

Emergency and Hospital Care for Food-Related Anaphylaxis in Children

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ABSTRACT **OBJECTIVES:** Among patients with food-related anaphylaxis, to describe trends in emergency and hospital care and determine the revisit rate.

METHODS: This retrospective cohort study included children 6 months to 18 years of age with food-related anaphylaxis from 37 children's hospitals between 2007 and 2012. Summary statistics and trends for patient characteristics were evaluated. Multivariable regression was used to identify predictors for hospital admission. Revisit rates to either the emergency department (ED) and/or inpatient unit were calculated.

RESULTS: 7303 patients were evaluated in the ED; 3652 (50%) were admitted to the hospital. Hospital admission rates varied widely (range, 20%–98%). Food-related anaphylaxis increased from 41 per 100 000 ED visits to 72 per 100 000 while hospital admission rates did not change. Males (odds ratio [OR], 1.2 [95% confidence interval (CI), 1.0–1.4]), patients <1 year old (OR, 1.8 [95% CI, 1.3–2.5]), those with anaphylaxis to either peanut (OR, 1.2 [95% CI, 1.0–1.5]) or tree nut (OR, 1.7 [95% CI, 1.3–2.1]), and patients with asthma (OR, 7.4 [95% CI, 5.8–9.3]) or a chronic complex condition (OR, 5.2 [95% CI, 3.0–9.0]) were more likely to be admitted to the hospital. The 3-day revisit rate was 3% for patients discharged from the ED and 0.6% for those admitted on the index visit.

CONCLUSIONS: The incidence of food-related anaphylaxis in pediatric EDs is increasing, but rates of hospital admission are stable. Hospital admission is common but widely variable. Further research is needed to identify optimal management practices for this potentially life-threatening problem.



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Food allergy is a common condition affecting US children and, for unclear reasons, the prevalence seems to be rising.¹ A recent randomized, cross-sectional survey that evaluated nearly 40 000 US children in 2011 found that the prevalence of food allergy was ~8%, which is higher than previously reported.²

Nearly 40% of children with food allergies have a history of food-related anaphylaxis, a severe life-threatening reaction to an allergen that can lead to airway obstruction, shock, or death.² Food-related anaphylaxis is the most common type of anaphylaxis treated in emergency departments (EDs) in the United States.³ Anaphylaxis can present with a range of symptoms and variable degrees of severity (eg, breathing difficulties, hypotension, oropharyngeal swelling, vomiting). Time to complete resolution of symptoms can also vary, and up to one-quarter of patients will experience a biphasic reaction within 72 hours of initial allergen exposure.^{4,5} There is little evidence to help predict which patients are at high risk for recurrent or persistent symptoms and would therefore be more likely to benefit from prolonged observation periods or hospital admission.⁶ Nonetheless, 4 to 6 hours of observation are believed to be sufficient according to consensus-based national guidelines from the US National Institute of Allergy and Infectious Disease/ Food Allergy and Anaphylaxis Network symposium.⁷

Analysis of a large multicenter database of pediatric EDs provides an important opportunity to better understand hospital care for food-related anaphylaxis. Further information about hospital admission practices and outcomes will help differentiate between real and perceived risk of food-related anaphylaxis, better supporting patients with food allergy, their families, and policy makers. Variability in hospital practices may also indicate targets for quality improvement efforts and future research. The goal of the present study therefore was to describe the trends in emergency and hospital care and determine the revisit rate for anaphylaxis-related problems in patients with food-related anaphylaxis presenting to pediatric EDs.

METHODS

Study Design and Data Sources

This retrospective cohort study used the Pediatric Health Information System (PHIS), an administrative database of 47 US children's hospitals. The PHIS was developed by the Children's Hospital Association and represents the majority of freestanding children's hospitals. These hospitals are located in 17 of the 20 largest metropolitan areas. PHIS contains information on demographic characteristics, diagnosis and procedure codes, service locations, and line item charges for imaging studies, clinical services, laboratory tests, pharmacy, supplies, and bed-days. Furthermore, it is possible to track patients across ED and hospital visits, allowing for longitudinal analysis. Data quality is ensured through specific processes, including bimonthly coding consensus meetings, coding consistency reviews, and quarterly data quality reports, that occur across hospitals. The institutional review board at Seattle Children's Hospital approved this study with an informed consent waiver.

