Incidence of Peptic Ulcer Bleeding in the US Pediatric Population

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See ''Clinical Applicability of the Incidence of Pediatric Peptic Ulcer Bleeding in the United States'' by Park on page 718.

ABSTRACT

Objectives: The aim of the present study was to determine the incidence of peptic ulcer bleeding (PUB) in pediatric patients.

Methods: A hospital inpatient database, Premier Perspective, and an insurance claims database, MarketScan, were analyzed to estimate upper and lower limits for the annual incidence of PUB in the US pediatric population.

Results: Using data from the Premier Perspective database and database-specific projection methodology, the total number of cases of hospitalization of pediatric patients for PUB in the United States in 2008 was estimated to be between 378 and 652. This translated to an incidence of 0.5 to 0.9/100,000 individuals in the pediatric population. Using data from the MarketScan database, the incidence of PUB in the insured pediatric population was estimated to be 4.4/100,000 individuals. Overall, 17.4% of insured pediatric patients diagnosed as having any upper gastrointestinal ulcer in 2008 were reported to have developed PUB.

Conclusions: The estimated incidence of PUB in the US pediatric population in 2008 ranged from 0.5 to 4.4/100,000 individuals. The total number of cases of PUB in pediatric patients in the United States each year was thus estimated to be between 378 and 3250. Such estimates provide a likely lower and upper limit for the total number of cases of the condition annually.

Key Words: bleeding, incidence, pediatric, peptic ulcer

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In adults, peptic ulcer bleeding (PUB) is a common problem in emergency medicine (1) and presents a substantial clinical and economic burden (2–4). The most common risk factors for PUB are infection with *Helicobacter pylori* (5), increasing age (6), treatment with nonsteroidal anti-inflammatory drugs (7), smoking (8), and previous gastrointestinal (GI) complications (9).

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The clinical course and presentation of peptic ulcer disease and its complications such as PUB are presumed to be similar in children and adults, and most practitioners treat pediatric patients who have PUB using therapies that have been approved only in adults (10,11). Most risk factors for PUB are absent in children; thus, the incidence of PUB in the pediatric population is likely to be much lower than that in adults; however, there is presently little direct evidence to support this expectation (12–14). We have therefore conducted a retrospective study using both an inpatient and a health care claims database to estimate the annual incidence of PUB in pediatric patients in the United States.

METHODS

Data Source

Two databases were analyzed: Premier Perspective (Charlotte, NC), an inpatient database of hospitalized patients, and MarketScan (Thomson Reuters, New York, NY), an insurance claims database that includes information on inpatient and outpatient visits and prescription claims, including pharmacy dispensary information. The Premier Perspective inpatient database includes information on discharge diagnoses and drug prescriptions during hospitalization from >5 million patients across approximately 500 hospitals each year, including pediatric hospitals. The MarketScan database contains information on person-specific health care use, expenditures, and enrollment from 125 large employers and 13 additional contributing health care plans across the United States. The 2008 dataset includes information on >34.6 million patients (active employees and their dependents, and retirees).

Disease Definition

International Classification of Diseases, 9th revision Clinical Modification (ICD-9-CM) codes were used to identify patients with PUB in both the Premier Perspective and MarketScan databases. The following diagnoses were used to define an overall set of PUB: gastric ulcer with bleed/perforation (*ICD-9-CM* codes 531.0X, 531.1X, 531.2X, 531.4X, 531.5X, 531.6X), duodenal ulcer with bleed/perforation (*ICD-9-CM* codes 532.0X, 532.1X, 532.2X, 532.4X, 532.5X, 532.6X), gastrojejunal ulcer with bleed/perforation (*ICD-9-CM* codes 534.0X, 534.1X, 534.2X, 534.4X, 534.5X, 534.6X), peptic ulcer with bleed/perforation (*ICD-9-CM* codes 533.0X, 533.1X, 533.2X, 533.4X, 533.5X, 533.6X), and esophagus ulcer with bleed (*ICD-9-CM* code 530.21). Upper GI perforations and esophageal ulcers were included to identify every patient who may have had PUB. These *ICD-9* codes have been shown previously to have a positive predictive value of close to 90% (15). In addition, in the MarketScan database, the following diagnoses were used to identify GI ulcers without bleeding: gastric ulcer without bleed/perforation (*ICD-9-CM* codes 531.3X, 531.7X, 531.9X), duodenal ulcer without bleed/perforation (*ICD-9-CM* codes 532.3X, 532.7X,

532.9X), gastrojejunal ulcer without bleed/perforation (*ICD-9-CM* codes 534.3X, 534.7X, 534.9X), peptic ulcer site unspecified without bleed/perforation (*ICD-9-CM* codes 533.3X, 533.7X, 533.9X), and esophagus ulcer without bleed (*ICD-9-CM* code 530.20).

