

Hospitalizations for Anaphylaxis in Florida: Epidemiologic Analysis of a Population-Based Dataset

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Key Words

Anaphylaxis • Epidemiology • Hospitalization • Mechanical ventilation

Abstract

Background: Previous epidemiologic studies of anaphylaxis have been single-institution investigations. The objective of this study was to determine the annual hospital discharge rate and risk factors for anaphylaxis outcomes throughout Florida. **Methods:** 464 patients who were hospitalized in Florida for anaphylaxis and discharged in 2001 were identified using a statewide database and ICD-9-CM (International Classification of Diseases, 9th revision, Clinical Modification) codes. Linear regression was used to determine the predictors of length of stay (LOS) and total charges. Relative risks (RR) for ventilator-assisted respiration and anaphylaxis due to food were calculated using binomial regression. **Results:** Annual hospital discharge rate for anaphylaxis was 2.8/100,000 population. Hospital mortality rate was 0.86%. Median LOS was 1 day. Median total charges was USD 4,982. Asthmatics had increased risk of receiving ventilator-assisted respiration (adjusted RR = 2.72, $p = 0.04$). Likelihood of hospitalization for anaphylaxis increased with age for both sexes ($p < 0.0001$). Patients who were <18 years old were three times as likely to be hospitalized for food anaphylaxis

(versus other causes) compared to patients who were 71+ years old (adjusted RR = 3.25, $p = 0.004$). **Conclusion:** Young age was associated with increased risk of hospitalization for anaphylaxis to foods. Asthmatics had increased risk of receiving ventilator-assisted respiration. Likelihood of hospitalization increased with age. Copyright © 2007 S. Karger AG, Basel

Introduction

Anaphylaxis is a potentially life-threatening syndrome usually following exposure to an antigen to which an individual is allergic [1]. This antigen exposure then results in mast cell degranulation [1]. Nonallergic anaphylaxis may result from exposure to a nonspecific mast cell activator [1]. Two US population-based studies of anaphylaxis have previously been reported. One based on a medical record review in Olmsted County, Minn., USA, reported 9 hospitalizations during a 5-year period [2]. The other study of 229,422 children and adolescents enrolled in a health maintenance organization also reported 9 hospitalizations during a 5-year period [3]. We conducted a retrospective cohort study to elucidate the clinical epidemiology of hospitalization for anaphylaxis. Our goals were to evaluate the incidence of hospitalization for ana-

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phylaxis, the in-hospital mortality, and the impact of demographic and clinical factors on total patient charges, the risk of receiving ventilator-assisted respiration, length of stay (LOS), venom-associated anaphylaxis, and food-associated anaphylaxis among patients hospitalized for anaphylactic shock throughout Florida and discharged during a 1-year period. To our knowledge, this use of a statewide hospital database represents a novel approach in the study of the outcomes of anaphylaxis in the United States.

Materials and Methods

Source Population and Inclusion Criteria

A hospital discharge dataset was obtained from the Florida Agency for Health Care Administration. This public-use database includes discharge summaries from all non-federal Florida hospitals except state tuberculosis and state mental health hospitals. After data are entered into this system, they are subjected to formatting and logic checks. The primary hospital submitting patient information must then certify the data are correct and verify the accuracy of a summary report before it is released by the Florida Agency for Health Care Administration.

This dataset contained clinical and demographic information for 2,343,330 patients who were hospitalized for at least 1 day and discharged in calendar year 2001. The principal discharge diagnosis and up to nine secondary discharge diagnoses were coded using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM). Procedures performed during the hospital stay were also coded using ICD-9-CM. The Florida Agency for Health Care Administration allowed for up to nine secondary procedure codes in addition to the principal procedure code.

Records were included in our analysis if the principal discharge diagnosis was anaphylactic shock/allergic shock/anaphylactic reaction/anaphylaxis which was not otherwise specified or due to the adverse effect of a correct medicinal substance that was administered properly (ICD-9-CM code 995.0), anaphylactic shock due to an adverse reaction to a nonpoisonous food such as peanuts or crustaceans (ICD-9-CM codes 995.60 through 995.69) or anaphylaxis due to anesthesia (ICD-9-CM 995.4). The broad category of 'other anaphylactic shock' (ICD-9-CM code 995.0) also included patients who had adverse reactions to one or more antibiotics. A select group of these patients were identified using ICD-9-CM codes E930.0-E931.0 and their data were summarized.

