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Epidemiologic Patterns of In-Hospital Anaphylaxis in Pediatric Surgical Patients

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Capsule Summary

The incidence of in-hospital anaphylaxis in pediatric surgical patients has more than doubled between 2003 and 2012. Patients with hematological and myeloproliferative disorders, particularly when admitted for bone marrow transplant, are at especially heightened risk.

Keywords

Anaphylaxis; children; pediatric; surgical; inpatients; United States; bone marrow transplant

To the Editor

While several population-based epidemiological studies have evaluated the incidence of anaphylaxis in children and its change over time, few have focused specifically on anaphylaxis occurring during hospitalization. The purpose of this study is to assess the incidence and risk factors of in-hospital anaphylaxis in children admitted for surgery.

Data for this study came from the Kids' Inpatient Database (KID), which accounts for over 95% of all pediatric inpatient hospital admissions in the United States.[1,2] The KID is released every three years. This study was based on the 2003, 2006, 2009, and 2012 KID datasets. In-hospital birth admissions and patients aged 18 years or older at admission were excluded from analysis. Children were identified as having had anaphylaxis if they received a primary or secondary diagnosis with International Classification of Diseases, Ninth Revision (ICD-9) codes for anaphylaxis or anaphylactic shock (995.0) or for an anaphylactic reaction to serum (999.4). These two codes were chosen because they have shown a high positive predictive value (PPV) for anaphylaxis when evaluated in inpatient samples (77.4%).[3] Medical admissions were identified by a medical diagnosis-related group (DRG)

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code and surgical admissions by a surgical DRG.[4] Since children who present to the hospital with anaphylaxis are unlikely to be admitted for a surgical procedure, diagnoses of anaphylaxis during surgical admissions were interpreted as having developed during hospitalization, and likely iatrogenic in nature.

Descriptive statistics and regression analyses in this study were calculated using weighted data.[5] Using all available years of data, a total of 315 surgical admissions were found to have a diagnosis of anaphylaxis, while 1,750,151 did not. A total of 3,320 medical admissions had a diagnosis of anaphylaxis, while 7,817,791 did not. Of anaphylaxis diagnoses, the ICD-9 code 995.0 was used in 96.4% of surgical admissions and 97.0% of medical admissions, while the code 999.4 was used in the remaining admissions. The overall incidence of anaphylaxis in medical and surgical admissions more than doubled between 2003 and 2012 (Figure 1). Of anaphylactic episodes that occurred during medical admissions, depending on the year, 64–68% were coded as the primary diagnosis, whereas 97–100% of anaphylaxis diagnoses in surgical admissions were coded as a secondary diagnosis.

The overall in-hospital mortality ratio for children was 0.38% (0.75% for surgical admissions and 0.43% for medical admissions). The in-hospital mortality ratio for children who developed anaphylaxis during surgical admission was 2.47%, significantly higher than the in-hospital mortality ratio for pediatric surgical patients who did not develop anaphylaxis (0.75%, $p = 0.0004$). Yet, the in-hospital mortality ratio for children with any diagnosis of anaphylaxis during medical admission, 0.29%, was not significantly different from the in-hospital mortality ratio for pediatric medical patients without a diagnosis of anaphylaxis (0.43%, $p = 0.21$).

The characteristics of children with and without anaphylaxis during a surgical admission were evaluated. Of the 315 pediatric surgical patients with anaphylaxis, 15.6% were admitted for hematological and myeloproliferative disorders, compared to 1.5% of all pediatric surgical patients (see ETable I in Online Repository). All characteristics were included as covariates in a multivariable logistic regression model and the independent association between each covariate and the diagnosis of anaphylaxis was evaluated. Records with missing covariate data were excluded from analysis. To accommodate small cell sizes, some major diagnostic categories (MDCs) were merged together for regression analysis (see ETable II in Online Repository). Factors associated with significantly increased odds ratios of anaphylaxis included older age, larger hospital size, teaching hospital status, Western region of the United States, and admissions for respiratory and cardiovascular diseases (Table I). The strongest association, however, was with hematological and myeloproliferative disorders, with an estimated odds ratio of 13.47 (95% confidence interval, 8.99–20.19) compared to digestive, hepatobiliary, and endocrine disorders, the most common reason for pediatric surgical admissions. Of the children admitted for hematological and myeloproliferative disorders, bone marrow transplant admissions accounted for 68.2% of admissions with an anaphylactic event, but only 21.4% of admissions without anaphylaxis. The incidence of anaphylaxis in children undergoing bone marrow transplant was 485.9 per 100,000 admissions, 27 times the incidence in the general pediatric surgical population (18.1 events per 100,000 surgical admissions). Overall,

children who underwent bone marrow transplant accounted for 13.3% of the anaphylaxis incidence in surgical admissions.

