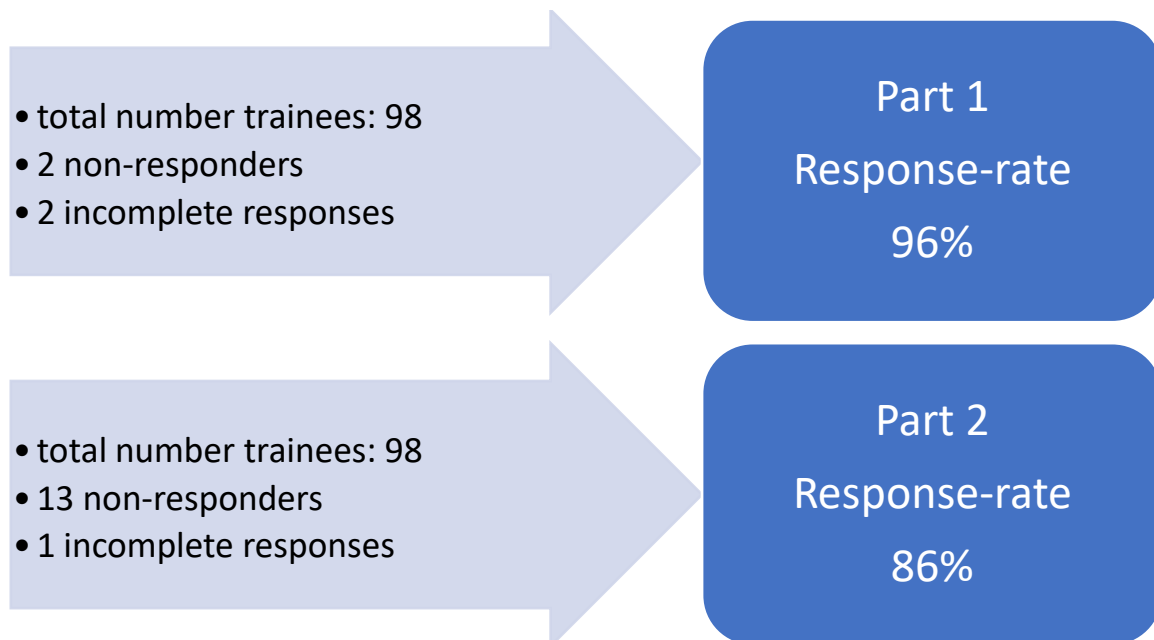


Figure 1: Sample size

e) *Study tools*

Participants were informed verbally about the questionnaire and paper surveys were distributed to the trainees for both phases one and two. Survey administered questions were in English language. The interview questions were created based on previous

studies and the clinical expertise of the investigator group.

A total number of 12 questions was given to the trainees (Table1). In each phase one and two, there were two demographic questions plus four knowledge related questions.

Table 1: Questionnaire Part 1

What's your Gender	Male	Female						
What's your Level of training?	Intern	PGY-1	PGY-2	PGY-3	PGY-4	Fellow		
Question 1 Do you know how to treat Anaphylactic shock due to Food Allergy?	1.1 Yes, and I got training about it.	1.2 Yes, but I did not get training about it	1.3 Maybe, I forgot how to treat despite my training	1.4 No, and I did not get any training.				
Question 2 What is the lifesaving drug in this case?	2.1 Antihistamine	2.2 Methylprednisolone	2.3 Terbutaline	2.4 Norepinephrine	2.5 Epinephrine	2.6 IV fluids	2.7 oxygen	
Question 3 Which route would you use to administer the treatment?	3.1 Oral	3.2 Nebulizer or inhaler	3.3 IV	3.4 SC	3.5 IM	3.6 Rectal	3.7 Via continuous mask inhalation	3.8 In the heart
Question 4 What dose would you give?	4.1 0.001mg/kg from 1:1,1000 solution	4.2 0.01mg/kg from 1:1,1000 solution	4.3 1mg/kg	4.4 2mg in 2ml nebulizer solution	4.5 1 liter / minute	4.6 I don't know		

