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Intravenous Immune Globulin in Children with Streptococcal Toxic Shock Syndrome

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Abstract

Background—Streptococcal toxic shock syndrome (TSS) is a rare and severe manifestation of group A streptococcal infection. The role of intravenous immune globulin (IVIG) for streptococcal TSS in children is controversial.

Objective—To describe the epidemiology of streptococcal TSS in children and to determine whether adjunctive therapy with IVIG is associated with improved outcomes.

Methods—A multicenter retrospective cohort study of children with streptococcal TSS from 2003-2007 was conducted. Propensity scores were used to determine each child's likelihood of receiving IVIG. Differences in the primary outcomes of death, hospital length of stay, and total hospital costs were compared after matching IVIG-recipients and non-recipients on propensity score.

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Results—The median age was 8.2 years. IVIG was administered to 84 (44%) of 192. Overall mortality was 4.2% (95% confidence interval: 1.8% to 8.0%). Differences in mortality between IVIG recipients (n=3, 4.5%) and non-recipients (n=3, 4.5%) were not statistically significant (P=1.00). While patients receiving IVIG had higher total hospital and drug costs than non-recipients, differences in hospital costs were not significant once drug costs were removed (median difference between matched patients, $6,139; interquartile range: -$8,316 to $25,993; P=0.06). There were no differences in length of stay between matched IVIG recipients and non-recipients.

Conclusion—This multicenter study is the largest to describe the epidemiology and outcomes of children with streptococcal TSS and the first to explore the association between IVIG use and clinical outcomes. IVIG use was associated with increased costs of caring for children with streptococcal TSS but was not associated with improved outcomes.

Keywords for indexing

Toxic shock syndrome; Streptococcus pyogenes; immunoglobulins; intravenous; epidemiology; treatment outcome

Introduction

Streptococcal toxic shock syndrome (TSS) is a rare and severe manifestation of infection caused by group A beta-hemolytic streptococci. In adults, mortality rates range from 30% to 70% despite prompt antimicrobial therapy.[1-3] Streptococcal pyrogenic exotoxins, acting as superantigens, are thought to mediate systemic disease by bypassing traditional antigen presenting mechanisms and attaching directly to T-cell receptors.[4] In this manner, they induce a cascade of cytokine-mediated inflammation, leading to capillary leak and multi-organ failure.

Patients who develop streptococcal TSS often lack neutralizing antibody against pyrogenic exotoxins and other major streptococcal virulence factors.[5-8] Polyclonal human intravenous immunoglobulin (IVIG) contains neutralizing antibody to these streptococcal virulence factors,[9] suggesting a potential mechanism for effective adjunctive therapy with IVIG. *In vitro*, IVIG inhibits T-cell activation by blocking or inactivating streptococcal superantigens, thereby decreasing the production of pro-inflammatory cytokines.[9] In a transgenic model of streptococcal TSS, mice treated with IVIG at the time of infection have improved survival.[10] Extension of these findings to clinical practice is controversial. In an observational study of 53 adults with streptococcal TSS, IVIG therapy was associated with an 8-fold reduction in mortality.[11] However, the difference in mortality between IVIG and placebo adult recipients was not statistically significant in a subsequent randomized trial involving 21 patients from 17 hospitals.[12]

The role of IVIG for streptococcal TSS in children is even less clear for several reasons: 1) Children are less likely to develop streptococcal TSS than adults,[1,13,14] limiting the available epidemiologic and outcome data; 2) Mortality rates are substantially lower in children compared with adults, making this a less desirable outcome measure in pediatric studies of streptococcal TSS;[13,15,16] and 3) Data regarding IVIG use in children with streptococcal TSS has been limited to case reports, making assessment of therapeutic effectiveness difficult.[17-20] We undertook this study to describe the epidemiology of streptococcal TSS in children and to determine whether adjunctive therapy with IVIG is associated with improved outcomes. The present study comprises the largest multicenter cohort of children with streptococcal TSS.

