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Toxic Shock Syndrome in Patients Younger than 21 Years of Age, United States, 2006–2018

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Abstract

We examined the incidence of toxic shock syndrome in the United States during 2006–2018 among persons <21 years old with commercial or Medicaid-insurance using administrative data. There were 1008 commercially-insured and 481 Medicaid-insured toxic shock syndrome cases. The annual rate was 1 per 100,000 and stable over time. Rates were even lower in children <5 years old and stable over time.

Keywords

Toxic shock syndrome; TSS; staphylococcus TSS; streptococcus TSS; MarketScan

Introduction:

Toxic shock syndrome (TSS) is a rare, severe, potentially life-threatening illness, mainly caused by infection with Staphylococcus aureus or Streptococcus pyogenes. It is characterized by high fever, hypotension, a generalized rash and multiorgan system involvement. Mortality rate estimates for TSS in the United States vary from 2% to 38%.[1, 2] Because TSS patients require hospital treatment for clinical management, TSS hospitalization rates can be used as reasonable surrogates for TSS incidence.

Staphylococcal TSS incidence rates substantially declined in the 1980s following changes to manufacturing of tampons, whereas rates of streptococcal TSS have remained stable over time.[3] The incidence of TSS in the United States has been estimated to be 0.5 for

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staphylococcal TSS and 0.2 per 100,000 for streptococcal TSS.[2, 3] Rates of TSS are thought to be lower in children than in adults.[3] However, there are limited data published on rates of TSS in US children, last published from studies in 2012–2013[4, 5] and neither provided national estimates of TSS incidence in children. Updated national data of the epidemiology and rates of pediatric TSS will help improve our understanding of TSS and provide data to help distinguish from other illnesses in children with clinical features similar to TSS, such as Kawasaki disease and multisystem inflammatory syndrome in children (MIS-C), a newly identified syndrome in children linked to severe coronavirus disease 2019 infection.[6]

In this report, we describe the incidence of TSS during 2006–2018 among persons <21 years old enrolled in commercial employer-sponsored insurance or Medicaid-insurance programs.

Methods:

Data sources

The 2006–2018 IBM MarketScan Commercial Claims and Encounters and Multi-State Medicaid Databases were used in our analysis. Annually, the MarketScan Commercial database includes healthcare claims for approximately 20–50 million employees and their beneficiaries with employer-sponsored insurance in the United States.[7] The MarketScan Medicaid database includes data for approximately 6–13 million persons annually from 8–12 unidentified, geographically dispersed states. Only the Medicaid databases include information on race/ethnicity.

Case definitions

The study population consisted of MarketScan enrollees from both databases <21 years old enrolled for the full calendar year. TSS cases were identified using inpatient diagnostic codes for TSS (any diagnostic and principal code) based on the International Classification of Diseases, 9th or 10th revisions, Clinical Modification (ICD-9-CM code 040.82 or ICD-10-CM code A48.3); these codes alone do not distinguish between staphylococcus or streptococcus TSS.

Analysis

We calculated annual incidence by insurance type and age group (<21 years and <5 years). Logistic regression was used to assess changes in TSS rates over time and by selected variables (insurance type, sex, region, urban/rural and race). We assessed the following outcomes among TSS patients: hospital duration, intensive care unit (ICU) admission, intubation and death in the hospital; data on deaths was not available after 2016. We compared selected characteristics (demographics and outcomes) of TSS patients <21 years old by insurance status using Pearson χ^2 or Fisher exact test for categorical variables and the Mann-Whitney-Wilcoxon test for numeric variables (SAS, version 9.4; SAS Institute Inc., Cary, NC). $P < 0.05$ were statistically significant.

Because the analysis only included deidentified data, it was deemed not to be human subjects research and did not require Institutional Review Board approval by the Centers for Disease Control and Prevention.

Results:

An annual average of 8 million (range, 3–11 million) commercially-insured and 3 million (range, 2–5 million) Medicaid-insured persons <21 years old were included in this analysis. Among commercially-insured persons <21 years old, there were 1008 TSS patients identified; 544 (54%) had TSS coded in the principal diagnostic code. Among Medicaid-insured persons, there were 481 TSS patients identified; 230 (48%) had TSS coded in the principal diagnostic code (Table 1). The median age of TSS patients was 14 years among commercially-insured patients and 12 years among Medicaid-insured patients ($P < 0.01$). Two-thirds (66%) of commercially-insured patients were in the 13–20 years old age group, whereas half (51%) of the Medicaid-insured patients were in the 0–4 and 5–12 years old age groups. Sixty-nine percent of commercially-insured TSS patients <21 years old were female compared with 60% among Medicaid-insured ($P < 0.01$). However, when data were stratified by age group, differences by gender were no longer statistically significant. Among 421 (88%) Medicaid-insured patients <21 years old with data on race/ethnicity, 58% of TSS patients were White, 30% were Black and 8% were Hispanic.

