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A Retrospective Cohort Study of the Management and Outcomes of Children Hospitalized with Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis

James W. Antoon, MD, PhD[a], **Jennifer L. Goldman, MD, MS**[b,c], **Samir S. Shah, MD, MSCE**[d], **Brian Lee, PhD**[c]

[a]Department of Pediatric and Adolescent Medicine, Children's Hospital, University of Illinois at Chicago College of Medicine, Chicago, Ill

[b]Division of Clinical Pharmacology, Children's Mercy Hospitals and Clinics, Kansas City, Mo

[c]Division of Infectious Diseases, Children's Mercy Hospitals and Clinics, Kansas City, Mo

[d]Divisions of Hospital Medicine and Infectious Diseases, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

Abstract

BACKGROUND: Severe cutaneous adverse reactions are rare yet life-threatening conditions. The current management and outcomes of these conditions in US children are unclear.

OBJECTIVE: To characterize the current management and outcomes of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) across US children's hospitals.

METHODS: We performed a retrospective cohort study of children younger than 18 years hospitalized with a primary diagnosis of SJS or TEN at 47 US freestanding children's hospitals. We compared treatment (intravenous immunoglobulin [IVIG], steroids, antibiotics, and others) and outcomes (length of stay [LOS], hospital mortality, readmission, recurrence, related complications, and adjusted hospital costs) across hospitals and by SJS versus TEN diagnoses.

RESULTS: We identified 898 pediatric patients hospitalized with a primary diagnosis of SJS or TEN. Of these patients, 167 (18.6%) were prescribed steroids only, 229 (25.5%) IVIG only, and 153 (17.04%) both IVIG and steroids. Median LOS was 8 days (interquartile range, 5–13) with median hospital-adjusted costs of $16,265. Readmissions were common, with 88 (9.9%) patients readmitted within 30 days of discharge and a recurrence rate of 2.7%. Overall hospital mortality in children was low at 0.56%. TEN was associated with higher mortality (3.23%) compared with SJS (0.13%). There was no association between the use of IVIG, systemic steroids, or IVIG and steroids during the first 2 days of hospitalization and decreased LOS or mechanical ventilation. Complex chronic conditions and TEN diagnoses were associated with increased LOS and increased odds of mechanical ventilation.

Corresponding author: James W. Antoon, MD, PhD, Department of Pediatric and Adolescent Medicine, Children's Hospital, University of Illinois at Chicago College of Medicine, 840 S. Wood St, CSB 1404, Chicago, IL 60612. jantoon@uic.edu.

CONCLUSION: Survival in children with SJS and TEN is significantly better than that observed in adults. However, there is variability in the management and outcomes in children diagnosed with these severe cutaneous reactions. Further studies are needed to determine the most effective treatment strategies given the extent of health care utilization and high rate of readmissions observed in this population.

Keywords

Stevens-Johnson syndrome; Toxic epidermal necrolysis; Pediatric hospital medicine; Drug adverse effects; Severe cutaneous adverse reactions

INTRODUCTION

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are uncommon but potentially devastating severe cutaneous adverse reactions, classically in response to drugs or infections. The incidence of SJS or TEN is estimated to be 2 to 12 cases per million per year in adults.[1–4] The incidence of SJS and TEN varies by race, ethnicity, and sex, and differences in reporting of incidence may be due to differences in patient populations studied. It is now widely accepted that SJS and TEN constitute a single disease of varying severity on the same spectrum.[5,6] These conditions occur in all ages (including neonates), sexes, and ethnicities.[7,8]

Care for milder cases remains largely supportive, whereas moderate to severe SJS or TEN typically requires immunosuppression and intensive or burn unit care.[9] Currently, there is no standardized treatment regimen resulting in variability in care for these patients. Because cases are rare and unpredictable, randomized controlled studies to evaluate the most effective treatment strategies are lacking. Specific pharmacological therapies remain controversial and include systemic corticosteroids, intravenous immunoglobulin (IVIG), plasmapheresis, cyclosporine, or TNF inhibition.[10–17] Most studies of treatment of SJS and TEN were performed in adults and the question of generalizability to children remains.

The short- and long-term outcomes of children with SJS and TEN are not well understood and a better understanding of the current disease management is needed to identify potential opportunities for treatment improvement and reduction in complications. The objectives of this study were to (1) characterize the management and outcomes of SJS and TEN across US children's hospitals and (2) determine the association between treatment (IVIG, steroids, and antibiotics) and SJS- and TEN-related complications.