Methods

Data Source

Data for this retrospective cohort study were obtained from the Pediatric Health Information System (PHIS), a national administrative database containing resource utilization data from 36 freestanding, tertiary care children's hospitals affiliated with the Child Health Corporation of America (Shawnee Mission, KS). Data quality and reliability are assured through a joint effort between the Child Health Corporation of America and participating hospitals. Systematic monitoring occurs on an ongoing basis to ensure data quality. For the purposes of external benchmarking, participating hospitals provide discharge data including patient demographics, diagnoses, and procedures. Billing data is also available that details all of the drugs, radiologic imaging studies, laboratory tests, and supplies charged to each patient. The protocol for the conduct of this study was reviewed and approved by The Children's Hospital of Philadelphia Committees for the Protection of Human Subjects with a waiver of informed consent.

Patients

Children less than 18 years of age with streptococcal TSS were eligible for this study if they were discharged from any of the 36 participating hospitals between January 1, 2003 and December 31, 2007.

Study Definitions

Study participants were identified using International Classification of Diseases, 9th revision (ICD-9) discharge diagnosis codes for the diagnosis of TSS (040.82) in combination with an ICD-9 code for *Streptococcus* (041.xx) or with a billing charge for intravenous penicillin. Similar to previous studies,[21-25] participants with varicella were identified using ICD-9 discharge diagnosis code 052.x. Comorbid conditions considered in the study included cancer (hematologic and non-hematologic), congenital heart disease, human immunodeficiency virus infection, prematurity, post-operative infection, and sickle cell disease using previously reported ICD-9 codes.[26] Adjuvant corticosteroid therapy was defined as the receipt of dexamethasone, hydrocortisone, or methylprednisolone intravenously. Blood product transfusions included administration of packed red blood cells, cryoprecipitate, fresh frozen plasma, or platelets. Vasoactive infusions included dobutamine, dopamine, epinephrine, norepinephrine, and milrinone. Surgical debridement was defined using ICD-9 procedure codes for excisional debridement of wound, infection or burn (86.22) and nonexcision debridement of wound, infection, or burn (86.28).

Measured Outcomes

The primary outcomes of interest in this study were death, hospital length of stay (LOS), and total hospital costs. We used hospital costs because hospital charges, which represent the amount that hospitals billed for services, may vary depending on factors such as reimbursement contracts. Total hospital charges in the PHIS database were adjusted for hospital location using the Centers for Medicare and Medicaid price/wage index. We then used hospital-level cost-to-charge ratios to convert the charges from the hospital billing data to costs. Secondary outcomes included the intensive care unit LOS and the following specific subcategories of hospital cost: drug, supply, laboratory, clinical (e.g., clinical evaluation and consultation, surgical and non-surgical procedures, wound care, mechanical ventilation), and all other costs.

Measured Exposures

The primary exposure of interest was the use of IVIG.

Statistical Analysis

Categorical variables were described using frequencies and percents while continuous variables were described using mean, median, range, and interquartile range (IQR) values. We then characterized the variability among hospitals in the use of IVIG for streptococcal TSS. To account for a small signal (in this case, hospital effect) to noise (variation due to unmeasured patient factors) ratio, a Bayesian “shrinkage” factor was applied to each hospital's observed IVIG prescribing practices. This process weights the proportion of patients with streptococcal TSS who received IVIG at a particular hospital based on the degree of uncertainty in the calculation of prescribing rates. In this situation, Bayesian shrinkage would help account for expected regression to the mean in IVIG prescribing.[27]

