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Algorithm for the Diagnosis of Anaphylaxis and its Validation Using Population Based Data on Emergency Department Visits for Anaphylaxis in Florida

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Abstract

Background—Epidemiological studies of anaphylaxis have been limited by significant under-diagnosis.

Objective—The purpose of this study was to develop and validate a method for capturing previously unidentified anaphylaxis cases by using *International Classification of Disease Ninth Revision Clinical Modification (ICD-9-CM)* based data sets.

Methods—Florida emergency department data for 2005–2006 from the Florida Agency for Health Care Administration were used. Patients with anaphylaxis were identified using ICD-9-CM codes specifically indicating anaphylaxis or an ICD-9-CM algorithm based on the definition of anaphylaxis proposed at the 2005 National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network symposium. Cases ascertained with the algorithm were compared to the traditional case ascertainment method. Comparisons included demographic and clinical risk factors, proportion of monthly visits, and age/sex specific rates. Cases ascertained with anaphylaxis ICD-9-CM codes were excluded from those ascertained with the algorithm.

Results—1149 patients were identified by anaphylaxis ICD-9-CM codes and 1602 cases were identified using the algorithm. The clinical risk factors and demographics of cases were consistent between the two methods. However, the algorithm was more likely to identify older individuals ($p < 0.0001$), those with hypertension or heart disease ($p < 0.0001$), and individuals with venom-induced anaphylaxis ($p < 0.0001$).

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Conclusion—This study introduces and validates an ICD-9-CM based diagnostic algorithm for the diagnosis of anaphylaxis to capture individuals missed using the ICD-9-CM anaphylaxis codes. 58% of anaphylaxis cases would be missed without the use of the algorithm, including 88% of venom-induced cases.

Keywords

Anaphylaxis; epidemiology; emergency; ICD-9-CM; Under-diagnosis

INTRODUCTION

Anaphylaxis is an acute generalized allergic reaction which may be life threatening. This syndrome usually involves more than one organ system. Signs and symptoms can include respiratory distress, hypotension, angioedema, urticaria, nausea, vomiting, diarrhea, abdominal/pelvic cramps, tachycardia, and cyanosis. The exception is hypotensive shock without other symptoms in the context of contact with a known or likely allergen¹. Because of the wide range of symptoms, the diagnosis is often unclear, especially to physicians who are unfamiliar with the syndrome. Unfamiliarity with and misdiagnosis of this multiple symptom, multi-organ system syndrome may play a large part in the under-diagnosis of anaphylaxis.² A few hospital-based studies have demonstrated that under-diagnosis occurs. A four month study in a community hospital emergency department (ED) revealed only 4 patients with a diagnosis of anaphylaxis. An additional 13 patients were identified as having anaphylaxis through a review of their medical records. The original diagnosis for these 13 patients was an unspecified allergic reaction.³ The authors concluded that the majority of cases would not have been identified using anaphylaxis specific *International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM) codes.

A recent paper by Campbell and colleagues which examined the use of prescription epinephrine further supports the contention that anaphylaxis is commonly under-diagnosed.⁴ The study identified 157 cases using the ICD-9-CM codes for anaphylactic shock. An additional 54 cases of anaphylaxis were identified by reviewing a random sample of 600 medical records where the ICD-9-CM codes indicated an associated diagnosis (food/venom). Finally, recent reviews of Florida death certificate and hospitalization data suggest that some anaphylactic deaths in hospitalized patients reported on death certificates are not recorded in the hospital discharge diagnosis records as such.^{5,6} The under-diagnosis of this syndrome presents a public health risk since proper treatment of anaphylaxis depends upon its timely diagnosis and prevention depends on an accurate understanding of the determinants of the disease.^{7,8,9}

The objective of this study was to develop and validate a method for capturing previously unidentified anaphylaxis cases from ED discharge data. The authors present an algorithm based on a clinical definition for anaphylaxis proposed at the 2005 National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network (NIAID/FAAN) symposium.¹ The ICD-9-CM codes needed for record review, and for the use of this definition with hospital discharge and ED data, are included in the authors' algorithm. This paper explores and compares the commonly used ICD-9-CM codes to identify patients with

anaphylaxis versus coding based on the NIAID/FAAN proposed clinical definition in the context of a population based analysis of emergency department visits for anaphylaxis in Florida for 2005 through 2006.