Table 2: Questionnaire Part 2

What's your Gender	Male	Female				
What's your Level of training	Intern	PGY-1	PGY-2	PGY-3	PGY-4	Fellow
Question 5 Have you heard of Epinephrine Autoinjector / EpiPen?	5.1 Yes	5.2 No	5.3 I can't remember			
Question 6 Do you know when to use it (which case)? -> Advised to stop here if answer "no"	6.1 Yes	6.2 No				
Question 7 Please write down which case it is used for	7.1 No answer	7.2 Correct answer (anaphylaxis)	7.3 Other answer (wrong)			
Question 8 Where would you give it?	8.1 lateral part upper arm SC	8.2 lateral part thigh IM	8.3 frontal part upper arm IM	8.4 frontal part thigh SC	8.5 lateral part thigh IM or SC	8.6 no answer

f) *Variables*

Three variable themes were included in the questionnaire:

1. Demographic data i.e. gender and training level,
2. Anaphylaxis-related questions i.e., lifesaving medications, route of administration and dosage,

3. Epinephrine auto-injector (EpiPen®) knowledge-related questions. Outcomes

The outcomes of importance were:

1. Knowledge related to anaphylaxis management and EpiPen® use among pediatric trainees;

2. Identification of possible gaps in trainees' knowledge among different levels of training related to anaphylaxis management, with the aim to target teaching accordingly.

g) *Data sources/measurement*

This study aimed to assess pediatric trainees' knowledge in acute management of anaphylaxis as primary objective. Secondary objective was to assess possible knowledge gaps between the different trainees' levels, to evaluate whether the educational deficiencies are found at medical school or postgraduate training, so targeted training can be implemented accordingly. Statistical Analysis Descriptive statistics were used to summarize the demographics and level of training of the participants. We assessed knowledge related responses amongst trainees using frequencies along with percentages (univariate analysis). To compare

knowledge between the most junior and most senior trainees, we used the fisher exact test (multivariate analysis).

A two-sided P value <0.05 was considered statistically significant. Surveys with missed data were not included in the analysis. All statistical analyses were performed using statistical package SPSS, version 19.0 (IBM Corporation, Armonk, NY).

III. RESULTS

A total of 98 trainees were approached for both phases one and two, from whom we analysed 94 (96% response rate) for phase one and 84 surveys (86% response rate) in phase two (Figure 1). Most participants were females and pediatric fellows in both parts as seen in table 3.

Table 3: Demographics for phases 1 and 2*

Variable	Part 1 N=94	Part 2 N=84
Gender		
a. Male	40 (41.5%)	39 (46%)
b. Female	56 (58.5%)	45 (54%)
Training level		
a. Interns	7 (7%)	4 (5%)
b. Pgy1	20 (21%)	15 (18%)
c. Pgy2	19 (20%)	17 (20%)
d. Pgy3	11 (12%)	10 (12%)
e. Pgy4	9 (9%)	7 (8%)
f. Pediatric fellows	30 (31%)	31 (37%)

Knowledge related responses

Table 4: Knowledge related responses

Knowledge related responses	Trainees N (%)
Q1. Do you know how to treat Anaphylaxis? Did you receive any training about it?	
a. Yes and I got training about it.	46 (48)
b. Yes, but I did not get training about it.	40 (42)
c. May be, I forget how to treat despite my training.	4 (4)
d. No, and I did not get any training.	4 (4)
Q2. What is the lifesaving drug in this case?	
a. Antihistamine	3 (3)
b. Norepinephrine	2 (2)
c. Epinephrine	89 (92)
Q3. Which route would you use to administer the treatment?	
a. I.V	6 (6)
b. S.C	12 (13)
c. I.M	76 (80)
Q4. What dose would you give?	
A. 0.001mg/kg from 1:1000 solution	4 (4)
B. 0.01mg/kg from 1:1000 solution	77 (80)
C. 1mg/kg	4 (4)
D. 2mg in 2ml nebulizer solution	1 (1)
F. Not sure	8 (8)
Q5. Have you heard about the EpiPen®?	
A. Yes	71 (85)
B. No	11 (13)
C. Not sure	2 (2)

Q6. Do you know when to use it (which case)? A. Yes B. No	60 (72) 24 (28)
Q7. Please write down which case it is used for Not sure Anaphylaxis Other	23 (27) 60 (72) 1 (1)
Q8. Where would you give it? a. Lateral part upper arm SC b. Lateral part thigh IM c. Frontal part upper arm IM d. Frontal part thigh SC e. Lateral part thigh IM or SC f. Not sure	3 (4) 43 (51) 4 (5) 5 (6) 12 (14) 17 (20)

Table 4 shows knowledge related responses for all participants. Of notice 44 (46%) of the trainees responded they received no training about how to treat anaphylaxis. While 86 (89%) claimed they know how to treat anaphylaxis, 41 (49%) trainees were unaware that epinephrine should be administered in the lateral part of the thigh by intramuscular route and 24 (28%) trainees did not know that the EpiPen® is used in case of anaphylaxis.