Study Population

The study included patients aged >6 months and <18 years cared for in the ED or inpatient setting of a PHIS hospital between January 1, 2007, and December 31, 2012. Inpatients included those initially cared for in the ED as well as any direct admissions. We included patients with either a primary or secondary *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM), code indicating food-related anaphylaxis (995.60–995.69) (Supplemental Table 4). Patients aged <6 months were excluded because exposure to food causing anaphylaxis in this age group is unlikely. Also excluded were patients with an underlying diagnosis, as indicated by a PHIS flag of a comorbid condition (eg, malignancy and immunologic disorders) or use of a specific medication (eg, chemotherapy or immunotherapy), that would alter the risk or management of food-related anaphylaxis (Fig 1, Supplemental Table 5).

To describe the patient characteristics associated with ED and hospital care, all

cases ($N = 7303$) from the 37 hospitals that submitted ED data during the study period (Fig 1) were included. To analyze time trends, the analysis was limited to a subset of 5947 patients from 31 hospitals that had submitted data for the entire study period. For the model-based analysis of hospital admission, we excluded cases if the hospital submitted incomplete demographic data (>10% missing data for race or primary payer). Consequently, this evaluation was conducted in 4067 patients from 23 hospitals. Data were extracted from PHIS in November 2013.

Covariates

Covariates measured were gender, age (<1 year, 1–5 years, 6–11 years, or >11 years), insurance (private, public, self-pay, or other/unknown), season, geographic region, race, and type of allergen. Allergen was further categorized according to discharge ICD-9-CM codes indicating peanut, tree nut/seeds, egg, fish, crustacean, milk, fruit/vegetable, food additive, multiple, or other. Patients with the comorbid discharge diagnoses of asthma or complex chronic conditions were also further categorized because these conditions may affect severity, medical decision-making, or risk for revisits for anaphylaxis-related problems.⁸

ICD-9-CM codes beginning with 493 were used to identify patients with asthma. Patients with chronic complex conditions were identified with an established PHIS flag.⁸

Main Outcome Measures

Incidence was calculated by dividing the number of cases of food-related anaphylaxis by the total number of ED visits. Hospital admission rates were calculated by dividing the number of patients admitted with food-related anaphylaxis by the number presenting to the ED with food-related anaphylaxis, expressed in cases per 100 000 total ED visits. Patients coded as observation status were classified as inpatient because hospitals differ in whether they classify patients under observation as ED patients, inpatients, or a separate observational unit.⁹ We also measured revisits to the index ED or hospital within 3 days after discharge from