METHODS

Source Population and Inclusion Criteria

Non-federal ED data for 2005 and 2006 were obtained from the Florida Agency for Health Care Administration (AHCA). Diagnosis information was coded using the ICD-9-CM. For each record AHCA allows for the reporting of one primary diagnosis, nine secondary diagnoses (a total of 10 diagnosis fields), and 3 external injury codes (Ecodes).

Anaphylaxis cases were defined in one of two ways. Method I identified patients who had an ICD-9-CM code specific to anaphylaxis within one of the ten diagnosis fields (Table 1). Method II identified patients through an algorithm based on the definition of anaphylaxis proposed at the 2005 meeting of the NIAID/FAAN.¹ Analyses of cases ascertained through the algorithm, Method II, excluded all cases which were first ascertained through Method I. This algorithm identifies patients with features of the anaphylactic syndrome sufficient to make a diagnosis of anaphylaxis. A case of anaphylaxis was identified through Method II if respiratory compromise or skin-mucosal involvement was found in conjunction with shock due to anesthesia; respiratory compromise or reduced BP was found in conjunction with skin-mucosal involvement; or a combination of gastrointestinal symptoms, respiratory compromise, reduced BP, or skin mucosal involvement were found in conjunction with a potential allergen (including venom, drugs, or a biological substance). These were identified through ICD-9-CM codes found within the ten diagnosis fields and three Ecode fields (Table 1).

Exclusion Criteria

A total of 3024 records of anaphylaxis were identified using Method I (1283) and Method II (1741). Analysis was restricted to records for Florida residents. 254 nonresident records were excluded which yielded 2770 Florida cases. Subjects were also excluded from the analysis if the envenomation, as determined through ICD-9-CM code 989.5, was from an animal or plant whose venom is likely to produce signs and symptoms which result from direct venom toxicity rather than anaphylaxis [snakes/lizards (E905.0), venomous spiders (E905.1), and marine animals/plants (E905.6)]. Nineteen such cases were identified; two were envenomation from snakes/lizards, eight were envenomation from venomous spiders, and ten were envenomation from marine animals/plants. There were 2751 records used in the analysis that met either definition of anaphylaxis in Florida residents.

Anaphylaxis Triggers

After a case of anaphylaxis was identified, either by Method I or Method II, the causes of anaphylaxis were examined. Each trigger was identified by searching for a related ICD-9-CM code. A patient was identified as having a food related reaction if they experienced dermatitis due to food (693.1), anaphylaxis due to a food allergy (995.60–995.69) or an adverse food reaction that was not classified elsewhere (995.7). Due to the relationship

between the two methods of case ascertainment, individuals with an ICD-9-CM code of 995.60 to 995.69 (anaphylaxis due to a food allergy) were automatically identified using Method I. It is not possible to identify the specific food trigger for the few individuals identified with food-induced anaphylaxis using the algorithm (Method II). Medication-induced anaphylaxis was identified using the algorithm when a patient record indicated dermatitis due to medication (693.0), an adverse reaction to a drug (995.2 and 995.4), or the patient had taken an antibiotic/anti-infective (E930-E930.9 and E931-E931.9). Patients with Hymenoptera- venom induced anaphylaxis presented with a sting(s) from a hornet/wasp/bee (E905.3), a sting from other venomous arthropods (E905.5), or included patients whose record indicated the toxic effect of venom (989.5). The code ICD-9-CM code 989.5 is often used to categorize patients with Hymenoptera insect stings.¹⁰

Demographic Factors

Demographic factors examined included age of patient at the time of an ED visit, race, ethnicity, and gender. The principal payer was used as a proxy for the patient's socioeconomic status and was combined into three categories; commercial insurance, governmental insurance, and no insurance. Commercial insurance carriers included non-Medicaid health maintenance organizations and preferred provider organizations. Governmental insurance carriers included Medicare, Medicaid, Department of Veteran Affairs, and government sponsored health care plans such as prison and health department clinics. Patients whose principal payer was through charity, self-pay, or other, were categorized as no insurance. Employees of the federal government have employer provided commercial health insurance.