In table 5 we compared the knowledge related responses between the most junior and most senior

trainees in the residency program, to explore whether the training programs were well equipped with the necessary tools to provide trainees with the necessary knowledge and skills to treat anaphylaxis. Comparing the most junior and most senior trainees, there was no statistical difference in knowledge related responses except that all 9 (100%) senior residents claimed to know how to treat anaphylaxis compared to only 14 (74%) of junior residents (p-value 0.01).

Table 5: Comparing knowledge related responses of PGY1 to PGY4

Correct responses to knowledge questions Questionnaire Part 1	PGY1 N=19 (%)	PGY4 N=9 (%)	P value (fischer exact test)
Q1. Do you know how to treat anaphylactic shock due to food allergy? Yes, and I got training about it.	4 (21)	7 (78)	0.01
Yes, but I didn't get training about it.	10 (53)	2 (22)	0.27
Maybe/No.	5 (26)	0	0.24
Q2. What is the lifesaving drug in this case? Epinephrine	18 (95)	9 (100)	0.9
Q3. Which route would you use to administer the treatment? I.M	19 (100)	8 (89)	0.6
Q4. What dose would you give? 0.01mg/kg from 1:1000 solution	15 (79)	9 (100)	0.3
Correct response to knowledge questions Questionnaire Part 2	PGY1 N=15(%)	PGY4 N=7(%)	P value
Q5. Have you heard about EpiPen®? Yes	11 (73)	7 (100)	0.3
Q6. Do you know when to use it? Yes	10 (67)	7 (100)	0.2
Q7. Please write down which case it is used for? Anaphylaxis	10 (67)	7 (100)	0.2
Q8. Where would you give it? Lateral part of the thigh	7 (47)	5 (71)	0.5

As summarized in figure 2, pediatric fellows (12 fellows or 30%) and PGY1 (10 residents or 25%) were

more likely to report that they did not receive training compared to other categories.

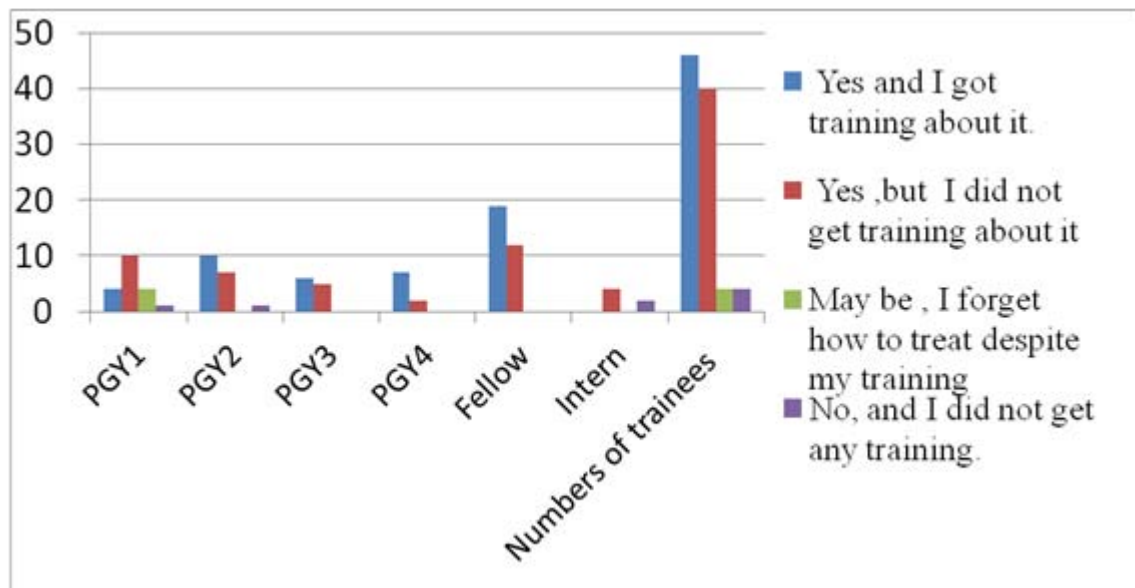


Figure 2: Knowledge of anaphylaxis treatment and training received among all trainees (% of total number by trainee level)

