RESEARCH ARTICLE

National Trends in the Epidemiology and Resource Use for Henoch-Schönlein Purpura (IgA Vasculitis) Hospitalizations in the United States From 2006 to 2014

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ABSTRACT

OBJECTIVES: We examined the trends in the rate of Henoch-Schönlein purpura (HSP) hospitalizations and the associated resource use among children in the United States from 2006 through 2014.

METHODS: Pediatric hospitalizations with HSP were identified by using *International Classification of Diseases, Ninth Revision*, code 287.0 from the National Inpatient Sample. HSP hospitalization rate was calculated by using the US population as the denominator. Resource use was determined by length of stay (LOS) and hospital cost. We used linear regression for trend analysis.

RESULTS: A total of 16 865 HSP hospitalizations were identified, and the HSP hospitalization rate varied by age, sex, and race. The overall HSP hospitalization rate was 2.4 per 100 000 children, and there was no trend during the study period. LOS remained stable at 2.8 days, but inflation-adjusted hospital cost increased from $2802.20 in 2006 to $3254.70 in 2014 ($P < .001$).

CONCLUSIONS: HSP hospitalization rate in the United States remained stable from 2006 to 2014. Despite no increase in LOS, inflation-adjusted hospital cost increased. Further studies are needed to identify the drivers of increased hospitalization cost and to develop cost-effective management strategies.

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Henoch-Schönlein purpura (HSP), now renamed IgA (immunoglobulin A) vasculitis, is the most common childhood vasculitis.[1] It affects small vessels and has multiorgan involvement including skin, gastrointestinal tract, joints, and kidneys. HSP is a benign, self-limiting condition, typically resolving within 4 to 6 weeks of onset. The etiology of HSP is not clearly understood, but some triggers like infections and drugs have been reported.[2–6]

The incidence of HSP across the world (expressed as per 100 000 children) ranges from 3.3 in Norway to 26.7 in the United Kingdom.[7] Most cases of HSP are first diagnosed in children <10 years of age. HSP is more common in male individuals with higher incidence in white than African American individuals in North America.[8] Before 2016, studies in which authors examined the epidemiology of pediatric HSP in the United States came from a single-center,[4] a single-county,[9] and a retrospective multicenter cohort study from 36 children's hospitals.[10] The drawback of such epidemiological studies is the presence of a referral bias and smaller study cohort. Hence, data from these studies may have poor external validity and may not be nationally representative. Okubo et al[11] in 2016 investigated the national rate of HSP hospitalization in the United States using the Kids' Inpatient Database (KID), a nationally representative administrative health care database. Authors of the study found that HSP hospitalization rate in the United States from 2003 to 2012 ranged from 1.89 to 2.45 per 100 000 children. This hospitalization rate is much lower than the predicted or estimated incidence of 13.5 to 18 per 100 000 in the United States and North America.[12,13] We thus sought to examine temporal trends in HSP hospitalizations rate according to age, sex, and race and the associated resource use among the US children from 2006 to 2014 using the National Inpatient Sample (NIS).

METHODS

Database

Our study sample was derived from the NIS database from 2006 to 2014. The raw data were derived from the following resources available in the public online domain: https://www.hcup-us.ahrq.gov (the Agency for Healthcare Research and Quality). The NIS is part of a family of databases and software tools developed for the Healthcare Cost and Utilization Project (HCUP) and is sponsored by the Agency for Healthcare Research and Quality.[14] As of 2014, the NIS sampling frame consisted of 44 states and the District of Columbia (Supplemental Fig 4), covering >96% of the US population. It is the largest publicly available inpatient health care database in the United States. When weighted, the NIS estimates >35 million hospitalizations nationally. This sampling frame represents >97% of the US population. For example, a query of the 2014 NIS yields 67 978 discharge records with an asthma diagnosis. This represents the unweighted number of discharges in the 20% stratified sample. To determine the estimated number of records with asthma diagnosis for the entire United States, the unweighted number of discharge records is multiplied with sample weights to generate the nationwide number of discharge records with asthma. In this example, the result is 339 890, representing the weighted number of discharges nationwide with an asthma diagnosis in 2014. The NIS provides sample weights for each year. Each individual hospitalization is deidentified and maintained as a unique entry with a single primary diagnosis and <30 secondary diagnoses along with <15 procedural codes. The NIS has been used to estimate population-level trends in numerous conditions.[15–19] Researchers and policymakers use the NIS to make national estimates of health care use, access, charges, quality, and outcomes. The NIS is released annually, which makes it an excellent database for longitudinal analysis. The study involved publicly available deidentified data and was thus exempt from review by the institutional review board.

