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RESEARCH ARTICLE

Temporal trends of splenectomy in pediatric hospitalizations with hereditary spherocytosis from 2000 to 2019: A national survey

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Abstract

Background: Total and partial splenectomy are used in pediatric patients with hereditary spherocytosis to resolve anemia and hemolytic complications.

Procedure: Data from the Healthcare Cost and Utilization Project's Kid's Inpatient Database was used to profile and describe temporal trends in pediatric (≤18 years) hospital admissions in the United States from 2000 to 2019 data release years. Survey sampling methods were used to produce national estimates.

Results: From 2000 to 2019, the use of splenectomy declined overall, from 427 to 206 weighted procedures (difference = 222, 95% confidence interval [CI]: 124–320; $p < .0001$); the risk of undergoing splenectomy during admission also declined from 56.7% to 38.7% (risk difference = 17.9 percentage points [p.p.], 95% CI: 9.7–26.1; $p < .0001$). Total splenectomy was mostly used. Age at time of splenectomy increased 10.2 years (difference = 1.6 years, 95% CI: 0.6–2.7; $p = .0018$). The risk of splenectomy increased with age until 10 years, then leveled off until 18 years. The proportion of children aged ≤5 years undergoing splenectomy decreased from 27.7% to 11.2% in 2019 (risk difference: 16.5 p.p., 95% CI: 7.3–25.7; $p = .0004$). The strongest clinical predictors of splenectomy, adjusting for patient- and hospital-level characteristics, were a co-diagnosis of symptomatic cholelithiasis (adjusted odds ratio [aOR] = 3.18, 95% CI: 1.92–5.28; $p < .0001$) and splenomegaly or hypersplenism (aOR = 2.52, 95% CI: 1.74–3.65; $p < .0001$). Risk of splenectomy with splenomegaly or hypersplenism increased over time.

Conclusion: Splenectomy was delayed until age greater than 10 years. Older age, co-diagnosis with splenomegaly or hypersplenism, or symptomatic cholelithiasis were strongest clinical predictors of splenectomy. Conservative management of hereditary spherocytosis appears to be more common.

KEYWORDS
hemolytic anemia, hereditary spherocytosis, splenectomy

Abbreviations: AHRQ, Agency for Healthcare Research and Quality; aOR, adjusted odds ratio; CI, confidence interval; HCUP, Healthcare Cost and Utilization Project; HS, hereditary spherocytosis; ICD-10-CM, International Classification of Diseases, Tenth edition, Clinical Modification; ICD-10-PCS, International Classification of Diseases, Tenth edition, Procedure Coding System; ICD-9-CM, International Classification of Diseases, Ninth edition, Clinical Modification; ICD-9-PCS, International Classification of Diseases, Ninth edition, Procedure Coding System; KID, Kids' Inpatient Database; NIS, National Inpatient Sample; OPSS, overwhelming post-splenectomy sepsis; OR, odds ratio; p.p., percentage point(s).

1 | INTRODUCTION

Hereditary spherocytosis (HS) is a congenital hemolytic disorder characterized by structural abnormalities in erythrocytes, resulting in osmotic and mechanical fragility. The spleen is the primary site of premature hemolysis of spherocytes, resulting in anemia. Hemolytic anemia is also associated with jaundice, fatigue, and splenomegaly. While HS is mostly a mild benign disease found worldwide, moderate-to-severe symptomatology is occasionally detected in children and adolescents.[1,2] The incidence of HS is most commonly associated with populations of northern European ancestry, with an incidence of approximately one in 2000 and approximately one in 5000 in the United States.[1,2] The definitive treatment for severely symptomatic HS has been total splenectomy, stopping the process of hemolysis and ameliorating hemoglobin, bilirubin, and reticulocyte levels.[3,4] However, this surgical intervention poses a unique set of clinical considerations and potential life-long consequences.

Total splenectomy results in an increased risk of infection by encapsulated bacteria, most commonly by *Streptococcus pneumoniae*, *Neisseria meningitides*, and *Haemophilus influenzae*.[5] Overwhelming post-splenectomy sepsis (OPSS) due to any cause is a result of impaired clearance of encapsulated bacteria, with older estimates of incidence of OPSS up to 4.4% in children and mortality rates up to 2.2%.[6–8] One meta-analysis observed postoperative sepsis rates of 5%–12% and 0%–11% for total and partial splenectomy, respectively.[9] However, these mortality rates included both adult and pediatric patients across several hemolytic disorders. Asplenic individuals are also at risk for less common infections due to *Capnocytophaga*, *Babesia*, and malaria.[10]

Primarily as a reaction to the high risk of mortality due to OPSS, the partial splenectomy procedure was introduced in 1993.[11] Meta-analyses of several case series found that the improvement of common hematologic parameters following partial splenectomy is less or as effective than total splenectomy.[9,12] Residual hemolysis following partial splenectomy carries risk of later need for cholecystectomy, risk of splenic regrowth, and subsequent re-operation for total splenectomy.[13] However, the theoretical benefit of preserving splenic immune function is less clear, especially in the era of increased vaccination against micro-organisms.

