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Prevalence of Bacteremia in Hospitalized Pediatric Patients With Community-acquired Pneumonia

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Abstract

Background—National guidelines recommend obtaining blood cultures in children hospitalized with moderate or severe community-acquired pneumonia (CAP). The objectives of this study were to determine the prevalence of bacteremia in children, identify factors associated with bacteremia and quantify the influence of positive blood cultures on clinical management in children hospitalized with CAP.

Methods—This multicenter retrospective study included children from 60 days to 18 years of age requiring hospitalization for CAP. Categories analyzed were bacteremia, culture negative and no culture.

Results—Blood cultures were performed in 369 (56%) of 658 children with CAP. The prevalence of bacteremia was 7% (4.7–10.1%) in patients with a blood culture obtained. Bacteremia occurred in 21% of patients with a pleural drainage procedure and 75% of patients with distant site of infection (eg, osteomyelitis). Patients with bacteremia had longer duration of fever before admission and higher C-reactive protein values compared with those with negative or no blood culture. However, differences in white blood cell count and erythrocyte sedimentation rate between those with bacteremia and those without were not significant. Contamination rates were low and similar across institutions, ranging from 1% to 3.8% ($P = 0.63$). Blood culture–

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directed changes in antibiotic management occurred in 33% of patients with a contaminated culture and 65% of bacteremic patients. Antibiotic therapy was narrowed in 26% of bacteremic patients at hospital discharge.

Conclusion—The prevalence of bacteremia was higher than previously reported in children hospitalized with CAP and consistent across children’s hospitals. Positive blood cultures should prompt change to narrow-spectrum antibiotic therapy.

Keywords

bacteremia; children; community-acquired pneumonia; hospitalized

Blood cultures are often performed in the diagnostic evaluation of children hospitalized with community-acquired pneumonia (CAP). Recent clinical practice guidelines for the management of pediatric CAP recommend that blood cultures be performed routinely in children requiring hospitalization for moderate or severe CAP, but the quality of evidence supporting this recommendation is low.¹

Guidelines for adult patients also recommend obtaining a blood culture in patients hospitalized with CAP, and this recommendation has been cited as a quality indicator by The Joint Commission and the Centers for Medicare and Medicaid Services.² Sandora et al³ reviewed the blood culture recommendations for adults and applied this recommendation in a hospitalized pediatric population with CAP, revealing a bacteremia rate of 1.4% and bringing into question the utility of obtaining a blood culture on a routine basis in this patient group. Most other studies have also reported a low prevalence of bacteremia among children hospitalized with uncomplicated CAP, with rates ranging from 1.1% to 2.7%.^{3–8} However, a single-center study of children in Utah documented a substantially higher prevalence of bacteremia (11.4%) in children with uncomplicated CAP.⁹

The prevalence of bacteremia is higher in children with pneumonia complicated by effusion or empyema, ranging from 13% to 26%, and obtaining a blood culture in this setting has been shown to confirm a pathogen in 7–21% of patients with negative pleural fluid cultures.^{5,9–12} However, some of these data are in the prepneumococcal conjugate vaccine period and all were obtained from single-center studies. A multicentered study conducted in Italy revealed a pathogen by blood culture alone for 2 patients (4.3%), raising the possibility that blood culture may not provide added clinical data over molecular testing (eg, polymerase chain reaction for *Streptococcus pneumoniae* and *Staphylococcus aureus*) performed on blood and pleural fluid.¹³ Although children with complicated pneumonia have a higher rate of bacteremia, only 1 study to date has determined the impact of positive results on patient management.⁵

The objectives of this study were to (1) determine the prevalence of documented bacteremia in children hospitalized with CAP across 4 children’s hospitals, (2) determine differences in clinical characteristics and outcomes of patients with documented bacteremia compared with those without and (3) quantify the influence of positive and contaminated blood cultures on antibiotic management.

MATERIALS AND METHODS

Study Design, Setting and Participants

This multicenter retrospective study was conducted from a cohort of children evaluated to validate International Classification of Diseases, 9th revision, Clinical Modification codes for CAP. The previous study used billing codes from the Pediatric Hospital Information System (Children’s Hospital Association, Overland Park, KS) and included patients from 60

days to 18 years of age, with a discharge code of pneumonia or effusion, radiographically confirmed pneumonia and/or clinical features and laboratory results consistent with pneumonia from 1 of 4 free-standing children's hospitals (Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN; Children's Mercy Hospitals & Clinics, Kansas City, MO; Seattle Children's Hospital, Seattle, WA and Cincinnati Children's Hospital Medical Center, Cincinnati, OH) from January 1, 2010, to December 31, 2010. A 25% random sample (N = 998) of 3646 hospital discharges were identified as possible CAP by International Classification of Diseases, 9th revision, Clinical Modification codes and were selected for medical record review. Patients hospitalized since birth, with a chronic comorbid condition or whose primary admitting diagnosis was trauma, were excluded (n = 243). In addition, patients were excluded if no blood culture information was available (n = 19) or there was no provider diagnosis of pneumonia (n = 78). Patients meeting inclusion criteria were categorized into 3 mutually exclusive categories: those with documented bacteremia, those without bacteremia as documented by a negative or contaminated blood culture (culture negative) and those in whom a blood culture had not been performed (no culture). All culture data were obtained within 48 hours of hospital admission.