Study Population

We identified all pediatric hospitalizations (age ≤18 years) using the NIS database from the years 2006 to 2014. Because each record in the NIS database corresponds to a discharge, children whose final disposition was coded as transferred out to another short-term facility, skilled nursing care, or intermediate care facility were identified by using the "DISPUNIFORM" variable and were excluded to avoid duplication of the data at the receiving facility. This exclusion criterion has been used in previous studies in which authors used the NIS.[20,21] Pediatric hospitalizations with HSP were identified by using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code 287.0 in any diagnosis field.

We excluded conditions that could be confounded with HSP using ICD-9-CM codes (Supplemental Table 3). Details of the population derivation are shown in Fig 1. We excluded the 2015 and 2016 editions of the NIS from the current study because the 2015 edition contained both *International Classification of Diseases, Ninth Revision* (ICD-9), and *International Classification of Diseases, 10th Revision* (ICD-10) codes, whereas the 2016 edition has only ICD-10 codes. Details of the population derivation are shown in Fig 1.

Definition of Variables

Hospital-level characteristics and encounter-level characteristics were studied for HSP hospitalizations. Encounter-level information such as age in years (0–4, 5–9, 10–14, and 15–18), sex, race, median household income as per zip code (<$36000, $36000–$44999, >$45000), primary payer (Medicare or Medicaid, private insurance, other), and hospital-level characteristics such as teaching status (rural, urban nonteaching, urban teaching), hospital bed size (small, medium, large), and hospital region (northeast, Midwest, south, west) were studied. The HCUP provides cost-to-charge ratio files to estimate cost. The cost-to-charge ratio allows for the conversion of charge data to cost estimates. Inflation-adjusted cost for each year was calculated in terms of the 2014 cost, according to the consumer price index data released by the US government.[22] This enabled the cost to be standardized over the study period.

Statistical Analysis

Baseline characteristics of the study population were analyzed. Median and

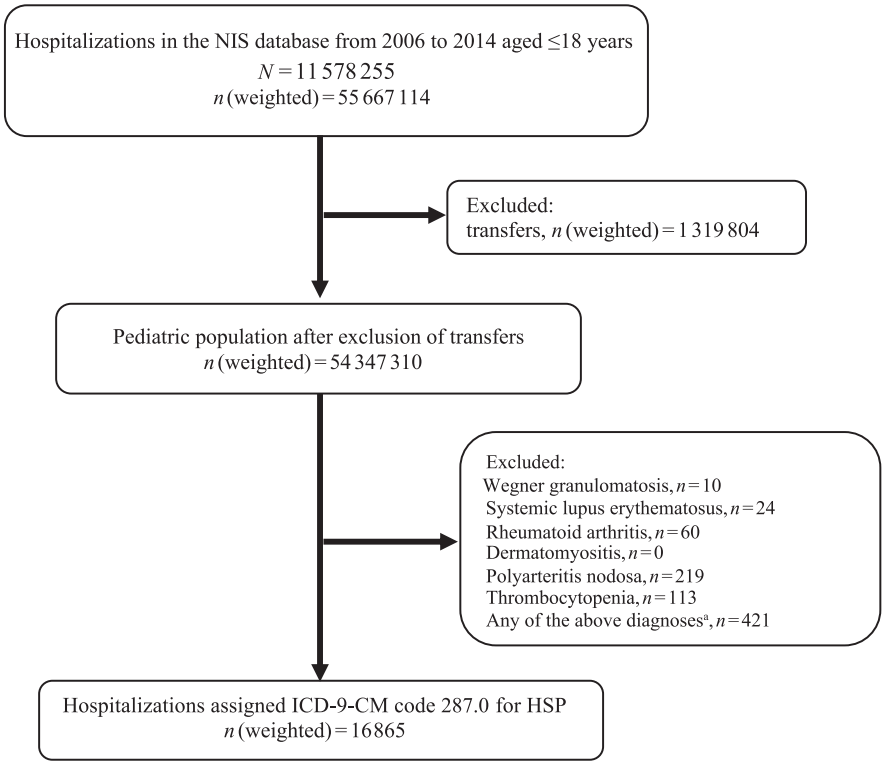

FIGURE 1 Study population and eligibility flowchart. [a] There could have been overlapping diagnosis.