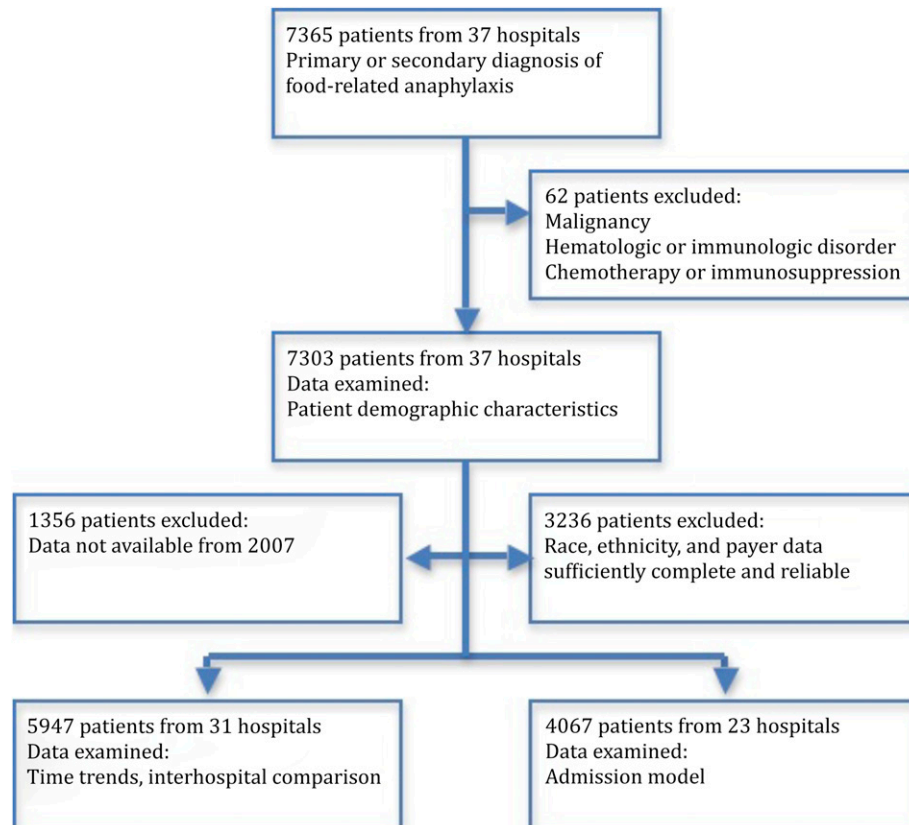


FIGURE 1 CONSORT diagram of study population.

the index visit. Three days was chosen as the revisit end point because biphasic anaphylactic reactions occur within 72 hours after initial allergen exposure, and it is extremely rare that anaphylaxis would last >72 hours.^{4,5,10} We only examined revisits to the ED for the same cause or a cause known to be a complication of anaphylaxis (eg, urticaria). Two investigators (J.P.P. and J.S.T.) reviewed all the ICD-9-CM codes for inclusion as a revisit. These included a discharge diagnosis code for food-related anaphylaxis or another allergic condition (Supplemental Table 4).

Analysis

Descriptive statistics were used to compare case counts, demographic characteristics, hospital admission, and revisits. Trends in hospital admission over time were calculated by dividing overall annual food-related anaphylaxis case counts across all hospitals by the overall ED volume. Linear regression was used to estimate the annual rate of increase and its significance.

Hospital-level raw admission and revisit rates were calculated. Multivariable generalized linear mixed model logistic regression was used to examine factors associated with admission, adjusting for age group, gender, race, ethnicity, insurance type, asthma, and indicators for the 2 most common types of food allergies in the data set (peanuts and tree nuts). Hospital was adjusted for as a random intercept. A similar model was performed to evaluate factors affecting the revisit rate but was omitted because readmission was too infrequent to render its findings useful. Thus, only unadjusted rates are reported for revisit rates.

RESULTS

Overall and Trends

Over the study period, 7303 patients met inclusion criteria. Of those, 3651 (50%) were discharged from the ED, and 3652 (50%) were admitted to the hospital. Male subjects accounted for 60% of patients. The largest group of patients were aged 1 to 5 years (52%). The most common race was white

(43%) followed by black (31%). Thirty-five percent of patients had public insurance or were listed as self-pay. Peanut was the most commonly identified allergen (37%), followed by tree nut or seed (21%) (Table 1). There were 6 ED or hospital deaths reported (mortality rate, 0.08%).

From 2007 to 2012, the number of cases of food-related anaphylaxis increased from 41 to 72 per 100 000 ED visits ($P < .01$). Despite this increase in ED care, however, the inpatient (mean, 50%) and ICU (mean, 4%) admission rates, when accounting for ED volumes, remained stable over the same interval (Table 2). Food allergens associated with the anaphylaxis admissions also remained stable for the 6-year study period (Supplemental Fig 3).

