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Patterns of hospital readmission in children with food-induced anaphylaxis

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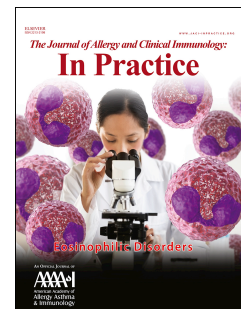
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Title: Patterns of hospital readmission in children with food-induced anaphylaxis

Short Title: Readmission in food-induced anaphylaxis

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BT Cheng had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

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46 **Clinical statement:** There is an increased risk of inpatient hospital readmission for food-induced
47 anaphylaxis in our pediatric cohort due to seeds and tree nuts amongst adolescents admitted to a
48 teaching hospital on the weekend. These children may benefit from additional food allergy
49 education and careful counseling to prevent repeat hospitalizations.

To the editor:

Previous studies have found increasing inpatient utilization for food-induced anaphylaxis (FIA) among children.¹ However, these data do not address frequency of readmission. Children with inpatient admission for FIA are a high-risk group for mortality, and readmission indicates further risk for fatality from food allergy.² This study examined patterns and predictors of readmission among US children hospitalized for FIA. Our objective was to identify sociodemographic characteristics in patients requiring readmission within one year for FIA.

We analyzed all children (<18 years) from the 2012-2016 National Readmissions Database (NRD), a cross-sectional sample of US hospitalizations from the Agency for Healthcare Research and Quality. NRD contains an anonymized patient linkage variable that allows tracking of a patient across multiple hospitalizations within a calendar year. FIA was identified using *International Classification of Diseases (ICD)* codes; NRD contains up to 35 discharge diagnoses per hospitalization. Based on previous studies, index admission was defined as first discharge diagnosis of either (1) a specific FIA code or (2) history of food allergy and current anaphylaxis episode (Table E1).¹

Prevalence and median time to first readmission were tabulated in children with FIA who were vs were not readmitted for the indication of FIA. We determined 30-/60-/90-/any day readmission rate for FIA. Hospitalizations were limited to January-November, January-October and January-September to determine 30-, 60- and 90-day readmission rates, respectively. Inpatient cost of care was calculated, adjusted for inflation and cost-to-charge ratio provided by the NRD.

Bivariable and multivariable Cox regression models invoking stepwise selection ($\alpha=0.10$) were constructed to determine patient- and hospital-level characteristics associated with

readmission among children with FIA. Time-to-event outcome was time from index discharge to first readmission with FIA. Models included sex, age, household income, insurance payer, number of chronic conditions (defined by the Healthcare Cost and Utilization Project Chronic Comorbidity Indicator),³ length of index hospitalization, admission on a weekend, hospital size and teaching status, comorbid asthma, and season. Cox regression models, adjusted for all significant variables in the final stepwise model, were constructed to examine intubation and particular food antigens as predictors of readmission. Crude and adjusted hazard ratios (HR) and 95% confidence intervals (CI) were estimated.

All analyses were conducted in SAS v9.4 (SAS Institute, Cary, NC). A two-sided P-value <0.05 was considered statistically significant.

There were 28,105,752 (unweighted: 6,152,409) pediatric discharges captured in the 2012-2016 NRD. Out of 5,872 index admissions with FIA over the five-year period, 62 (proportion [95% CI]: 1.1% [0.7-1.5%]) were readmitted with FIA within the calendar year (median [IQR] time to readmission: 54.2 [120.9] days). The 30-day readmission rate for FIA was 0.3% [95% CI: 0.1-0.5%], increasing to 0.5% [0.3-0.8%] and 0.7% [0.4-1.0%] within 60 and 90 days, respectively. Having multiple readmissions was rare: 0.8% [0.5-1.1%] were readmitted once, 0.2% [0.0-0.3%] twice, and 0.1% [0.0-0.2%] ≥ 3 times (maximum=6). The median cost of index admission and first readmission with FIA were \$2506 [IQR: \$2550] and \$4416 [\$6151], respectively. For comparison, median hospitalization cost for non-FIA hospitalizations was \$1674 [\$3243].

In multivariable Cox regression models invoking stepwise selection, higher risk of readmission with FIA was associated with ages 13-17 years (adjusted HR [95% CI]: 2.67 [1.32-

5.40]), admission on a weekend (2.23 [1.08-4.61]), and hospital teaching status (2.26 [1.41-3.63]), and inversely associated with ages 6-12 years (0.28 [0.11-0.68]) (Table 1).

In models adjusted for age, weekend admission, and hospital teaching status, intubation did not predict higher rates of readmission with FIA (adjusted HR [95% CI]: 0.65 [0.07-6.42], $P=0.70$). In similarly adjusted models, readmission risk was increased in children initially hospitalized for anaphylaxis triggered by seeds and tree nuts (3.25 [1.30-8.11]) (Table 2).