In addition, records were included if the principal discharge diagnosis was 'toxic effect of other substances, venom' (ICD-9-CM code 989.5). There were 453 such records. However, many records with ICD-9-CM code 989.5 also contained procedure codes for treatment of animal bites which suggested that the envenomation was not from a Hymenoptera insect. Therefore this group of records was further analyzed for E codes that confirmed that the envenomation was from a source other than a Hymenoptera insect. 295 records were found to contain codes for venomous snakes and lizards (E905.0), venomous spiders (E905.1), scorpion

(E905.2), centipede and venomous millipede (tropical) (E905.4), venomous marine animals and plants (E905.6), and poisoning and toxic reactions caused by other plants (E905.7). These records were excluded leaving 158 other records with ICD-9-CM code 989.5 toxic effect of other substances, venom. ICD-9-CM code 989.5 is commonly used to denote allergic reactions to Hymenoptera insect stings [4].

The database did not contain a unique patient identifier and therefore the records of patients who were discharged to another hospital were deleted to minimize the probability of including multiple records for a single patient in the multivariate analysis. Multiple regression analyses can only be performed if every patient record has complete data for all of the independent variables and the dependent variable. Records that had missing values for the dependent and/or independent variables and records of patients who were discharged to another hospital were deleted. Seven records were deleted due to missing values (after applying our inclusion and exclusion criteria). There were 464 records available for the regression analyses after also deleting the records of the seven patients who were discharged to another hospital.

Calculation of Hospital Discharge Rates

A total of 442 of the 464 patients were Florida residents. Age- and sex-specific hospital discharge rates for Florida residents were calculated by dividing the appropriate number of cases that were discharged in 2001 by the stratum-specific Florida population estimate for 2001 [5]. χ^2 tests for a linear trend in proportions (Mantel extension) were calculated for both the male and female rates using the Epi Info software package (Version 6.04d, Centers for Disease Control and Prevention, Atlanta, Ga., USA).

Definition of Outcomes Used in the Regression Analyses

Five outcomes were studied. The first dependent variable was LOS recorded in days. According to the Florida Agency for Health Care Administration, discharges on the admission date were counted as 1 day. The second dependent variable, total patient charges, was also a continuous outcome. This was defined by the Florida Agency for Health Care Administration as the amount charged to the patient (before any discounts) and rounded to the nearest US dollar. The third outcome was being placed on a mechanical ventilator and receiving respiratory assistance via an endotracheal tube or tracheostomy. This outcome was defined as the presence of ICD-9-CM codes 96.70 (continuous mechanical ventilation of unspecified duration), 96.71 (continuous mechanical ventilation for less than 96 consecutive hours), or 96.72 (continuous mechanical ventilation for 96 consecutive hours or more) in any of the ten procedure fields. The fourth outcome was anaphylaxis due to food as opposed to anaphylaxis caused by other factors (see ICD-9-CM disease codes above). The final outcome was anaphylaxis due to exposure to venom (see ICD-9-CM disease codes above).

Definition of Potential Risk Factors

Several demographic and clinical risk factors were studied. Age at the time of admission was a continuous variable recorded in years for the linear regression analyses. For the binomial regression models, the following four clinically relevant age categories were created: 0-17, 18-30, 31-70, and ≥ 71 years. We created a binary race-ethnicity variable: White non-Hispanic versus other race ethnicity. The patient's principal health insurance payer

was used as a proxy of socioeconomic status and was defined as commercial insurance compared to noncommercial insurance. Commercial carriers were defined as non-Medicaid health maintenance organizations (HMO) and preferred provider organizations. Noncommercial carriers included Medicare, Medicaid, charity, self-pay, Department of Veterans Affairs, etc. Heart disease was defined as the presence of any of the following ICD-9-CM codes in any of the nine secondary discharge diagnosis positions: 401.0–402.9 and 404.00–405.99 (hypertensive disease), 414.00–414.05 (coronary atherosclerosis), and 428.0–428.9 (congestive heart failure). Asthma was defined as ICD-9-CM codes 493.00 to 493.92. Finally, we examined the impact of receiving continuous mechanical ventilation (defined above) on LOS and total charges.

