Bloodstream Infections in Children With Sickle Cell Disease: 2010–2019

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abstract

BACKGROUND: Children with sickle cell disease (SCD) are at increased risk for bloodstream infections (BSIs), mainly because of functional asplenia. Immunizations and antibiotic prophylaxis have reduced the prevalence of invasive bacterial infections, but contemporary analysis of BSI in children with SCD is limited.

METHODS: We conducted a retrospective cohort study of children aged <18 years with SCD who had blood cultures collected at our institution from 2010 to 2019 to identify BSI. Probable contaminant organisms were identified and not included as BSI. We calculated the annual incidence of BSI at our institution with 95% confidence intervals (CIs) and used multivariate logistic regression to evaluate associations.

RESULTS: There were 2694 eligible patients with 19 902 blood cultures. Excluding repeated cultures and contaminant cultures, there were 156 BSI episodes in 144 patients. The median age at BSI was 7.5 years. The average incidence rate of BSI was 0.89 per 100 person-years (95% CI 0.45–1.32). The most common pathogens were *Streptococcus pneumoniae* (16.0%), *Streptococcus* viridans group (9.0%), *Escherichia coli* (9.0%), *Staphylococcus aureus* (7.7%), *Bordetella holmesii* (7.7%), *Haemophilus influenzae* (7.1%), and *Salmonella* species (6.4%). Odds of BSI were higher with sickle cell anemia genotypes (odds ratio [OR] 1.88; 95% CI 1.20–2.94) and chronic transfusions (OR 2.66; 95% CI 1.51–4.69) and lower with hydroxyurea (OR 0.57; 95% CI 0.39–0.84).

CONCLUSIONS: BSI remains a risk for children with SCD. Overall incidence, risk factors, and spectrum of pathogens are important considerations to guide prevention and empirical treatment of suspected infection in SCD.

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WHAT'S KNOWN ON THIS SUBJECT: Children with sickle cell disease are at risk for bloodstream infection. Antibiotic prophylaxis and advancements in pneumococcal immunization have reduced but have not eliminated risk. Central venous catheters pose an additional infection risk.

WHAT THIS STUDY ADDS: We reviewed all blood cultures obtained over a 10-year period after the licensure of the 13-valent pneumococcal conjugate vaccine. In this study, we provide a contemporary update on potential causes of bloodstream infections in sickle cell disease.

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Children with sickle cell disease (SCD) are at increased risk for bloodstream infections (BSIs), particularly with encapsulated bacteria, such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. This infection risk is related to impaired or absent splenic function, other immune defects, and anatomic predisposition as occurs with osteomyelitis.[1–4] The placement of a central venous catheter (CVC) also increases the risk of BSI.[5–8] The Cooperative Study of Sickle Cell Disease, which was conducted in an era before routine penicillin prophylaxis or pneumococcal immunizations, provided a prospective longitudinal assessment of bacteremia risk, revealing that incidence rates were highest in patients with hemoglobin SS aged <3 years and decreased with age during the first 2 decades of life, predominantly because of *S pneumoniae* and *H influenzae*.[9,10] Later retrospective studies from 1993 to 2010 demonstrated *S pneumoniae*, *Salmonella, Escherichia coli*, and *Staphylococcus aureus* as causes of bacteremia in SCD.[11,12]

Interventions to prevent BSI, namely prophylactic penicillin in children aged <5 years and the introduction of the 23-valent pneumococcal polysaccharide vaccine (PPSV23) in the mid-1980s, the *H influenzae* type b vaccine in 1990, the 7-valent pneumococcal conjugate vaccine (PCV7) in 2000, and the 13-valent pneumococcal conjugate vaccine (PCV13) in 2010, have reduced the incidence of invasive bacterial infections in children with SCD.[13–19] Despite these advances, BSI remains a concern in children with SCD. Increased prevalence of microorganisms not included in current immunizations,[20–23] low rates of penicillin adherence, and antibiotic resistance may be contributors to invasive infection.[13,24,25] Large-scale studies of BSI in children with SCD in the current era are needed to understand the contemporary infection rate, guide empirical antibiotic therapy during febrile episodes, and guide policy decisions for targeted immunization schedules.

Our aims for this study are (1) to determine the annual incidence and associated features of BSI in children with SCD at our health care system over a 10-year period from 2010 to 2019 and (2) to delineate the specific microorganisms responsible for BSI in this era.