interquartile range (IQR) were used to describe continuous variables, whereas proportions were used for categorical variables. χ^2 test, *t* test, Wilcoxon rank test, or analysis of variance (ANOVA) with post hoc Tukey's highly significant difference test depending on the data and their distribution were used for unadjusted analysis. Discharge weights ("DISCWT" variable) provided by NIS were used to generate national estimates of the number of HSP-related pediatric hospitalizations for each year from 2006 to 2014. Because of changes in sampling and weighting strategies from 2012, the HCUP has provided trend weights for years 1993 to 2011 to make estimates comparable to the new design (2012 and beyond).

Secular trends in HSP hospitalizations were analyzed by using linear regression, whereas trends among continuous variables such as length of stay (LOS) were analyzed by using survey regression procedures. The annual rate of HSP hospitalization was estimated by dividing the number of HSP hospitalizations (numerator) by the corresponding subgroup population (denominator). Hospitalization rate was expressed as per 100 000 children. The population of children ≤18 years old and their respective subgroup populations were derived from the Centers for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research online database.[23] SAS 9.4 (SAS Institute Inc, Cary, NC) was used for analyses. A *P* value <.05 was considered significant for all the analyses.

RESULTS

From 2006 to 2014, out of 55 667 114 pediatric hospitalizations, 16 865 were assigned an *ICD-9* diagnosis of HSP (Fig 1). There were 705 381 929 children aged ≤18 years during 2006 to 2014. The HSP hospitalization rate in the United States was 2.4 per 100 000 children from 2006 to 2014. Baseline and demographic characteristics of the HSP hospitalizations are shown in Table 1. HSP-related hospitalizations by age are shown in Figure 2.

Trends in HSP hospitalization rates by age, sex, race, and hospital census region are shown in Table 2. The overall rate of HSP hospitalization (expressed as per 100 000 children) decreased from 2.4 in 2006–2008 to 2.3 in 2012–2014, which was not statistically significant ($P = .62$). HSP hospitalization peaked at 4.5 among children aged 5 to 9 years, whereas the lowest rate was 0.8 for >15 years. Except for children aged ≤4 years, there were no trends in the HSP hospitalization rate among children aged ≥5 years. Boys were more prone to HSP compared with girls (2.7 vs 2 per 100 000 children; $P = .005$).

The HSP hospitalization rate was 1.9 in Hispanic, 1.6 in white, and 0.6 in African American patients. The difference between Hispanic and white patients was not statistically significant. There were no significant trends in the HSP hospitalization rate according to race. The differences in the HSP hospitalizations among the 4 census regions in the United States were not significant ($P = .65$). The Northeast region however recorded a statistically significant decrease in HSP hospitalization rate from 3.4 to 2.4 per 100 000 children ($P < .01$). The seasonal distribution of HSP hospitalization is shown in Figure 3. The lowest proportion of HSP hospitalizations ($P < .001$) was recorded in the summer. Differences between hospitalizations during winter, fall, and spring were not significant. Half of all the hospitalizations (52.4%) occurred during the fall and winter.

The trends in the LOS and hospital cost for HSP hospitalizations are shown in Table 2. Mean LOS was 2.8 days, and there was no significant trend from 2006 to 2014. However, the median inflation-adjusted cost of hospitalization significantly increased from $2802.20 in 2006 to $3254.70 in 2014 ($P < .001$). No mortality was recorded during the study period.

DISCUSSION

In the current study, we used the NIS database to highlight important findings regarding the epidemiology of pediatric HSP hospitalizations and associated resource use in the United States from 2006 to 2014. We found that the median age was 5.9 years and 79% were aged <9 years. Additionally, we have shown that there was a male preponderance, and the highest HSP

TABLE 1 Baseline and Demographic Characteristics of HSP Hospitalizations in the United States From 2006 Through 2014

