
Anaphylaxis in the obstetric patient: analysis of a statewide hospital discharge database

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Background: Previous reports of anaphylaxis during pregnancy typically have involved single institutions and a few cases.

Objective: To describe the epidemiologic features of anaphylaxis in women who gave birth in Texas.

Methods: Statewide public use hospital discharge data for 2004 and 2005 provided by the Texas Department of State Health Services were accessed. Diagnoses and procedures in this data set were recorded using *International Classification of Diseases, Ninth Revision, Clinical Modification* codes. The records of women who delivered a neonate and simultaneously had a diagnosis of anaphylaxis were selected for study. The prevalence of maternal anaphylaxis noted at the time of delivery of the neonate and the 95% Wilson's confidence interval were calculated. The *International Classification of Diseases, Ninth Revision, Clinical Modification* E codes were examined to determine the possible anaphylactic trigger. Finally, the impact of 4 selected maternal comorbidities and complications on length of stay was assessed.

Results: A total of 19 maternal anaphylaxis cases were identified. The prevalence was 2.7 cases per 100,000 deliveries (95% confidence interval, 1.7–4.2 cases per 100,000 deliveries). Penicillins and cephalosporins were the anaphylactic trigger in 11 of the patients. Five patients were emergent admissions. There were no maternal deaths. Most of the patients (14 [74%]) delivered by cesarean section. Patients who had 1 or more of 4 selected comorbidities or complications had a median length of stay of 5 days, whereas those patients free of these conditions had a median length of stay of 3 days ($P = .07$, exact Wilcoxon rank sum test).

Conclusions: Anaphylaxis during pregnancy is a rare event. In this large case series, we found that β -lactam antibiotics were the most common triggers of anaphylaxis.

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INTRODUCTION

Anaphylaxis is a potentially life-threatening systemic allergic reaction that is rapid in onset and involves the activation of mast cells and/or basophils.¹ Anaphylaxis is typically triggered by exposure to insect venom, natural rubber latex, foods, or medications through a mechanism that is mediated by IgE.¹ The lifetime prevalence of anaphylaxis has been estimated to be between 0.05% and 2%.²

Although anaphylaxis is a rare event during pregnancy, it has the potential to lead to serious maternal and/or fetal morbidity.³ The objective of our retrospective study was to identify the epidemiologic features of anaphylaxis in women

who delivered a neonate throughout Texas during a 2-year period. To our knowledge, this is the first published report of the prevalence of anaphylaxis during pregnancy using the Texas hospital inpatient discharge data set. Statewide hospital and vital statistics databases allow clinicians and epidemiologists to rapidly and efficiently quantify the frequency and triggers of anaphylaxis.^{4,5}

METHODS

Source of Patient Records and Inclusion Criteria

Retrospective analyses were performed using hospital inpatient discharge data that were obtained from the Texas Department of State Health Services in Austin. These data are from all state-licensed hospitals except those that are exempt from reporting to the Texas Health Care Information Council. According to the data user manual, "Exempt hospitals include those located in a county with a population of less than 35,000, or those located in a county with a population more than 35,000 and with fewer than 100 licensed hospital beds and not located in an area that is delineated as an urbanized area by the United States Bureau of the Census." Hospitals that do not seek insurance payment or government reimbursement are also exempt from the reporting requirement.

Only public use data were used in this study. This data set contained clinical and demographic information for patients who were discharged in calendar years 2004 and/or 2005. The principal diagnosis and up to 24 secondary diagnoses were evaluated in our study. These variables were coded

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using the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*.

The study sample included only the records of individuals who delivered during that particular hospitalization. Deliveries were enumerated using *ICD-9-CM* diagnosis codes. If a patient had a code beginning with V27 in any of her diagnosis fields, then she was considered to have delivered a singleton or multiples during that hospital stay.

Records were included in our analysis if the principal discharge diagnosis or a secondary diagnosis was other anaphylactic shock (allergic shock, anaphylactic reaction, or anaphylaxis that 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), anaphylaxis due to anesthesia (*ICD-9-CM* code 995.4), or anaphylactic shock due to serum (*ICD-9-CM* code 999.4).