METHODS

We conducted a retrospective cohort study to review all blood cultures from children with SCD obtained at Children's Healthcare of Atlanta (CHOA) in Atlanta, Georgia, from January 1, 2010, to December 31, 2019. CHOA is the primary pediatric health care system in the metropolitan region, with 3 academic hospitals that provide outpatient, emergency, and inpatient care to the vast majority (>95%) of children with SCD in the Atlanta metropolitan area. Two tertiary care hospitals use CHOA laboratories, whereas 1 nontertiary hospital uses the laboratory at Grady Health System. This study was approved by the Institutional Review Board of CHOA and the Research Oversight Committee of Grady.

The Sickle Cell Disease Clinical Database of CHOA is a comprehensive prospective database housed in Research Electronic Data Capture (REDCap), capturing use data from all patients with a laboratory-confirmed diagnosis of SCD with ≥1 health care encounter at CHOA from 2010 onward. Data capture includes the laboratory-verified SCD genotype, SCD treatment history (hydroxyurea, chronic transfusions, hematopoietic stem cell transplant), and dates of all health care use at CHOA. The SCD database is linked to CHOA's enterprise electronic health record database (Epic Systems, Verona, WI), allowing comprehensive data searches for this manually validated SCD population. All blood cultures reported for patients with SCD at CHOA laboratories from January 2010 to December 2019 and at the Grady laboratory from June 2013 to December 2019 were identified through the electronic health record. Blood cultures from Grady from January 2010 to May 2013 were obtained directly from Grady microbiology laboratory records.

All patients in the SCD database aged 0 to 18 years, including those without blood cultures, contributed to incidence rate determination. Patients with at least 1 blood culture during the 10-year period were included for specific review of culture results as well as age, sex, SCD genotype, and treatment history. SCD genotypes were categorized into 2 groups: sickle cell anemia (SCA) genotypes (hemoglobin SS, $S\beta^0$ thalassemia, SD, and SO-Arab) and non-SCA genotypes (hemoglobin SC, $S\beta^+$ thalassemia, and *Staphylococcus epidermidis*). Patients were censored 21 days before hematopoietic stem cell transplant, and all subsequent blood cultures were excluded. Any patients with a concomitant diagnosis of cancer were identified through our institution's tumor registry and were censored at the date of their cancer diagnosis. Deaths that occurred within the same health care encounter during which the blood culture was collected were identified, and medical record review was performed to determine if death was attributable to infection or another cause.

Blood cultures at CHOA laboratories were processed in automated, continuous monitor systems (Bactec FX; Becton-Dickinson, Franklin Lakes, NJ). Isolates were identified by phenotypic tests or matrix-assisted laser desorption ionization mass spectrometry time of flight

(Bruker Microflex MS; Bruker Daltonics, Billerica, MA). Blood cultures at the Grady Health System laboratory were performed with the BacT/ALERT 3D system (bioMérieux; Durham, NC). Isolates were identified by phenotypic tests or matrix-assisted laser desorption ionization mass spectrometry time of flight (Vitek-MS system; bioMérieux). Antimicrobial susceptibility testing and interpretation were in compliance with Clinical and Laboratory Standards Institute standards M07 and M100, respectively, for the appropriate years.[26,27] Minimum inhibitory concentration was performed by using the MicroScan Walkaway (Danaher Corp, Pasadena, CA) or Vitek 2 (bioMérieux) system.

Blood cultures that were collected within 14 days of a previous culture and either had the same result or a negative result after a positive one were considered to represent repeat testing from the same episode and were excluded. Contaminated blood cultures with positive results were defined as cultures in which (1) the identified organism is one commonly associated with common skin flora contamination (eg, coagulase-negative *Staphylococcus*, *Bacillus, Micrococcus*, common skin flora, or polymicrobial)[8,28] and (2) the culture source was not from a CVC. Any culture organism from blood obtained from a CVC was considered a true BSI, regardless of the organism's identity, including polymicrobial results.

For identified cases of BSI, an individual medical record review was performed to determine if the patient had an active prescription for antibiotic prophylaxis at the time of the BSI or had a history of surgical splenectomy and, in cases of *S pneumoniae*, to review immunization records.

The serotypes of *S pneumoniae* and *H influenzae* isolates were determined by the Centers for Disease Control and Prevention Emerging Infections Program, which provides surveillance for the 20-county Atlanta area.[29] Serotypes were determined by quellung reaction before 2016 and by whole genome sequencing in 2016 onward.