Statistical Analysis: LOS and Total Charges

Linear regression was used to model the association between the potential risk factors and the continuous outcomes of LOS and total charges. The patients were clustered in 153 hospitals. Conventional linear regression assumes that the outcome data are not correlated. This assumption was most likely violated since patients were nested by hospital and therefore patients treated for anaphylactic shock within a particular hospital may have similar risks for prolonged LOS or elevated total charges. Failure to adjust for this correlation may affect point estimates and p values. We used generalized estimating equations to account for the correlated outcome data [6, 7].

LOS was not included as a predictor while modeling correlates of total charges since it is in the causal pathway of several of our predictor variables [8, 9]. For example, one would expect that severely ill patients who were intubated and placed on a ventilator may have an extended hospital stay which would lead to a higher total charges figure. A result was considered statistically significant if p was 0.05 or less.

Statistical Analysis: Mechanical Ventilation, Food Anaphylaxis, and Venom

Binomial regression was used to calculate crude and adjusted relative risks (RR) for three dichotomous outcomes: receipt of mechanical ventilation, anaphylaxis due to food, and anaphylaxis due to venom [10].

The GENMOD procedure in SAS was used to perform binomial regression [10]. A RR was considered statistically significant if the 95% confidence interval for the population RR excluded the value of one, which is the null value (the value of no association). We used generalized estimating equations to account for potential correlations between patients treated at the same hospital [6, 7]. The study protocol was approved by the Committee for the Protection of Human Subjects at The University of Texas Health Science Center at Houston.

Results

Florida's population in 2001 is estimated to be 16,410,669 [5]. A total of 464 cases were included in our analyses, yielding an annual period prevalence of hospitalization for anaphylaxis of approximately 19.8 cases per

Table 1. Detailed principal discharge diagnoses of patients hospitalized for anaphylaxis (n = 464)

ICD-9-CM code	Description of diagnosis	n	%
989.5	Toxic effect venom	158	34.1
995.0	Other anaphylactic shock	227	48.9
	Penicillins	21	
	Cephalosporins*	17	
	Other specified* and unspecified antibiotics	7	
	Sulfonamides*	5	
	Macrolides	2	
	Tetracycline group	1	
	Antifungal antibiotics	1	
995.4	Shock due to anesthesia	4	0.9
	Anaphylactic shock due to:		
995.60	Unspecified food	6	1.3
995.61	Peanuts	9	1.9
995.62	Crustaceans	11	2.4
995.63	Fruits and vegetables	7	1.5
995.64	Tree nuts and seeds	4	0.9
995.65	Fish	12	2.6
995.66	Food additives	1	0.2
995.67	Milk products	3	0.7
995.68	Eggs	1	0.2
995.69	Other specified food	21	4.5

* One patient from each group with a reaction to more than one class of antibiotic. ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

100,000 patients hospitalized for all causes (464 cases/2,343,330 discharges) and 2.8 hospitalizations for anaphylaxis per 100,000 population.

The distribution of principal discharge diagnoses is presented in table 1. The 'other anaphylactic shock' category (ICD-9-CM code 995.0) was used in several patients who had adverse reactions to various antibiotics including beta-lactams (table 1). Approximately 16% of the cohort was hospitalized for anaphylaxis caused by foods. Hospital discharge rates for anaphylaxis among Florida residents are shown in figure 1. Overall, rates for both sexes increased between the ages of 20 and 79 years. p was < 0.0001 for male and female subjects.

Selected characteristics of these 464 patients are shown in table 2. The majority of the patients were White non-Hispanics (78.2%). Asthma was noted to be present in 30 individuals (6.5%). Review of the discharge diagnoses revealed that 9 of the 30 asthmatics (30%) had a principal discharge diagnosis code for food anaphylaxis. Venom

Table 2. Demographic and clinical characteristics of patients hospitalized for anaphylactic shock (n = 464)

Demographic variables	
Age, years (median; range)	53;0–94
Male	223 (48.1%)
White non-Hispanic	363 (78.2%)
Commercial insurance	211 (45.5%)
Clinical variables	
Asthma	30 (6.5%)
Heart disease	157 (33.8%)
Mechanical ventilation	34 (7.3%)