Premier Perspective

Discharge data from January 2004 to December 2008 were analyzed for the pediatric population from newborns (younger than 1 month) to adolescents up to 17 years of age (inclusive). PUB was identified using either primary discharge diagnosis alone or primary and secondary discharge diagnoses considered together. Projection weights were applied to each hospital based on geographic region, urban/rural location, teaching status, hospital ownership, and number of beds (16). These weights were used to extrapolate the observed number of cases of pediatric PUB in the database to the total US hospitalized pediatric population. The incidence of PUB in the hospitalized pediatric population was estimated by dividing the projected total number of cases of PUB in the hospitalized pediatric population by the total number of US pediatric individuals (per 100,000).

MarketScan

All of the medical claims data from 2008 were analyzed (approximately 24.6 million patients). All of the children ages 1 to 17 years who were continuously enrolled in a MarketScan-covered insurance plan for the entire 2008 calendar year were included. In addition, all of the infants born in 2008 were included regardless of length of enrollment and are described as being younger than 1 year.

MarketScan National Weights (*http://www.medstatmarketscan.com*) were applied to extrapolate the data to the total US pediatric population that has employer-sponsored health insurance coverage (approximately 29.3 million children and adolescents). The incidence of PUB per 100,000 individuals in this population was estimated by dividing the projected number of pediatric patients with employer-sponsored health insurance coverage who had $\geq$1 PUB diagnosis during 2008 by the total projected insured pediatric population in 2008 (per 100,000). This incidence estimate was used to estimate the total number of cases of PUB in the overall US pediatric population by multiplying the incidence per 100,000 individuals by the total US pediatric population (per 100,000) in 2008 (73.9 million, estimated from the US Census Bureau [*http://www.census.gov/*]).

Statistical Analysis

Data were extracted from both databases using SAS software, and analyses were conducted using SAS version 9.1 (SAS Institute, Cary, NC).

RESULTS

Premier Perspective

Estimates of the total number of cases of PUB and the incidence of PUB in pediatric patients from 2004 to 2008 in the US hospitalized population, extrapolated from data in the Premier Perspective database, are shown by age group in Table 1. When only the primary discharge diagnosis was considered, the estimated total number of cases per year ranged from 333 to 456 during the study period, with a slight decreasing trend over time. When both primary and secondary discharge diagnoses were considered, the range of the estimated total number of cases per year was 639 to 806, and the decreasing trend was maintained. In 2008, the estimated total number of cases was 378 when only primary discharge diagnosis was considered, and 652 when both primary and secondary discharge diagnoses were considered. The total number of cases of PUB in 2008 translated to an incidence of between 0.5 (primary discharge diagnosis) and 0.9 (primary and secondary discharge diagnoses) per 100,000 individuals in the pediatric population.

MarketScan

The estimated total numbers of cases of PUB in the insured US pediatric population in 2008 by age group extrapolated from data in the MarketScan database are shown in Table 2. The total

TABLE 1. Total number of cases and incidence per 100,000 individuals of peptic ulcer bleeding in hospitalized US pediatric patients according to age group, 2004–2008

	2004		2005		2006		2007		2008	
Age group, y	Cases (total)	Incidence (/100,000)	Cases (total)	Incidence (/100,000)	Cases (total)	Incidence (/100,000)	Cases (total)	Incidence (/100,000)	Cases (total)	Incidence (/100,000)
Primary discharge diagnosis										
<1	18	0.4	30	0.7	23	0.6	0	0	4	0.1
1–3	23	0.2	49	0.4	24	0.2	26	0.2	39	0.3
4–11	117	0.4	38	0.1	53	0.2	41	0.1	30	0.1
12–17	298	1.2	255	1.0	279	1.1	266	1.0	305	1.2
Total	456	0.6	372	0.5	379	0.5	333	0.4	378	0.5
Primary and secondary discharge diagnoses										
<1	58	1.4	139	3.4	96	2.3	76	1.8	76	1.8
1–3	70	0.6	79	0.6	56	0.5	50	0.4	77	0.6
4–11	225	0.7	88	0.3	127	0.4	106	0.3	71	0.2
12–17	453	1.8	411	1.6	379	1.5	407	1.6	428	1.7
Total	806	1.1	717	1.0	658	0.9	639	0.9	652	0.9

Data from the Premier Perspective database.

TABLE 2. Incidence of peptic ulcer bleeding in pediatric patients in 2008 in the total insured US population

Age group, y	Total cases	Incidence (/100,000 insured)
<1	103	6.5
1–3	147	3.7
4–11	367	2.9
12–17	671	6.0
Total	1288	4.4

Data from the MarketScan database.

number of cases was estimated to be 1288, giving an incidence of 4.4 cases per 100,000 insured children. Assuming a similar incidence of pediatric PUB in the entire US pediatric population, the estimated total number of US pediatric patients with PUB during 2008 was 3250.

Upper GI Ulcers

The total number of cases of upper GI ulcer with or without bleeding in the 2008 total US insured pediatric population, extrapolated from the MarketScan database, was 7280, translating to an incidence of 24.8 cases per 100,000 pediatric individuals. Of these, 17.4% were estimated to have PUB.