METHODS

Study design and data source

We performed a retrospective study using data from the Pediatric Health Information System (PHIS) to describe a cohort of hospitalized pediatric patients diagnosed with SJS or TEN. PHIS is an administrative database that contains inpatient, emergency department, ambulatory surgery, and observation encounter-level data from 47 not-for-profit, tertiary care pediatric hospitals in the United States. These hospitals are affiliated with the Children's

Hospital Association. Data quality and reliability are assured through a joint effort between the association and participating hospitals.

Study population

The study population included children hospitalized with severe cutaneous reactions. Patients were included if they were younger than 18 years at the time of admission, classified as either an inpatient or observation patient, and discharged from 1 of the hospitals in the PHIS system between January 1, 2008, and December 31, 2015, with a primary *International Classification of Diseases, Ninth Revision* (ICD-9), discharge diagnosis code of 695.13 (SJS), 695.14 (SJS/TEN overlap syndrome), or 695.15 (TEN and length of stay [LOS] ≥3 days).[4,18] Incorporating LOS can improve retrospective identification of SJS/TEN cases.[19] An LOS of 3 or more days was chosen on the basis of previously published studies.[18–20] ICD-9 diagnoses of SJS/TEN overlap syndrome and TEN were combined for data analysis and compared with SJS. In this study, the term TEN refers to combined ICD-9 diagnoses of SJS/TEN overlap syndrome and TEN. We limited our study to no earlier than 2008 because of the reclassification of ICD-9 codes for SJS, TEN, and SJS/TEN overlap syndrome in 2007 to improve the accuracy and precision of these codes for cutaneous reactions. The newer ICD-9 codes used in this study have been shown to better reflect true SJS or TEN compared with codes before 2008.[2,4,19]

To ensure that the cohort represented children hospitalized for index SJS or TEN, subjects with a known previous diagnosis of SJS or TEN were excluded. Subjects were also excluded if they had a concurrent diagnosis (ICD-9) of diseases associated with cutaneous reactions including Kawasaki disease, graft versus host disease, toxic shock syndrome, staphylococcus scalded skin syndrome, streptococcus scalded skin syndrome, or paraneoplastic pemphigus. To ensure consistent capture of data, patients transferred in and out of the hospital were excluded. Finally, subjects with no billing data available were excluded from the study.

Outcomes and definitions

The primary outcomes of the study were to describe the management strategies and outcomes of children hospitalized with SJS or TEN. The outcomes included adjusted charges (in dollars) of hospitalization, hospital LOS, hospital mortality, recurrence, hospital readmission, and SJS- or TEN-related complications. For comparison of treatments and outcomes, admission was defined as the first 2 days of hospitalization. Readmission was defined as any hospitalization after discharge from initial SJS or TEN hospitalization. Readmissions within 30 days and 6 months were analyzed. Recurrence was defined as repeated admission(s) with a primary discharge diagnosis of SJS or TEN anytime from 6 months to 5 years after the initial SJS or TEN hospitalization. For example, if a patient was discharged with a diagnosis of SJS and admitted later for TEN, this was considered a recurrence (and vice versa). Short-term complications were those known to be associated with SJS or TEN during initial hospitalization and any 30-day readmission, including sepsis, septic shock, respiratory distress, respiratory insufficiency, respiratory failure, acute kidney injury, and hypotension. Adjusted costs were determined by applying an annual cost-to-charge ratio (submitted to the Center for Medicare & Medicaid Services) to the total billed charges.

Data analyses

Data from index (initial) hospitalizations were analyzed. The overall distributions of select clinical and demographic characteristics were determined using the Pearson chi-square statistic when comparing categorical distributions. The Mann-Whitney test was used to compare the distribution of continuous variables. Multivariable linear regression models were used to examine the factors associated with log-transformed LOS. In this model, for example, a positive coefficient is associated with an increased LOS, whereas a negative coefficient is associated with a decreased LOS. Multivariable logistic models were used to examine the odds of mechanical ventilation after the first 2 admission days. All regression models treated PHIS hospitals as a random effect and used compound symmetry for the covariance matrix. All analyses were completed using SAS version 9.4 statistical software (SAS Institute, Cary, NC).