Insect stings are a common cause of anaphylaxis.⁶ The order Hymenoptera contains various insect species, including bees, wasps, and ants. In an effort to decrease the possibility that cases of Hymenoptera anaphylaxis were missed, we also searched the database for records with *ICD-9-CM* code 989.5 (toxic effect of venom). This code is commonly used to record allergic reactions to the stings of insects classified in the order Hymenoptera.⁷ Eight women satisfied the previously mentioned inclusion criteria and had code 989.5 in their electronic records, but only 3 of these women had *ICD-9-CM* E codes indicating that the source of the venom may have been a Hymenoptera insect (codes E905.3 and E905.5). E codes are supplementary codes that identify external causes of injury and poisoning. None of these 3 patients was considered to have carried the diagnosis of anaphylaxis because they did not have 2 or more of the following: involvement of skin-mucosal tissue, respiratory compromise, reduced blood pressure, or persistent gastrointestinal symptoms.⁶

Data Analysis

Analysis of this data set was approved by the Institutional Review Board for the Protection of Human Subjects of the Texas Tech University Health Sciences Center in El Paso. The data were primarily analyzed using SAS 9.1.3 software (SAS Institute Inc, Cary, North Carolina). The number of cases of anaphylaxis noted in women at the time of delivery of the neonate from January 1, 2004, through December 31, 2005, was divided by the number of deliveries during this time that were found in this Texas data set to arrive at a period prevalence. The denominator for the prevalence calculation was 705,183.

A small proportion (0.75%) of the 705,183 deliveries, representing 5,260 records, had an unknown or missing value for the patient's sex. A very small proportion (0.04%), representing 304 records, had a male sex code. In the latter situation, miscoding of the patient's sex was assumed to be present because these records, as previously described, had an

ICD-9-CM delivery code (V27) that is to only be used on the mother's record. Given the public health and financial implications of coding births, it was assumed that the sex of the patient, rather than the delivery outcome status of the patient, had been misclassified. Therefore, the records with the male code or a missing or unknown code were not excluded before calculating the prevalence. The electronic record of each of the maternal anaphylaxis cases did have a female sex code. A 95% Wilson's confidence interval was calculated for the population prevalence of maternal anaphylaxis noted at the time of delivery of the neonate.⁸

A line listing of the anaphylaxis cases summarizing key demographic, epidemiologic, and clinical features was created. The series of cases was sorted by quarter and year of discharge. The exact age of each patient was not available, but the data set did contain each patient's age group. Patients who underwent a cesarean delivery were enumerated by searching for the following *ICD-9-CM* procedure codes in the principal procedure field and the 24 secondary procedure fields: 74.0, 74.1, 74.2, 74.4, or 74.99.

Laboratory data, such as serum tryptase levels, and treatment regimens, such as antihistamines and epinephrine, were not available in this database. However, using *ICD-9-CM* E codes, it was possible to determine the likely trigger of the episode of anaphylaxis.

Women who had selected chronic conditions and/or certain pregnancy complications were compared with women who did not have these conditions or complications with respect to their length of stay. The 4 diagnoses of interest (2 chronic diseases and 2 complications) were identified using *ICD-9-CM* codes: hypertensive disease (codes 401–405), diabetes mellitus (code 250), hypertension complicating pregnancy (codes 642.0, 642.1, 642.2, and 642.3), and gestational diabetes/abnormal glucose tolerance (code 648.8). The median length of stay was calculated for both groups and reported along with a 2-sided *P* value from the exact Wilcoxon rank sum test. The exact Wilcoxon statement in the NPAR1WAY procedure was used to calculate this *P* value. Finally, the general epidemiologic features of anaphylaxis during pregnancy were summarized.

RESULTS

A total of 19 maternal anaphylaxis cases were identified using *ICD-9-CM* delivery codes and anaphylaxis codes (Table 1). The prevalence was 2.7 cases per 100,000 deliveries (95% confidence interval, 1.7–4.2 cases per 100,000 deliveries). All of the patients had a single *ICD-9-CM* code for anaphylaxis (code 995.0), which is described as other anaphylactic shock, allergic shock not otherwise specified, or allergic shock due to an adverse effect of a correct medicinal substance properly administered (data not shown). A cutaneous sign or symptom, such as urticaria or pruritus, was noted in 5 patients: patients 2, 7, 10, 12, and 14 (Table 1). β -Lactam antibiotics (specifically, a penicillin or a cephalosporin) were the anaphylactic trigger in 11 of the patients.

Table 1. Selected Demographic, Epidemiologic, and Clinical Features of 19 Women Who Simultaneously Gave Birth in Texas in 2004 or 2005 and Were Diagnosed as Having Anaphylaxis