The first aim of this paper was to describe nationally representative rates of splenectomy among discharges from pediatric patients with HS. The second aim was to describe temporal trends and associations among patients who underwent splenectomy.

2 | METHODS

2.1 | Data source and availability

Data release years from 2000 through 2019 from the Kids' Inpatient Database (KID) is produced by the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ).[14] The KID is the largest publicly available all-payer pediatric inpatient care database in the United States, containing data from approximately two to three million hospitalizations (weighted, this estimates ~7 million hospitalizations).[15] The large sample size is suitable for analyses of rare conditions, such as congenital anomalies, as well as uncommon treatments.[15] KID data releases are available every 3 years from 1997 through 2012 using ICD-9-CM/PCS (International Classification of Diseases, Ninth edition, Clinical Modification/Procedure Coding System) coding, and again from 2016 to 2019 to align with the transition to ICD-10-CM/PCS (International Classification of Diseases, Tenth edition, Clinical Modification/Procedure Coding System) coding.

2.2 | Study population

The target study population was defined as any discharge of pediatric patients aged 18 years or younger with a primary diagnosis code of HS (ICD-9-CM code: 282.0; ICD-10-CM code: D58.0). To eliminate double-counting, transfers to a skilled nursing facility, intermediate care facility, another type of facility, or to short-term facility were excluded using the "DISPUNIFORM" variable.[16] Encounters with splenic trauma were excluded, as were other hemolytic conditions that may require splenectomy, including sickle-cell disorders, thalassemia, and immune thrombocytopenic purpura. A full list of diagnostic and procedure codes used are provided in Table S1. The target population was further divided by those who may have undergone either total or partial splenectomy during their encounter.

2.3 | Definition of variables

Age at admission is reported in integer values from 0 to 20 years, which was then categorized as ≤5, 6–10, 11–15, and 16–18 years to ensure sufficient counts of records within each category and to balance risk of complications among age groups. Some analyses consider age ≤5 versus more than 5 years, as the former group is most at risk of serious complications of splenectomy. Hospital-level characteristics (e.g., region and hospital bed size) and encounter-related characteristics such as age, sex, race (White vs. non-White), median household annual income category as per zip codes, and expected primary payer status (private vs. Medicaid/other) were abstracted from the data. The type of admission (elective vs. non-elective) were derived from the KID database variable "ATYPE" and "ELECTIVE."[16] The definition of any splenectomy captures both total and partial splenectomy procedural codes. In case discharge records contained procedural codes for both partial and total splenectomy, they were assigned as total splenectomy. Splenomegaly and hypersplenism were defined based on secondary diagnosis codes. Anemia or jaundice were combined to indicate presence of either secondary diagnosis code. Receiving any red blood cell transfusion was defined as the presence of one or more such procedure code during the encounter.

2.4 | Statistical analyses

Per the Data Use Agreement with HCUP, all statistics involving cells with ≤10 unweighted records (or those that could be reasonably used to identify such records) were suppressed in order to protect patient anonymity.[17]

Taking into consideration the complex survey sampling design of the KID database, survey procedures were used for all estimates, accounting for discharge weights and survey stratification. Trend weights were supplied by HCUP and must be used to produce unbiased and accurate estimates. These weights produce nationally representative estimates that are suitable for assessing temporal trends across survey years.[18,19] Taylor-series (linearization) variance estimates were used, which are appropriate for the survey design.

Baseline characteristics of HS encounters were descriptively summarized by means and standard errors for continuous variables or counts, and percentages for categorical variables. Univariate comparisons were made using the survey-adjusted Wald test or survey regression methods, as appropriate. Temporal trends were also graphed. Logistic regression models were used to determine unadjusted and adjusted risk of any splenectomy. A two-sided 5% alpha level was used for statistical significance. Statistical analyses were performed using Stata 18 (StataCorp LLC).

3 | RESULTS

3.1 | Study population

The flow diagram of records included in this study is presented in Figure S1. In total, there were 2946 unweighted discharge records between 2000 and 2019 inclusive, which contain a primary diagnosis code for HS. After retaining pediatric patients and excluding those discharged to a secondary care facility, or those with splenic traumatic injury, sickle cell disorders, thalassemia, immune thrombocytopenic purpura, there were 2743 unweighted records identified representing 4356 weighted discharges.

Baseline patient demographics and hospital-level characteristics from the combined study population from 2000 to 2019 are reported in Table 1. Characteristics for each KID release year are reported in Table S2. The average age of patients was 7.2 years [95% confidence interval (CI): 7.0–7.5] years, of which 40.1% were ≤5 years old, 46.5% were female, and most were White (70.5%) (Table 1). The majority of encounters were primarily privately insured (60.7%), and half were elective procedures (49.2%). Patients tended to come from households with greater income quartiles (25.8% from the 51st to 75th percentile, and 28.7% from the 76th to 100th percentile). The majority of encounters occurred at hospitals in the South (35.7%) and were most commonly performed in large facilities (59.9%). Splenectomies were performed significantly less often in those aged ≤5 years compared to older patients (odds ratio [OR] = 0.21, 95% CI: 0.17–0.25; $p < .0001$). With each additional year of age, the rate of splenectomy increases

TABLE 1 Patient demographics and hospital-level characteristics of pediatric encounters with a primary diagnosis of hereditary spherocytosis (KID 2000–2019).