A higher proportion of commercially-insured TSS patients were admitted to the ICU compared with Medicaid-insured patients (66% vs. 55%; $P < 0.01$) (Table 1). The median duration of hospitalization was 4 days for both commercially- and Medicaid-insured patients ($P = 0.27$). There were 5 in-hospital deaths (0.5%), all among 1008 commercially-insured TSS patients 13–20 years old, none among Medicaid-insured.

Among persons <21 years old, the average annual rate of TSS hospitalizations was 1.0 (range, 0.8–1.1) per 100,000 among commercially-insured persons and 1.1 (range, 0.6–1.4) per 100,000 among Medicaid-insured persons with TSS coded as any diagnostic code (Fig. 1). Among children <5 years old, the average rate of TSS hospitalizations was 0.5 (range, 0.2–0.8) per 100,000 among commercially-insured persons and 0.8 (range, 0.2–1.5) per 100,000 Medicaid-insured patients with TSS as any diagnostic code. TSS rates were stable with no significant differences over time for all age and insurance groups ($P > 0.05$) (Fig. 1). There was no statistical difference in rates by insurance group for patients <21 years ($P = 0.63$) and <5 years ($P = 0.86$) of age.

The average annual TSS incidence was higher in females than males in both commercially-insured (1.4/100,000 vs. 0.6/100,000; $P < 0.01$) and Medicaid-insured patients (1.3/100,000 vs. 0.9/100,000; $P = 0.02$). Among commercially-insured patients, the average annual rate was higher in patients living in urban versus rural areas (1.0/100,000 vs. 0.8/100,000; $P < 0.01$) and in the Northeast versus other regions (1.2/100,000 vs. 0.9–1.0/100,000; $P = 0.01$). Among Medicaid-insured patients, the average annual rate was lower in Black (0.8/100,000) compared with White (1.2/100,000), Hispanic (1.0/100,000) and other race patients (1.0/100,000), although not statistically significant ($P > 0.05$).

Discussion:

In both claim databases analyzed, TSS hospitalization rates among persons <21 years old remained low (0.6–1.4/100,000); in comparison, TSS rates in the early 1980s had peaked

to 6–12 per 100,000 among women 12–49 years old.[8] Rates in our analysis were stable over time during 2006–2018. Rates among children <5 years old were even lower (0.2–1.5/100,000) and also stable during the study period. Rates did not differ by insurance group suggesting that socioeconomic status is not associated with TSS.

TSS rates in the present study are within the range of other published studies.[5, 8–10] National TSS rates for all ages in 1986 and 1996 were 1.0 and 0.5 per 100,000, respectively, and 0.7–1.0 per 100,000 during 2003–2012.[5, 8] Two studies using Minnesota and Colorado surveillance data reported average TSS rates of 0.5–0.6 per 100,000 and found rates to be stable during 2000–2006 and 1993–2006, respectively.[9, 10] Some studies have included children, although none provided national estimated pediatric TSS rates in the United States.[4, 5, 9–11] Studies in the United Kingdom and Australia estimated the average annual TSS rate in children to be approximately 0.4 per 100,000.[12, 13] The higher proportion of TSS cases in females has been documented in other studies,[4, 5, 10, 11] along with a mean or median age of 11–13 years.[4, 11] Similar to another analysis of hospitalization data, we also found lower rates in Blacks, although we did not find lower rates in Hispanic as compared with White patients.[5] In terms of disease severity in children, some studies found comparable rates to this study in mortality (0.6%–1.9%) and ICU admission (74%),[4, 5, 13] although mortality has also been reported to be much higher (16%–38%).[2, 12]

We were unable to distinguish between TSS streptococcal and staphylococcal infections using existing TSS codes. We attempted to identify these cases by pairing TSS codes with streptococcal or staphylococcal infection diagnostic codes but found only 12% (175/1489) had codes to potentially distinguish between the 2 types, with a higher proportion with staphylococcal diagnostic codes (7% TSS staphylococcal only, 3% TSS streptococcal only and 2% with both types). In the future, a diagnostic code to distinguish between these 2 types of TSS would be helpful for monitoring streptococcal and staphylococcal TSS.

Our study had limitations. We relied on diagnostic codes from claims databases and did not have access to medical records to verify the TSS diagnosis. We only captured in-hospital deaths, and data on deaths were unavailable after 2016. Last, our data are from persons with private employer-sponsored insurance and may not be generalizable to other populations, and Medicaid data are from a select number of states.