Statistical Analysis

For each calendar year from 2010 to 2019, the incidence rate of BSI was calculated by dividing the number of BSI episodes by the amount of person-time for all patients in the SCD database in that year. We defined person-years as the follow-up time for each child in that year until they were diagnosed with BSI or until the end of a particular calendar year, whichever came first. Subsequent BSIs in the same year were treated as independent events. Overall and age-stratified (<5 years and 5–18 years) annual incidence rates with 95% confidence intervals (CIs) were calculated. Characteristics of patients with BSI were compared with those of patients with negative blood culture results by using 2-tailed Student's t test, Pearson χ^2 test, and Fisher's exact test, as appropriate for the data. A 2-sided P value of .05 was assumed to reflect statistical significance. Covariates that had an adjusted odds ratio (OR) revealing a change >10% in the crude estimate or those of clinical importance were used in the final multivariate logistic regression models with forward stepwise selection. Traditional model diagnostics (eg, goodness-of-fit tests and residuals plots) were used to evaluate model fit. Statistical analysis was performed by using SAS software version 9.3.1 (SAS Institute, Inc, Cary, NC).

RESULTS

Study Population

In the 10-year period, which capture 3624 patients with SCD, 2694 (74.3%) patients with a total of 19 902 blood cultures met inclusion criteria, as shown in Fig 1. When repeat blood cultures were excluded, there remained 15 208 unique cultures. After exclusion of positive culture results from presumed contaminant growth (n = 168 cultures), there were 156 episodes of BSI (1.0% of blood cultures) among 144 patients. For BSI, the blood culture sources were peripheral blood in 123 and CVC in 33 (21.1%).

Baseline characteristics of the study population are summarized in Table 1. The mean age was slightly older for those with positive versus negative blood culture results (8.4 vs 7.5 years; P = .049). BSIs were more prevalent in patients with SCA (versus a non-SCA genotype) and patients on chronic transfusion therapy. Among BSI episodes, 25 (16.0%) occurred in patients with splenectomy, and 78 (50.0%) occurred in patients on antibiotic prophylaxis (71 on penicillin, 4 on amoxicillin, 3 on other).

Incidence Rates of BSI

The average annual incidence of BSI over the 10-year period was 0.89 per 100 person-years (95% CI 0.45–1.32). The incidence rate for children aged <5 years was 1.42 per 100 person-years (95% CI 0.31–2.52), compared with an incidence rate of 0.78 per 100 person-years (95% CI 0.29–1.26) for children aged ≥5 years. The incidence rates for the most common organisms in each year are shown in Fig 2. There was no major change in the other less common organisms over the 10-year period.

Risk Factors for BSI

In the multivariate analysis shown in Table 2, the final model included age, sex, SCD genotype, hydroxyurea, and chronic transfusion therapy. The odds of BSI were significantly higher for

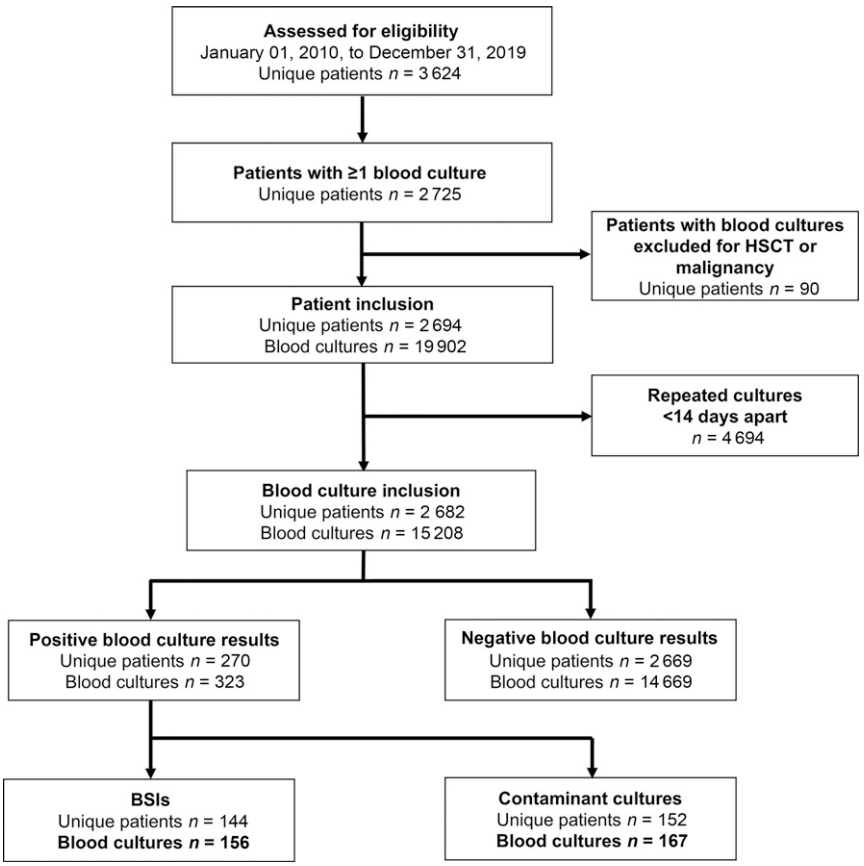

FIGURE 1
Flow diagram for identification of BSIs among a cohort of children with SCD, 2010–2019. HSCT, hematopoietic stem cell transplant.