Patient No.	Discharge year	Type of admission	Age group, y	Race/ethnicity	Cesarean delivery	Principal diagnosis and selected secondary diagnoses	Anaphylactic trigger
1	2004	Elective	25–29	Other/Hispanic	No	Complicated pregnancy, childbirth, or puerperium	Antiallergic/antiemetic
2	2004	Elective	30–34	White/Hispanic	Yes	Previous cesarean delivery, postterm pregnancy, unspecified pruritic disorder, abnormality in fetal heart rate or rhythm	Contrast media used for diagnostic x-ray procedures
3	2004	Emergency	20–24	White/non-Hispanic	No	Oligohydramnios, immediate postpartum hemorrhage	Oxytocic agents (ergot alkaloids or prostaglandins)
4	2004	Elective	35–39	Other/Hispanic	Yes	Abnormality in fetal heart rate or rhythm, diabetes, benign essential hypertension complicating pregnancy, childbirth, or puerperium	Penicillins
5	2004	Urgent	25–29	Black/non-Hispanic	Yes	Previous cesarean delivery, maternal hypotension syndrome	Cephalosporins
6	2005	Elective	25–29	Black/non-Hispanic	Yes	Previous cesarean delivery, obstetric shock	Cephalosporins
7	2005	Urgent	25–29	Other/Hispanic	Yes	Previous cesarean delivery, rash and other nonspecific skin eruption	Cephalosporins
8	2005	Urgent	30–34	Black/non-Hispanic	No	Mild or unspecified preeclampsia, abnormality in fetal heart rate or rhythm	Antihypertensive agent
9	2005	Urgent	30–34	White/non-Hispanic	No	Second-degree perineal laceration	Penicillins
10	2005	Urgent	25–29	Other/Hispanic	Yes	Previous cesarean delivery, rash and other nonspecific skin eruption	Cephalosporins
11	2005	Urgent	30–34	White/non-Hispanic	Yes	Very young maternal age (<16 y at expected date of delivery), acute respiratory failure, gestational diabetes, abnormality in fetal heart rate or rhythm	Penicillins
12	2005	Emergency	20–24	White/Hispanic	Yes	Complicated pregnancy, childbirth, puerperium, allergic urticaria	Penicillins
13	2005	Emergency	20–24	White/Hispanic	Yes	Other specified infectious and parasitic diseases abnormality in fetal heart rate or rhythm	Penicillins
14	2005	Emergency	30–34	Black/non-Hispanic	Yes	Fetopelvic disproportion, dermatitis due to medicines taken internally	Other antibiotics
15	2005	Elective	30–34	Black/non-Hispanic	Yes	Previous cesarean delivery, gestational diabetes, essential hypertension (unspecified as to malignant or benign)	Cephalosporins
16	2005	Emergency	18–19	Other/Hispanic	Yes	Oligohydramnios	Antirheumatics
17	2005	Elective	25–29	White/Hispanic	Yes	Previous cesarean delivery, acute posthemorrhagic anemia, maternal hypotension syndrome	Oxytocic agents (ergot alkaloids or prostaglandins)
18	2005	Urgent	35–39	White/non-Hispanic	No	Mild or unspecified preeclampsia, other cardiovascular diseases complicating childbirth, or puerperium	Other antibiotics
19	2005	Urgent	25–29	Other/Hispanic	Yes	Transient hypertension of pregnancy, previous cesarean delivery, unspecified hypotension (arterial)	Cephalosporins

Eight (42%) of the cases were urgent admissions, whereas 5 (26%) were emergent admissions. Hispanics comprised 53% of the case series ($n = 10$). Most patients underwent a cesarean delivery ($n = 14$ or 74%) (Table 1).

The length of stay of the 19 patients ranged from 2 to 7 days (data not shown). The impact of 4 maternal comorbidities and complications (hypertensive disease, diabetes, hypertension complicating pregnancy, and gestational diabetes or abnormal glucose tolerance) on length of stay was evaluated. Four of the patients had 1 or more of these complications, and their median length of stay was 5 days (Fig 1). In comparison, women who were free of these 4 conditions ($n = 15$) had a median length of stay of 3 days (exact Wilcoxon rank sum test, $P = .07$) (Fig 1).

Of the 19 patients, 6 were discharged in the fourth quarter (ie, October, November, or December) (Fig 2). Five of the patients were discharged in the first quarter of 2005. None of the patients died in the hospital, and all were discharged to their home or to self-care (data not shown).

The epidemiologic features of anaphylaxis during pregnancy can be summarized as follows. Although a specific incidence (risk) of maternal anaphylaxis during pregnancy has not been reported, the anecdotal clinical frequency is low. One of the earliest reports occurred in 1974.³ Most reported cases have occurred after 20 weeks' gestation,³ and the geographic trends are either unknown or not reported. There was an increase in antibiotic-related cases after the implementation of guidelines in 1996 to prevent neonatal group B streptococcal infection. The typical offending agents of anaphylaxis in the pregnant woman are as follows (in descending order of frequency): antibiotics (usually β -lactams), latex, succinylcholine, laminaria, and insect stings.³ Although the penicillins and cephalosporins are the most common triggers