	KID years combined (2000–2019)	
Characteristic	**Estimate**	**95% CI**
Unweighted *N*	2743	
Weighted *N*	4356	4075–4638
Sex		
Female	46.5%	44.3%–48.7%
Male	53.5%	51.3%–55.7%
Age, years		
Mean [95% CI)	7.2	7.0–7.5
IQR		3–11
Age categories		
≤5 years	40.1%	37.9%–42.4%
6–10 years	34.1%	32.1%–36.2%
11–15 years	17.6%	16.0%–19.3%
15–20 years	8.2%	7.0%–9.5%
Race		
White	70.5%	67.9%–72.9%
Non-White	29.5%	27.1% – 32.1%
Primary payer		
Non-private (Medicaid, others)	39.3%	37.0%–41.7%
Private	60.7%	58.3%–63.0%
Median household income category for ZIP code		
0–25th percentile	21.3%	19.3%–23.4%
26th–50th percentile (median)	24.2%	22.3%–26.2%
51st–75th percentile	25.8%	23.8%–28.1%
76th–100th percentile	28.7%	26.4%–31.0%
Admission type		
Non-elective	50.8%	50.8%–53.2%
Elective	49.2%	46.8%–51.7%
Hospital region		
Northeast	17.5%	14.8%–20.5%
Midwest	20.9%	18.1%–24.0%
South	35.7%	32.1%–39.4%
West	26.0%	22.7%–29.6%
Hospital bed size		
Small	12.1%	9.8%–14.9%
Medium	28.0%	24.3%–32.0%
Large	59.9%	56.3%–63.4%
Length of stay for those who underwent splenectomy, days		
Mean [95% CI)	2.7	2.6–2.9
IQR		2–3
Splenomegaly or hypersplenism diagnosis	19.8%	18.2%–21.5%
Symptomatic cholelithiasis diagnosis	11.4%	10.1%–12.7%

Abbreviations: CI, confidence interval; IQR, interquartile range; KID, Kids' Inpatient Database.

(OR = 1.21, 95% CI: 1.19, 1.24; $p < .0001$). However, the rate of splenectomy levels off by the age of 10 years, hence age categories are used throughout. Co-diagnoses of splenomegaly or hypersplenism (19.8%, 95% CI: 18.2%–21.5%) or of symptomatic cholelithias (11.4%, 95% CI: 10.1%–12.7%) were commonly observed complications of hemolysis. No mortality was observed in this study.

Approximately half (48.3%) of encounters resulted in splenectomy being performed, representing a total of 2103 weighted records. The age of patients who underwent splenectomy ranged from 0 to 18 years, with an average age of 9.3 years [95% CI: 9.1–9.6]. For those who underwent splenectomy, the average length of stay was 2.7 days [95% CI: 2.6–2.9], and nearly all were elective procedures (89.4%, 95% CI: 87.3%–91.5%). While total splenectomy was more preferred to partial splenectomy, the proportion of total splenectomy was lower in patients aged ≤5 years versus more than 5 years (90.4% vs. 95.1%; OR = 0.49, 95% CI: 0.29–0.81; $p = .0057$). Following the change to ICD-10 coding from KID 2016 onwards, the surgical approach can be distinguished on the basis of procedure codes. On average, the majority of splenectomies were performed laparoscopically compared to an open approach (90.3%, 95% CI: 87.0%–93.5%).

3.2 | Temporal trends in splenectomy

The total (weighted) number of all splenectomies decreased from 427 [95% CI: 339–516] in 2000 to 206 [95% CI: 164–247] in 2019 (Figure 1A and Table 2). As a proportion of encounters with a primary diagnosis of HS, the risk of splenectomy declined from 56.7% [95% CI: 49.9%–63.4%] to 38.7% [95% CI: 34.0%–43.4%] in the same period (Figure 1B), a 17.9 percentage point (p.p.) decrease (95% CI: 9.7–26.1; $p < .0001$). On average, the OR for encounters with splenectomy compared to those without was 0.96 for each additional year in the study period (95% CI: 0.95–0.98; $p < .0001$). The proportion of splenectomies that were performed as elective procedures was steady through the study period (linear trend, $p = .1012$; Table 2).