Data Source

Detailed medical record reviews were performed in all children in this study. Data collected included demographics, presenting signs and symptoms, physical examination findings and laboratory, radiograph, and microbiology results, including bacterial pathogens and antibiotic susceptibility patterns. The following clinical outcomes were also recorded: length of stay, presence of pneumonia-associated sequelae, supplemental oxygen requirement, intensive care unit admission and vasoactive medications. Treatment data during hospitalization were obtained from Pediatric Hospital Information System and discharge antibiotic therapy was obtained from medical record review. Data from medical record review were entered into a central web-based data collection system. All investigators who participated in medical record review underwent training and piloted the record review process to ensure consistency in data collection. Discrepancies were resolved by group consensus and changes were made to the data collection tool for clarification when necessary.

Study Definitions

Pathogenic bacteria included *S. pneumoniae*, *Staphylococcus aureus* and *Haemophilus influenzae*. Bacteria considered as contaminants included coagulase-negative *Staphylococcus* spp., α -hemolytic *Streptococcus* spp., *Corynebacterium* spp., *Bacillus* spp. and *Micrococcus* spp. Susceptibility data were determined at each individual site using current Clinical and Laboratory Standards Institute criteria.¹⁴ Antimicrobial therapy was recorded daily and defined in 2 categories: narrow (penicillin or aminopenicillin) and broad (any second- or third-generation cephalosporin, macrolide, lincosamide, quinolone or penicillin combined with a β -lactamase inhibitor).¹⁵ Blood culture-directed changes in antibiotics were classified as broadened, narrowed or unchanged relative to *S. pneumoniae* and *Staphylococcus aureus*. For example, a patient initially receiving vancomycin that was changed to ceftriaxone based on culture results was classified as "narrowed" due to a narrower spectrum of pneumococcal and *Staphylococcus aureus* coverage of ceftriaxone compared with vancomycin. Conversely, if ceftriaxone was added to vancomycin with a blood culture result revealing either *S. pneumoniae* or *Staphylococcus aureus*, therapy was considered to be unchanged based on no additional spectrum coverage of either pathogen.

Pneumonia was categorized as uncomplicated or complicated within the first 24 hours of hospitalization. Uncomplicated pneumonia was defined as alveolar or lobar infiltrate with or without a small effusion on chest radiograph or was determined to be clinically consistent

with pneumonia in the medical record. Complicated pneumonia was defined as at least 1 of the following: presence of moderate-to-large pleural effusion, lung abscess or necrosis, or bronchopleural fistula on radiologic imaging (eg, chest radiograph, ultrasound, computerized axial tomography scan) or requirement of a pleural fluid drainage procedure. Pneumonia sequelae were defined as presence of one or more of the following: complicated pneumonia, organ dysfunction, vasoactive support, intensive care admission or extrapulmonary complication. Organ dysfunction was based on consensus guidelines and defined as sepsis evidenced by bacteremia in the setting of intensive care admission requiring vasoactive medications, respiratory failure with the need for endotracheal intubation or noninvasive mechanical ventilation via positive pressure methods or dysfunction in cardiovascular, renal, hepatic, hematologic or neurologic systems.¹⁶ Metastatic complication was defined as at least 1 of the following sites of secondary infection: skin/soft tissue abscess, pyomyositis, septic arthritis or osteomyelitis at any time during hospitalization.

Statistical Analysis

Characteristics of the study population were described overall and within their blood culture group. Continuous variables were summarized using median and interquartile range (IQR) and compared between children with bacteremia, those with negative blood culture and without blood culture using the Wilcoxon rank-sum test. Categorical variables were described using counts and frequencies and compared between those with bacteremia and those with negative culture and no culture using χ^2 test or Fisher's exact test. The prevalence of bacteremia and contaminated blood cultures was determined for all patients, patients with uncomplicated pneumonia and patients with complicated pneumonia using binomial exact 95% confidence intervals. Descriptive statistics were used for susceptibility data and therapy at hospital discharge.