Clinical Factors

The clinical factors used in the analysis were hypertension, heart disease, asthma, shortness of breath, tachypnea, wheezing, and chronic obstructive pulmonary disease (COPD). Patients with these factors were identified by the presence of the related ICD-9-CM code. Patients with hypertension or heart disease had codes for hypertensive disease (401–402.9 and 404–405.99), coronary atherosclerosis (414.00–414.05) or congestive heart failure (428.0–428.9). Asthma patients were identified by the ICD-9-CM codes 493–493.92. COPD was defined by chronic airway obstruction (496) and obstructive chronic bronchitis with acute exacerbation (491.21). Shortness of breath, tachypnea and wheezing were identified using their specific ICD-9-CM code; 786.05, 786.06, and 786.07, respectively. Codes used to identify epinephrine use were ICD-9-CM codes E941.2, E933.0 and CPT codes J0170, J1200, J2920, and J2930.

Calculation of ED Visit Rates

Age and sex specific rates for patients treated in Florida EDs were calculated by dividing the appropriate number of anaphylaxis cases by the sum of the stratum-specific Florida population estimate for 2005 and 2006. The chi-square test for linear trend in proportions was calculated for both the male and female rates using SAS. Age-adjusted rates stratified by sex were calculated using the 2000 US standard population.¹¹ In addition, the proportion of anaphylaxis cases by month was compared with the proportion of monthly ED visits using the chi-square goodness of fit test.¹²

Comparison of Methods

Descriptive statistics and ED visit rates were presented stratified by the method of anaphylaxis case ascertainment. This separation of cases allowed for the comparison of patients' demographic and clinical risk factors by the two case ascertainment strategies. The risk factors were then compared using Pearson's chi-square test except for total patient charges and age, which were both defined as continuous. The median and means of these variables were compared using a z-test or the Mann-Whitney-Wilcoxon test. Demographic factors of age (defined as categorical), gender, race, and ethnicity were also compared with the distribution of these factors in the state population using the chi-square goodness of fit test.¹²

RESULTS

Emergency Department Cases Ascertained by Anaphylaxis Specific ICD-9-CM Codes (Method I)

A total of 1149 ED anaphylaxis cases were directly identified using only ICD-9-CM codes specific to this condition. The age-adjusted rate was 3.3 cases per 100,000 Floridians/year (95% CI = 1.4, 5.2). Eighty-seven percent (n = 1000) of cases had a primary diagnosis of anaphylactic shock. Anaphylactic shock was listed as a secondary diagnosis for the other cases. The demographic composition of individuals identified with anaphylaxis using Method I (Table 2) was slightly different from the general Florida ED population. However, the differences in proportions were less than 5 percent (Table E1). The mean age for individuals diagnosed with anaphylaxis in the ED was 35.1 years, which is lower than the mean age for the state population (39.8 years). The difference between the mean age of the anaphylactic patients (35.1 years) and the mean age (33.8 years) of all ED patients approached statistical significance with a p-value equal to 0.05. Additionally, the distribution of cases by age group differed by gender with a p-value of 0.001 (Figure E1).

Approximately half (596) of individuals identified with anaphylaxis using Method I had accompanying diagnosis codes indicating the anaphylaxis trigger. The most common trigger was food related (451) followed by medication (109) and venomous insect stings (36). Among the individuals with food-induced anaphylaxis, 408 had a primary diagnosis of anaphylactic shock due to food (ICD-9-CM codes 995.60–69). The most frequently (154) specified category for food-induced cases was anaphylaxis caused by an unknown food (995.69) or a food not specified (995.60). The most commonly specified foods were peanuts (89) and fish (79). Almost all (106) of medication-induced anaphylaxis was due to antibiotics or other anti-infectives (Table 3). When specified, the three most commonly identified drug groupings were penicillin (37), other or unspecified antibiotics (31) and cephalosporins (14). Sixty-seven percent (24) of the cases diagnosed with anaphylaxis triggered by a venomous insect sting were due to a hornet, wasp, or bee sting and 28 percent (10) of patients were bitten by a venomous arthropod (Table 3). There were 700 cases identified using Method I that had an ICD-9-CM code of 995.0 (other anaphylactic shock). A food trigger was identified in 2, a venom trigger in 36 and a medication trigger in 109.