In unadjusted analyses, patient characteristics and clinical outcomes of IVIG recipients and non-recipients were compared using chi-square or Fisher exact tests for categorical variables and the Wilcoxon Rank Sum test for continuous variables. Propensity scores accounted for potential confounding by observed baseline covariates because the number of covariates within our study was large relative to the number of outcomes, a situation in which multivariable modeling may create unreliable estimates.[28-30] Additionally, matching by propensity scores achieves a better balance of covariates between the exposed and unexposed groups than other matching strategies.[31,32] Propensity scores estimate the probability of receiving a specific treatment (in this case, IVIG) given an observed set of covariates, aiming to control for measured confounders in the treatment and no treatment groups in an observational study.[33,34] We created a propensity score using multivariable logistic regression to assess the likelihood of exposure to IVIG using age, sex, race, comorbid conditions and varicella diagnosis as risk factors for IVIG receipt. To account for severity of illness, the propensity model also included the following variables if they occurred within the first two days of hospital admission: intensive care unit admission, requirement for mechanical ventilation, vasoactive infusions, blood product transfusions, intravenous corticosteroids, surgical debridement, and arterial blood gas measurements. The model's calculated c-statistic was 0.776, which represents the predictive capability of the model. The model provides a better estimate than expected by chance alone (i.e., if the c-statistic was equal to 0.5), but remains in a range which allows for little concern over non-overlapping propensity score distributions between the treatment and no treatment groups, making comparisons possible.[35]

IVIG-recipients and non-recipients were matched on propensity score using nearest-neighbor matching with a caliper set at one quarter of the standard deviation of the logit of the propensity scores.[36] We forced matches on intensive care unit status. The difference in outcomes was computed as the difference in outcomes between an IVIG-recipient and his or her matched subject. The median and IQR values of these differences were reported. There were too few patients at individual hospitals to permit hospital-level clustering in the analysis. Statistical significance for the difference in use (LOS or costs) was determined using Wilcoxon's signed rank test and differences in mortality were determined using McNemar's test.

IVIG-recipients who could not be matched to a control subject were removed from the analysis. To assess whether bias occurred in the matching process and how such bias would affect our interpretation of the results, we compared the characteristics and outcomes of matched and unmatched IVIG recipients with chi-square or Fisher exact tests for categorical variables and the Wilcoxon rank sum test for continuous variables.

All statistical analyses were performed using SAS 9.1 (SAS Institute, Inc., Cary, NC). For unadjusted comparisons, $P<0.05$ was considered statistically significant. Since multiple comparisons were made on the same sample of discharges, we used the conservative Bonferroni correction to set the statistical significance at $P<0.006$ when determining the significance of the eight clinical outcomes in the propensity score analysis.[37]

Results

Patient Characteristics

During the study period, 192 patients were diagnosed with streptococcal TSS. There was a median of 4 patients (IQR, 3-8 patients) per hospital; one hospital contributed 16 patients. Forty-three (22.4%) patients were transferred to the participating hospital after initial evaluation elsewhere. The characteristics of study patients are shown in Table 1. The mean age was 8.8 years (median, 8.2 years; IQR, 5.0-13.4 years). Most patients (n=182; 94.8%) received adjunctive therapy with intravenous clindamycin in combination with either penicillin or vancomycin. Three patients (1.6%) had varicella zoster virus infection.

Intravenous Immune Globulin Use

IVIG was administered to 84 (44%) children either as a single dose (n=51, 61%) or once daily on 3 consecutive days (n=33, 39%). There was no significant change in the proportion of patients receiving IVIG over time: 2003, 44.1%; 2004, 29.7%; 2005, 50.0%; 2006, 50.0%; and 2007, 44.7% (chi-square test for trend, P=0.353). However, IVIG use varied by hospital; shrunken estimates of IVIG use ranged from 29% to 60% of patients with streptococcal TSS at any hospital. IVIG was administered to 12 (30%) of the 40 patients not requiring admission to the intensive care unit and 72 (47%) of 152 patients admitted to the intensive care unit; 5 (63%) of the 8 patients who died received IVIG.

Outcome Measures

The overall mortality was 4.2% (95% CI: 1.8% to 8.0%). The unadjusted difference in mortality between IVIG (n=5, 6.0%) and non-IVIG (n=3, 2.8%) recipients was not statistically significant (Fisher exact, P=0.300). The mean LOS was 14 days; approximately 25% of patients had a LOS >14 days while 17% of patients had a LOS >21 days. In unadjusted analysis, the total hospital LOS and intensive care unit LOS were significantly longer for IVIG recipients than non-IVIG recipients (Table 2).