	2006–2008	2009–2011	2012–2014	Total	*P*
No. HSP hospitalizations (unweighted)	1171	1254	1067	3492	—
No. HSP hospitalizations (weighted)	5537	5993	5335	16 865	—
Age, median (IQR)	5.5 (3.1–8.0)	6.1 (3.7–8.2)	6.1 (3.9–8.4)	5.9 (3.5–8.2)	—
Age group, %					<.0001
0–4	33.4	30.5	27.9	30.6	
5–9	45.8	50.2	50.3	48.8	
10–14	12.2	12.4	14.7	13.1	
15–18	8.6	7.0	7.0	7.5	
Sex, %					<.0001
Male	56.9	54.8	60.6	57.3	
Female	40.4	43.2	39.4	41.1	
Missing	2.6	2.0	0.0	1.6	
Race, %					.02
White	44.0	51.2	55.7	50.3	
African American	4.1	4.7	4.1	4.3	
Hispanic	15.1	19.1	20.0	18.1	
Other	8.6	11.7	11.4	10.6	
Missing	28.3	13.2	8.8	16.8	
Median household income category for patient's zip code, %					<.0001
0–25th percentile	25.8	26.8	24.7	25.8	
26–50th percentile	20.9	23.0	25.7	23.2	
51–75th percentile	24.3	24.7	24.0	24.3	
76–100th percentile	26.8	22.6	23.7	24.4	
Missing	2.2	2.9	2.0	2.4	
Expected payer and/or insurance status, %					<.0001
Private	58.5	52.8	50.6	54.0	
Medicare or Medicaid	35.5	39.4	43.0	39.3	
Others	5.8	7.5	6.4	6.6	
Hospital characteristics, %	0.2	0.3	0.0	0.2	
Hospital location and teaching status, %					<.0001
Rural	7.2	7.0	3.8	6.1	
Urban nonteaching	23.7	19.1	11.9	18.3	
Urban teaching	69.1	72.4	84.4	75.1	
Hospital region, %					<.0001
Northeast	24.6	15.0	17.7	19.0	
Midwest	20.1	16.3	24.8	20.3	
South	35.7	41.5	34.9	37.5	
West	19.6	27.2	22.6	23.2	
Bed size, %					<.0001
Small	12.7	8.8	11.4	10.9	
Medium	21.2	25.3	28.8	25.1	
Large	66.1	64.5	59.8	63.5	

—, not applicable.

hospitalization rate was in school-aged children (5–9 years old), and >50% of all the HSP hospitalizations occurred in the fall and winter months. These findings confirm what is already known on HSP hospitalizations from previous studies from the United States.[4,10,11] However, our study is the first to estimate and trend the national rate of HSP hospitalization in the United States. We demonstrated the HSP hospitalization rate in the United States was 2.4 per 100 000 children, and there was no

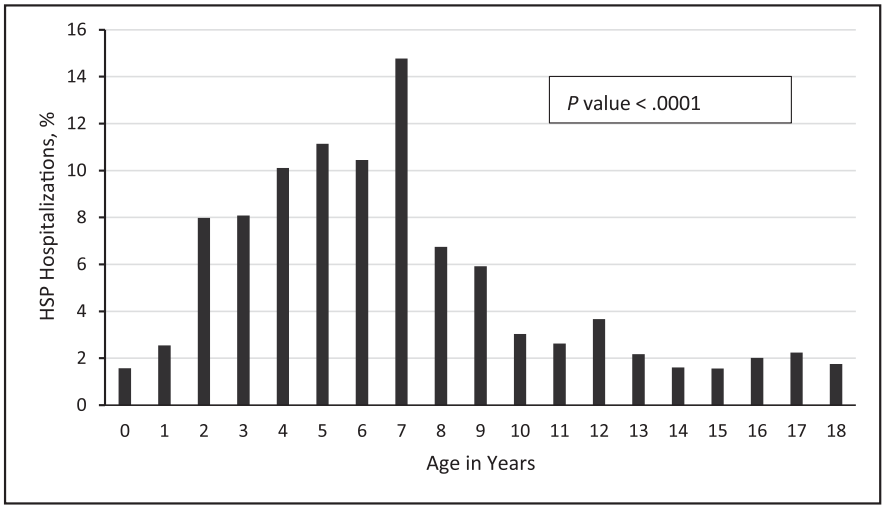

FIGURE 2 Distribution of HSP hospitalizations by age.

trend from 2006 to 2014. LOS remained stable, and inflation-adjusted hospital cost for HSP increased from 2006 to 2014. This extends our knowledge on pediatric HSP hospitalizations in the United States.