Anaphylaxis cases identified by Method I were seen in the ED less frequently during the first quarter (January, February, and March) of the year than at other times (Figure E2). The highest crude rate of anaphylaxis ED visits was found in December (12.4 per 100,000 ED visits). However, there was no statistically significant difference between anaphylactic monthly ED visits and the proportion of all ED visits made by Floridians. Among individuals whose anaphylactic trigger was identified, only those with venom-induced anaphylaxis had a significantly different proportion of monthly visits compared to the proportion of all ED visits ($p < 0.0001$), with 22 percent of cases occurring in September.

Emergency Department Anaphylaxis Cases Ascertained by Anaphylaxis Algorithm (Method II)

The anaphylaxis algorithm identified an additional 1602 ED cases among Floridians for 2005 and 2006, which produced an age adjusted rate of 4.4 cases per 100,000 Floridians (95% CI = 2.2, 6.6). The number of individuals identified in each algorithm criteria category is shown in Table E2. The demographic profile of individuals diagnosed with anaphylaxis identified using Method II (algorithm) (Table E1) was slightly different from that of the general ED Florida population. Again the differences in proportions were less than 10 percent. The mean age was 41.2 years for individuals ascertained by Method II, which was slightly higher than the mean age for the state population (39.8 years) and significantly higher than the mean age (33.8 years) of the overall ED population ($p < 0.0001$) (Table E1). Additionally, the distribution of cases by age group differed by gender ($p = 0.01$) (Figure E1).

Information on anaphylactic triggers, assessed using accompanying diagnosis codes, were found in the ED record less often for those patients identified through Method II (420, 26%) than for those patients identified through Method I (601, 41%). The most common trigger for patients identified using the algorithm was venomous insect stings (255) followed by medication (119) and food (46). Half (130) of individuals with venom-induced anaphylaxis were stung by a hornet, wasp or bee (Table 3). An additional 40 percent (104) of cases were due to a bite by a venomous arthropod. Using Method II, among anaphylaxis cases due to medication, less than half (51) were due to antibiotics or other anti-infectives (Table 3). The most commonly mentioned drug groupings were other or unspecified antibiotics (15), penicillins (9), cephalosporins (6), and sulfonamides (6). In the overall group identified using the algorithm, 22 cases were treated for dermatitis due to food and 24 cases were treated for other food reactions. Thus 46 cases of food-related anaphylaxis were identified with the algorithm. This is in contrast to anaphylaxis cases ascertained through Method I, where 451 food-related cases were identified but only 2 cases listed the ICD-9-CM code for dermatitis due to food (693.0) and none listed other food reactions (995.7). The specific food that caused the anaphylactic reaction for those cases ascertained using Method II (algorithm) could not be determined from the available diagnosis codes. Patients who had food-induced anaphylaxis where the food has a specific ICD-9-CM code are automatically identified using Method I.

The highest crude rate of anaphylaxis cases identified through the algorithm occurred in August (18.8 per 100,000 ED visits) and September (18.7 per 100,000 ED visits) (Figure E2). The difference between the distribution of anaphylactic cases by month and the

distribution of all monthly ED visits made by Floridians was statistically significant ($p<0.0001$). The majority of this difference can be attributed to venom-induced anaphylactic cases. Without these cases the difference in distributions is not significant ($p=0.06$). Venom-induced anaphylactic cases occur most frequently in August (15%), September (15%), and October (14%). It is important to note that the distribution of anaphylactic cases without a known trigger identified through Method II (1182) was not statistically different from the distribution of all monthly ED visits ($p=0.05$).

Comparison of ascertainment method

A total of 2751 ED cases of anaphylaxis were identified using either case ascertainment method; 42 percent were identified through Method I and 58 percent were identified using the algorithm, Method II. There were 26 cases, which could have been identified using either method. However due to study criteria, these cases were classified as Method I. The demographic information for anaphylaxis cases ascertained using the two methods was very similar (Table 2). The majority of all anaphylaxis cases were white non-Hispanic females. The main difference was in age at time of treatment. Those individuals identified using anaphylaxis specific ICD-9-CM codes were significantly younger (35 vs. 41 years) than individuals identified using the algorithm ($p<0.0001$). Twenty-two percent of cases ascertained using ICD-9-CM codes specific to anaphylaxis were 14 years or younger compared to only 10 percent of cases ascertained using the algorithm (Figure E1).

