



## Brief Report

# Bacterial blood cultures in children with sickle cell disease

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Received 20 March 2009; revised 1 April 2009; accepted 1 April 2009

## Abstract

**Background:** Children with sickle cell disease (SCD) are considered at risk for bacteremia, especially when they present to the emergency department (ED) with fever.

**Objective:** We aimed to determine the incidence of bacteremia in children with SCD presenting with or without fever to a pediatric ED.

**Methods:** A retrospective chart review of 692 pediatric ED visits of children with SCD during a 2-year period was conducted.

**Results:** Seven blood cultures (6 homozygous and 1 heterozygous) had bacterial growth (1.3%; 95% confidence interval, 0.5–2.1), 3 of which were among febrile children (1.7%; 95% confidence interval, 0–3.6). All identified microorganisms are part of the normal skin or oral flora and could represent contamination. None of the patients had growth of the *Streptococcus pneumoniae* species.

**Conclusion:** A very low rate of bacterial growth and no *S pneumoniae* were found. The absence of *S pneumoniae* in our cohort can be associated with the addition of the 7-valent pneumococcal conjugate vaccine.

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## 1. Introduction

Bacteremia in children with sickle cell disease (SCD) carries a significant risk for morbidity and mortality. Despite the success of routine vaccination against *Haemophilus influenzae* type b [1], splenic dysfunction, poor perfusion,

and immature immune response to polysaccharide antigens lead to increased vulnerability of these children to severe infections with encapsulated organisms. The use of penicillin prophylaxis and pneumococcal conjugate vaccine (PCV) has decreased the risk of bacteremia from *Streptococcus pneumoniae* [2]; however, penicillin-resistant strains and nonvaccine serotypes of *S pneumoniae* are becoming relatively more common [3].

Hence, children with SCD are considered at risk for bacteremia, especially when they present to the emergency department (ED) with fever. The latter also receive empirical antibiotic treatment until blood cultures are confirmed negative, and until recently, most of them were admitted

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to the hospital [4]. However, many sickle cell centers have long since adopted as standard practice the outpatient management of uncomplicated fever in children with SCD.

The objective of our study was to determine the incidence of bacteremia in children with SCD presenting with or without fever to a pediatric ED. Identifying this risk may help physicians to proactively plan and, in some cases, tailor their management accordingly, as well as identify potential sources for intervention.

## 2. Methods

We retrospectively reviewed the health records of all patients with SCD who are 18 years or younger who visited the ED at the Hospital for Sick Children (Toronto, Canada) between January 1, 2005, and December 31, 2006 (2-year period). In our tertiary pediatric ED, approximately 50 000 patients are seen annually, and we serve a catchment area of approximately 1 million children. The study was approved by the hospital research ethics board. Information collected included age, sex, presence of fever (defined as  $\geq 38^{\circ}\text{C}$  in the ED or 24 hours before arrival at the ED), bacterial blood culture results from the ED, and disposition. We also documented diagnosis, SCD type, white blood cell count, and antibiotics administered in patients with positive blood cultures.

Patient data were collected from the hospital computerized record system and downloaded onto a Microsoft Excel (Microsoft, Redmond, WA) spreadsheet. Statistical analysis was conducted using SPSS release 14.0 (SPSS, Chicago, IL). Results are expressed as mean (SD) for continuous variables and absolute numbers (percentage with 95% confidence interval [CI]) for categorical variables. Statistical significance was considered at  $P < .05$ .

## 3. Results

The patient flow is shown in Fig. 1. A total of 248 patients with SCD had 692 ED visits during the study period. The average age of the patients was 9 years (SD, 5 years), and 51% were women. One hundred eighty (26%; 95% CI, 22.7-29.3) patients were febrile in the 24 hours before arrival or in triage. Four hundred eighty-three (70%) of all patients (95% CI, 66.6-73.4) and 139 (77%) of 180 febrile children (95% CI, 70.9-83.1) were admitted.

Blood cultures were taken at the ED in 530 (77%) of 692 visits (95% CI, 73.9-80.1). Seven blood cultures (6 homozygous and 1 HbSC) had bacterial growth (1.3%; 95% CI, 0.5-2.1), 3 of which were among febrile children (1.7%; 95% CI, 0-3.6). All identified microorganisms are part of the normal skin or oral flora and could represent contamination. None of the patients had growth of the *S pneumoniae* species. All patients with possible bacte-

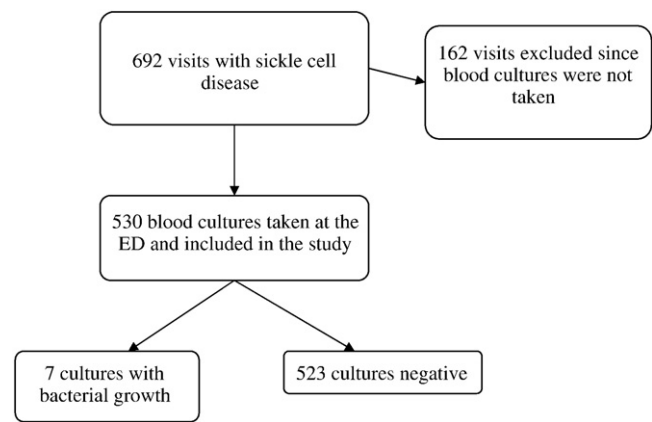


Fig. 1 Patient flow.

remia (except one receiving penicillin prophylaxis at home) were treated with intravenous cephalosporins and 5 were discharged. Only 1 patient was diagnosed with a serious bacterial infection (pneumonia with growth of diphtheroid). One patient with upper respiratory tract infection had growth of coagulase-negative *Staphylococcus*, and after 2 days, a second culture had grown *Rothia mucilaginosa* (*Stomatococcus mucilaginosus*).