IV. DISCUSSION

There are notable findings from our study. Despite the vital importance of knowing the emergency treatment of anaphylaxis, of significance is the observation that none of the trainees' categories answered all the questions correctly. Surprisingly significant number of the total trainees 44 (46%) claimed they did not receive any training about how to treat anaphylaxis. Almost half of the trainees 41 (49%) were not aware that the EpiPen® should be administered in the lateral part of the thigh by intramuscular route. Moreover, 24 (28%) of trainees did not know that EpiPen® is used in case of anaphylaxis. Our study showed that 13 (15%) have never heard about epinephrine auto-injectors from which the most junior trainees represent about half.

These worrisome results indicate that both medical schools and training programs need to consider restructuring their existing educational agenda to better address low prevalence high consequence conditions like anaphylaxis and other emergencies. There is an urgent need for improving training in the recent international consensus.²⁰ There was an obvious discrepancy between claimed and actual knowledge in our study. While 86 (89%) of the trainees claimed they knew how to manage anaphylaxis, when they were asked more detailed questions, half of them were unaware that epinephrine should be administered in the lateral part of the thigh by intramuscular route and one third did not know that the EpiPen® is used in case of anaphylaxis.

Studies suggested that doctors claim to know how to treat anaphylaxis but this is often not translated into practice.¹⁹ Unlike our findings, a large survey based study of doctors and nurses in a Singapore hospital indicated not only good recognition of anaphylaxis but also a trend to over-diagnose this condition.²¹ A systematic review study showed that participants reported high levels of confidence in diagnosing or managing anaphylaxis at baseline and follow-up despite their limited clinical experience.²² Physicians' overestimation of their own competence may compromise the safety and clinical outcomes of patients. It may be advantageous to help trainees at all levels to become more cognizant of this disconnect.²³ The incorporation of continuous medical education to practice skills is essential to maintain knowledge and competency.^{24 25} Though most participants knew that epinephrine is the drug of choice for treating anaphylaxis, few interns thought wrongly that antihistamine is the drug to use for treating anaphylaxis. While most of the pediatric trainees 76 (80%) acknowledged that the best mode of administering epinephrine during anaphylaxis is I.M, 18 (20%) assumed dangerously that IV and S.Q are the standard modes of treatment during anaphylaxis. Similar to our findings, in a questionnaire-based study done in UK with a sample size of 68 foundation doctors, 27/68 (40%) chose the correct route (IM), 17/68 (25%) wrongly chose the (IV) route and 1/68 (1%) incorrectly chose either subcutaneous or nebulized routes of administration.¹⁵ Regarding the dose and concentration of epinephrine, most of the trainees except the interns acknowledged

the right dose and concentration of epinephrine. A study of first- and second-year UK doctors in 2008 identified that even junior doctors who had completed ALS training had poor knowledge of adrenaline use and dose.²⁶

Our study showed that 13 (15%) have never heard about epinephrine auto-injectors from which the interns and PGY1 represent about half. This might indicate gaps in the educational programs at medical schools. We anticipate that trainees' performance will continue to decline in the absence of educational reinforcement. When we compared the knowledge-related responses of the most junior and most senior trainees, we found no statistical difference between the two categories in most of the core areas. Similar to our study, a survey-based study in adult medicine by Droste et al, which compared two district hospitals with different levels of trainees showed that there was a lack of knowledge in a significant number of senior and junior doctors regarding the dose, route, and concentration of epinephrine with no much difference among trainee levels.²⁷ Another study by Drupad HS et al of 265 subjects in which a pretested structured questionnaire was used showed no significant difference between senior and junior doctors.²⁸ Trainees of all grades who may be the first responders at a scene of anaphylaxis should solidify their knowledge about emergencies and should be well prepared if anaphylaxis ensued. Innovative educational interventions are essential to improve and maintain trainees' knowledge and clinical competency.

V. CONCLUSION

Although prompt treatment with epinephrine is critically important for survival in anaphylaxis, we continue to have gaps in the critical knowledge of the frontline trainees regarding anaphylaxis management. Knowledge about epinephrine injection site, mode of administration and the lack of overall training of anaphylaxis treatment were the most concerning findings.

Continuing medical education, coupled with training opportunities to apply knowledge and practice skills, is needed to improve trainees' knowledge.