Hospital Admissions and Revisits

The mean hospital admission rate on a patient level was 50% and ranged from 20% to 98% across hospitals; similarly, the mean ICU admission rate was 3.8% and ranged from 0%

TABLE 1 Patient Demographic Characteristics (*N* = 7303 Episodes)

Characteristic	Overall (<i>N</i> = 7303)		Discharged from ED (<i>n</i> = 3651)		Admitted to Hospital (<i>n</i> = 3652)		<i>P</i> *
	<i>N</i>	% Total	<i>N</i>	% Total	<i>N</i>	% Total	
Male	4378	60	2151	59	2227	61	.002
Age, y							.02
<1	428	6	186	5	242	7	
1–5	3831	52	1933	53	1898	52	
6–11	1663	23	859	24	804	22	
>11	1381	19	673	18	708	19	
Race							.35
White	3172	43	1611	44	1561	43	
Black	2228	31	1089	30	1139	31	
Latino	733	10	354	10	379	10	
Other/unknown	1170	16	597	16	573	16	
Insurance							.14
Commercial	3948	54	1990	55	1958	54	
Public/self	2531	35	1230	34	1301	36	
Other/unknown	824	11	431	12	393	11	
Season							.33
January–March	1516	21	770	21	746	20	
April–June	1926	26	944	26	982	27	
July–September	1837	25	945	26	892	24	
October–December	2024	28	992	27	1032	28	
Region							<.001
Northeast	1371	19	615	17	756	21	
South	2021	28	1036	28	985	27	
Midwest	2334	32	1195	33	1139	31	
West	1577	22	805	22	772	21	
Allergen							<.001
Peanut	2699	37	1409	39	1290	35	
Tree nut/seeds	1537	21	715	20	822	23	
Eggs	363	5	183	5	180	5	
Fish	571	8	298	8	273	7	
Crustacean	267	4	147	4	120	3	
Milk	445	6	203	6	242	7	
Fruit/vegetable	229	3	114	3	115	3	
Food additive	37	<1	15	<1	22	<1	
Multiple	110	2	24	<1	86	2	
Unspecified	1045	14	543	15	502	14	
Comorbidities							
Asthma	1434	20	351	10	1083	30	<.001
Complex chronic condition	184	3	37	1	147	4	<.001

**P* value indicates comparison of patients admitted versus discharged from the ED (χ^2 test).

a diagnosis of peanut (OR, 1.2 [95% CI, 1.0–1.5]) or tree nut (OR, 1.7 [95% CI, 1.3–2.1]) anaphylaxis, or a diagnosis of asthma (OR, 7.4 [95% CI, 5.8–9.3]) or a chronic complex condition (OR, 5.2 [95% CI, 3.0–9.0]) (Table 3). Insurance status was not significantly associated with admission. The unadjusted 3-day revisit rate was 3% for patients discharged from the ED and 0.6% for those admitted as an inpatient on the index ED visit.

DISCUSSION

In this large, multicenter analysis of pediatric hospitals from 2007 to 2012, we found that children are increasingly being diagnosed with food-related anaphylaxis. However, there has been no corresponding increase in the proportion of these patients (when adjusting for ED volumes) admitted to the hospital and ICU. We also found that although one-half of all patients were admitted, hospitals varied widely in their rates of admission and that revisits were uncommon, even when patients were initially discharged from the ED.

We found a >50% increase in episodes of food-related anaphylaxis from 2007 to 2012 presenting to the ED, paralleling the reported rise in the prevalence of food allergies. The reason for this increase is unknown and under debate. Food allergy is believed to result from a disruption in the development of tolerance to food proteins and/or the development of sensitization to allergens. A multitude of host and environmental factors, including changes in gut microflora, disruption of intestinal barrier functioning, and timing of early food introduction, have been implicated.^{11–13}

Clark et al¹⁴ evaluated time trends in the incidence of food-related anaphylaxis from 2001 to 2009. Using data extrapolated from 2 multicenter studies, they concluded that the incidence of ED visits among patients aged <18 years for acute food-related reactions was stable (0.29% of all ED visits in 2001 vs 0.28% in 2009). However, our study indicates that the increase in food-related anaphylaxis is a recent phenomenon, predominantly occurring from 2010 to 2012, after the study period of Clark et al had ended.

to 20% across hospitals. Figure 2 depicts wide variability in hospital and ICU admission rates across hospitals and very modest correlation between the 2 factors ($r = 0.21$).