The total cost for all patients was $9,392,968; drug costs accounted for $2,165,784 or 23.1% of the total hospital cost. The cost of hospitalization exceeded $115,000 for 10% of patients and $164,000 for 5% of patients. Drug costs were significantly higher for patients receiving the 3 day IVIG regimen (median, $18,472; IQR: 10,910-33,044) compared with the 1 day IVIG regimen (median, $9,447; IQR: 5,453-16,698; P=0.002). Patient outcomes are summarized in Table 2. In unadjusted analysis, the total hospital cost, drug cost, and all other cost subcategories were greater in IVIG recipients than non-recipients. There was no significant difference in the proportion of IVIG recipients (22%) or non-recipients (25%) admitted to the participating hospitals as transfers from other acute care institutions (chi-square, P=0.832).

When stratifying the unadjusted (i.e., unmatched) analysis by age, there was no difference in LOS (median, 13 days; IQR: 7-18 days) or total hospital costs (median, $35,886; IQR: $18,606-$76,893) between IVIG recipients and non-recipients <5 years of age. Among children ≥5 years of age, the LOS was significantly longer for IVIG recipients (median, 14 days) than non-recipients (median, 7 days; P<0.001). In this older age group, IVIG recipients also had higher total hospital costs (median, $43,488) than non-recipients (median, $13,705; P<0.001).

Analysis of Patients Matched by Propensity Scores

In the propensity score analysis, 67 (80%) of 84 patients receiving IVIG were matched to appropriate controls (i.e., IVIG non-recipients). Differences in demographic characteristics, comorbid conditions, and specific diagnostic and therapeutic interventions between patients matched by propensity scores were not statistically significant with one exception; IVIG recipients had more arterial blood gas measurements than non-recipients (Table 3). In

propensity-matched analysis, the differences in mortality between IVIG recipients (n=3, 4.5%) and non-recipients (n=3, 4.5%) were not statistically significant (McNemar's test, P=1.000). The other outcomes of the propensity-matched analysis are summarized in Table 4. Patients receiving IVIG had higher total hospital and drug costs than non-recipients. While patients receiving IVIG had a longer LOS and higher supply, clinical and laboratory costs compared with non-recipients, these differences were not statistically significant when accounting for multiple comparisons (Table 4). The difference in the cost of hospitalization between IVIG recipients and non-recipients was not significant once drug costs were subtracted from total hospital costs (median difference between matched patients, $6,139; IQR: -$8,316, to $25,993; P=0.060), suggesting that the differences in drug costs accounted for the differences in total costs.

In a secondary analysis, the characteristics and outcomes of unmatched and matched IVIG recipients were compared. There were no differences in age or sex between unmatched and matched patients. Unmatched patients had a greater number of arterial blood gas measurements and were more like to receive blood product transfusions and corticosteroids compared with matched patients. Unmatched IVIG recipients also had a significantly longer LOS (25 days vs. 12 days; P=0.003) and higher total ($115,500 vs. $38,120; P=0.001) and drug costs ($30,507 vs. $11,433; P=0.002) compared with matched IVIG recipients.

Discussion

This multicenter study is the largest to describe the epidemiology and outcomes of children with streptococcal TSS and the first to explore the association between IVIG use and clinical outcomes. There was variability in the use of IVIG among participating hospitals. While overall mortality was low, the costs of caring for children with streptococcal TSS were substantial. Importantly, IVIG use was not associated with reduction mortality or hospital LOS. The total hospital costs were higher for children receiving IVIG, a difference that was attributable to higher drug costs for IVIG recipients compared with non-recipients. The results of our study suggest that IVIG use increases the costs of caring for children with streptococcal TSS but does not improve their outcome.

There was significant variation in the use of IVIG for TSS between hospitals. Increased illness severity incompletely accounted for this variation. It is likely that the variability between hospitals indicates poor consensus on best practices for treatment, due in part to the lack of evidence supporting IVIG use. Institutional cultural differences also may drive variability; certain champions of therapies may define therapy at a particular institution, which may be more likely in the setting of a rare and potentially fatal disease entity.