Patients identified using anaphylaxis specific ICD-9-CM codes were also more likely to have commercial insurance than governmental insurance compared to individuals diagnosed using the algorithm ($p=0.01$). Of note, there was no difference between the two groups for the median patient cost of treatment before any discounts ($p=0.17$).

The same proportion (8%) of individuals in each case ascertainment group had a diagnosis indicating the presence of asthma. However, a larger proportion of individuals with anaphylaxis ascertained using the algorithm had hypertension or heart disease compared with those with anaphylaxis specific ICD-9-CM codes ($p<0.0001$). Forty percent of individuals identified with anaphylaxis using the algorithm had additional diagnosis codes for shortness of breath compared with only seven percent of individuals identified by ICD-9-CM codes for anaphylaxis ($p<0.0001$). Wheezing was also seen more often in patients identified through Method II compared with those patients identified through Method I ($p<0.0001$). The other respiratory conditions, COPD and tachypnea, were rarely seen in either group.

A greater proportion of anaphylaxis cases identified using the algorithm were related to insect stings than were cases identified using only anaphylaxis ICD-9-CM codes ($p<0.0001$). In contrast, a greater proportion of food-induced anaphylactic shock cases were found among individuals identified by anaphylaxis specific ICD-9-CM codes compared with the cases ascertained using the algorithm ($p<0.0001$). The differences in the proportion of medication-related anaphylaxis cases identified through Method I compared to the proportion identified through Method II approached statistical significance ($p=0.05$).

An epinephrine treatment code was used in 111 cases identified using Method I (10%) and 180 cases using Method II (11%) (Table 2). These frequencies were not statistically different ($p=0.19$).

The distribution of monthly anaphylactic visits to Florida EDs differs depending on the case ascertainment method ($p<0.0001$). The rate of ED visits for cases identified through Method I decreased slightly between January and April while the rate for cases identified through Method II increased during the same time period. Towards the end of the year the crude rate of ED visits increased for individuals identified through Method I and is relatively stable for patients identified through Method II. (Figure E2)

DISCUSSION

The epidemiology of anaphylaxis is not very well understood. This is exemplified by the fact that published estimates on the burden of disease within the population vary widely.⁸ This problem may be due, in a large part, to under-diagnosis and misdiagnosis of this multiple system, multi-organ syndrome. Under-diagnosis during clinical care can lead to the under-treatment of anaphylaxis.⁴ The lack of availability of ICD-9-CM codes for anaphylaxis diagnosis without shock contributes to this under-diagnosis.¹³ The need for a better definition and method of case ascertainment in the epidemiological study of anaphylaxis is important. In 2006 an anaphylaxis definition and diagnostic criteria were published based on the results of the 2005 NIAID/FAAN symposium.¹ This definition outlined a method for identifying and diagnosing patients with anaphylaxis. The use of this definition as in the algorithm used by Bohlke et al,¹⁴ lends itself to extracting cases during medical record review and capturing acuteness of onset of anaphylactic signs and symptoms. However, it cannot be used in epidemiological studies which depend upon ICD-9-CM based administrative data. We have modified the NIAID/FAAN anaphylaxis definition so that it may be used with ICD-9-CM based administrative data sets to capture previously unidentified cases of anaphylaxis. The algorithm presented in our work includes all the possible combinations of signs and symptoms necessary to make a diagnosis of anaphylaxis that can be included in ICD-9 CM coding. The algorithm case ascertainment method (Method II) was compared with the traditional method of extracting cases using ICD-9-CM codes specific to anaphylactic shock (Method I).