Our study revealed a mean LOS of 2.8 days, similar to 3 days reported by Weiss et al[10] using data from 36 US children's hospitals in the Pediatric Health Information System (PHIS) and 2.6 days by Okubo et al[11] using data from the KID. This is however lower than 5.9 and 5.1 days reported in South Korea and Taiwan, respectively.[4,7] It is noteworthy that only 17.6% of patients with HSP were hospitalized in the study in South Korea. Although the reasons for the hospitalizations were not outlined, it stands to reason that these hospitalizations represented a cohort of severe HSP cases, hence the longer LOS. Whereas the LOS in our study remained stable, the inflation-adjusted median cost for HSP hospitalization significantly increased. This is intriguing given that increased LOS is associated with increased costs of hospitalization for some pediatric conditions such as neonatal herpes simplex virus infections.[24]

From 2005 to 2015, the LOS for all children aged 0 to 17 years decreased from 6.8 to 5.6 days, whereas the average hospital cost increased from $5700 to $6700.[25] Thus, the impact of LOS on hospital cost may be minimal as studied by Taheri et al.[26] The reason for this increased cost of hospitalization is unclear but could stem from variability in the management practices and resource use across different hospitals and regions. Such variation in inpatient therapy and diagnostic evaluation was documented by Weiss et al[10] by using the PHIS database. Authors of a study from Israel involving 163 patients with HSP >15 years old suggested that 65% of the HSP hospitalizations were unnecessary.[27] Hospital costs are the expenses incurred by a hospital in providing patient care, and this includes the direct costs of patient care such as nursing, room and board, medicines and supplies, and indirect costs such as overhead for administrative expenses including complying with federal and state regulatory requirements, infection control, medical records, building maintenance, and equipment.[28–30] Hospital costs provided by the HCUP do not include professional or physician fees. Variation in any of these components could have led to the increased hospital cost of HSP hospitalization observed in this study. Establishment of clear admission criteria, clinical pathways, and treatment guidelines can reduce hospitalization rates, LOS, and hospital costs, which has been shown for childhood asthma.[10] Children-specific databases like the PHIS, which contains clinical data, could be used to delineate factors for increasing cost of hospitalization in future studies.

In the current study, the rate of HSP-related hospitalizations in the United States was 2.4 per 100 000 children. This is similar to the mean rate of 2.14 per 100 000 children using data from the KID.[11] These hospitalization rates are far lower than the estimated incidence of 10 to 14 per 100 000 children in the United States.[12] Because most cases of HSP are mild and self-limiting, they are managed in the outpatient setting. Indeed, authors of 2 recent studies from Taiwan and Korea found that <20% children with HSP diagnosis required hospitalization.[7,31] Therefore, our hospitalization rate of 2.4 per 100 000 children underestimates the true incidence of HSP in the United States because some patients are managed as outpatients only. The question arises as to what the rate of hospitalization is among children diagnosed with HSP in the United States. We could not determine this because of the lack of a national database focusing on pediatric outpatient management in the United States. Whereas Okubo et al[11] demonstrated a downward trend in the HSP hospitalization rate from 2.45 to 1.89 per 100 000 children from 2003 to 2012, the hospitalization rate from our study remained stable from 2006 to 2014. Our HSP hospitalization rate is also lower than the 3.3 to 26.9 per 100 000 children reported for other countries.[32,33] This may be due to the organization of the health care system in the United States, the establishment of the medical home for children,[34] and the guidelines on the child health supervision services provided by the American Academy of Pediatrics[35] that ensure the longitudinal follow-up of children as outpatients. The differences in the KID and the NIS may account for these differences. The KID is based on a stratified, random sample of pediatric discharges (patients <21 years of age) comprising 10% of normal newborns and 80% of other pediatric discharges (≤20 years at admission). It is released every 3 years, and its large sample size enables analyses of rare conditions (eg, congenital anomalies) as well as uncommon treatments (eg, cardiac surgery). The NIS does not oversample complicated newborns and other (nonnewborn) pediatric discharges, and because it is released each year, it is a good tool for longitudinal analysis.[36]

TABLE 2 Trends in the HSP Hospitalization Rate (per 100 000 Children) by Age Group, Sex, Race, and Geographic Region and Resource Use From 2006 to 2014