those with SCA compared with those with non-SCA genotypes (OR 1.88 [95% CI 1.20–2.94]) and for those receiving chronic transfusion therapy (OR 2.66 [95% CI 1.51–4.69]). Hydroxyurea therapy was associated with significantly lower odds of BSI (OR 0.57 [95% CI 0.39–0.84]).

TABLE 1 Demographic and Clinical Features of Children With SCD Who Had Health Care Encounters That Included Blood Culture

Characteristic	BSI Episode	Blood Culture Without BSI	*P*
Age, mean (SE), y	8.4 (0.5)	7.5 (0.04)	.049
Age ≤60 mo, *n* (%)	60 (38.5)	6147 (40.8)	.55
Sex (female), *n* (%)	79 (50.6)	7108 (47.2)	.4
SCA genotype, *n* (%)	131 (84)	11 299 (75.1)	.01
SS or $S\beta^0$ thalassemia	131 (84)	11 252 (74.8)	—
SD	0 (0)	14 (0.09)	—
SO-Arab	0 (0)	32 (0.21)	—
SC Harlem	0 (0)	1 (0.007)	—
Non-SCA genotypes, *n* (%)			
SC	21 (13.5)	2950 (19.6)	—
$S\beta^+$ thalassemia	4 (0.64)	761 (5.1)	—
SE	0 (0)	42 (0.28)	—
Hydroxyurea therapy, *n* (%)	38 (24.4)	4663 (30.9)	.08
Chronic transfusion therapy, *n* (%)	14 (8.9)	425 (2.8)	<.0001
Mortality, *n* (%)	3 (1.9)	11 (0.07)	<.0001

Patients with a BSI episode ($n = 156$) are compared with those without a BSI ($n = 15\,052$). —, not applicable.

Microbiologic Findings

A list of all microorganisms associated with BSI is shown in Table 3. The most prevalent pathogen was *S pneumoniae* ($n = 25$, 16.0% of BSIs), followed by *Staphylococcus* ($n = 12$ for *S aureus*, $n = 5$ for *S epidermidis*, $n = 3$ for other coagulase-negative *Staphylococcus*) and *Streptococcus* ($n = 23$ viridans group, $n = 1$ *Streptococcus pyogenes*). Prevalent Gram-negative organisms included *E coli* ($n = 14$, 9.0%), *Bordetella holmesii* ($n = 12$, 7.7%), *H influenzae* ($n = 11$, 7.1%), and *Salmonella* species ($n = 10$, 6.4%). *H influenzae* included serotypes f ($n = 6$) and a ($n = 1$) and nontypeable *H influenzae* ($n = 3$) and was not tested in 1 case.

Serotypes of *S pneumoniae* isolates were determined for 24 of 25 cases (Table 4), whereas 1 isolate was from a child who resided outside the Centers for Disease Control and Prevention surveillance area for *S pneumoniae*. Pneumococcal BSI occurred in 7 (25%) children <24 months of age, in 7 (28%) children 24 to 59 months of , and in 11 (44%) aged ≥60 months. There were 12 (48%) isolates of serotypes included in PPSV23 (10A, 12F, 15B/C, 22F). No serotypes included in PCV13 were isolated. Among children who had a PPSV23 serotype, 6 (50%) had received at least 1 PPSV23 immunization (5 with 1 dose, 1 with 2 doses), whereas among children with a non-PPSV23 serotype, 9 (75%) had at least 1 PPSV23 immunization ($P = .20$).

Antimicrobial susceptibility was available for select pathogens (Fig 3). For *S pneumoniae*, all isolates tested ($n = 23$) revealed susceptibility to ceftriaxone at both nonmeningitis (<1 μg/mL) and meningitis (≤0.5 μg/mL) breakpoints and to penicillin at