Among all encounters where a patient underwent splenectomy, the average age of patients has steadily increased from 8.6 years [95% CI: 7.7–9.4] in 2000 to 10.2 years [95% CI: 9.6–10.9] in 2019, an increase of 1.6 years (95% CI: 0.6–2.7; $p = .0018$). The proportion of patients aged ≤5 years decreased from 27.7% [95% CI: 20.4%–36.4%] to 11.2% [95% CI: 7.5%–16.4%] in 2019, a decrease of 16.5 p.p. (95% CI: 7.3–25.7; $p = .0004$); the proportion of 11–15-year-old patients rose from 19.1% [95% CI: 12.8%–25.5%] in 2000 to 32.3% [95% CI: 25.0%–39.6%] in 2019, an increase of 13.2 p.p. (95% CI: 3.5–22.9; $p = .0077$); whereas the patients aged 6–10 and 16–18 years remained relatively stable in the same period (Figure 2). Among patients who underwent splenectomy, the proportion of encounters with a co-diagnosis of splenomegaly or hypersplenism compared to no such co-diagnosis rose from 20.8% [95% CI: 13.2%–28.3%] in 2000 to 37.9% [95% CI: 30.5%–45.4%] in 2019, a difference of 17.1 p.p. (95% CI: 6.5–27.7; $p = .002$; Table 2 and Figure 3). The relative proportion of all splenectomies performed changed somewhat over the study period; however, these differences were not statistically significant (adjusted χ^2 test, $p = .9636$; Table 2). Length of stay for admissions involving splenectomy was stable through the study period (interquartile range [IQR]: 2–3; linear trend, $p = .9999$), as were those patients co-diagnosed with symptomatic cholelithiasis (linear trend, $p = .1173$).

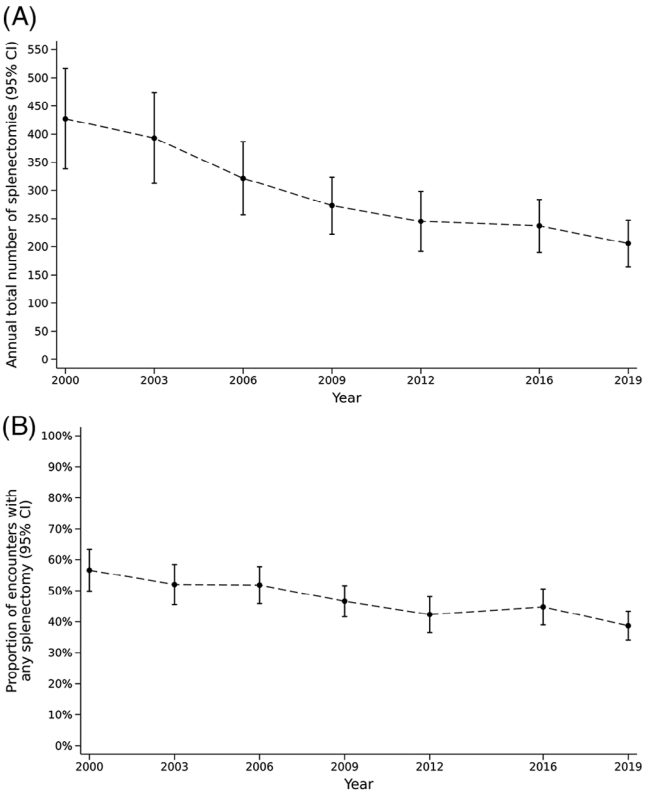

FIGURE 1 Trend in the (A) total number and (B) proportion of splenectomies performed in patient encounters with hereditary spherocytosis.

3.3 | Predictors of undergoing splenectomy

Unadjusted and adjusted predictors of splenectomy as determined by logistic regression are presented in Table 3. In multivariable logistic regression, elective surgery was the strongest predictor of splenectomy (adjusted OR = 72.99, 95% CI: 49.93–106.70; $p < .0001$). Age is statistically significant predictor ($p < .0001$), in which the risk of splenectomy rises through age 10 years, then remains similar from age 11 to 18 years. For co-morbidities, the strongest predictor was a co-diagnosis of symptomatic cholelithiasis (adjusted odds ratio [aOR] = 3.18, 95% CI: 1.92–5.28; $p < .0001$), and a co-diagnosis of splenomegaly or hypersplenism was also associated with higher odds of splenectomy (aOR = 2.52, 95% CI: 1.74–3.65; $p < .0001$). White patients (aOR = 1.39, 95% CI: 0.98–1.97; $p = .0669$) and those with private insurance (aOR = 1.52, 95% CI: 1.07–2.15; $p < .0206$) were also more likely to have surgery. Overall, there was no statistically significant variation among hospital care regions ($p = .0733$), though surgery was more likely in the Midwest compared to the rest of the country (aOR = 2.08, 95% CI: 1.17–3.68).

TABLE 2 Temporal trends in encounters with splenectomies in patients with hereditary spherocytosis from KID data release years (KID 2000–2019).