The demographic information (sex, race, and ethnicity) among the two groups was not statistically different. The median medical charges per visit were similar indicating comparable treatments between groups. Furthermore, prior studies examining the differences in the frequency of anaphylaxis during the progression of the seasons of the year show an increase in cases during the third quarter (July, August, and September).^{2, 5,15,16} These results were seen in both case ascertainment groups, although the increase during the third quarter was more pronounced in patients identified through Method II, further supporting the accuracy of this case ascertainment method. While the proportions of patients with medication-induced anaphylaxis approached statistical significance with a p-value equal to 0.05, the proportions only differed slightly with 9% and 7% in the Method I (ICD-9-CM codes specific to anaphylaxis) and Method II (algorithm) identified groups, respectively.

There were some demographic differences found between the two populations ascertained using Method I and Method II. The mean age (41 years) of patients identified by Method II (algorithm) is significantly older than the mean age (35 years) seen in patients identified using Method I, even when all food-triggered anaphylaxis cases are removed from the analysis. However, the difference in mean age between the groups is decreased by the removal of all food-triggered anaphylaxis cases (Table 2). Therefore, the true mean age of patients treated in the ED with anaphylaxis is may be somewhat older than previously reported.^{3,17,18}

The algorithm (Method II) identified proportionally more cases of venom-induced anaphylaxis than Method I. This indicates that the algorithm functions as expected. In addition, this finding was surprising since clinicians and the public are generally aware that Hymenoptera stings may cause anaphylaxis. It would be expected that this awareness would result in the use of the specific anaphylactic diagnostic codes indicating a Hymenoptera trigger. Our results suggest that the frequency of Hymenoptera sting anaphylaxis may be greater than previously appreciated. Previously reported prevalence estimates are based on expert history or questionnaires in community based studies and not on ICD-9-CM code-based case finding^{19,20,21}.

ICD-9-CM codes 995.60–995.69 amply identify food-induced anaphylaxis. The algorithm (Method II) identified very few additional food-induced anaphylaxis cases. This would suggest that data from our study can be compared with published estimates of the overall frequency of food-induced anaphylaxis cases previously identified using ICD-9-CM codes. Nevertheless, there may be an under-use of ICD-9-CM codes specific to food reactions as indicated in a 2006 study¹⁰. Clark et al. identified only half of their cohort of patients with food allergies through specific food-related ICD-9-CM codes.¹⁰ The rest of the patients were identified through a medical records review. Since a medical records review was not conducted in our study we cannot estimate the percentage of food-induced anaphylaxis cases which may still be unidentified.

ICD coding in ED's appears to be more likely to include an anaphylaxis code for food anaphylaxis, while Hymenoptera sting reactions are more likely to be coded "symptomatically" without the use of an anaphylaxis code. Another difference between Method I and II could be that when the case is coded with an anaphylaxis code (Method I) it is less likely that other descriptive codes, such as codes for the clinical variables of shortness of breath and wheezing, would have been used because the diagnosis was already clear. When the case is identified by the algorithm (Method II), these clinically important respiratory signs and symptoms are more likely to be documented.

A strength of this study includes the very large number of patients included and the large number of institutions from which they are drawn. This allows for robust statistical conclusions and minimizes coding and/or treatment biases specific to a single institution. Limitations of this study are first, that it was not possible to confirm the coding information by manual case abstraction or by the presence of an anaphylaxis expert at the patients' bedside. The report by Clark et al.¹⁰ discussing the under-use of ICD-9-CM codes to identify food reactions demonstrates the limitations of ICD-9-CM codes when compared

with medical record review. That notwithstanding, the frequency of use of epinephrine in the group identified by Method I (ICD-9-CM anaphylaxis codes) and in the group identified by Method II (algorithm) was not statistically different (Table 2). This suggests that both groups contained similar proportions of individuals who were treated acutely for anaphylaxis. The frequency of epinephrine use found in this study is lower than previously reported²². This may reflect the administration of epinephrine in some patients prior to their arrival in the ED. It also may result from the inadequate use of ICD-9-CM and CPT codes for epinephrine use. There is the possibility that there are scenarios that could be mistaken for anaphylaxis by the algorithm. However, a careful review of the algorithm components only revealed two possible cases (of 1602) in which there were clinical scenarios that could have been mistakenly identified as anaphylaxis. These two individuals were identified by Method II on the basis of having had stridor and cutaneous angioedema. Finally, it is not possible to determine the positive and negative predictive values for either method because an anaphylaxis expert was not present to make critical real time observations. This study has not elucidated the epidemiology of anaphylaxis in the population as a whole, since many patients with anaphylaxis may not present to an ED.