RESULTS

Study subjects

We identified 914 pediatric patients hospitalized with a primary diagnosis of SJS or TEN and a hospital LOS of 3 days or more. Sixteen patients with prespecified concurrent diagnosis with known cutaneous reactions as described earlier (eg, Kawasaki disease) were excluded. A total of 898 patients were included in the final analysis. Most of the patients (86.2%) were diagnosed with SJS. There was an overall male predominance (59.0%), and median age on admission was 10.8 years (interquartile range, 6.7–14.3). A diagnosis of SJS was more common in males (61.2%) and that of TEN was more common in females (54.8%). Diagnosis of SJS and TEN varied by race and ethnicity, with a higher frequency of patients being white or other/unknown (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). Demographic characteristics are presented in Table I.

Outcomes

Clinical outcomes are presented in Table II. Almost one-fourth of patients (23.3%) were admitted to the intensive care unit (ICU) and 9.8% of patients required mechanical ventilation. TEN was associated with a higher frequency of mechanical ventilation compared with SJS (33.9% vs 5.9%; $P < .001$). TEN was also associated with a higher frequency of overall ICU care (55.7% vs 5.94%; $P < .001$) and significantly more transfers to ICU after admission (10.5% vs 3.36%; $P = .001$) compared with SJS.

The overall median LOS was 8 days (interquartile range, 5–13), varying from a median of 7 days in SJS to 15.5 days in TEN ($P < .001$). Overall hospital mortality in this hospitalized pediatric population was 0.56%. TEN diagnoses were associated with higher mortality (3.23% vs 0.13%; $P = .002$), shock/sepsis (12.1% vs 6.33%; $P = .04$), respiratory complications (31.5% vs 4.91%; $P < .001$), and higher costs ($44,362 vs $14,510; $P < .001$) compared with SJS.

All-cause readmissions to the hospital after discharge were common, with 88 (9.85%) children readmitted within 30 days and 169 (18.9%) children readmitted within 6 months. There was no difference in the 30-day or 6-month readmissions between SJS and TEN

diagnoses. Overall disease recurrence was 2.69%. Mean time to recurrence was 1.71 years with a median of 1.33 years. There was no statistically significant difference in recurrence between SJS and TEN.

Pharmacological management

There was variability in treatment strategies used across hospitals (Figure 1). There was a high variation in frequency of antibiotic and antiviral use across hospitals (Figure 1, *A*). Most patients received antibiotics (542, 60.4%) during their admission, and patients with TEN were more likely to receive antibiotics than those with SJS (76.6% vs 57.8%; $P < .001$) (Table III). Of those who received antibiotics, most were administered on admission compared with later in the hospitalization (45.3% vs 15.0%; $P < .001$). There was no correlation between hospital volume of admissions due to severe cutaneous adverse reactions and frequency of antibiotic use.

Overall, 18.6% patients were prescribed steroids only, 25.5% IVIG only, and 17.04% both IVIG and steroids. Adjunctive therapies initiated within 2 days of admission included IVIG (25.6%), systemic steroids (13.4%), or both (8.35%). Patients with TEN were more likely to receive IVIG only in the first 2 days of hospitalization compared with patients with SJS ($P < .001$). As seen in Figure 1, *B*, there was no association between hospital volume of SJS and TEN admissions and frequency of steroid or IVIG treatment.

There was variation in adjunctive therapy choice based on region, with those patients in the Middle Atlantic and East North Central geographic regions receiving more IVIG and steroids compared with IVIG or steroids alone. The West North Central region had the lowest rate of combination therapy use at 7.45% compared with 26.0% and 23.7% in the Middle Atlantic and East North Central regions, respectively.

Predictors of LOS and mechanical ventilation

The initial treatments of SJS and TEN were analyzed to determine whether initial treatment in the first 2 days of hospitalization was associated with differences in LOS or need for mechanical ventilation. As can be seen in Table IV, factors associated with an increased LOS include TEN diagnosis, mechanical ventilation, antiviral use, antibiotics both on admission and after admission, and complex chronic condition. In addition, treatment with IVIG alone and treatment with a combination of IVIG and steroids were both associated with a significantly longer LOS compared with receipt of neither of those therapies. In stratified analysis, the factors associated with increased LOS within diagnoses (either SJS or TEN) were similar to the combined analysis (Table IV).