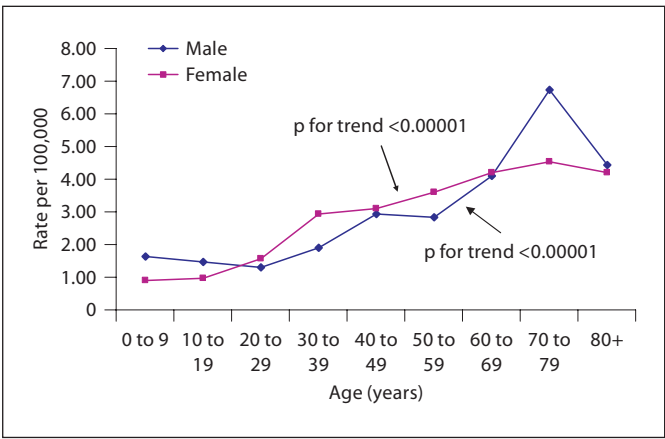


Fig. 1. Anaphylaxis hospital discharge rates, Florida, USA, 2001.

Table 3. Crude and adjusted* parameter estimates of potential risk factors for length of stay from linear regression models (n = 464)

	Crude		Adjusted	
	parameter estimate	p value	parameter estimate	p value
<i>Demographic variables</i>				
Age (1-year increments)	0.045	0.21	0.043	0.39
Sex				
Male	0.32	0.76	0.86	0.54
Female	referent	–	referent	–
Race-ethnicity				
White non-Hispanic	0.29	0.71	–0.33	0.49
Other race ethnic groups	referent	–	referent	–
Health insurance				
Commercial insurance	–2.02	0.03	–1.01	0.02
Other insurance payer	referent	–	referent	–
<i>Clinical variables</i>				
Asthma present?				
Yes	–1.50	0.01	–2.15	0.04
No	referent	–	referent	–
Heart disease present?				
Yes	–0.019	0.98	–1.53	0.47
No	referent	–	referent	–
Mechanical ventilation				
Placed on ventilator	9.85	0.13	9.75	0.13
Was not put on ventilator	referent	–	referent	–
* Each parameter estimate is adjusted for the remaining variables in the table.				

anaphylaxis comprised 6 of the 30 asthmatic patients’ anaphylaxis triggers. Drug-induced anaphylaxis occurred in an additional 3 asthmatic subjects. Because the charts are not available to the authors, it is not possible to

review the charts to determine the other 12 asthmatic patients’ trigger factors. Four patients expired in the hospital. Two of the patients had a principal discharge diagnosis of ‘toxic effect due to venom of other venomous ar-

Table 4. Crude and adjusted* parameter estimates of potential risk factors for total patient charges from linear regression models (n = 464)

	Crude		Adjusted	
	parameter estimate	p value	parameter estimate	p value
<i>Demographic Variables</i>				
Age (1-year increments)	193.23	0.22	183.79	0.39
Sex				
Male	1,998.29	0.67	4,698.20	0.44
Female	referent	–	referent	–
Race ethnicity				
White non-Hispanic	2,273.67	0.50	–455.23	0.82
Other race ethnic groups	referent	–	referent	–
Health insurance				
Commercial insurance	–8,950.52	0.03	–4,370.52	0.04
Other insurance payer	referent	–	referent	–
<i>Clinical Variables</i>				
Asthma present?				
Yes	–5,636.87	0.03	–9,287.34	0.06
No	referent	–	referent	–
Heart disease present?				
Yes	–991.55	0.78	–7,830.59	0.39
No	referent	–	referent	–
Mechanical ventilation				
Placed on ventilator	50,893.75	0.07	50,729.12	0.07
Was not put on ventilator	referent	–	referent	–
* Each parameter estimate is adjusted for the remaining variables in the table.				

thropods'. They died as the result of anaphylaxis to ant bites (presumably fire ants). Of the remaining 2 patients, 1 was an asthmatic and the other had an adverse reaction to one of the penicillins.

The distributions of LOS and total charges were skewed to the right (data not shown). The median LOS was 1 day (minimum = 1 day, maximum = 225 days) while the median total charges was USD 4,982 (minimum = USD 633, maximum = USD 983,797). Cumulative total charges for the entire cohort were USD 5,421,314, of which USD 1,999,430 was incurred by 34 patients who required mechanical ventilation.