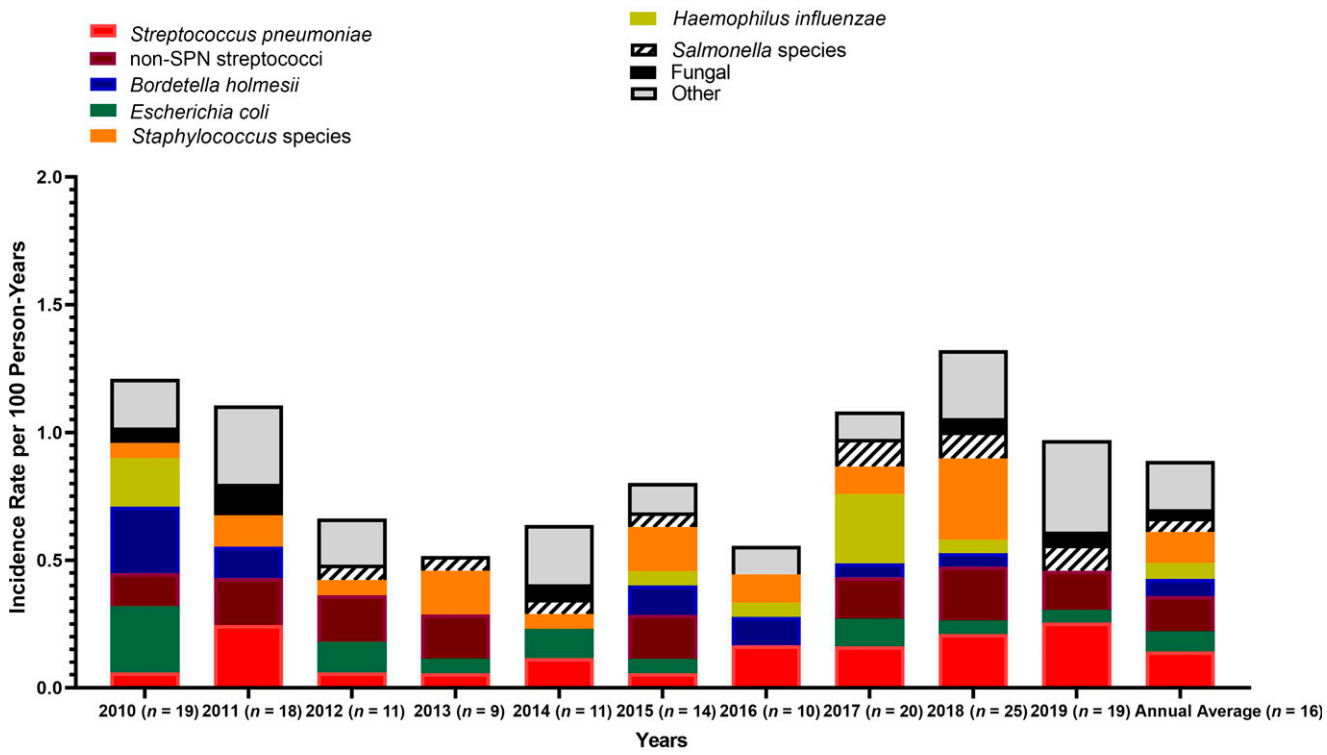

FIGURE 2
Annual incidence rates of BSI episodes among children with SCD, 2010–2019. SPN, *S pneumoniae*.

nonmeningitis breakpoints; however, only 61% were susceptible to penicillin at the meningitis breakpoint (≥0.12 μg/mL).[30] Susceptibility to ceftriaxone was observed in 100% of *Salmonella* and *E coli* isolates. Susceptibility to ampicillin was observed in 9 of 10 (90%) of *Salmonella* and 5 of 13 (38.5%) of *E coli* isolates.

Mortality

There were 14 deaths within the study inclusion cohort: 3 deaths during illnesses associated with a BSI and 11 deaths during illness in which blood culture results at CHOA were negative. Two deaths were attributable to *S pneumoniae* sepsis, and 1 death in a patient with CVC-associated BSI (methicillin-resistant *S aureus*) was attributed to a coexistent non-SCD medical condition. Within the non-BSI group, 2 deaths occurred in patients transferred to CHOA after positive blood culture results reported by outside hospitals (1 *H influenzae*, 1 Gram-negative rod), 2 deaths were associated with ceftriaxone-induced hemolytic anemia, and 7 deaths were not associated with an known infection or antibiotic adverse event. Mortality was significantly higher within the BSI group (1.9% of BSI events versus 0.09% of non-BSI events; $P < .0001$). In multivariate analysis of all mortality, the odds of death were significantly higher in those with BSI (OR 22.4 [CI 6.1–82.6]), whereas age, sex, genotype, and hydroxyurea were not associated with mortality.