There were several factors associated with increased odds of mechanical ventilation after the first 2 days of hospitalization. Compared with SJS, TEN had greater odds of mechanical ventilation (Table V). Similarly, complex chronic conditions were associated with increased odds of mechanical ventilation. Treatment with steroids on admission did not decrease the odds of mechanical ventilation compared with no treatment. Similarly, treatment with both IVIG and steroids on admission did not decrease the odds of mechanical ventilation. The use of IVIG alone was associated with an overall increase in odds of mechanical ventilation.

DISCUSSION

In this large multicenter study, we found wide variation in the treatment of pediatric SJS and TEN. In contrast to affected adults, mortality is rare and recurrences are uncommon among children. SJS and TEN have been associated with high mortality, up to 34% in adults.[10,21,22] A recent study comprising primarily of adult patients found a recurrence rate of 7.2% and short-term mortality of 23.4% and 9.0% in TEN and SJS, respectively.[23] Pediatric studies have reported mortality ranging from 0% to 0.12% in SJS and 4.17% to 16.0% in TEN in the pediatric population.[18,20] We identified an overall recurrence rate of 2.43% and mortality of 3.23% and 0.13% in TEN and SJS, respectively. Our results also differed from those of smaller studies performed in the pediatric population. Finkelstein et al[24] retrospectively reviewed 55 cases of SJS or TEN at 2 children's hospitals and reported a hospital mortality and recurrence rate of approximately 2% and 18%, respectively. We found an overall mortality rate of 0.56% and markedly lower recurrence rate. The difference in mortality rate is likely due to the low number of patient deaths and differences in study design, comparing small local populations or community hospitals in previous studies to a tertiary care population such as in our study.

There is a paucity of pediatric data on SJS and TEN, with data limited to case series and local retrospective studies with small sample sizes.[9,25–31] The current management of SJS and TEN in US children is not well studied. Consistent with previous data, we found that the treatment strategies for children with SJS and TEN are variable, ranging from supportive care to combination therapy of IVIG and steroids.[24] Antibiotics were the most commonly prescribed agent in children. It can be challenging to diagnose SJS and TEN because symptoms may be confused for an infectious process and infection is a frequent complicating factor in these cases. Infectious complications have been associated with mortality in adults; however, data in children are lacking.[32] The number of SJS and TEN cases cared for at an institution did not appear to influence the selected treatment, confirming that a consensus approach to treatment has not been adapted, even in higher volume centers.

The optimal medical management for SJS and TEN has not been defined. Removal of the inciting agent is critical. Whether steroids, IVIG, or other immunomodulators improve or worsen outcomes remains unclear. Differences in therapeutic efficacy appear to be age-related; thus, analysis specific to pediatric patients is critical to achieve a better understanding of therapeutic optimization.[33] Our findings do not demonstrate a benefit of early immunosuppression on LOS or need for mechanical ventilation. There was an increased association between antibiotic and antiviral use and LOS in the hospital. It is possible that children with severe illness disproportionately received these therapies. However, the frequent use of antibiotics in pediatric cases of SJS and TEN warrants additional evaluation of associated risks and benefits.

Although SJS and TEN are severe conditions, the general outcome measures in children are not well characterized. We found that SJS and TEN were associated with high hospital charges, prolonged LOS, and high rates of both 30-day and 6-month all-cause readmissions, suggesting areas for improvement in the care of these hospitalized children. Because these

cases are rare, a coordinated approach to investigate the most effective treatment strategies for these children is needed.

Unlike the adult population, we found that SJS was more common in males and TEN more common in females. These findings are consistent with recently published data in the pediatric population.[18,20] The mechanism for this sex variation between adults and children is unclear. It is possible that there is a biological predisposition or differences in dose effect in the pediatric population. It is also possible, however, that some erythema multiforme cases were misclassified as mild SJS by coding physicians.