DISCUSSION

We have produced 2 estimates for the total number of cases of pediatric PUB in the US population in 2008: 378 to 652 in the hospitalized population and 3250 in the overall population, translating to an incidence of between 0.5 to 0.9 and 4.4/100,000 individuals. Of the 2 databases, the Premier Perspective inpatient database is likely to be more indicative of the pediatric population under review because it would be unusual for a pediatric patient satisfying the parameters of the indication (maintenance of hemostasis and risk reduction of rebleeding in patients following therapeutic endoscopy for acute PUB) to be treated on an outpatient basis; however, analyzing 2 databases increases the robustness of the results, and the estimate from the MarketScan database gives a likely upper estimate for the annual incidence of the condition. Thus, we consider that the total number of cases of PUB in pediatric patients annually in the United States is approximately 378 to 652, and $\leq$3250, or 4.4 cases per 100,000 people. This is much lower than the present estimate of 19.4 to 57.0 cases of PUB per 100,000 individuals in the general population (including both adult and pediatric patients) (17), supporting the hypothesis that PUB is rare in pediatric patients. Data from the Premier Perspective database appear to show a slight decreasing trend in the incidence of PUB in pediatric patients over time, which is likely to be the result of the decreasing prevalence of *Helicobacter pylori* infection (18,19). We have also shown that among pediatric patients in the MarketScan database who had an upper GI ulcer with or without bleeding, 17.4% developed PUB.

Previous literature reporting on the epidemiology of PUB in pediatric patients is scarce. Lacroix et al (12) showed in a 1992 article an incidence of 6.4% (63/984 patients) for upper GI bleeding in patients admitted to a pediatric intensive care unit (ICU); however, of these patients, only 0.4% (4/984) experienced clinically significant bleeding (defined as an occurrence of hypotension, death, or the necessity for transfusion within 24 hours after the bleeding episode). The rate of clinically significant bleeding (defined as decreased hemoglobin concentration, hypotension, or the necessity for transfusion or surgery because of the bleeding episode), was somewhat higher in a subsequent study (13), in which it was detected in 1.6% (16/1006) of pediatric ICU patients; however, neither of these studies detailed the rate of bleeding caused by peptic ulcers, and both dealt with highly vulnerable ICU patient populations.

A third study used the Pediatric Endoscopic Database System-Clinical Outcomes Research Initiative (PEDS-CORI), a US database of pediatric endoscopy results, to analyze upper endoscopic findings among children and adolescents with hematemesis (14). During an approximately 5-year period, 6337 upper GI endoscopy reports in the database were reviewed to identify 327 that were performed for the indication of hematemesis. Boys and girls were equally represented and no age-related differences in endoscopic findings were observed. A specific diagnosis of peptic ulcer was made for 6.4% (21/327); however, the present study was limited by the lack of a population denominator, which precludes any conclusion about the prevalence of the condition in the general population, other than that PUB is uncommon in pediatric patients.

To our knowledge, the present study is the first to offer an estimate of the overall incidence of PUB in the general US pediatric population. Two European registries provide information on the incidence of peptic ulcer disease in pediatric patients, although neither provides information on bleeding status. The Federal Statistical Office in Germany reported that for 2003, the total number of hospitalizations resulting from peptic ulcer disease for patients ages 0 to 20 years was 738 (20). The total population in the same age group was 16,980,619 children, thus corresponding to an incidence of 4.3 cases of hospitalization for peptic ulcer disease per 100,000 individuals. In Sweden, according to hospital discharge statistics the incidence of hospitalization for stomach ulcers among children ages 0 to 19 years is approximately 0.5/100,000 individuals in the general population (21). These estimates are both considerably lower than our estimate of the incidence of upper GI ulcer with or without bleeding of 24.8/100,000 pediatric individuals and are consistent with our finding that PUB in pediatric patients is rare.

A significant strength of our study was the use of 2 databases, one of which gives a conservative estimate of the total number of cases of PUB in pediatric patients, whereas the other gives a likely upper limit. Both databases contain information on a large number of patients. In addition, the breadth of *ICD-9-CM* codes used for diagnosis means that we are likely to have identified almost all of the cases of pediatric PUB in each of the 2 databases. Although the *ICD-9-CM* codes used have not been formally validated, results of a previous study have shown that they have a positive predictive value of close to 90% (15); however, because each database contains data on only a subset of the total US population, our projections may be limited by bias in the included patients. For example, it is unknown whether the incidence of pediatric PUB is the same in the insured and uninsured US population, which may lead to inaccuracy in the estimate of the total number of cases in the overall US population extrapolated from the MarketScan database. Likewise, the hospitals included in Premier Perspective may not be fully representative of the US population as a whole. In addition, other factors that could affect the prevalence of PUB in the patient population, such as sex, family history of the condition, and *H pylori* infection, were not taken into account. Nevertheless, we are able to conclude that PUB is rare in the pediatric population in the United States.

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