This study found readmission after FIA hospitalization was rare (1.1% of children were readmitted within a calendar year), yet we were able to identify certain characteristics which increased odds of readmission. In particular, seeds and tree nuts (which are a joint ICD code) were the food triggers associated with the highest risk of readmission. It is possible this is due to sesame allergen, which is not required for advisory labelling under the current Food Allergen Labeling and Consumer Protection Act (FALCPA).⁴ This places even the most vigilant families at risk for accidental exposures. In fact, one survey study of patients with sesame allergy found accidental exposure rates were comparable for sesame and peanut (15.9% vs 12.4%), and epinephrine in sesame reactions were underutilized.⁵ Anaphylaxis induced by seeds and tree nuts may describe a higher-risk cohort at particular need for careful counseling.

Other demographic characteristics associated with increased readmission risk were older children originally admitted to a teaching hospital and during a weekend. Higher rates of readmission to teaching hospitals likely reflects the complexity of patients admitted to these facilities.^{6,7} Our findings also suggest children hospitalized during the weekend might not receive adequate education about how to manage food allergy. Previous studies have proposed differences in nursing and clinician staffing contribute to increased inpatient mortality on the weekends.^{8,9} It may also be that children and adolescents tend to engage in less routine behavior

over the weekend and might introduce different foods than on a weekday.¹⁰ There may be additional opportunities to reduce readmission through careful evaluation and counseling by a clinician with specific training in management of food allergy. Additional studies are needed to determine optimal strategies to reduce readmissions. For now, older children and those admitted on the weekend should be specifically targeted for more in-depth food allergy education to potentially prevent readmission.

Strengths of this study include the large all-payer cohort collected over a 5-year period and the population-based survey sampling that allows for accurate estimates of nationwide readmissions. A few limitations merit mention. First, the readmission rate was very low, which reduces the power of predictive models; stepwise variable selection was used to minimize collinearity and increase the events per variable in multivariable models. Our study cohort comprised US hospitalizations and results may not be generalizable to other countries. Moreover, these data only reflect inpatient care delivered; data were unavailable on outpatient care, emergency department (ED) visits, and individual access to epinephrine. Additional studies are needed to investigate these points. We excluded patients in whom “anaphylaxis” was coded without evidence of food allergy to increase positive predictive value; as such, our results likely underestimate the true prevalence of food-induced anaphylaxis. Additionally, data on specific allergens are limited to what is available in ICD coding, such as the joint code for seed and tree nut anaphylaxis. Future studies will determine optimal strategies to educate children with FIA and prevent readmissions.

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Table 1. Predictors of food-induced anaphylaxis readmission in patients who were hospitalized with food-induced anaphylaxis.