In conclusion, the present study used data from large national healthcare claims databases over a 13-year period to provide the most current incidence of TSS among insured children in the United States. The incidence remained rare and stable at about 1 per 100,000 persons <21 years old during 2006–2018. Although there are limitations with hospitalization data, they can be used to examine national trends for more rare conditions and are typically less resource-intensive than other types of surveillance methods. TSS is one of the potential differential diagnoses for MIS-C as both conditions share similar clinical features. Baseline data on pediatric TSS in the United States can be useful for better understanding rates of other hyperinflammatory conditions such as MIS-C.

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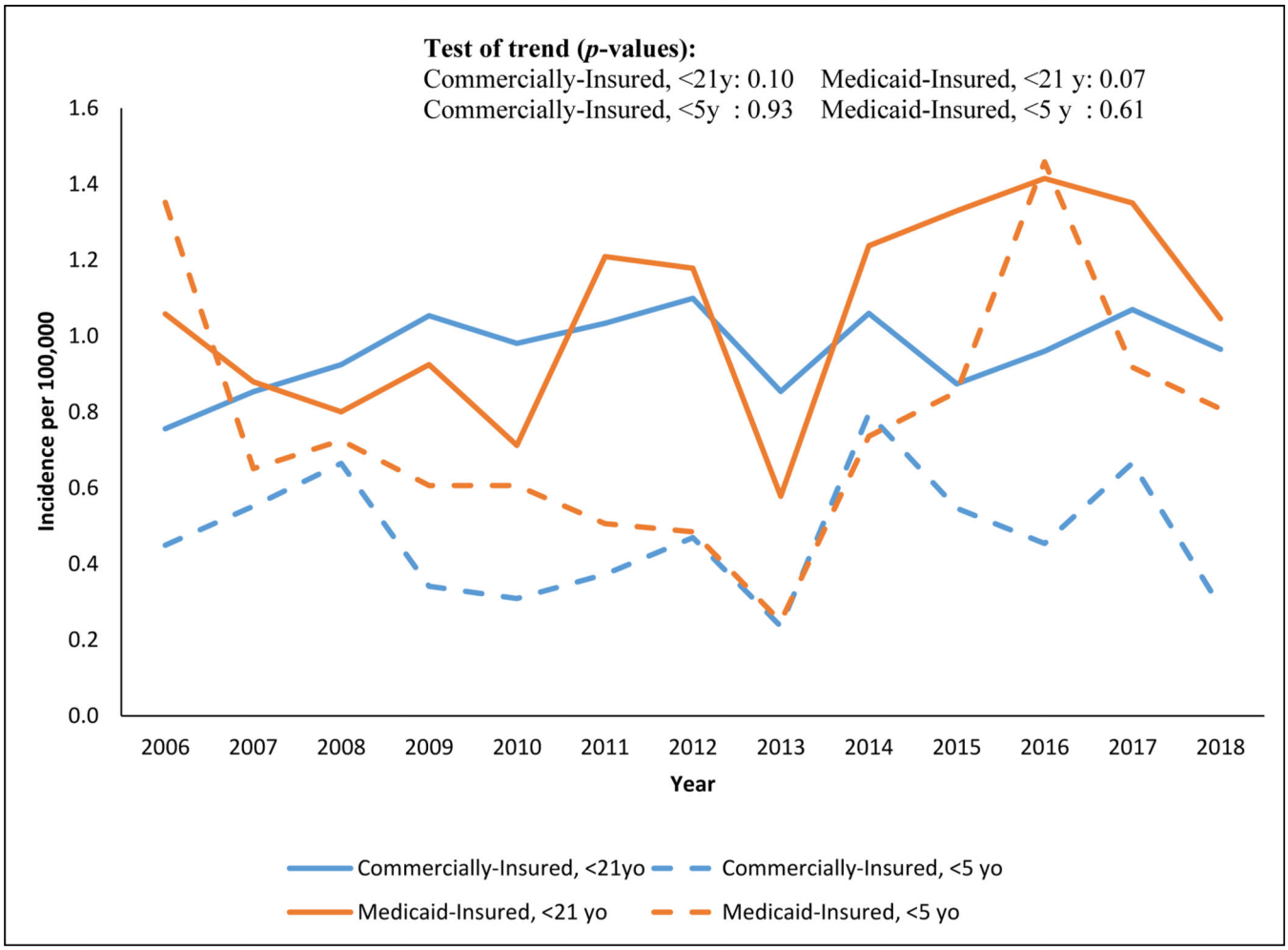

FIGURE 1.

Incidence of TSS per 100,000 among persons <21 years old, by age group and insurance type, United States, 2006–2018[a].