This study is the first to develop and validate a diagnostic algorithm for anaphylaxis which identifies cases based on ICD-9-CM codes for anaphylactic signs and symptoms. We have demonstrated that 58% of anaphylaxis cases remain undiagnosed if only the ICD-9-CM codes for anaphylaxis are used to identify cases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ABBREVIATIONS

ICD-9-CM	International Classification of Disease, Ninth Revision Clinical Modification
NIAID/FAAN	National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network
AHCA	Agency for Health Care Administration
CI	Confidence Interval
CPT	Current Procedural Terminology
ED	Emergency Department
Ecodes	External Cause of Injury Codes

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CLINICAL IMPLICATIONS

The ICD-9-CM based diagnostic algorithm allows for a more accurate estimate of anaphylaxis incidence by capturing previously unidentified cases, especially venom-induced cases.

Table 1

ICD-9-CM Criteria for Case Ascertainment Methods

Method I: Codes for anaphylactic shock	<ul style="list-style-type: none"> Anaphylactic shock due to food (995.60–995.69) Other anaphylactic shock (995.0)
Method II: ICD-9-CM algorithm	<ul style="list-style-type: none"> Skin-mucosal tissue involvement was found in conjunction with shock due to anesthesia (995.4) Respiratory compromise was found in conjunction with shock due to anesthesia (995.4) or angioneurotic edema (995.1) Reduced blood pressure (BP) was found in conjunction with skin-mucosal involvement, angioneurotic edema (995.1), the toxic effect of venom (989.5), or an Ecode indicating the cause of poisoning was a venomous animal/plant (E905, E905.3, E905.5, E905.8, E905.9) Reduced BP and gastrointestinal symptoms were found in conjunction with an unspecified adverse effect due to the correct administration of a drug, medicinal, and biologic substance (995.2), or an unspecified allergic reaction (995.3) Reduced BP and skin-mucosal tissue involvement were found in conjunction with an unspecified adverse effect due to the correct administration of a drug, medicinal, and biologic substance (995.2), or an unspecified allergic reaction (995.3) Respiratory compromise and reduced BP were found in conjunction with an unspecified adverse effect due to the correct administration of a drug, medicinal, and biologic substance (995.2), or an unspecified allergic reaction (995.3) Respiratory compromise and gastrointestinal symptoms were found in conjunction with an unspecified adverse effect due to the correct administration of a drug, medicinal, and biologic substance (995.2), an unspecified allergic reaction (995.3), skin-mucosal involvement, the toxic effect of venom (989.5), or an Ecode indicating the cause of poisoning was a venomous animal/plant (E905, E905.3, E905.5, E905.8, E905.9) Respiratory compromise and skin-mucosal tissue involvement were found in conjunction with an unspecified adverse effect due to the correct administration of a drug, medicinal, and biologic substance (995.2), an unspecified allergic reaction (995.3), the toxic effect of venom (989.5), or an Ecode indicating the cause of poisoning was a venomous animal/plant (E905, E905.3, E905.5, E905.8, E905.9) Gastrointestinal symptoms and skin-mucosal tissue involvement were found in conjunction with an unspecified adverse effect due to the correct administration of a drug, medicinal, and biologic substance (995.2), an unspecified allergic reaction (995.3), the toxic effect of venom (989.5), or an Ecode indicating the cause of poisoning was a venomous animal/plant (E905, E905.3, E905.5, E905.8, E905.9)
Definition of symptom categories	<ul style="list-style-type: none"> Respiratory compromise: acute respiratory failure (518.81), acute respiratory distress (518.82), dyspnea/respiratory distress (786, 786.00–786.09), stridor (786.1), extrinsic asthma (493.0) or unspecified asthma (493.9). Reduced BP: hypotension (458, 458.0, 458.2, 458.8, 458.9), or syncope/collapse (780.2). Gastrointestinal symptoms: allergic gastroenteritis/colitis (558.3), nausea/vomiting (787.0), nausea with vomiting (787.01), vomiting alone (787.03), or abdominal pain (789.0). Skin-mucosal involvement: Conjunctival edema (372.73), Edema of eyelid (374.82), Edema of larynx (478.6), Edema of pharynx or nasopharynx (478.25), Flushing (782.62), Urticaria (708), Allergic urticaria (708.0), Idiopathic urticaria (708.1), Urticaria due to cold and heat (708.2), Dermatographic urticaria (708.3), Vibratory urticaria (708.4), Cholinergic urticaria (708.5), Other specified urticaria (708.8), Urticaria, unspecified (708.9), Pruritus and related conditions (698), Pruritus of genital organs (698.1), Other specified pruritic conditions (698.8), Unspecified pruritic disorder (698.9)