Patients more likely to be admitted to the hospital were <1 year of age (OR, 1.8 [95% CI, 1.3–2.5]), male (OR, 1.2 [95% CI, 1.0–1.4]), of black race (OR, 0.8 [95% CI, 0.6–1.0]), had

TABLE 2 Time Trends in Food-Related Anaphylaxis and Hospital Management (*N* = 5947 episodes)

Variable	2007	2008	2009	2010	2011	2012	Overall
Total ED visits	1 580 299	1 624 821	1 951 977	1 855 677	1 929 471	2 061 317	11 003 562
Food-related anaphylaxis cases	645	716	836	1005	1255	1490	5947
Food-related anaphylaxis cases per 100 000 visits*	41	44	43	54	65	72	54
Hospital admission rate, %	49	51	45	49	47	50	50
ICU admission rate, %	3.6	4.5	3.0	4.6	3.3	3.7	3.8

**P* < .05.

Although ED visits for food-related anaphylaxis are increasing, we found no increase in the proportion of ED patients hospitalized or admitted to the ICU when correcting for ED patient volume. Only 3.8% of hospitalized patients required ICU admission, and hospital mortality was extremely uncommon.

The decision to discharge a patient from the ED rather than admit to the hospital must be carefully weighed against the risk of recurrent or recalcitrant symptoms and the cost and risk of hospitalization. National organizations state that the risk of recurrent or recalcitrant symptoms is substantially low for most children with food anaphylaxis, and they therefore recommend against routine admission for the vast majority of these patients.⁷

However, we found that one-half of patients presenting to the ED with anaphylaxis are admitted to the hospital and that adjusted rates of hospitalization vary widely, with nearly fivefold differences between hospitals. Our findings indicate these national recommendations have not yet been implemented at all hospitals. Moreover, we found that 3-day revisits after ED discharge were uncommon (3%), indicating diminished value in routinely admitting all patients to the hospital. Our results may be useful to ED providers when counseling patients after allergen exposure regarding the risk of symptom recurrence. Inpatient monitoring or prolonged observation should be reserved for selected patients with established risk factors, such as asthma or severe disease, and should be carefully weighed against the

associated cost, hazards, and family preference.⁷ Quality improvement collaborative efforts could provide an opportunity for hospitals to share best practices to improve the value of care for this condition.^{15,16}

We identified the patients most likely to be admitted and, therefore, perceived to be at risk for severe, persistent, or recurrent disease. The strongest characteristics associated with hospital admission included age <1 year, tree nut exposure, and asthma or other comorbid conditions. Although patients with asthma are known to be at higher risk for fatality from anaphylaxis, no reliable clinical predictors are available that indicate which patients are most at risk for severe or recurrent symptoms.⁷ Additional study is therefore needed to identify which patients would benefit most from