Crude and adjusted coefficients from the linear regression when LOS was the outcome are shown in table 3. In the crude (unadjusted) analysis patients who had commercial health insurance had a LOS that was approximately 2 days shorter than the LOS of Medicaid patients and others who did not have commercial health insurance (p = 0.03). After adjusting for age, sex, and the remaining four variables, insurance status remained a risk factor for a shorter LOS (p = 0.02). The presence of asthma was associated with a decrease of 2.15 days in

the LOS after controlling for the other covariates (p = 0.04).

Table 4 presents coefficients from the linear regression models where total charges was the outcome. Patients with commercial health insurance incurred a USD 4,371 reduction in total charges as compared with the charges of those with non-commercial insurance (p = 0.04). Asthma was associated with a reduction in total patient charges in the crude analysis. There was a trend for patients who received ventilator-assisted respiration to have an increase in their total charges by approximately USD 50,729 (p = 0.07).

Crude and adjusted RRs for receipt of ventilator-assisted respiration are shown in table 5. Patients who were 0 to 17 years of age appeared to have an 85% reduction in the risk of being placed on a ventilator compared to patients who were ≥71 years (adjusted RR = 0.15, p = 0.06). Adults who were 31–70 years of age were also less likely than the referent group to receive ventilator-associated respiration (p = 0.01). Adjusted analysis for receiving mechanical ventilation indicates that the risk increase due to heart disease is actually due to increased age in patients

Table 5. Crude and adjusted* relative risks for receipt of mechanical ventilation from binomial regression models (n = 464)

	Crude			Adjusted		
	relative risk	95% CI	p value	relative risk	95% CI	p value
Age						
0–17 years	0.17	0.03–0.995	0.05	0.15	0.02–1.05	0.06
18–30 years	1.02	0.34–3.05	0.97	0.93	0.28–3.05	0.90
31–70 years	0.42	0.23–0.77	0.005	0.43	0.22–0.83	0.01
≥71 years	1	referent	–	1	referent	–
Asthma present?						
Yes	2.51	0.97–6.53	0.06	2.72	1.07–6.91	0.04
No	1	referent	–	1	referent	–
Heart disease present?						
Yes	1.32	0.70–2.49	0.39	1.09	0.55–2.18	0.80
No	1	referent	–	1	referent	–

* Each relative risk is adjusted for the remaining variables in the table. CI = Confidence interval.

Table 6. Crude and adjusted* relative risks for anaphylaxis due to food among patients hospitalized for various types of anaphylactic shock from binomial regression models (n = 464)

	Crude			Adjusted		
	relative risk	95% CI	p value	relative risk	95% CI	p value
Age						
0–17 years	3.58	1.68–7.65	0.001	3.25	1.45–7.25	0.004
18–30 years	4.15	1.85–9.33	0.001	3.42	1.41–8.33	0.01
31–70 years	2.15	1.06–4.34	0.03	1.89	0.91–3.92	0.09
≥71 years	1	referent	–	1	referent	–
Race ethnicity						
White non-Hispanic	0.63	0.40–0.99	0.05	0.70	0.43–1.13	0.15
Other race ethnic groups	1	referent	–	1	referent	–
Sex						
Male	0.85	0.58–1.27	0.43	0.82	0.55–1.21	0.32
Female	1	referent	–	1	referent	–
Health insurance						
Commercial insurance	1.41	0.93–2.15	0.11	1.20	0.76–1.89	0.44
Other insurance payers	1	referent	–	1	referent	–

* Each relative risk is adjusted for the remaining variables in the table. CI = Confidence interval.

with concomitant heart disease. Asthmatics were 2.72 times as likely as non-asthmatics to receive mechanical ventilation ($p = 0.04$).

The results of the univariate and multivariate modeling of anaphylaxis hospitalizations due to food are presented in table 6. Among these 464 patients hospitalized for anaphylaxis, those who were 0–17 years of age and

those who were 18–34 years of age at the time admission were more than three times as likely to have a discharge diagnosis of anaphylaxis due to food (versus other types of anaphylaxis) than patients who were 70 years of age or older. Both of these results are statistically significant.