Characteristic	2000	2003	2006	2009	2012	2016	2019	Overall
Primary diagnosis of hereditary spherocytosis, *N* [95% CI]	754 [617–891]	756 [625–887]	621 [519–722]	586 [495–677]	579 [484–674]	529 [438–620]	531 [445–618]	4356 [4075–4638]
Number with any splenectomy, *N* [95% CI]	427 [339–516]	393 [312–474]	322 [257–387]	273 [222–324]	245 [192–298]	237 [190–284]	206 [164–247]	2103 [1936–2270]
Proportion with any splenectomy, % [95% CI]	56.7 [49.9–63.4]	52.0 [45.5–58.4]	51.8 [45.9–57.8]	46.6 [41.6–51.6]	42.3 [36.6–48.1]	44.8 [39.0–50.6]	38.7 [34.0–43.4]	48.3 [46.0–50.6]
Number with total splenectomy, *N* [95% CI]	[a]	[a]	[a]	254 [206–303]	221 [171–271]	210 [166–254]	184 [145–223]	1978 [1815–2141]
Proportion with total splenectomy of all splenectomies, % [95% CI]	[a]	[a]	[a]	93.1 [88.4–97.9]	90.0 [83.3–96.8]	88.7 [83.1–94.2]	89.5 [84.2–94.7]	94.1 [92.4–95.7]
Number of splenectomies performed laparoscopically, *N* [95% CI]	[a]	[a]	[a]	[a]	[a]	215 [169–261]	184 [146–223]	400 [340–459]
Proportion of all splenectomies performed laparoscopically, *N* [95% CI]	[a]	[a]	[a]	[a]	[a]	90.8 [86.4–95.2]	89.6 [84.9–94.4]	90.3 [87.0–93.5]
Number of elective splenectomies, *N* [95% CI]	384 [299–469]	339 [265–412]	298 [234–362]	241 [193–290]	222 [174–271]	220 [175–265]	187 [146–227]	1793 [1640–1946]
Proportion of elective splenectomies of all encounters, % [95% CI]	87.4 [81.5–93.3]	85.8 [79.3–92.3]	92.5 [88.1–97.0]	88.4 [83.5–93.3]	90.6 [85.4–95.9]	92.9 [89.0–96.7]	90.7 [85.7–95.8]	89.4 [87.3–91.5]

(Continues)

TABLE 2 (Continued)

Characteristic	2000	2003	2006	2009	2012	2016	2019	Overall
Age at time of splenectomy, years								
Mean [95% CI]	8.6 [7.7–9.4]	8.9 [8.3–9.5]	9.6 [9.0–10.3]	9.4 [8.8–10.1]	9.6 [8.9–10.3]	9.9 [9.2–10.5]	10.2 [9.6–10.9]	9.3 [9.1–9.6]
IQR	5–12	6–12	5–13	6–13	6–13	6–13	6–14	6–13
Proportion of all splenectomies by age group, % [95% CI]								
≤5 years	27.7 [20.4–36.4]	23.1 [17.2–30.2]	24.9 [19.2–31.6]	21.3 [15.6–28.5]	17.8 [12.7–24.4]	18.4 [12.7–25.9]	11.2 [7.5–16.4]	21.8 [19.2–24.6]
6–10 years	44.0 [35.5–52.8]	44.9 [38.0–52.1]	33.1 [26.9–40.0]	39.4 [32.7–46.5]	44.5 [37.5–51.7]	37.3 [30.3–44.9]	40.8 [33.0–49.2]	40.9 [37.9–43.9]
11–15 years	19.1 [13.6–26.3]	23.7 [18.5–29.7]	25.5 [19.5–32.7]	24.4 [18.6–31.3]	24.6 [18.0–32.7]	30.9 [24.4–38.3]	32.3 [25.5–40.0]	24.9 [22.4–27.5]
16–18 years	9.2 [4.9–16.8]	8.3 [5.3–13.0]	16.5 [11.7–22.6]	15.0 [10.5–20.8]	13.1 [8.6–19.4]	13.4 [8.8–19.9]	15.7 [10.7–22.5]	12.5 [10.6–14.7]
Proportion of all splenectomies performed within region, % [95% CI]								
Northeast	18.4 [10.7–29.7]	16.3 [10.4–24.7]	16.6 [10.7–25.1]	16.0 [9.6–25.4]	13.0 [6.6–23.8]	19.0 [11.7–29.3]	15.6 [9.2–25.4]	16.6 [13.6–20.0]
Midwest	22.6 [13.6–35.2]	30.0 [20.3–41.9]	21.1 [13.8–30.9]	26.2 [17.7–36.8]	24.3 [16.6–34.0]	21.6 [13.9–32.0]	22.6 [14.2–34.0]	24.3 [20.6–28.4]
South	28.9 [20.4–39.3]	25.7 [16.6–37.5]	30.7 [21.9–41.1]	36.7 [27.4–47.0]	35.1 [25.1–46.8]	34.4 [25.4–44.7]	38.9 [28.8–50.2]	31.9 [28.1–36.0]
West	30.0 [19.9–42.5]	28.0 [17.4–41.9]	31.5 [20.9–44.4]	21.2 [14.4–30.2]	27.6 [17.7–40.4]	24.9 [16.1–36.5]	22.9 [14.3–34.5]	27.2 [23.0–31.8]
Proportion of all splenectomies with co-diagnosis of splenomegaly or hypersplenism, % [95% CI]	20.8 [13.2–28.3]	17.2 [12.0–22.4]	22.8 [16.7–28.8]	28.9 [22.2–35.6]	33.1 [25.8–40.4]	34.6 [26.5–42.8]	37.9 [30.5–45.4]	26.2 [23.4–28.9]
Proportion of all splenectomies with co-diagnosis of symptomatic cholelithiasis, % [95% CI]	17.4 [10.6–24.2]	16.4 [11.4–21.4]	20.2 [14.0–26.4]	21.1 [15.4–26.8]	22.8 [17.0–28.7]	20.6 [14.1–27.0]	23.0 [15.9–30.0]	19.6 [17.3–22.0]