	2006–08	2009–11	2012–14	Total	*P*[a]	*P* for Trend
HSP hospitalization rate[b]						
Overall	2.4 ± 0.1	2.5 ± 0.1	2.3 ± 0.1	2.4 ± 0.004	—	.62
Age groups,[c] y					<.001	
≤4	3 ± 0.1	3 ± 0.1	2.5 ± 0.1	2.8 ± 0.008		.04
5–9	4.9 ± 0.1	4.9 ± 0.1	4.3 ± 0.1	4.5 ± 0.009		.88
10–14	1.1 ± 0.07	1.2 ± 0.08	1.2 ± 0.08	1.1 ± 0.004		.46
≥15	0.9 ± 0.07	0.8 ± 0.07	0.7 ± 0.07	0.8 ± 0.004		.64
Sex					.005	
Male	2.6 ± 0.08	2.7 ± 0.08	2.7 ± 0.08	2.7 ± 0.005		.93
Female	1.9 ± 0.07	2.2 ± 0.07	1.8 ± 0.07	2.0 ± 0.004		.71
Race[d]					<.001	
White	1.3 ± 0.05	1.7 ± 0.05	1.6 ± 0.05	1.6 ± 0.003		.21
African American	0.6 ± 0.07	0.7 ± 0.07	0.5 ± 0.07	0.6 ± 0.004		.81
Hispanic	1.6 ± 0.1	2.1 ± 0.1	1.9 ± 0.1	1.9 ± 0.007		.66
Others	2.9 ± 0.2	4 ± 0.2	3.3 ± 0.2	3.4 ± 0.01		.41
Hospital region					.65	
Northeast	3.4 ± 0.1	2.2 ± 0.1	2.4 ± 0.1	2.7 ± 0.01		.01
Midwest	2.1 ± 0.1	1.9 ± 0.1	2.6 ± 0.1	2.2 ± 0.006		.14
South	2.3 ± 0.9	2.8 ± 0.9	2.1 ± 0.9	2.4 ± 0.05		.87
West	1.9 ± 0.1	2.8 ± 0.1	2.1 ± 0.1	2.3 ± 0.008		.96
Resource use						
LOS, d						.99
Median (IQR)	1.6 (1.5–1.7)	1.6 (1.5–1.7)	1.6 (1.5–1.7)	1.6 (1.5–1.6)	—	
Mean ± SD	2.8 ± 0.1	2.8 ± 0.1	3.0 ± 0.2	2.8 ± 0.1	—	
Cost of hospitalization, US $						<.01
Median (IQR)	2802.2 (2591.9–3012.5)	3081.2 (2784.8–3377.6)	3254.7 (3060.9–3448.6)	3051.0 (2914.9–3187.0)	—	
Mean (SD)	4562.8 ± 232	4976.5 ± 442	6713.8 ± 568	5400.1 ± 250	—	

—, not applicable.
[a] *P* value for ANOVA or Student's *t* test as appropriate. ANOVA was followed by pairwise comparisons with Tukey's honestly significant difference test.
[b] Data presented as mean ± SEM.
[c] 10 to 14 y vs ≥15 y, $P = .29$; $P = .001$ for comparisons between other groups.
[d] White patients versus Hispanic patients, $P = .61$; $P < .001$ for all other group comparisons.

The onset of HSP is often preceded by respiratory tract infections.[2,3,9,37,38] The observation by multiple studies, including the present 1, that most cases of HSP hospitalizations occur in the winter and fall months supports the role of infections in HSP pathogenesis. If infections alone were the inciting trigger for HSP, one would expect children <5 years old, the group with the highest risk of infections such as acute respiratory infections, to have the highest rate of hospitalizations.[39,40] However, children 5 to 9 years have consistently been the most affected age group in several largest studies.[2,6,41] This raises the possibility of other factors such as race and genetics in the onset or pathogenesis of HSP. Indeed, we found that HSP hospitalization rate was highest in Hispanic patients and lowest in African American patients, similar to observations from previous studies from the United States.[9] Among 342 Spanish patients, López-Mejías et al[42] found an association between HSP and HLA-DRB1*01 in white patients. Also, a protective effect against the development of HSP appears to exist in white patients carrying the HLA-DRB1*03 phenotype.[42] Different genes including the HLA family of genes as well as genes for synthesis of inflammatory and antiinflammatory proteins, endothelial function regulation, synthesis of antioxidant proteins, and the complement gene family are associated with susceptibility to or protection against HSP.[43] We therefore speculate that racial and ethnic differences in the expression of these genes may be associated with the occurrence of HSP. Another possible reason for the racial differences in the HSP hospitalization rate may be the result of racial disparities in the health and health care of children in the United States.[44] More studies are needed to unravel the role of genetic or ethnic factors in HSP pathogenesis.