TABLE 2 Adjusted Multivariate Analysis for BSI and Associated Features Among Children With SCD

	OR	95% CI
Age, y	1.03	1.01–1.06
Sex, female	1.17	0.85–1.61
SCA genotype	2.13	1.33–3.40
Hydroxyurea therapy	0.56	0.38–0.83
Chronic transfusion therapy	2.68	1.52–4.74

DISCUSSION

The present comprehensive review of blood culture findings among nearly 2700 children provides a contemporary update to the incidence of and specific pathogens associated with invasive BSI in children with SCD. Significant advances have occurred in infection prevention since the Cooperative Study of Sickle Cell Disease (1978–1994),[31] including antibiotic prophylaxis in children aged <5 years and the development of pneumococcal conjugate vaccines. The BSI incidence rates of 0.89 per 100 person-years overall and 1.42 per 100 person-years in children <5 years are lower than the rates in the Cooperative Study of Sickle Cell Disease, which ranged from 7.87 per

TABLE 3 Microorganisms Isolated From Cases of BSI Among Children With SCD ($n = 156$)

Microorganism Group	$n = 156$, Frequency (%)	Culture from CVC ($n = 33$), n (%)
Gram-negative bacteria		
Enterobacteriaceae		
E coli	14 (9.0)	3 (9.1)
Salmonella species[a]	10 (6.4)	0 (0)
Klebsiella pneumoniae	2 (1.3)	0 (0)
Pantoea agglomerans	2 (1.3)	0 (0)
Citrobacter koseri	1 (0.6)	0 (0)
Morganella morganii	1 (0.6)	0 (0)
Shigella sonnei	1 (0.6)	0 (0)
Miscellaneous Gram-negative (non-Enterobacteriaceae)		
B holmesii	12 (7.7)	1 (3.0)
H influenzae	11 (7.1)	1 (3.0)
Moraxella species[a]	4 (2.6)	0 (0)
Acinetobacter species[a]	3 (1.9)	0 (0)
Stenotrophomonas maltophilia	1 (0.6)	0 (0)
Pseudomonas aeruginosa	1 (0.6)	0 (0)
Pseudomonas stutzeri	1 (0.6)	0 (0)
Gram-positive bacteria		
SPN	25 (16.0)	1 (3.0)
Viridans *Streptococcus* group (non-SPN)		
Viridans *Streptococcus* group[a]	14 (9.0)	1 (3.0)
Streptococcus mitis group	9 (5.8)	0 (0)
S pyogenes	1 (0.6)	0 (0)
Staphylococcus aureus		
Methicillin-susceptible SA	8 (5.1)	1 (3.0)
Methicillin-resistant SA	4 (2.6)	1 (3.0)
Staphylococcus Epidermidis	5 (3.2)	5 (15.1)
Coagulase-negative staphylococci (non-SE)		
Staphylococcus capitis	1 (0.6)	1 (3.0)
Staphylococcus hominis	2 (1.3)	2 (6.1)
Propionibacterium species[a]		
Cutibacterium (Propionibacterium) acnes	6 (3.9)	6 (18.2)
Propionibacterium species[a]	1 (0.6)	1 (3.0)
Bacillus species, not *Bacillus anthracis*	1 (0.6)	1 (3.0)
Abiotrophia and *Granulicatella* species		
Abiotrophia defectiva	1 (0.6)	0 (0)
Abiotrophia and *Granulicatella* species	2 (1.3)	1 (3.0)
Gemella species		
Gemella haemolysans	1 (0.6)	0 (0)
Gemella morbillorum	1 (0.6)	0 (0)
Rothia species[a]	1 (0.6)	0 (0)
Miscellaneous		
Polymicrobial	3 (1.9)	2 (6.1)
Yeast[a]		
Candida albicans	4 (2.6)	4 (100)
Candida tropicalis	1 (0.6)	1 (100)
Candida parapsilosis	1 (0.6)	1 (100)
Total	156 (100)	33 (100)

SA, *S aureus*; SE, *S epidermidis*; SPN, *S pneumoniae*.

[a] No further identification.

100 person-years for children with hemoglobin SS <3 years age to 0.63 per 100 person-years for children with hemoglobin SS aged 10 to 19 years.[9] However, our findings demonstrate the ongoing prevalence of BSI in children and adolescents of all ages with SCD. These rates are informative to guiding the prevention, identification, and empirical treatment of infection in SCD.