Limitations

Our study was based on self-reports. Our institution is the only tertiary center in the area and is comprised of pediatric trainees from all over the world.

Strengths

Our training program enrolls medical school graduates from multiple different countries, which makes our findings more generalizable and consists of a large number of 98 trainees within a single institution. We handed out surveys at 2 time points to ascertain our findings and included comprehensive questions on anaphylaxis knowledge and treatment/ EpiPen® use,

both of which are important to successfully recognize and treat such condition. We had a high response rates using both paper and electronic version of the questionnaire.

VI. SUMMARY-BOX

What is known about the subject? 1. Pediatric trainees are at the frontline managing children with anaphylaxis in the hospital and at community level. Their fundamental knowledge of anaphylaxis treatment is crucial. 2. Studies showed that poor knowledge of anaphylaxis management impairs patients' quality of life, and leads to increased healthcare costs and preventable deaths. 3. There is limited data about pediatric trainees' knowledge of anaphylaxis management according to their level of training.

What this study hopes to add: 1. Deficient knowledge about Epinephrine injection site, concentration and mode of administration among pediatric trainees were the most concerning outcome. 2. Overconfidence in anaphylaxis management in senior trainees was worrisome. 3. Continuing medical education, coupled with training opportunities to apply knowledge and practice skills, is needed to improve trainees' knowledge.

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Disclosure Statement

The authors declare no conflict of interests.

Authors Contribution MA (Principal investigator) conceptualized the study, CB collected the data analyzed, drafted and edited the manuscript. SME analysed data and wrote the manuscript. AA presented the data in the PAAM conference. All authors read and approved the final manuscript.

REFERENCES RÉFÉRENCES REFERENCIAS

1. Simons FE, Arduzzo LR, Bilò MB, et al. 2012 Update: World Allergy Organization Guidelines for the assessment and management of anaphylaxis. *Curr Opin Allergy Clin Immunol* 2012; 12(4):389-99. doi: 10.1097/ACI.0b013e328355b7e4
2. Stewart AG, Ewan PW. The incidence, aetiology and management of anaphylaxis presenting to an accident and emergency department. *QJM* 1996; 89(11): 859-64. 3. Lieberman P, Camargo CA, Bohlke K, et al.
3. Epidemiology of anaphylaxis: findings of the American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis Working Group. *Ann Allergy Asthma Immunol* 2006; 97(5): 596-602. doi:10.1016/S1081-1206(10)61086-1.