Any study of this nature relying on administrative data has some limitations, and our findings must be interpreted with

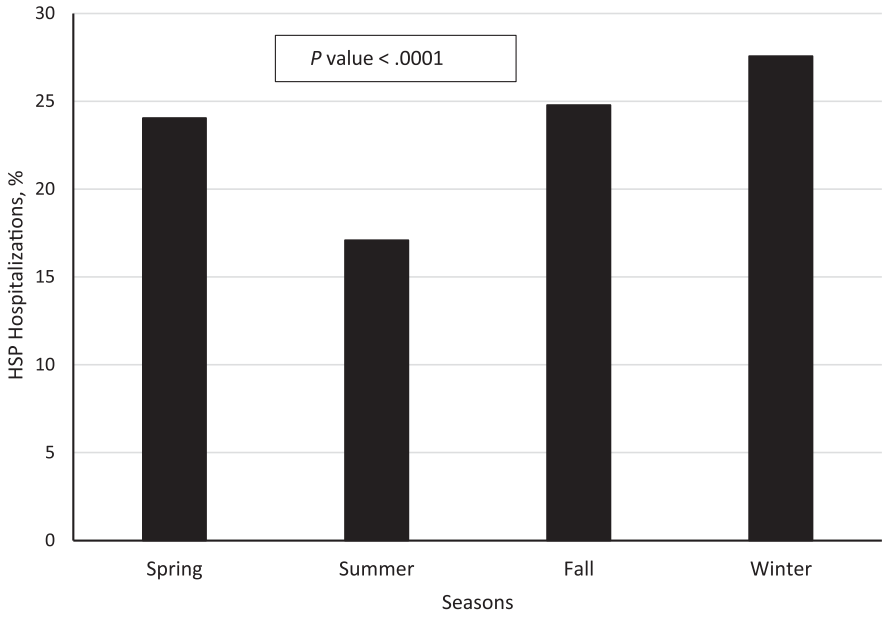

FIGURE 3 Seasonal distribution of HSP hospitalizations.

these limitations in mind. Large databases such as the NIS are susceptible to coding errors, omissions, and duplications. However, the HCUP has instituted mechanisms to ensure the validity of the NIS data.[45] Additionally, HSP is a major discharge diagnosis and more likely to be coded correctly because it is related to reimbursement. The NIS database had no data on clinical parameters such as preceding illnesses, diagnostic tests, and inpatient pharmacologic treatments. In addition, because we used discharge data rather than individual patient data, data on some patients could have been duplicated for any given year. Not all individuals with HSP are hospitalized, making it impossible to calculate true incidence of HSP in children. Rather, we estimated the HSP hospitalizations rate in the general population of children. In addition, we could not estimate the rate of hospitalization among patients with HSP because the NIS contains data on hospitalized patients only. The NIS database lacks follow-up information, so we could not study the long-term outcomes of HSP hospitalizations. The ICD-9 code for HSP has not been validated in any previous study. Therefore, the sensitivity, specificity, and the positive predictive value of this code is unknown. Hospital costs are usually higher at children's hospitals than at community hospitals.[46] The NIS data cannot be used to differentiate freestanding children's hospitals from nonchildren's hospital. We were therefore unable to study the influence of care at a children's hospital on the LOS and cost of hospitalization for HSP. Furthermore, the NIS data could not be used to differentiate between observation status and inpatient status. Hence, we could not estimate whether the cost of hospitalization could have been different if the admissions were billed as observation status as compared to inpatient status.

Notwithstanding these limitations, our study possesses several strengths. The NIS is the largest health care database in the United States, containing data on all discharges in the United States regardless of payer and is uniquely equipped to capture almost all HSP cases. Thus, our study findings are nationally representative. To our knowledge, the current study is 1 of the largest to characterize the epidemiology of HSP hospitalizations in children and their associated resource use in the United States.

CONCLUSIONS

Using nationally representative database, we showed that HSP disproportionately affects school-aged children, and the hospitalization rate remained stable from 2006 to 2014. LOS remained stable, whereas inflation-adjusted hospital cost increased. The increased cost of HSP hospitalizations suggests that standardized, cost-effective management strategies are needed.

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