## 4. Discussion

We found a very low rate of bacterial growth (1.3% overall and 1.7% in febrile patients) and no growth of *S pneumoniae* among children with SCD arriving at the ED. This is one of the first studies to determine the incidence of bacteremia among pediatric patients with SCD after the introduction of the routine PCV vaccination, and the main questions arising are why was the rate of bacterial growth so low and is the absence of *S pneumoniae* related to the PCV vaccination?

In the era preceding the PCV, the rate of severe pneumococcal infections among homozygous SCD patients was reported to be 2.4 and 0.35 events per 100 patient-years in children younger than 5 years and children older than 5 years, respectively [5]. Among febrile children with SCD in 1993-2001 in the United States, *S pneumoniae* accounted for 42% of bacteremias, followed by *Salmonella* species (17%), coagulase-negative *Staphylococci* (9%), *Staphylococcus aureus* (7%), *Escherichia coli* (5%), and others [1].

The 7-valent PCV was licensed in February 2000 and recommended for all children younger than 2 years and for selected children aged 2 to 4 years with high-risk conditions such as SCD [6]. Starting in January 2005, the Ontario Government is providing the vaccine for free for all children, and as of January 2006, all provincial/territorial governments in Canada provide for routine immunization of children with 7-valent PCV. The 23-valent pneumococcal polysaccharide vaccine has been available through Ontario's publicly funded immunization program since 1996. The

vaccine is provided for the immunization of persons 2 years or older who have a “high-risk” medical condition, including SCD, that puts them at increased risk of invasive pneumococcal disease.

According to Halasa et al [2], in comparing the pre-PCV period (1995-1999) with the post-PCV period (2001-2004), the rate of invasive pneumococcal disease decreased by 93% in children younger than 5 years (from 2044 to 134 cases per 100 000 person-years).

In a retrospective pre-PCV study from California (1989-1999), 4.6% (8/175) of febrile events in children with SCD resulted in true bacteremia (3 *S pneumoniae*, 3 *Streptococcus viridans*, 1 *H influenzae*, and 1 *Moraxella catarrhalis*) [4]. This was much higher than the incidence of possible bacteremia among febrile patients in our cohort (1.7%); however, children in the study by West et al [4] were, on average, younger (mean age, 5.9 years) and there is a significant tapering of invasive pneumococcal disease after the age of 5 years (although they are more deadly in older patients with homozygous SCD). Occurrence of bacteremia among 53 503 blood cultures taken from the general population of hospitalized children in Israel was reported at a level of 3.1% [7], whereas the rate of bacterial growth was 1.3% in our cohort of the ED patients with SCD.

Vernacchio et al [8] have shown that IgG pneumococcal antibody concentrations are higher if 7-valent PCV and the 23-valent pneumococcal vaccine group are combined, compared with single 23-valent vaccine, in children 2 years or younger with SCD. The rate of pediatric invasive pneumococcal infections caused by included in the conjugate vaccine strains, nonsusceptible to penicillin and multiple antibiotics, significantly decreased after the introduction of the conjugate vaccine, with an increase in infections caused by serotypes not included in the vaccine [9]. We therefore suggest that the absence of the *S pneumoniae* species in our cohort could be associated with the addition of the 7-valent PCV. As the previously reported rate of invasive pneumococcal disease in children with HbSS 5 to 10 years old ranged from 0.4 to 0.9 per 100 patient-years before the introduction of PCV and is now approximately 60% to 90% lower with PCV, it is not surprising that no pneumococcal bacteremia were detected.

Physicians admitted 77% of febrile children in our cohort, similar to a previous study [10]. Several criteria for admission of febrile children with SCD had been suggested in the past [11]. We suggest that because of the very low rate of possible bacteremia in our cohort, fever alone may not be an indication for admission.

Among positive cultures, 58% and 61% were considered a contamination in the studies of Pavlovsky et al [7] and Norris et al [1], respectively. In our study, all identified microorganisms could be part of the normal skin or oral flora and could represent contamination.

Our study was limited because it was retrospective and low-risk children (23% in our cohort) did not have blood cultures taken, of which some, theoretically, could be

positive. Also, we did not have data on how many children had actually received the PCV and the 23-valent unconjugated vaccine, which are routinely indicated for all children with SCD [6], and how many were actually taking penicillin. In addition, we did not collect the follow-up data on admitted patients who could have further positive blood cultures and could experience significant complications such as acute chest syndrome and osteomyelitis when in the hospital. Furthermore, our data are from a single ED at a tertiary care hospital and did not include children who were seen in the outpatient setting and those who were directly admitted to the hospital, which limits the generalizability of our findings.

In conclusion, we found a very low rate of bacterial growth (1.3%) and no growth of *S pneumoniae*, whether the children were febrile or not. The absence of *S pneumoniae* in our cohort can be associated with the addition of the 7-valent PCV. Although large prospective studies are needed to determine the current incidence of bacteremia in children with SCD from different medical settings and to detect specific risk factors, our results confirm the practice of outpatient management of uncomplicated fever in children with SCD. Knowledge of the low risk of bacteremia in children with SCD presenting to the pediatric ED will help physicians in planning, managing, and identifying potential sources for intervention for these patients.

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