The mortality rate of 4.2% in this study is similar to the 7.7% mortality rate in a previous United States study by O'Loughlin et al.[38] which included 26 children <10 years of age from 2000-2004, and dramatically lower than the 38-44% case fatality rate for those ≥10 years of age in the same study, or two recent European studies that included all patient ages from 2002-2004.[39,40] The difference in pediatric outcomes could be due to differences in the study populations, recognition of disease, case definitions or care provided. In particular, virtually all patients in our study received adjunctive treatment with clindamycin, which has greater efficacy than penicillin alone in experimental infections with group A beta-hemolytic streptococci.[41]

IVIG has been suggested as a potential adjunctive therapy for streptococcal TSS because of its ability to neutralize a wide variety of superantigens and to facilitate opsonization of streptococci.[42,43] In an observational study of adults, the unadjusted 30-day mortality was significantly lower among 21 IVIG recipients (33%) compared with 32 non-recipients (66%, P=0.02).[11] The odds of survival was 8-fold higher among IVIG recipients (adjusted odds

ratio, 8.1; 95% confidence interval: 1.6-45.0) after adjusting for illness severity at presentation.[11] However, a disproportionate number of IVIG non-recipients studied by Kaul et al. did not receive clindamycin.[11] Darenberg et al.[12] conducted a randomized trial involving 21 adults from 17 European hospitals. The trial was terminated early because of low enrollment. Although mortality was lower in IVIG recipients (10%) compared with placebo recipients (36%), this difference was not statistically significant.[12]

Our large multicenter study of children with streptococcal TSS did not find an association between IVIG use and mortality or LOS. While there was substantial variability in IVIG use for children with streptococcal TSS, clindamycin was administered almost routinely. When given to mice at the time of experimental group A beta-hemolytic streptococcal infection (and in the absence of antibiotic therapy), IVIG neutralized circulating superantigens and reduced systemic inflammatory response.[10] However, when used in combination with penicillin and clindamycin in a delayed treatment setting (to more closely mimic what occurs in the clinical setting), IVIG did not confer additional therapeutic benefit.[10] These experimental results raise two important points that lend credence to our findings that IVIG use was not associated with improved outcomes in children with streptococcal TSS. First, the benefit of IVIG may depend predominantly and perhaps exclusively on the timing of administration. IVIG may not have any clinical benefit if it is not administered sufficiently early in the course of infection, a goal that may be difficult to accomplish in clinical practice. Second, the concurrent use of clindamycin therapy may improve outcomes to such an extent that detection of any additional benefit conferred by IVIG would require prohibitively large numbers of study subjects.

This study has several limitations. First, the use of administrative data precluded the use of the formal case definition of streptococcal TSS[44] to identify the study cohort. We attempted to minimize such misclassification bias by using a rigorous definition of streptococcal TSS that incorporated ICD-9 discharge diagnosis codes and billing data for receipt of intravenous penicillin. However, discharge diagnosis coding may be unreliable for specific diseases or pathogens. Furthermore, it is possible that IVIG recipients were more likely to have streptococcal TSS than non-recipients. If the outcomes of these groups of patients differed, then our approach would underestimate the actual benefit of IVIG.

Second, it is likely that we were underpowered to detect small benefits of IVIG use on mortality in streptococcal TSS. However, since the overall mortality rate in children with streptococcal TSS is considerably lower than mortality in adults, any absolute reduction in mortality attributable to IVIG in children with streptococcal TSS is likely to be minimal. Furthermore, given the relative rarity of streptococcal TSS in children, it is unlikely that a randomized controlled trial of IVIG use in children with streptococcal TSS will ever be conducted. Despite the fact that streptococcal TSS occurs more commonly in adults, the only randomized trial of streptococcal TSS and IVIG use in adults was terminated early due to low enrollment; the numbers of patients in our study was 6-fold greater than the number enrolled in the adult randomized trial.