In this study, we found anaphylaxis during pediatric surgical admissions to be associated with several patient and hospital variables, as well as an increased risk for mortality not seen in medical admissions. A particularly strong association with anaphylaxis was found with admissions for hematological and myeloproliferative disorders, especially for bone marrow transplants. While it is not possible to determine the triggering agent for anaphylaxis using this dataset, chemotherapeutic agents and more recent monoclonal antibody treatments have been recognized causes of immediate hypersensitivity and anaphylaxis in bone marrow transplant patients, but these events have typically only been documented in case reports or as adverse events in clinical trials.[6–8] The exact mechanism for hypersensitivity to these agents is unclear, and while mild to moderate reactions are relatively common, severe hypersensitivity reactions are thought to be rare.[9] Since severe hypersensitivity after treatment with chemotherapy has not been well described in a population-based study, its incidence may be underestimated, resulting in inadequate preparation for responding to these events.

Despite its relatively rare occurrence, in-hospital anaphylaxis is a serious event that can lead to significant morbidity and mortality. It is worth noting that while the PPV for anaphylaxis diagnostic codes 995.0 and 999.4 in inpatient records is relatively high, the sensitivity of these codes is unclear. Thus, it is likely that these codes still underestimate the true incidence of anaphylaxis in the pediatric population. Given the potentially life-threatening nature of an anaphylactic episode, our findings of a strong association between bone marrow transplant and anaphylaxis may direct future studies to evaluate reasons for this association and methods to reduce its occurrence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

KID	Kids' Inpatient Database
ICD-9	International Classification of Diseases, Ninth Revision
DRG	diagnosis-related group
MDC	major diagnostic category
PPV	positive predictive value
OR	odds ratio
CI	confidence interval

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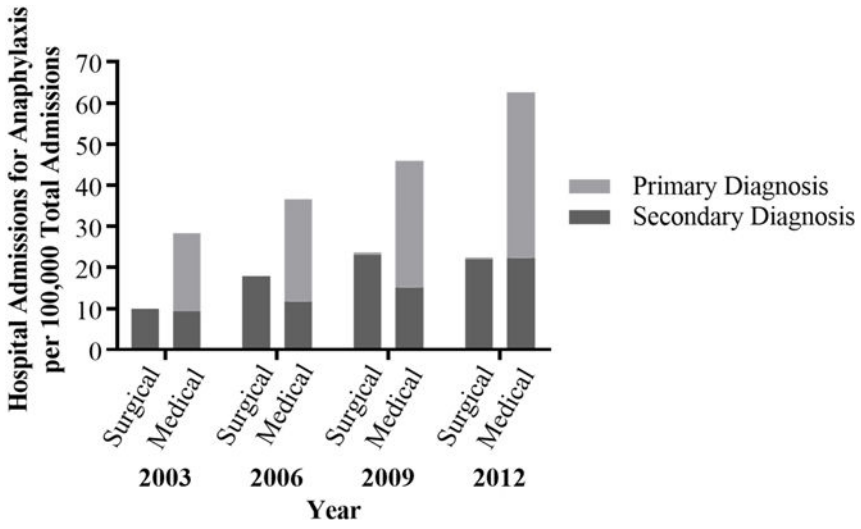

Figure 1.

Incidence of Anaphylaxis as a Primary or Secondary Diagnosis in Surgical and Medical Admissions.

Table I

Multivariable Logistic Regression including Risk Factors for Anaphylaxis in Surgical Admissions.

Risk Factors	OR Estimate (95% CI)
Age	1.05 (1.03–1.07)
Sex	
Male	(Reference)
Female	1.07 (0.85–1.35)
Admission type	
Elective	(Reference)
Emergent	0.83 (0.65–1.05)
Hospital bed size	
Large	(Reference)
Medium	0.66 (0.50–0.87)
Small	0.63 (0.43–0.93)
Hospital location	
Urban	(Reference)
Rural	0.79 (0.36–1.71)
Hospital teaching status	
Non-teaching	(Reference)
Teaching	2.86 (1.87–4.37)
Hospital region	
South	(Reference)
Northeast	0.95 (0.66–1.36)
Midwest	1.34 (0.97–1.86)
West	1.72 (1.28–2.31)
Major diagnostic category	
Digestive, hepatobiliary, endocrine disorders	(Reference)
Nervous system disorders	1.20 (0.73–1.98)
Eye, ear, nose, throat disorders	0.68 (0.37–1.26)
Respiratory disorders	3.00 (1.78–5.07)
Cardiovascular disorders	2.43 (1.55–3.80)
Musculoskeletal and skin disorders	1.18 (0.81–1.72)
Hematological and myeloproliferative disorders	13.47 (8.99–20.19)
Other disorders	1.17 (0.78–1.76)

OR = odds ratio, CI = confidence interval, (Reference) = reference value for each variable