Variable	Readmission with anaphylaxis							
	No	Yes	% Prev [95% CI]	Median [IQR]*	Crude HR [95% CI]	P-Value	Adjusted HR [95% CI]	P-Value
	Wtd Freq	Wtd Freq						
Sex								
Male	3320	33	1.0 [0.5-1.5]	53.6 [142.5]	1.00 [ref]	–		
Female	2403	29	1.2 [0.6-1.8]	54.7 [88.8]	1.78 [0.89-3.55]	0.10		
Age (years)								
≤5	2299	16	0.7 [0.2-1.2]	20.0 [150.8]	1.00 [ref]	–	1.00 [ref]	–
6-12	1713	12	0.7 [0.2-1.2]	102.7 [141.2]	0.39 [0.17-0.91]	0.03	0.28 [0.11-0.68]	0.006
13-17	1711	35	2.0 [1.0-3.0]	55.7 [86.7]	3.06 [1.71-5.50]	0.0003	2.67 [1.32-5.40]	0.007
Annual household income								
<50 th %'ile	2617	34	1.3 [0.6-1.9]	63.7 [86.1]	1.21 [0.63-2.32]	0.57		
≥50 th %'ile	3061	29	0.9 [0.5-1.4]	44.6 [164.6]	1.00 [ref]	–		
Insurance payer								
Private	2773	31	1.1 [0.5-1.7]	32.2 [65.1]	1.00 [ref]	–		
Public	2582	30	1.1 [0.5-1.8]	91.0 [119.9]	0.46 [0.22-0.98]	0.04		
No insurance/other	363	≤10	0.5 [0.0-1.5]	2.0 [0.0]	0.46 [0.05-4.38]	0.49		
Number of chronic conditions								
0-1	3542	30	0.8 [0.3-1.3]	110.5 [139.9]	1.00 [ref]	–		
≥2	826	28	3.3 [1.8-4.8]	41.1 [63.1]	1.45 [0.83-2.54]	0.19		
Length of stay								
0-1 days	4351	26	0.6 [0.3-0.9]	47.1 [119.9]	1.00 [ref]	–		
2+ days	1370	37	2.6 [1.4-3.8]	73.1 [112.6]	2.08 [1.03-4.20]	0.04		
Weekend admission								
No	3803	42	1.1 [0.6-1.6]	86.3 [115.2]	1.00 [ref]	–	1.00 [ref]	–
Yes	1920	20	1.0 [0.5-1.6]	41.6 [52.1]	1.64 [0.83-3.24]	0.15	2.23 [1.08-4.61]	0.03
Hospital bed size								
Small/medium	1935	19	1.0 [0.4-1.6]	72.0 [131.8]	1.00 [ref]	–		
Large	3788	43	1.1 [0.6-1.6]	49.4 [95.2]	0.89 [0.44-1.81]	0.74		
Hospital teaching status								
Non-teaching	743	≤10	0.6 [0.0-1.3]	33.0 [63.3]	1.00 [ref]	–	1.00 [ref]	–
Teaching	4980	58	1.1 [0.7-1.6]	54.7 [114.8]	0.62 [0.43-0.89]	0.009	2.26 [1.41-3.63]	0.001
Asthma								
No	3463	24	0.7 [0.3-1.1]	40.2 [63.2]	1.00 [ref]	–		
Yes	2260	39	1.7 [0.9-2.5]	80.6 [128.7]	0.80 [0.43-1.48]	0.46		
Season								
Autumn/winter	2678	22	0.8 [0.3-1.3]	55.8 [162.2]	0.34 [0.16-0.71]	0.005	0.41 [0.15-1.14]	0.09
Spring/summer	3045	41	1.3 [0.8-1.8]	53.4 [96.1]	1.00 [ref]	–	1.00 [ref]	–

165 Gray cells indicate that the variable was not included in the final selection models. Bold text indicates P-value was
 166 statistically significant.

167 Values ≤10 are bottom-coded to preserve anonymity.

168 *Refers to median and interquartile range of time to readmission in days

Table 2. Association of food allergen trigger and readmission for food-induced anaphylaxis.

Variable	Readmission with anaphylaxis					
	No	Yes	% Prev [95% CI]	Median [IQR]*	Adjusted HR* [95% CI]	P- Value
	Wtd Freq	Wtd Freq				
Food allergen						
Peanuts	1582	13	0.8 [0.3-1.4]	82.9 [156.7]	1.51 [0.65-3.50]	0.33
Shellfish/seafood	521	≤10	1.2 [0.0-2.5]	22.0 [30.4]	1.96 [0.48-8.02]	0.34
Fruits, vegetables	488	≤10	0.0 [0.0-0.0]	–	–	–
Seeds and tree nuts	767	20	2.5 [0.8-4.1]	39.5 [74.6]	3.25 [1.30-8.11]	0.01
Food additives	40	≤10	0.0 [0.0-0.0]	–	–	–
Milk products	436	≤10	0.4 [0.0-1.2]	157.0 [0.0]	0.53 [0.05-5.47]	0.59
Eggs	315	≤10	0.0 [0.0-0.0]	–	–	–
Not specified	1574	22	1.4 [0.6-2.1]	75.6 [148.1]	1.00 [ref]	–

169 *Models adjusted for age, weekend admission, and hospital teaching status. Bold text indicates P-value was
 170 statistically significant.

171 Values ≤10 are bottom-coded to preserve anonymity.

172 *Refers to median and interquartile range of time to readmission in days

Table E1. International Classification of Disease and Current Procedure Terminology codes identified.

Diagnosis	International Classification of Disease (ICD) code
Food-induced anaphylaxis	ICD-9: 995.6x ICD-10: T78.00XA-T78.09XA
History of food allergy	ICD-9: V15.01-V15.05 ICD-10: Z91.010-Z91.013, Z91.018
Anaphylaxis	ICD-9: 995.0 ICD-10: T78.2XXA
Asthma	ICD-9: 493.x ICD-10: J45.x
Procedure	Current Procedure Terminology code
Intubation	ICD-9: 960.1-960.5 ICD-10: 09HN7BZ, 09HN8BZ, 0CHY7BZ, 0CHY8BZ, 0DH57BZ, 0DH58BZ, 0BH17EZ, 0BH18EZ, 0B717DZ, 0B718DZ, 0BH07DZ, 0BH07YZ, 0BH172Z, 0BH17YZ, 0BH182Z, 0BH18YZ, 0BHK7YZ, 0BHK8YZ, 0BHL7YZ, 0BHL8YZ, 0WHQ7YZ