Abbreviations: CI, confidence interval; IQR, interquartile range; KID, Kids' Inpatient Database.

[a] Suppressed for privacy reasons due to 10 records or fewer in a cell.

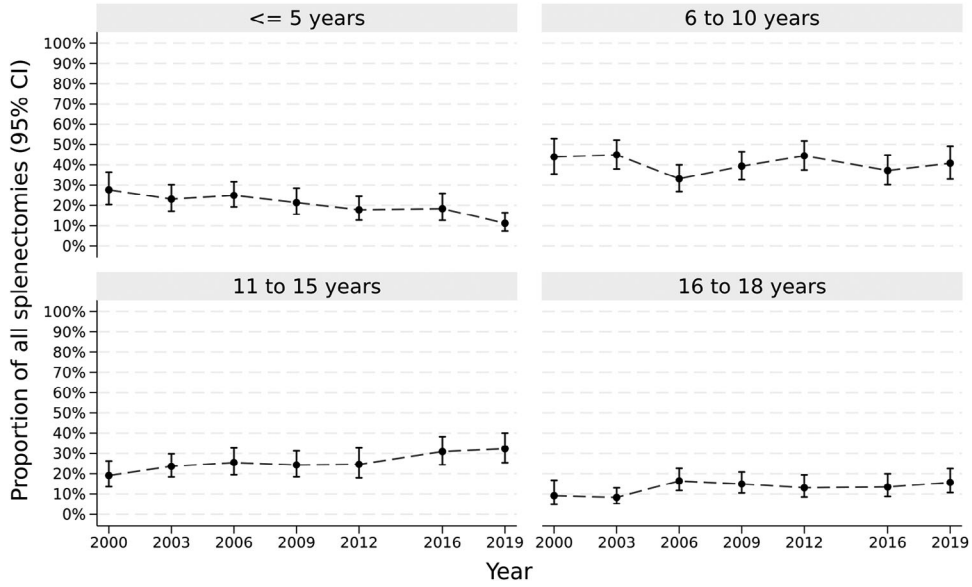

FIGURE 2 Trends in the rate of any splenectomy in patients with hereditary spherocytosis across age groups.

TABLE 3 Unadjusted and adjusted associations with undergoing splenectomy during hospitalization in patients with hereditary spherocytosis (KID 2000–2019).

	Unadjusted		Adjusted[a]	
Factor	**Odds ratio [95% CI]**	***p*-Value**	**Odds ratio [95% CI]**	***p*-Value**
Year of survey (per decade)	0.70 [0.61–0.81]	<.0001	0.97 [0.95–1.00]	.0613
Age group		<.0001		<.0001
≤5 years	Reference		Reference	
6–10 years	3.86 [3.11–4.78]		3.62 [2.48–5.29]	
11–15 years	6.09 [4.73–7.84]		5.66 [3.16–10.13]	
16–18 years	7.84 [5.51–11.17]		6.92 [3.44–13.89]	
Female sex (Ref. male)	1.10 [0.94–1.29]	.2379	—	
White race (Ref. not white)	1.65 [1.37–1.99]	<.0001	1.42 [1.00–2.00]	.0487
Elective admission (Ref. non-elective)	60.82 [45.80–80.78]	<.0001	72.99 [49.93–106.70]	<.0001
Primary payment, private (Ref. Medicaid/other)	1.81 [1.53–2.13]	<.0001	1.52 [1.07–2.15]	.0206
Hospital region		.0003		.0733
Northeast	Reference		Reference	
Midwest	1.52 [1.15–2.00]		2.08 [1.17–3.68]	
South	0.90 [0.71–1.14]		1.05 [0.70–1.57]	
West	1.20 [0.91–1.58]		1.13 [0.73–1.77]	
Co-diagnosis of splenomegaly or hypersplenism (Ref. no diagnosis)	2.19 [0.72–0.89]	<.0001	2.52 [1.74–3.65]	<.0001
Co-diagnosis of symptomatic cholelithiasis (Ref. no diagnosis)	6.40 [4.60–8.90]	<.0001	3.18 [1.92–5.28]	<.0001

Abbreviations: CI, confidence interval; KID, Kids' Inpatient Database.