Limitations of our findings include the retrospective nature of the study as well as the absence of biometric data in the PHIS data set. For this reason, we could not account for patient-level physiological and laboratory assessments to determine disease severity or assess validity of the diagnosis. Because of the change in ICD-9 coding for SJS and TEN in 2008, our look-back period was limited to 2008 and later. It is possible that patients may not return to the same hospital for a recurrence episode. Therefore, we may have underestimated the frequency of recurrences. Adjudication of SJS and TEN is important because misdiagnosis is common and use of ICD-9 codes alone may overrepresent true cases. For example, it is possible that erythema multiforme may be misrepresented as mild SJS. Recently described approaches to enhance the validity of SJS and TEN were applied in this study to identify patients.[4] PHIS does not include data from the outpatient setting or from community hospitals. Given that the exposure or precipitating event causing SJS and TEN (eg, drug and infection) often occurs before admission for management of SJS and TEN, PHIS data cannot be used to evaluate causation, incidence, or prevalence of SJS and TEN. Similarly, we were unable to identify specific drugs leading to hospitalization for SJS or TEN. Given the overall positive outcomes in children and low prevalence of children hospitalized with SJS and TEN, it is possible that treatment effects may be underappreciated because of the low number of patients in comparison cohorts. In addition, long-term sequelae could not be evaluated given that the data are limited to the inpatient setting and do not capture outpatient follow-up. Finally, although PHIS includes children’s hospitals that contain burn centers, the database cannot distinguish between those cared for in a burn unit and those in a pediatric ICU. Despite these limitations, our findings represent a first step in understanding the treatment approaches used for SJS and TEN in the pediatric population across several institutions. Standardizing treatment strategies and effectively measuring both short- and long-term clinical outcomes are necessary to optimize care in these challenging clinical cases.

CONCLUSIONS

SJS and TEN are severe conditions resulting in high hospital costs and prolonged hospitalizations in the case of children. Children have a lower mortality and recurrence rate than do adults. Treatments with IVIG and steroids were not associated with decreased LOS or need for mechanical ventilation. Further studies are needed to determine the most cost-effective treatment strategy in these patients.

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TABLE E1.

Frequency of SJS and TEN by race and sex

	Female				Male			
	SJS		TEN		SJS		TEN	
Race	Frequency	Column %	Frequency	Column %	Frequency	Column %	Frequency	Column %
American Indian	4	1.33%	0	0.00%	6	1.27%	0	0.00%
Asian	13	4.33%	3	4.41%	12	2.53%	4	7.14%
African American	44	14.67%	15	22.06%	57	12.03%	9	16.07%
Other/ unknown	56	18.67%	15	22.06%	91	19.20%	15	26.79%
Pacific Islander	2	0.67%	0	0.00%	0	0.00%	0	0.00%
White	178	59.33%	35	51.47%	305	64.35%	28	50.00%
Multiracial	3	1.00%	0	0.00%	3	0.63%	0	0.00%
Total	300	100%	68	100%	474	100%	56	100%

Abbreviations used

ICU	intensive care unit
IVIG	intravenous immunoglobulin
LOS	length of stay
PHIS	Pediatric Health Information System
SJS	Stevens-Johnson syndrome
TEN	toxic epidermal necrolysis

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What is already known about this topic?

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare yet life-threatening conditions. Treatments with steroids and intravenous immunoglobulin are controversial. The current management and outcomes in children are unclear.

What does this article add to our knowledge?

We provide evidence of the management strategies used in children with SJS and TEN. We also determine clinical outcomes such as length of stay, mortality, readmission, recurrence, complications, and hospital costs for children with SJS and TEN.

How does this study impact current management guidelines?

Our findings represent a first step in understanding the treatment approaches used for SJS and TEN in children. Standardizing treatment strategies and effectively measuring both short- and long-term clinical outcomes are necessary to optimize care.

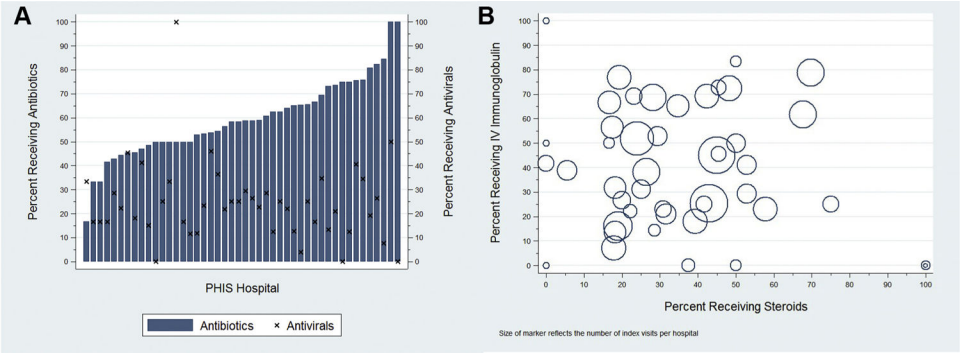

FIGURE 1.