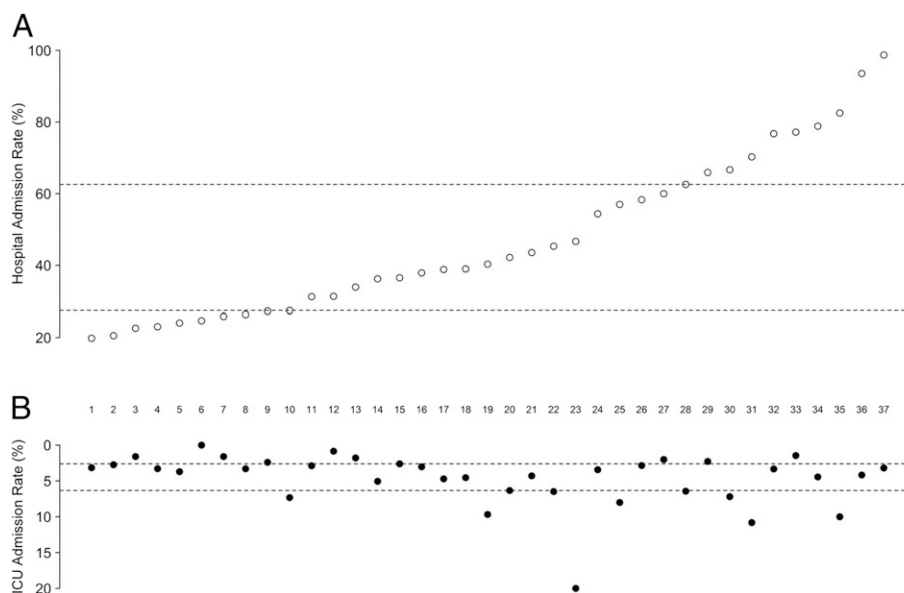


FIGURE 2 Variability in and correlation of (A) hospital and (B) ICU admissions. Hospital and ICU admission rates were calculated across 37 hospitals, and the correlation coefficient between hospital and ICU admission rates was 0.21. The dashed lines represent the first and third hospital quartiles.

TABLE 3 Factors Associated With Hospital Admission (*N* = 4067 Episodes)

Factors	OR (95% CI)
Male	1.2 (1.0–1.4)*
Non-white race	
Black	0.8 (0.6–1.0)*
Latino	0.9 (0.7–1.2)
Other or unknown	1.0 (0.8–1.3)
Non-private insurance	
Government	1.1 (0.9–1.3)
Self-insured	1.3 (0.7–2.5)
Other/unknown	1.3 (0.6–3.1)
Age, y	
<1	1.8 (1.3–2.5)**
6–11	0.9 (0.7–1.1)
>11	1.2 (1.0–1.5)
Peanut diagnosis	1.2 (1.0–1.5)*
Tree nut diagnosis	1.7 (1.3–2.1)**
Asthma	7.4 (5.8–9.3)**
Complex chronic condition	5.2 (3.0–9.0)**

The reference group included white female subjects aged 1 to 5 years with private insurance. **P* < .05, ***P* < .01.

hospitalization and whether this approach correlates with the populations that are actually admitted. It is also likely that age <1 year was a proxy for a child's first reaction, and ED clinicians and families may perceive these patients as more vulnerable and more likely to benefit from admission.

Our study has several limitations common to retrospective cohort studies using administrative data. First, to reduce the chance for misclassification bias, we narrowly defined the inclusion criteria. This strategy excludes nonclassified cases of food-related anaphylaxis and is therefore a conservative estimate of cases of food-related anaphylaxis. Although there is no a priori reason to suspect it, this strategy has the potential to lead to an overestimation of variability across hospitals if some hospitals tend to use nonspecific codes for food anaphylaxis compared with others. In addition, if there was a change in coding over time, it could lead to an overestimation or an underestimation of temporal trends in cases. Second, although we adjusted for differences in covariates across hospitals, we cannot be certain that residual confounding did not contribute to the observed variability in care.

For example, the prehospital availability and administration of epinephrine autoinjectors could not be determined. Finally, actual revisit and mortality estimates may be higher for some hospitals because we were only able to capture events occurring at the index hospital.

CONCLUSIONS

The incidence of food-related anaphylaxis in pediatric EDs is increasing but markers of disease severity have remained proportionally stable in this population. Despite national guidelines recommending against routine hospital admission and the uncommon occurrence of 3-day revisits, the practice remains common at some but not all hospitals. Taken together, these findings indicate opportunities to improve health care delivery and reduce costs. Factors associated with hospital admission were identified, but more research is needed to identify the patients most at-risk for either persistent or recurrent symptoms and, therefore, most likely to benefit from inpatient management.

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