Table 2

Demographic and clinical characteristics of patients treated for anaphylactic shock in Florida EDs for the years 2005 and 2006 (n = 2,751)[‡]

	Type of Case Definition				
	Method I (n = 1149)		Method II-Algorithm (n = 1602)		p-value
	Number	(Percentage)	Number	(Percentage)	
Demographic Variables					
Total charges *	\$1,307	(\$1422)	\$1,257	(\$1484)	0.17
Age in years **	35	(21.97)	41	(20.72)	< 0.0001
Male	507	(44)	666	(42)	0.08
Female	642	(56)	936	(58)	
White	914	(81)	1276	(80)	0.61
Black	176	(16)	260	(16)	
Other	44	(4)	52	(3)	
Hispanic	175	(15)	216	(14)	0.18
Non-Hispanic	959	(85)	1372	(86)	
Commercial Insurance	603	(52)	766	(48)	0.04^
Government Insurance	313	(27)	497	(31)	
No Insurance	233	(20)	339	(21)	
Clinical Variables					
Asthma	91	(8)	129	(8)	0.90
Heart disease	134	(12)	310	(19)	< 0.0001
Shortness of breath (786.05)	81	(7)	638	(40)	< 0.0001
Tachypnea (786.06)	2	(0)	5	(0)	0.71
Wheezing (786.07)	26	(2)	173	(11)	< 0.0001
COPD (491.2, 496)	10	(1)	22	(1)	0.23
Venom (ecode)	36	(3)	255	(16)	< 0.0001
Food related	451	(39)	46	(3)	< 0.0001
Medical related	109	(9)	119	(7)	0.05
Epinephrine administration	111	(10)	180	(11)	0.19

[†] 14 individuals in Method II and 15 in the Method I did not provide race/ethnicity.

^{*} Reported median (interquartile range) used mann-whitney-wilcoxon test

^{**} Reported mean (standard deviation) used z-test. Note: when cases with food-related triggers are removed there is still a difference between mean ages ($p=0.01$).

[^] There is a difference between commercial and governmental insurance $p=0.01$.

Table 3

Patients treated in Florida EDs for anaphylactic shock due to antibiotics or anti-infectives, food and Hymenoptera insect venoms for the years 2005 and 2006

Description of Diagnosis	Type of Case Definition			
	Method I		Method II-Algorithm	
	Number	(Percentage)	Number	(Percentage)
<i>Antibiotics or Anti-infectives</i>				
Penicillins	37	(35)	9	(18)
Erythromycin and other macrolides	4	(4)	4	(8)
Tetracycline group	0	(0)	2	(4)
Cephalosporin group	14	(13)	6	(12)
Other/unspecified antibiotics*	31	(29)	15	(29)
Sulfonamides	8	(8)	6	(12)
Quinoline and hydroxyquinoline derivatives	4	(4)	4	(8)
Other antiprotozoal drugs	0	(0)	2	(4)
Other and unspecified anti-infectives	8	(8)	3	(6)
Total	106	(100)	51	(100)
<i>Hymenoptera insect venoms</i>				
Hornets, wasps, or bees	24	(67)	130	(51)
Other venomous arthropods	10	(28)	104	(41)
Toxic effect of venom	2	(6)	21	(8)
Total	36	(100)	255	(100)
<i>Food</i>				
Dermatitis due to food	2	(0)	22	(48)
Anaphylaxis due to a food allergy	449	(100)	0	(0)
Adverse food reaction not classified elsewhere	0	(0)	24	(52)
Total	451	(100)	46	(100)

* Other antibiotics = E930, E930.8, and E930.9