Variation in SJS and TEN treatments across US children's hospitals. **A**, Variation in antibiotic and antiviral use across hospitals. **B**, Variation in immunosuppression use across hospitals.

TABLE I.

Demographic characteristics of patients admitted with SJS and TEN

Characteristic	n (%) (total N = 989)
Classification	
SJS	774 (86.19)
TEN	124 (13.81)
Sex	
Female	368 (40.98)
Male	500 (59.02)
Age (y), median (IQR)	10.8 (6.67–14.33)
Race	
American Indian	10 (1.11)
Asian	32 (3.56)
African American	125 (13.92)
Other/unknown	177 (19.71)
Pacific Islander	2 (0.22)
White	546 (60.8)
Multiracial	6 (0.67)
Ethnicity	
Hispanic	139 (15.48)
Non-Hispanic	626 (69.71)
Unknown	133 (14.81)
Insurance type	
Commercial	462 (51.45)
Medicaid	287 (31.96)
Other government	64 (7.13)
Self-pay	16 (1.78)
Other/unknown	69 (7.68)
Geographic location	
New England	52 (5.79)
Middle Atlantic	73 (8.13)
East North Central	48 (13.48)
West North Central	94 (10.47)
South Atlantic	121 (13.47)
East South Central	48 (5.35)
West South Central	127 (14.48)
Mountain	134 (13.59)
Pacific	135 (15.03)
Concurrent complex chronic condition	147 (16.37)

IQR, Interquartile range.

TABLE II.

Outcomes and hospital charges of children hospitalized with SJS and TEN

Outcome	All diagnoses	SJS*	TEN†	*P* value
Mortality	5 (0.56%)	1 (0.13%)	4 (3.23%)	.002
ICU	170 (18.93%)	114 (14.73%)	56 (45.16%)	<.001
Admission (first 2 admission days)	39 (4.34%)	26 (3.36%)	13 (10.48%)	<.001
Transfer to ICU after admission	39 (4.34%)	26 (3.36%)	13(10.48%)	.001
Mechanical ventilation	88 (9.80%)	46 (5.95%)	42 (33.8%)	<.001
<2 d after admission	50 (5.57%)	29 (3.75%)	21 (16.94%)	<.001
>2 d after admission	38 (4.23%)	17 (2.20%)	21 (16.94%)	<.001
Acute kidney injury	18 (2.00%)	15 (1.94%)	3 (2.42%)	.727
Shock/sepsis‡	64 (7.13%)	49 (6.33%)	15 (12.10%)	.036
Respiratory complications§	77 (8.57%)	38 (4.91%)	39 (31.45%)	<.001
Recurrence	24 (2.69%)	23 (2.98%)	1 (0.83%)	.235
All-cause 30-d readmission	88 (9.85%)	74 (9.57%)	14 (11.67%)	.509
All-cause 6-mo readmission	169 (18.92%)	144 (18.63%)	25 (20.83%)	.616
LOS, median days (IQR)	8 (5–13)	7 (4–11)	15.5 (8–23)	<.001
Median adjusted charges (IQR)	$16,265 ($7,422-$34,132)	$14,510 ($7,013-$29,682)	$44,362 ($19,077-$82,919)	<.001

BSA, Body surface area; *IQR*, interquartile range.

*SJS defined as SJS cases (<10% BSA).

†TEN defined as TEN + SJS/TEN overlap (>10% BSA).

‡Defined as hypotension, sepsis, and septic shock.

§Defined as respiratory distress, respiratory insufficiency, and respiratory failure.

TABLE III.

Treatment strategies in children

Treatment	Total (n = 986)	SJS	TEN	*P* value
Antivirals	205 (22.83%)	184 (23.77%)	21 (16.94%)	.106
Antibiotics				
Total	542 (60.35%)	447 (57.75%)	95 (76.61%)	<.001
Hospital antibiotics admission	407 (45.32%)	353 (45.61%)	54 (43.55%)	.698
Antibiotics after admission	135 (15.03%)	94 (12.14%)	41 (33.06%)	<.001
Immunosuppression on admission				
Systemic steroids only	120 (13.36%)	108 (13.95%)	12 (9.68%)	.254
IVIG only	230 (25.61%)	174 (22.48%)	56 (45.16%)	<.001
Both IVIG and steroids	75 (8.35%)	60 (7.75%)	15 (12.10%)	.115
No IVIG or steroids	473 (52.67%)	432 (55.81%)	41 (33.06%)	<.001
Vasopressors	72 (8.02%)	39 (5.04%)	33 (26.61%)	<.001
Length of treatment				
Total IVIG days, median (IQR)	3 (2–3)	2 (1–3)	3 (2–3)	<.001
Total systemic steroids days, median (IQR)	4 (2–6)	4 (2–6)	3 (2–8)	.679

IQR, Interquartile range.