Third, the effectiveness of IVIG may be underestimated in our study because neutralizing activity against various streptococcal superantigens could not be determined for any of the IVIG doses administered. Titers against streptococcal superantigens vary in different IVIG preparations[45,46] and such differences, at least in theory, could influence IVIG effectiveness. Fourth, there may be confounding by indication for IVIG use in streptococcal TSS. We attempted to account for this possibility by including variables associated with increased illness severity (e.g., vasoactive infusions, blood product administration) in our propensity score. The matched patients had a similar distribution of these factors. However, as in any observational study, there may still be residual confounding from unmeasured confounders. Finally, while matching patients on propensity score balances covariates between two groups (in this case,

IVIG recipients and non-recipients) better than other matching methods, the exclusion of unmatched patients may bias the study. This form of spectrum bias (i.e., the most ill patients are excluded) would cause us to overestimate the benefit of IVIG.

In conclusion, the role of IVIG in children with streptococcal TSS has been controversial. Until now, pediatricians have had to decide the extent to which findings from experimental animal models and adult studies are applicable to the treatment of children with streptococcal TSS. In our large multicenter observational study of children with streptococcal TSS, mortality was substantially lower than reported in studies of adults. IVIG use increased the costs of hospitalization but was not associated with improved clinical outcomes. While it may be reasonable to recommend IVIG as adjunctive therapy for adults with streptococcal TSS, our data do not support its use in children with streptococcal TSS.

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Table 1

Characteristics of patients with streptococcal toxic shock syndrome.

	Overall* (N=192)	No IVIG (N=108)	IVIG (N=84)	P**
Male sex	95 (49.5)	61 (56.5)	34 (40.5)	0.028
Age				
<2y	20 (10.4)	9 (8.3)	11 (13.1)	0.640
2-4y	27 (14.1)	13 (12.0)	14 (16.7)	
5-9y	69 (35.9)	41 (38.0)	28 (33.3)	
10-14y	49 (25.5)	30 (27.8)	19 (22.6)	
15-18y	27 (14.1)	15 (13.9)	12 (14.3)	
Race				
Non-Hispanic White	88 (48.1)	54 (52.4)	34 (42.5)	0.100
Non-Hispanic Black	29 (15.9)	19 (18.5)	10 (12.5)	
Hispanic	30 (16.4)	12 (11.7)	18 (22.5)	
Asian	12 (6.6)	8 (7.8)	4 (5.0)	
Other	24 (13.1)	10 (9.7)	14 (17.5)	
Comorbid conditions				
Malignancy	3 (1.6)	1 (0.9)	2 (2.4)	0.420
Hematologic disorder or immunodeficiency	7 (3.7)	1 (0.9)	6 (7.1)	0.023
Diagnostic and therapeutic interventions				
Arterial blood gas measurements***	2 [0, 8]	1 [0 - 4]	6 [2-10]	<0.001
Blood product receipt	91 (47.4)	40 (37.0)	51 (60.7)	0.001
Corticosteroid receipt	77 (40.1)	32 (29.6)	45 (53.6)	<0.001
Vasoactive infusions	127 (66.2)	58 (53.7)	69 (82.1)	<0.001
Intensive care unit admission	152 (79.2)	80 (74.1)	72 (85.7)	0.049
Dialysis	3 (1.6)	0(0.0)	3 (3.6)	0.048
Mechanical ventilation	13 (6.8)	5 (4.6)	8 (9.5)	0.181
Surgical debridement	15 (7.8)	6 (5.6)	9 (10.7)	0.186

* Values listed as number (percent) unless otherwise noted.

** P<0.05 considered statistically significant

*** Value listed as median (interquartile range).

Table 2

Unadjusted outcomes of patients with streptococcal toxic shock syndrome.