[a]Adjusted model included only statistically significant factors from unadjusted analyses.

In separate analyses looking at overall associations with patient age, the odds of splenectomy with co-diagnosis of symptomatic cholelithiasis in older (>5 years) children were threefold higher than in younger (≤5 years) children (OR = 3.21, 95% CI: 2.03–5.09; $p < .0001$), where the risk among older children by age group was similar. The odds of splenectomy with co-diagnosis of splenomegaly or hypersplenism in older children was also greater than for younger children (OR = 1.52, 95% CI: 1.09–2.13; $p = .0141$). Odds for the same outcome increased with older age, where the OR was 1.23 [95% CI: 0.85–1.78] for 5–10 years, 1.57 [95% CI: 1.07–2.32] for 11–15 years, and

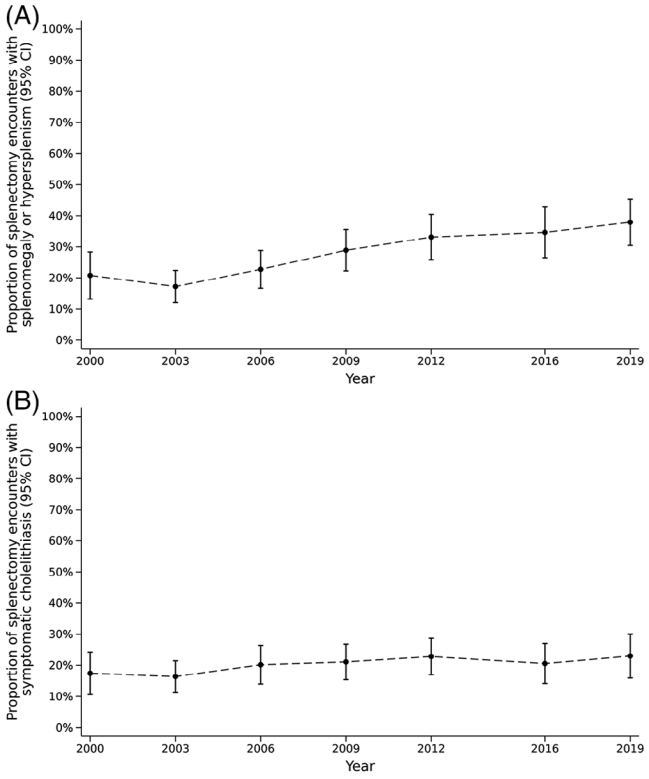

FIGURE 3 Trends in the proportion of splenectomies with a co-diagnosis of (A) splenomegaly or hypersplenism, or (B) symptomatic cholelithiasis in patients with hereditary spherocytosis.

2.62 [95% CI: 1.66–4.15] in 16–18 years as compared to ≤5 years ($p = .0002$).

3.4 | Non-splenectomy encounters with anemia, jaundice, or red blood cell transfusions

To determine if non-autologous red blood cell transfusions are differently used to conservatively manage splenectomy in younger children, encounters that did not result in a splenectomy were examined. This also removes potential confounding by peri-operative transfusion, which cannot be distinguished from other reasons for red blood cell transfusions based on ICD procedure codes alone. Trends in the need for any red blood cell transfusions were examined between younger (≤5 years) and older (>5 years) children (Figure S2; Table S3). Both age groups saw an initial increase and then fall in the use of transfusions over the entire study period, with the younger children statistically more likely to receive transfusions (quadratic trend interaction, $p = .0014$). However, both age groups reach a similar proportion of transfusion need by 2019.

Trends by age group for the presence of anemia or jaundice are also described (Figure S3; Table S3). Both age groups have similar proportions of co-diagnosis in earlier study years, and gradually diverge until 2019. There was a statistically significant linear interaction over this period ($p = .024$), resulting in a significantly higher proportion of co-diagnosis among older children compared to younger children.

4 | DISCUSSION

A substantial proportion of patients with diagnosed HS underwent splenectomy, suggesting that these patients tend to present with greater symptomatic burden. As expected, children older than 5 years, co-diagnosis with splenomegaly or hypersplenism, and White individuals were more likely to undergo splenectomy. The majority of procedures were performed as elective surgeries and as total splenectomy. In this analysis of pediatric hospital discharge data from 2000 to 2019 inclusive, the national trend shows an overall reduction in the total frequency and associated risk of undergoing splenectomy.

Despite the noted advantages of partial splenectomy, the data suggest that total splenectomy is still preferred across all age groups with little variation in rate by year, even in younger patients (<5 years) for whom partial splenectomy may be most beneficial. A shift toward performing partial splenectomy might have been expected over the study period as the procedure seems to be gaining in popularity for children from the early 2000s.[13,20] The risk of splenectomy is strongly increased with a co-diagnosis of splenomegaly or hypersplenism, suggesting this is an important clinical factor to perform surgery. Some have advocated that spleen size per se is an important consideration,[21] though others disagree as there are no clear data for the possibly increased risk due to splenic rupture or interruption of daily activities.[22] While partial splenectomy may be gaining in popularity, guidelines suggest that partial splenectomy requires further follow-up study.[21,22] The present study finds relatively low adoption for the partial splenectomy over the past two decades.