In this contemporary cohort, organisms classically known to affect individuals with SCD and asplenia, such as *S pneumoniae*, *H influenzae*, *Salmonella*, and *E coli*, continue to be among the most common pathogens identified. Our study period is unique because it began only 1 month before the licensure of PCV13 in February 2010, which replaced PCV7 in the routine childhood immunization schedule.[19] We found no *S pneumoniae* serotypes included in PCV7 or PCV13, suggesting a change in the epidemiology of infection in children with SCD concurrent with population-wide immunization practices. However, nearly half of the 25 pneumococcal BSIs were serotypes that were included in PPSV23. Almost all cases of vaccine-included serotypes occurred in children with either no doses or only 1 primary dose of PPSV23 without a booster dose. Regardless of PPSV23 immunization status, children with SCD remain at risk for pneumococcal BSI because non-PPSV23 serotypes may also cause invasive infection. The importance of antibiotic prophylaxis thus must be considered in children at highest risk of pneumococcal infection. Notably, when considering all BSIs in our series, 50% occurred in individuals who were prescribed antibiotic prophylaxis. This observation is not a reflection of the effectiveness of prophylaxis because our study was not designed to evaluate this measure. Additionally, this observation in our BSI group likely reflects our clinical practice of prescribing antibiotic prophylaxis in higher-risk patients (younger age or those undergoing splenectomy).

In addition to pneumococcus, several Gram-negative bacteria and organisms associated with CVC contamination were found. *B holmesii*, a fastidious Gram-negative organism, was the third most common BSI organism in this study.[32] Although not identified until 1995, *B holmesii* bacteremia

TABLE 4 Serotypes of *S pneumoniae* BSI Among Children With SCD, at CHOA, 2010–2019

Serotype	Frequency (%)
PPSV23 serotypes (n = 12)	
10A	1 (4.2)
12F	1 (4.2)
15B/C	7 (28.0)
22F	3 (12.5)
Non-PPSV23 serotypes (n = 12)	
6C	1 (4.2)
7C	1 (4.2)
15A	2 (8.3)
23B	3 (12.5)
35B	3 (12.5)
38	2 (8.3)

The serotype of 1 *S pneumoniae* isolate was not determined.

has been described predominantly among individuals with functional or anatomic asplenia, including those with SCD, typically without a severe disease course, and therefore should be included as a consideration in the empirical treatment of infection in SCD.

Risk factors for BSI identified in our cohort included SCA (hemoglobin SS or Sβ^0 thalassemia) and chronic transfusion therapy, whereas hydroxyurea revealed a significant risk reduction in the multivariate analysis. A similar observation with hydroxyurea was reported in the Realizing Effectiveness Across Continents with Hydroxyurea (REACH) trial in sub-Saharan Africa, which revealed lower incidence rates of infection and septicemia in children receiving hydroxyurea. A potential explanation may be that hydroxyurea therapy is associated with increased access to medical care and therefore also to preventive care in SCA. Among patients who are chronically transfused, the increased risk of BSI may be related in part to the frequent use of CVCs among patients receiving this therapy. The benefits of vascular access with CVCs must be balanced against the increased infectious risks in a population with asplenia that is already at increased