Outcome	Overall*	No IVIG	IVIG	P**
Overall length of stay (days)	10 (5 - 16)	7 (5 - 14)	14 (8 - 23)	<0.001
ICU length of stay (days)***	4 (2 - 9)	3 (2 - 5)	6 (3 - 11)	<0.001
Total cost ($)	24,206 (12,448 – 60,865)	15,520 (8,706 – 34,824)	43,546 (24,358 – 93,466)	<0.001
Drug cost ($)	6,315 (2,383 – 14,002)	2,665 (1,520 – 6,553)	13,060 (7,202 – 21,972)	<0.001
Supply cost ($)	739 (179 – 2,603)	521 (116 – 1,577)	1,486 (413 – 4,208)	<0.001
Laboratory cost ($)	3,784 (1,483 – 10,778)	2,464 (1,186 - 4963)	7,002 (3,004 – 16,728)	<0.001
Clinical cost ($)	1,352 (259 – 5,515)	743 (212 – 3,183)	3,179 (655 – 7,396)	<0.001
Other cost ($)	9,006 (5,039 – 19,216)	6,406 (3,859 – 13,274)	13,638 (7,992 – 31,246)	<0.001

Abbreviations: ICU, intensive care unit; IVIG, intravenous immune globulin

* Values are listed as median (interquartile range).

** P<0.05 considered statistically significant

*** Only patients requiring intensive care until hospitalization were included.

Table 3

Characteristics of patients with streptococcal toxic shock syndrome who were matched by propensity score.*

	No IVIG (N=67) No. (%)	IVIG (N=67) No. (%)	P**
Male sex	31 (46.3)	26 (38.8)	0.382
Age			
<2y	8 (11.9)	8 (11.9)	0.900
2-4y	10 (14.9)	11 (16.4)	
5-9y	20 (29.9)	23 (34.3)	
10-14y	19 (28.4)	14 (20.9)	
15-18y	10 (14.9)	11 (16.4)	
Race			
Non-Hispanic White	34 (51.5)	32 (50.8)	0.382
Non-Hispanic Black	14 (21.2)	8 (12.7)	
Hispanic	7 (10.6)	14 (22.2)	
Asian	4 (6.1)	3 (4.8)	
Other	7 (10.6)	6 (9.5)	
Comorbid conditions			
Malignancy	1 (1.5)	2 (3.0)	0.559
Hematologic disorder or immunodeficiency	1 (1.5)	0 (0.0)	0.316
Diagnostic and therapeutic interventions			
Arterial blood gas measurements***	2 (0-7)	5 (1-9)	0.048
Blood product receipt	34 (50.8)	36 (53.7)	0.729
Corticosteroid receipt	29 (43.3)	32 (47.8)	0.603
Vasoactive infusions	49 (73.1)	54 (80.6)	0.306
Intensive care unit admission	59 (88.1)	59 (88.1)	1.000
Dialysis	0 (0.0)	1 (1.5)	0.316
Mechanical ventilation	4 (6.0)	6 (9.0)	0.511
Surgical debridement	3 (4.5)	6 (9.0)	0.300

* Values listed as number (percent) unless otherwise noted.

** P<0.05 considered statistically significant

*** Value listed as median (interquartile range).

Table 4

Results of the propensity-matched analysis comparing differences in outcomes between intravenous immune globulin recipients and non-recipients with streptococcal toxic shock syndrome.

	Median Difference	Interquartile Range of Differences	P**
Overall length of stay (days)	2	-4 – 9	0.036
ICU length of stay (days)*	2	-1 – 6	0.033
Total Cost ($)	12,056	-8,014 – 42,328	0.002
Drug cost ($)	6,555	301 – 14,079	<0.001
Supply cost ($)	346	-282 – 2,270	0.018
Laboratory cost ($)	1,029	-2,031 – 5,707	0.098
Clinical cost ($)	300	-1,426 – 3,747	0.294
Other cost ($)	3,723	-3,324 – 12,456	0.008

Abbreviations: ICU, intensive care unit

* Only patients requiring intensive care until hospitalization were included.

** P<0.006, applying the Bonferroni correction, was considered statistically significant because of multiple comparisons.