4. Rudders SA, Arias SA, Camargo CA. Trends in hospitalizations for food-induced anaphylaxis in US children, 2000-2009. *J Allergy Clin Immunol* 2014; 134(4):960-2.e3. doi: 10.1016/j.jaci.2014.06.018 [published Online First: 2014/08/07]
5. Nocerino R, Leone L, Cosenza L, et al. Increasing rate of hospitalizations for food-induced anaphylaxis in Italian children: An analysis of the Italian Ministry of Health database. *J Allergy Clin Immunol* 2015; 135(3):833-5.e3. doi: 10.1016/j.jaci.2014.12.1912 [published Online First: 2015/01/25]
6. Mullins RJ, Dear KB, Tang ML. Time trends in Australian hospital anaphylaxis admissions in 1998-1999 to 2011-2012. *J Allergy Clin Immunol* 2015; 136(2):367-75. doi: 10.1016/j.jaci.2015.05.009 [published Online First: 2015/07/14]
7. 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(4): 956-63.e1. doi: 10.1016/j.jaci.2014.10.021 [published Online First: 2014/11/25]
8. Ma L, Danoff TM, Borish L. Case fatality and population mortality associated with anaphylaxis in the United States. *J Allergy Clin Immunol* 2014; 133(4):1075-83. doi: 10.1016/j.jaci.2013.10.029 [published Online First: 2013/12/14]
9. 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(1):32. doi: 10.1186/s40413015-0080-1 [published Online First: 2015/10/28]
10. Sampson HA, Muñoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol* 2006; 117(2):391-7. doi: 10.1016/j.jaci.2005.12.1303
11. Simons FE, Arduzzo LR, Bilò MB, et al. World Allergy Organization anaphylaxis guidelines: summary. *J Allergy Clin Immunol* 2011; 127(3): 587-93.e1-22. doi: 10.1016/j.jaci.2011.01.038
12. Sampson HA, Mendelson L, Rosen JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. *N Engl J Med* 1992; 327(6):380-4. doi: 10.1056/NEJM199208063270603
13. Pumphrey RS, Gowland MH. Further fatal allergic reactions to food in the United Kingdom, 1999-2006. *J Allergy Clin Immunol* 2007; 119(4):1018-9. doi: 10.1016/j.jaci.2007.01.021 [published Online First: 2007/03/08]
14. Campbell RL, Bellolio MF, Knutson BD, et al. Epinephrine in anaphylaxis: higher risk of cardiovascular complications and overdose after administration of intravenous bolus epinephrine compared with intramuscular epinephrine. *J Allergy Clin Immunol Pract* 2015; 3(1):76-80. doi: 10.1016/j.jaip.2014.06.007 [published Online First: 2014/08/29]
15. Plumb B, Bright P, Gompels MM, et al. Correct recognition and management of anaphylaxis: not much change over a decade. *Postgrad Med J* 2015; 91(1071): 3-7. doi: 10.1136/postgradmedj-2013-132181
16. Tanno LK, Ganem F, Demoly P, et al. Under notification of anaphylaxis deaths in Brazil due to difficult coding under the ICD-10. *Allergy* 2012; 67(6):783-9. doi: 10.1111/j.1398-9995.2012.02829.x [published Online First: 2012/04/23]
17. Gibbison B, Sheikh A, McShane P, et al. Anaphylaxis admissions to UK critical care units between 2005 and 2009. *Anaesthesia* 2012; 67(8):833-9. doi: 10.1111/j.1365-2044.2012.07159.x [published Online First: 2012/05/18]
18. NICE-Guideline. Anaphylaxis, 2016.
18. Torey P, Fitzharris P. Adrenaline in anaphylaxis: overtreatment in theory, under treatment in reality. *Postgrad Med J* 2015; 91(1071):1-2. doi: 10.1136/postgradmedj-2014-133185
19. Simons FE, Arduzzo LR, Bilò MB, et al. International consensus on (ICON) anaphylaxis. *World Allergy Organ J* 2014; 7(1):9. doi: 10.1186/1939-4551-7-9 [published Online First: 2014/05/30]
20. Ibrahim I, Chew BL, Zaw WW, et al. Knowledge of anaphylaxis among Emergency Department staff. *Asia Pac Allergy* 2014; 4(3):164-71. doi: 10.5415/apallergy.2014.4.3.164 [published Online First: 2014/07/29]
21. Davis DA, Mazmanian PE, Fordis M, et al. Accuracy of physician self-assessment compared with observed measures of competence: a systematic review. *JAMA* 2006; 296(9):1094-102. doi: 10.1001/jama.296.9.1094
22. Jongco AM, Bina S, Sporter RJ, et al. A Simple Allergist-Led Intervention Improves Resident Training in Anaphylaxis. *J Allergy (Cairo)* 2016; 2016:9040319. doi: 10.1155/2016/9040319 [published Online First: 2016/02/21]
23. Hernandez-Trujillo V, Simons FE. Prospective evaluation of an anaphylaxis education mini-handout: the AAAAI Anaphylaxis Wallet Card. *J Allergy Clin Immunol Pract* 2013; 1(2):181-5. doi: 10.1016/j.jaip.2012.11.004 [published Online First: 2013/01/26]
24. Kennedy JL, Jones SM, Porter N, et al. High-fidelity hybrid simulation of allergic emergencies demonstrates improved preparedness for office emergencies in pediatric allergy clinics. *J Allergy Clin Immunol Pract* 2013; 1(6):608-17.e1-14. doi: 10.1016/j.jaip.2013.07.006 [published Online First: 2013/09/21]

25. Gopalakrishnan S, Alexander R. Anaphylaxis-Junior doctors' knowledge of guidelines. *Resuscitation* 2009; 80(3):383-4. doi: 10.1016/j.resuscitation.2008.11.004 [published Online First: 2008/12/31]
26. Droste J, Narayan N. Anaphylaxis: lack of hospital doctors' knowledge of adrenaline (epinephrine) administration in adults could endanger patients' safety. *Eur Ann Allergy Clin Immunol* 2012; 44(3):122-7.
27. Drupad HS, Nagabushan H. Level of knowledge about anaphylaxis and its management among health care providers. *Indian J Crit Care Med* 2015; 19(7):412-5. doi: 10.4103/0972-5229.160288.