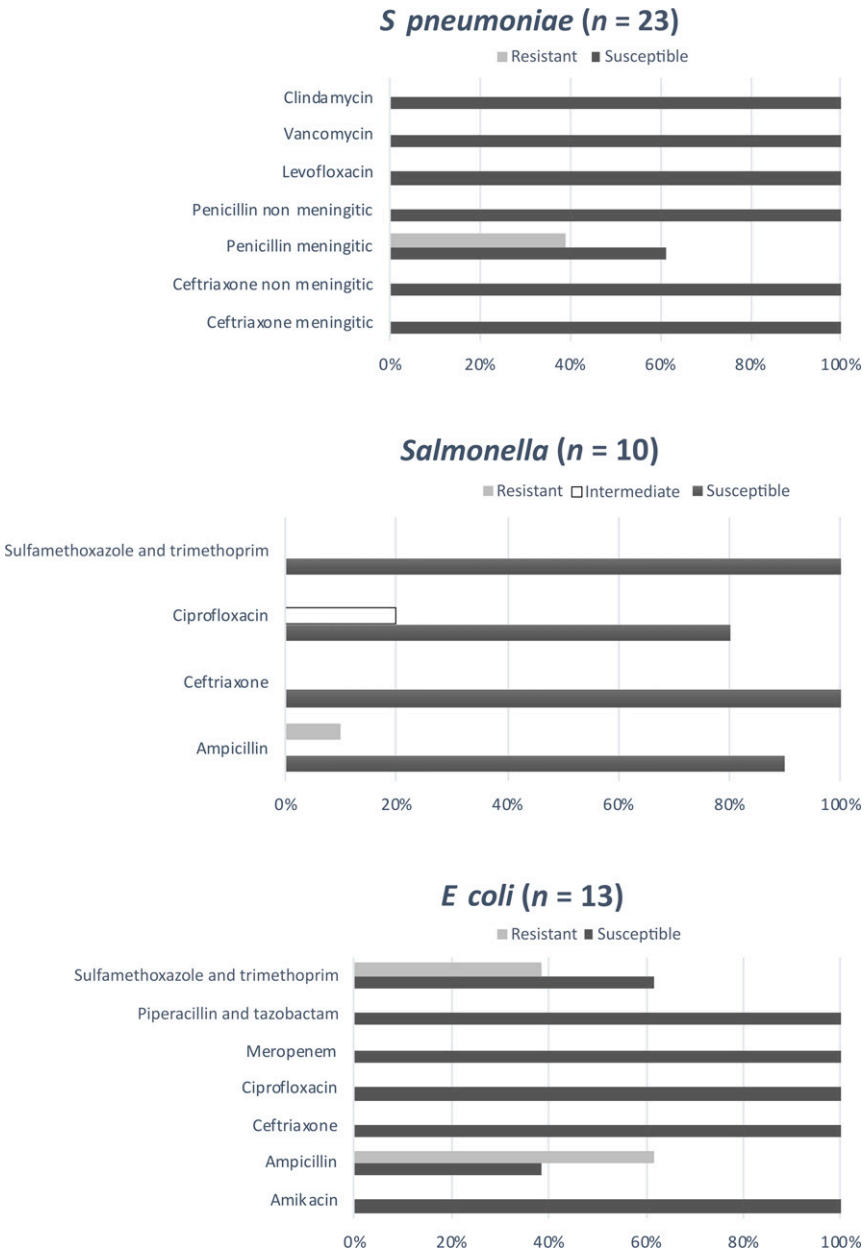

FIGURE 3
Antimicrobial susceptibility testing among isolates of *S pneumoniae*, *Salmonella*, and *E coli*.

risk of invasive bacterial infection. BSI in the presence of a CVC may lead to increased hospitalization, longer duration of exposure to antibiotics, or surgical procedures to remove the CVC in some cases.

Within this cohort, there were 4 deaths at our institution related to infection: 2 deaths from *S pneumoniae* sepsis and 2 deaths from septic shock in patients with Gram-negative bacteremia in cultures obtained at outside hospitals. One other death that occurred in a patient with a CVC-associated BSI was attributed to complications of a comorbid non-SCD medical condition. Given that our review does not include cultures from surrounding outside hospitals, our study likely underrepresents the

frequency of death due to infection. This highlights an important limitation of the study because the analysis was based on results of blood cultures drawn at CHOA facilities and does not capture blood culture results from other hospitals, thus underestimating the true incidence of BSI as compared with a population-based surveillance study.

Given the risk of BSI in children with SCD, national consensus guidelines recommend that all individuals with SCD and fever should have a blood culture obtained and treatment with empirical antibiotics.[33] Our study revealed that ~2% of blood culture results from children with SCD were positive, half of which represented true BSI; the other half, culture contamination. Considerations for empirical antibiotic choice should include adequate treatment of *S pneumoniae* as well as other Gram-positive and Gram-negative bacteria. Although antibiotic susceptibility results in our cohort revealed high susceptibility to ceftriaxone, empirical antibiotic therapy should reflect local susceptibility patterns; thus, these findings may not be extrapolated to other geographic regions. The risk of adverse events, including drug-induced immune hemolytic anemia, also bear consideration. For individuals with a CVC, a broader range of organisms must be considered. Past studies of CVCs in individuals with SCD have shown a rate of infection from 1.5 to 5.5 infections per 1000 catheter days, underscoring the infectious risks associated with these devices and the need for vigilance with BSI prevention and empirical treatment in these patients.[5,34–36]

CONCLUSIONS

This 10-year cohort study is one of the largest reviews of blood culture results and BSI in children with SCD. Although infection and its associated mortality have decreased substantially over the past decades, children with SCD remain at risk for BSI, particularly those with SCA genotypes or a CVC. The findings of this study continue to inform clinical practices for immunization, prevention, and treatment of BSI in SCD.

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ABBREVIATIONS

BSI: bloodstream infection
CHOA: Children's Healthcare of Atlanta
CI: confidence interval
CVC: central venous catheter
OR: odds ratio
PCV7: 7-valent pneumococcal conjugate vaccine
PCV13: 13-valent pneumococcal conjugate vaccine
PPSV23: 23-valent pneumococcal polysaccharide vaccine
SCA: sickle cell anemia
SCD: sickle cell disease

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Deidentified individual participant data (including data dictionaries) will be made available, in addition to study protocols, the statistical analysis plan, and the informed consent form. The data will be made available after publication to researchers who provide a methodologically sound proposal for use in achieving the goals of the approved proposal. Proposals should be submitted to memcphe@emory.edu.

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