The results of the univariate and multivariate modeling of anaphylaxis hospitalizations due to venom are pre-

Table 7. Crude and adjusted* relative risks for anaphylaxis due to venom among patients hospitalized for various types of anaphylactic shock from binomial regression models (n = 464)

	Crude			Adjusted		
	relative risk	95% CI	p value	relative risk	95% CI	p value
Age						
0–17 years	1.14	0.73–1.78	0.55	1.43	0.93–2.22	0.11
18–30 years	1.07	0.67–1.71	0.78	1.38	0.85–2.26	0.20
31–70 years	0.91	0.66–1.26	0.57	1.11	0.79–1.55	0.56
≥71 years	1	referent	–	1	referent	–
Race ethnicity						
White non-Hispanic	2.10	1.36–3.23	0.001	2.24	1.43–3.51	0.0004
Other race ethnic groups	1	referent	–	1	referent	–
Sex						
Male	1.41	1.08–1.84	0.01	1.36	1.05–1.76	0.02
Female	1	referent	–	1	referent	–
Health insurance						
Commercial insurance	0.88	0.68–1.13	0.32	0.79	0.62–1.02	0.07
Other insurance payers	1	referent	–	1	referent	–

* Each relative risk is adjusted for the remaining variables in the table. CI = Confidence interval.

sented in table 7. Among these 464 patients hospitalized for anaphylaxis, those who were White were approximately two times as likely as other racial/ethnic groups to have a discharge diagnosis of anaphylaxis due to venom (versus other types of anaphylaxis): adjusted RR = 2.24, $p = 0.0004$. Men were 36% more likely than women to have a discharge diagnosis of anaphylaxis due to venom (versus other types of anaphylaxis) ($p = 0.02$).

Discussion

We report that the annual hospital discharge rate for anaphylaxis in Florida to be 2.8/100,000 in 2001. This compares with 9 hospitalizations for anaphylaxis in Olmsted County, Minn., USA (approximate population of 100,000 people in 1990 [11]) over the 1983–1987 5-year interval (1.8/100,000/year). However, 3 of these latter 9 diagnoses were made only upon chart review by the investigators [2]. If there were also an underdiagnosis rate of 50% in Florida, there would have been approximately three times as many hospitalizations for anaphylaxis in Florida than in Minnesota. A possible explanation of this disparity includes differences in the socioeconomic strata between the two populations. The population in Olmsted County is mostly Caucasian and a large proportion of those working are employed as health care workers

suggesting a higher than average educational level [2]. Another possible explanation may be differences in medical practice patterns between the two locations. It is also possible that the incidence of anaphylaxis has increased in the 20 years since the Olmsted County data were collected. Overdiagnosis of anaphylaxis among the patients hospitalized in Florida is unlikely since the diagnoses recorded were at discharge and there would have been ample opportunity to correct any initial misdiagnoses. For example, because some patients with anaphylaxis may be erroneously coded as having angioedema, the database was searched for a primary diagnosis of angioedema with a secondary diagnosis of anaphylaxis. There were 12 such individuals.

There were four deaths among the hospitalized Florida patients resulting in a hospital mortality rate of 0.86%. The Office of Vital Statistics of the Florida Department of Health possesses death certificates which indicated seven inpatient deaths among a total of 11 deaths in Florida from anaphylaxis during 2001. A possible explanation for the discrepancy between the coding of the hospital discharge diagnoses and the death certificate diagnoses is that a hospital discharge diagnosis of anaphylaxis indicates that anaphylaxis is most responsible for the patient's hospitalization while anaphylaxis on the death certificate may signify that anaphylaxis was the cause of death but was not responsible for the majority of the patient's inpa-

tient care. It was not possible for these investigators to review the medical records of the patients to confirm the diagnosis of anaphylaxis on the death certificates. In addition, the Office of Vital Statistics of the Florida Department of Health death certificate records include deaths in military and Department of Veterans Affairs hospitals as well as the Florida State (psychiatric) Hospital in Chattahoochee and the A.G. Holley State Tuberculosis Hospital in Lantana. Deaths in these institutions are not included in the Florida Agency for Health Care Administration dataset used for this analysis. Therefore, the number of inpatient anaphylactic deaths in Florida may have been greater than the number provided by the Florida Agency for Health Care Administration.