[a]TSS cases were identified using inpatient diagnostic codes for TSS coded in any diagnostic position. yo indicates years old.

TABLE 1.

Annual Rates and Characteristics of Patients With TSS <21 Years Old by Insurance Type, United States, 2006–2018[ab]

	Toxic Shock Hospitalizations, Any Diagnostic Code					Toxic Shock Hospitalizations, Principal Diagnostic Code				
	Commercially-insured N=1008		Medicaid-insured N=481			Commercially-insured N=544		Medicaid-insured N=230		
Case Characteristics	**#**	**%**	**#**	**%**	***p*-value[c]**	**#**	**%**	**#**	**%**	***p*-value[c]**
Age in years, median (IQR)	14 (9–16)		12 (7–16)		<0.01	15 (12–16)		13 (8–15)		<0.01
Age group [d]					<0.01					<0.01
0–4	94	9.3%	83	17.3%		38	7.0%	31	13.5%	
5–12	254	25.2%	162	33.7%		113	20.8%	74	32.2%	
13–20	660	65.5%	236	49.1%		393	72.2%	125	54.3%	
Gender					<0.01					<0.01
Male	318	31.5%	191	39.7%		128	23.5%	82	35.7%	
Female	690	68.5%	290	60.3%		416	76.5%	148	64.3%	
MSA					NA					NA
Urban	876	86.9%	---	---		474	87.1%	---	---	
Rural	132	13.1%	---	---		70	12.9%	---	---	
Region					NA					NA
1. Northeast	191	18.9%	---	---		87	16.0%	---	---	
2. North Central	247	24.5%	---	---		150	27.6%	---	---	
3. South	379	37.6%	---	---		199	36.6%	---	---	
4. West	164	16.3%	---	---		93	17.1%	---	---	
5. Unknown	27	2.7%	---	---		15	2.8%	---	---	
Race					NA					NA
White	---	---	246	58.4%		---	---	116	56.9%	
Black	---	---	126	29.9%		---	---	66	32.4%	
Hispanic	---	---	34	8.1%		---	---	14	6.9%	
Other	---	---	15	3.6%		---	---	8	3.9%	
Missing	---	---	60	0.0%		---	---	26	0.0%	
Clinical Course										
ICU admission	666	66.1%	262	54.5%	<0.01	355	65.3%	123	53.5%	<0.01
Intubation	70	6.9%	39	8.1%	0.46	18	3.3%	8	3.5%	1.00
Died[e]	5	0.5%	0	0.0%	0.18	2	0.4%	0	0.0%	1.00
Duration of Hospitalization in days, median (IQR)	4 (2–6)	0.0%	4 (3–7)	0.0%	0.27	4 (2–6)	0.0%	4 (3–7)	0.0%	0.27

Abbreviations: MSA, metropolitan statistical area; IQR, interquartile range; NA, not available

[a]We used the 2006–2018 IBM MarketScan® Commercial Claims and Encounters and Multi-State Medicaid Databases. The MarketScan Commercial databases include employer-sponsored insurance healthcare claims for employees and their beneficiaries which include data for

approximately 20–50 million persons annually with employer-sponsored insurance. An average of 11 million persons aged <21 years were enrolled annually (~30% of the total commercially-insured annual enrolled population), of whom approximately 50% were male, 80% lived in an urban residence, 40% were from the South, 24% from North Central, 15% from the Northeast, and 19% in the West. An annual average of 8 million (range, 3–11 million) persons who fulfilled the study criteria (MarketScan enrollees aged <21 years who were enrolled for the calendar year) were included in this analysis. Data on race is not available for commercially-insured persons.

[b] The MarketScan Medicaid databases include data for approximately 6–13 million persons each year from 8–12 unidentified, geographically dispersed states. Only the Medicaid databases include information on race/ethnicity. An average of 5 million persons aged <21 years were enrolled annually (~60% of the total Medicaid-insured annual enrolled population), of whom approximately 50% were male, 46% were white, 33% black, and 8% Hispanic. An annual average of 3 million (range, 2–5 million) persons who fulfilled the study criteria (MarketScan enrollees aged <21 years who were enrolled for the calendar year) were included in this analysis. Data on MSA and region are not available for Medicaid-insured persons.

[c] We compared selected characteristics (demographics and outcomes) of TSS patients aged <21 years by insurance status (commercially-insured versus Medicaid-insured) using Pearson chi square or Fisher's exact test for categorical variables and the Mann Whitney Wilcoxon test for numeric variables. These are unadjusted *p*-values.

[d] We calculated the incidence of TSS in <5 year-olds as a comparison with other early childhood conditions, such as Kawasaki disease, with similar clinical features.

[e] Only information on in-hospital deaths were available and data on deaths were unavailable after 2016.