The temporal trends for splenectomy by age group could be explained by differences in symptomatology. Splenectomy is the definitive treatment to improve quality of life and correct the hemolytic process in severe cases; however, whether and how to handle splenectomy in moderate cases is more controversial, with some authors arguing for the necessity of splenectomy in adolescents with moderate symptomatology,[1,3,21–23] as guidelines have recommended for a delay in splenectomy until the child is older than 5 years.[1,3,21,22] This is supported by the shift in age at the time of splenectomy and accompanying decline in rate of splenectomy in patients ≤5 years. Interestingly, the shift in age occurred mainly in the group without co-diagnosis of splenectomy or hypersplenism, so an enlarged spleen still increases the likelihood of splenectomy. Younger children were found to be more likely to receive red blood cell transfusions, while older children were more likely to have a co-diagnosis of anemia or jaundice, supporting the notion of a shift conservative management.

Cholelithiasis is a common complication of HS due to bilirubin turnover, and may occur in young children (<5 years old), but is more common in older children and young adults.[24] While it is common to undergo cholecystectomy and related procedures for symptomatic gallstones at the same time as splenectomy, it is questionable to perform splenectomy in the absence of hemolytic symptoms at the same

time as cholecystemctomy.[22] A previous study of the KID and National Inpatient Sample (NIS) surveys found that pediatric patients with HS commonly undergo cholecystectomy in the same operation as the splenectomy.[25] This study selected patients with a primary diagnosis of HS, rather than including secondary diagnostic codes for HS, which would be expected to exclude gallbladder-related issues as the primary indication where admissions result in concomitant cholecystectomy and splenectomy. The current study found that co-diagnosis of symptomatic cholelithiasis was a strong predictor of performing splenectomy, independent of splenomegaly or hypersplenism. While co-diagnosis of symptomatic cholelithiasis in patients ≤5 years was not common, the odds of surgery were similar in older children regardless of age group. Symptomatic cholelithiasis co-diagnosis in this sample was relatively rare, so temporal trends could not be examined.

Taken together, this suggests that the guidelines are having some impact on surgical behavior, where young children are increasingly managed conservatively (i.e., folate supplementation, transfusions, and close observation). Splenectomy was delayed by approximately 2 years on average over the study period. However, splenomegaly and hypersplenism are still strong predictors of splenectomy, especially in children older than 5 years.

A major advantage in this study is that the KID is a large, nationally representative sample of pediatric hospital discharges, and this study included data release years (seven in total) from 2000 to 2019, inclusive. Therefore, the results are generalizable among all care regions within the United States. This is the only study to the author's knowledge that used the KID to examine national trends of splenectomy in pediatric patients with HS. A prior study combined data from the KID and NIS up to 2004; however, the focus was on pediatric quality indicators, whereas national (weighted) estimates were not produced.[25]

There are also important limitations to this study. As secondary data from an administrative survey are subject to reliance on administrative codes, and as such, coding errors or inconsistencies are possible. To mitigate this risk, the sample was defined using primary diagnoses of HS, and common potential confounding conditions that may necessitate splenectomy for reasons other than HS have been removed. Diagnostic codes for both HS and splenectomy are also readily mapped between ICD-9 and ICD-10 codes, facilitating the combination of survey data. Data in any given year are cross-sectional in nature, and as such, the survey is not designed to follow patients longitudinally. Indeed, the sampling unit of analysis for the KID is the discharge. Therefore, data are not available, which might shed light on follow-up outcomes, such as through re-admission records. It would have been interesting to examine trends based on the surgical approach (open vs. laparoscopic); however, this was not possible under ICD-9, where conversion of a laparoscopic to open procedure is rarely reported and the codes do not readily differentiate the surgical approach. While this is possible with ICD-10 coding, there were insufficient data to examine temporal trends with only two data years. Due to the popularity of total splenectomy, data were too sparse to further examine associations among discharges with partial splenectomy.

5 | CONCLUSION

This study used a large cross-sectional sample of pediatric discharges from hospitals across the United States from 2000 to 2019 to study trends in splenectomy in patients with HS. Over the study period, the number and proportion of encounters resulting in splenectomy are on the decline. Splenectomy is increasingly being delayed until the child is older (>10 years). Age, co-diagnosis with splenomegaly or hypersplenism, or with symptomatic cholelithiasis were the strongest clinical predictors of splenectomy. While most surgeries were elective procedures, the length of stay did not change over time. Overall, HS appears to be more often managed conservatively.

CONFLICT OF INTEREST STATEMENT

The author declares no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Healthcare Cost and Utilization Project. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from https://hcup-us.ahrq.gov/ with the permission of Healthcare Cost and Utilization Project.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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