The median LOS among the Florida patients was one day. We have preferred to use the median LOS because of the skewed nature of this variable. However, in order to allow comparison with the data from Olmsted County, Minnesota, we also calculated the mean LOS for the Florida patients. The mean LOS $\pm$ SD in Florida was 2.94 ± 11.01 days. The mean LOS ($\pm$ SD) in Minnesota was 2.1 ± 2.3 days.

Food allergy was responsible for the anaphylactic event in approximately 16% of this hospitalized cohort. Our analysis found the unadjusted risk of hospitalization for food anaphylaxis (versus other types of anaphylaxis) was 26.5% among patients who were 0 to 17 years of age while this risk was 14.9% among the adults (unadjusted relative risk = 1.78, $p = 0.04$). Bohlke et al. [3] reported a higher prevalence of food-induced anaphylaxis (42.4%) in all children and adolescents under 18 years of age with anaphylaxis in an HMO population. The increased likelihood of food as a cause of anaphylaxis in younger individuals is consistent with previous survey of food-induced anaphylactic deaths in which none of the victims was greater than 33 years of age [12]. The likelihood of hospitalization for anaphylaxis increased with age in this cohort. This confirms similar findings in a British population [13]. However, hospitalization rates increased through age 79, while those in the British study declined in those greater than 55 years of age.

The diagnosis of asthma was associated with shorter length of hospitalization and lower hospital charges. This is more remarkable since asthmatic patients were almost three times as likely to need mechanical ventilation. The result concerning LOS and total costs among asthmatic patients appears to be counter-intuitive. This is explained by the fact that 29 of the 34 patients who required mechanical ventilation did not have asthma. They had a mean LOS of 13.7 days. The five asthmatic patients who

required mechanical ventilation had a mean LOS of 2.2 days. Therefore the increased LOS of the entire group of patients who required mechanical ventilation was largely due to the nonasthmatic individuals.

The present report has several strengths. The use of a state discharge database is a novel approach to studying the outcomes of anaphylaxis. It is the first to study the epidemiology of patients hospitalized in the United States for anaphylaxis using a database derived from a population of more than 16,000,000 people. By examining a large number of cases throughout the state of Florida, our approach limits the possibility of institutional bias. A search of the PubMed/MEDLINE database did not reveal any similar large population-based studies using a state administrative health care database. This study is also the first to report on length of stay and hospital charges for anaphylaxis hospitalizations and the associated comorbidities in the US. The previous US [2, 3] and British [13] studies did not report hospital charges and the associated comorbidities. Furthermore, we accounted for any possible correlation in the development of the outcomes of interest among patients within a particular hospital by using generalized estimating equations. Failure to account for this violation of independence would lead to erroneous associations.

Our analysis had several limitations. Underdiagnosis of anaphylaxis has been reported [14]. It is possible that some very ill anaphylactic patients might have been diagnosed as having other causes of respiratory failure or hypotension. As discussed above, death certificate data suggest that three anaphylactic in hospital deaths were not recorded in the discharge diagnosis records. Some patients with envenomation, which included bites from snakes, scorpions, and jellyfish among other animals, may have been included among those with anaphylaxis due to Hymenoptera stings if their diagnoses were coded using the same ICD-9-CM code and the records omitted the E code which defines the source of the envenomation. Due to the retrospective nature of the study, we were unable to verify any of the diagnoses or procedures. The sensitivity and specificity of the coding of discharge diagnoses and procedures in the Florida Agency for Health Care Administration database is unknown. Misclassification is a possibility for some variables. However, as discussed in our 'Methods' section, each reporting hospital must certify that their data are correct.

In summary, this large, retrospective investigation of patients hospitalized for anaphylaxis in the State of Florida found a median LOS of 1 day and median total charges of USD 4,982. Asthmatics had a shorter LOS

than nonasthmatics. After adjustment for age, sex, race/ethnicity, asthma, mechanical ventilation, and heart disease, the patient's insurance status remained associated with LOS. Patients who were 0 to 17 years of age were three times as likely to have been hospitalized for anaphylaxis due to food (versus other types of anaphylaxis) compared to patients who were 71 years of age or older.

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