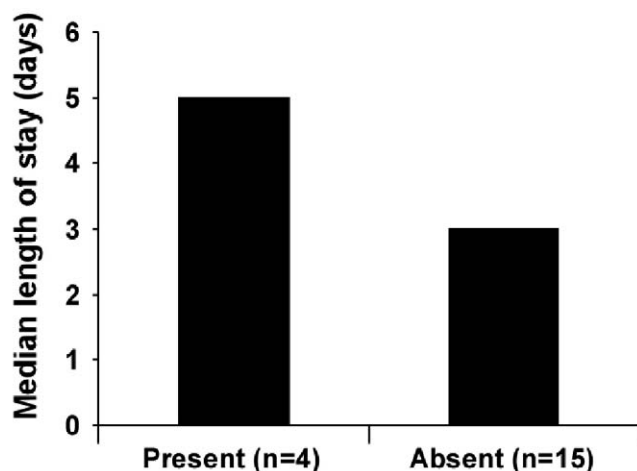


Figure 1. Median length of stay of 19 women noted to have anaphylaxis at the time of delivery of the neonate by presence or absence of selected maternal complications and/or comorbidities (ie, hypertensive disease, diabetes, hypertension complicating pregnancy, or gestational diabetes or abnormal glucose tolerance).

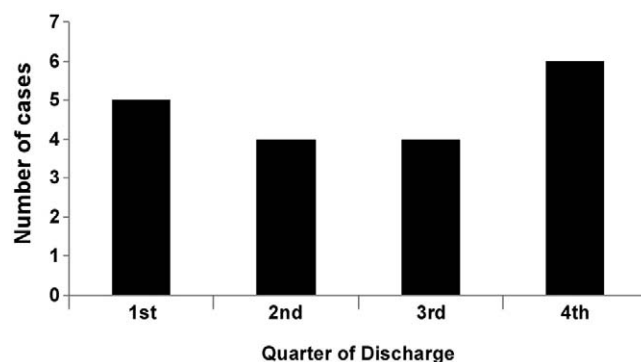


Figure 2. Frequency of maternal anaphylaxis noted at the time of delivery of the neonate by quarter of discharge from reporting hospitals in Texas, 2004 to 2005.

of anaphylaxis in the obstetric patient, which is likely in part because of their high frequency of use, other agents (eg, iron and latex) have also been implicated.³ The placement of laminaria tents in the cervixes of women undergoing elective abortions has also led to anaphylaxis.³

Fatal cases of maternal anaphylaxis are rare. In a previous investigation, the epidemiologic characteristics of 89 deaths due to anaphylaxis in Florida during a 10-year period were reported.⁵ Death certificates were available for 84 of these 89 deaths. Florida's death certificate can identify a woman who was pregnant in the past 3 months. A second review of these death certificates revealed that although several female decedents had missing or illegible responses to the pregnancy question, only 1 woman was pregnant at the time of death or pregnant within 3 months of her death due to anaphylaxis.

DISCUSSION

Anaphylaxis during pregnancy is an uncommon event. Using a statewide database, we have identified the epidemiologic characteristics of a relatively large series of maternal anaphylaxis cases ($N = 19$). The offending agent in most of the cases ($n = 13$) was an antibiotic. Of these 13 cases of anaphylaxis, 11 were triggered by a β -lactam antibiotic. It is likely that these antibiotics were used for intrapartum prophylaxis to prevent group B streptococcal infection in the neonate^{3,9} or to treat chorioamnionitis. A 0% hospital mortality was observed in our study, and all of the mothers were discharged to their home or to self-care. These positive outcomes are consistent with a relatively young and healthy population and a recent summary of case reports involving anaphylaxis during pregnancy.³

None of our patients experienced anaphylaxis due to the venom of a stinging insect. In addition, the highest number of discharges occurred in the fourth quarter (October–December) (Fig 2). In contrast, a previous study of individuals (both sexes and all ages) who were hospitalized in Florida and carried a principal discharge diagnosis of anaphylaxis found that anaphylaxis hospital discharges peaked in the third quarter (July, August, or September) and that the

proportion of anaphylaxis cases triggered by Hymenoptera insect stings also peaked during the third quarter.¹⁰ Insect venom has rarely been implicated as the offending agent in maternal anaphylaxis during pregnancy.^{11,12}

The focus of our report was the descriptive epidemiology of anaphylaxis in women who gave birth in Texas during a 2-year period rather than the management of maternal anaphylaxis. The reader is referred elsewhere for details on the treatment of anaphylaxis in the pregnant woman,^{3,9} although it is worth mentioning that a variety of agents (eg, epinephrine, steroids, and diphenhydramine) have been used in this situation. The administration of epinephrine to the mother is controversial because of the risk of placental perfusion problems secondary to uterine vasoconstriction.

A limitation of our study is the possibility of underascertainment. Some cases of anaphylaxis may not have received an ICD-9-CM anaphylaxis code and, therefore, would not have been identified using our computer program.⁶ A second limitation is the lack of information on neonatal outcomes. These data were provided by the Texas Department of State Health Services, which is currently prohibited from linking maternal and neonatal hospital discharge records. Future similar epidemiologic investigations should strive to capture detailed information on both maternal and neonatal outcomes.

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