TABLE IV.

Adjusted predictors of LOS

Clinical predictor	All diagnoses log LOS (95% CI)	% Change in LOS	*P* value	SJS* log LOS (95% CI)	*P* value	TEN† log LOS (95% CI)	*P* value
Severe cutaneous adverse reaction							
SJS	Reference	–	–	–	–	–	–
TEN	0.24 (0.13 to 0.35)	27.3%	<.001	–	–	–	–
Mechanical ventilation	0.67 (0.55 to 0.80)	95.5%	<.001	0.72 (0.56 to 0.87)	<.001	0.60 (0.34 to 0.85)	<.001
Antivirals	0.17 (0.08 to 0.30)	18.8%	<.001	0.17 (0.08 to 0.26)	<.001	0.18 (0.13 to 0.48)	.251
Antibiotics							
No antibiotics	Reference		–	–	–	–	–
Antibiotics on admission	0.27 (0.20 to 0.35)	31.5%	<.001	0.24 (0.16 to 0.33)	<.001	0.58 (0.26 to 0.90)	<.001
Antibiotics after admission	0.50 (0.39 to 0.61)	65.4%	<.001	0.55 (0.43 to 0.67)	<.001	0.54 (0.21 to 0.86)	<.001
Immunosuppression on admission							
No IVIG or steroids	Reference		–	–	–	–	–
Systemic steroids only	−0.08 (−0.18 to 0.03)	−7.6%	.151	−0.12 (−0.23 to 0.007)	.037	0.31 (−0.11 to 0.73)	.155
IVIG only	0.15 (0.06 to 23)	15.7%	<.001	0.14 (0.05 to 0.24)	.002	0.14 (−0.13 to 0.42)	.310
IVIG and steroids	0.18 (0.05 to 0.32)	19.9%	.008	0.15 (0.01 to 0.30)	.035	0.27 (−0.11 to 0.64)	.2
Complex chronic condition	0.21 (0.12 to 0.31)	23.0%	<.001	0.21 (0.08 to 0.33)	<.001	0.22 (−0.04 to 0.47)	.097

Note. Log LOS: positive coefficient indicates increased LOS, negative coefficient indicates decreased LOS, and 0 indicates no changes in LOS.

BSA, Body surface area.

*SJS defined as SJS cases (<10% BSA).

†TEN defined as TEN + SJS/TEN overlap (>10% BSA).

TABLE V.

Predictors of mechanical ventilation after admission

	All diagnoses, OR (95% CI)	*P* value	SJS,* OR (95% CI)	*P* value	TEN,† OR (95% CI)	*P* value
Severe cutaneous adverse reaction						
SJS	Reference	–	–	–	–	–
TEN	7.65 (3.73–15.7)	<.001	–	–	–	–
Antibiotics on admission	0.665 (0.30–1.33)	.22	1.09 (0.41–2.96)	.85	0.36 (0.11–1.23)	.10
Immunosuppression on admission						
No IVIG or steroids	Reference	–				
Steroids only	0.40 (0.08–1.89)	.25	0.41 (0.05–3.44)	.42	0.37 (0.03–3.96)	.40
IVIG only	2.24 (1.04–4.84)	.04	2.23 (0.78–6.34)	.14	2.47 (0.76–7.99)	.13
IVIG and steroids	0.76 (0.19–3.00)	.69	0.68 (0.08–5.79)	.72	0.82 (0.13–5.22)	.83
Complex chronic condition	4.63 (2.20–9.73)	<.001	6.81 (2.52–18.4)	<.001	0.85 (1.71–12.6)	.03

BSA, Body surface area; OR, odds ratio.

*SJS defined as SJS cases (<10% BSA).

†TEN defined as TEN + SJS/TEN overlap (>10% BSA).