RESULTS

Clinical, Laboratory and Radiographic Features

There were 658 children with a provider diagnosis of CAP and blood culture information available. The median patient age was 3.1 years (IQR: 1.3–6.7). Intensive care unit admission, indicating severe disease, occurred in 11.9% (78/658) of patients; 47.4% (37/78) required endotracheal intubation and 33.3% (26/78) received vasopressor support. Blood cultures were performed in 369 (56.1%) of 658 children. Bacteremia was present in 26 (3.9%) of 658 children hospitalized with CAP overall and in 26 (7.1%) of 369 of those who had a blood culture obtained (Table, Supplemental Digital Content 1, <http://links.lww.com/INF/B562>). Differences in age, gender, race, insurance type, duration of illness, outpatient visits and antibiotic therapy before admission were not significant between patients with bacteremia compared with those with either a negative blood culture or no blood culture (Table, Supplemental Digital Content 2, <http://links.lww.com/INF/B563>). However, children with either complicated pneumonia or pneumonia-associated metastatic complications were significantly more likely to have bacteremia than those with uncomplicated pneumonia. In addition, patients with bacteremia compared with those without blood culture were more likely to be admitted to the intensive care unit (Table, Supplemental Digital Content 2, <http://links.lww.com/INF/B563>).

Patients with bacteremia had longer fever duration before admission and supplemental oxygen requirement during hospitalization than those without a blood culture obtained. This was not true when compared with those with a negative blood culture (Table, Supplemental Digital Content 2, <http://links.lww.com/INF/B563>). Median length of stay was longer in

children with bacteremia than those with negative blood cultures and those without blood cultures.

Most children underwent laboratory evaluation, the most common of which was a white blood cell count in 480 (73.0%) children. C-reactive protein was obtained in 153 (23.3%) patients, and an erythrocyte sedimentation rate was obtained in 54 (8.2%) patients. Patients with bacteremia had higher median C-reactive protein values than those who had a negative culture or no blood culture. However, no differences were found in median white blood cell counts or erythrocyte sedimentation rate values across groups (Table, Supplemental Digital Content 2, <http://links.lww.com/INF/B563>).

Differences across age groups for findings on initial chest radiograph were not significant. Three-fourths of all children with metastatic complications had bacteremia compared with 6–10% of children without metastatic complications (Table 1). In addition, bacteremia was more common among children who underwent a pleural drainage procedure than those who did not have a pleural drainage procedure (Table 1).

Microbiologic Features

The most common pathogen was *S. pneumoniae*, which was identified in 19 (73.1%) of 26 children with bacteremia and in 19 (5.1%) of 369 of patients with CAP who had a blood culture obtained. The remaining pathogens causing bacteremia included *H. influenzae* (n = 1) and *Staphylococcus aureus* (n = 6); 3 of the 6 *Staphylococcus aureus* isolates were methicillin-resistant. Penicillin susceptibilities were available for 16 (84.2%) pneumococcal isolates; 75% were penicillin susceptible, 6.3% were intermediate and 18.8% were resistant. Two of the 3 isolates that were penicillin resistant were also resistant to third-generation cephalosporins. All isolates tested were susceptible to levofloxacin, but 2 (18%) of 11 isolates were resistant to meropenem. All methicillin-resistant *Staphylococcus aureus* isolates were susceptible to clindamycin and vancomycin. The *H. influenzae* isolate did not exhibit β -lactamase production.

Eleven (9.8%) of 112 pleural fluid cultures were positive. Pleural fluid isolates included *S. pneumoniae* (n = 8) and *Staphylococcus aureus* (n = 3); 2 of the *Staphylococcus aureus* pleural fluid isolates were methicillin resistant. Thirty-three patients had both blood and pleural fluid cultures performed; 20 (60.6%) had negative results for both pleural fluid and blood culture, whereas 6 (18.2%) patients had positive pleural fluid and negative blood cultures. Of the remaining patients, both blood and pleural fluid were positive in 3 (9.1%) and blood culture alone revealed a pathogen in 4 (12.1%) of patients.

Hospital Variation

The proportion of children with blood cultures obtained ranged from 42.5% to 65.0% of CAP admissions across hospitals (Table 2). In addition, pneumonia sequelae and pleural drainage procedures were low and similar across institutions. Discharge antibiotic therapy varied across the 4 hospitals with a mean of 55.8% (range: 27.6–77.8%) receiving a broad spectrum agent. In addition, while most patients received enteral antibiotics at discharge, there was a significant variation across hospitals ranging from 82.0% to 96.7%; the remaining patients received parenteral therapy in the home setting (Table 2).

Discharge Antibiotic Therapy

Overall, 591 patients (89.8%) were discharged with enteral therapy, 22 (3.3%) received parenteral therapy and 45 (6.8%) were discharged without antibiotic therapy. The median length of stay was longer for children discharged without antibiotic therapy (110 hours [IQR: 45–290]) compared with patients discharged with antibiotic therapy (51 hours [IQR:

38–87]; $P < 0.001$). In addition, most patients with bacteremia (96%) were discharged home with antibiotic therapy. Patients with bacteremia or any pneumonia-related sequelae were more likely to be discharged home with parenteral therapy than those with uncomplicated pneumonia (29.5% versus 1.5%, $P < 0.001$). Furthermore, patients with bacteremia were more likely to be discharged with a broad spectrum agent either parenterally or orally administered (80.0% versus 57.7%, $P = 0.026$).

Overall, 10 (38.5%) of 26 patients with bacteremia had their therapy broadened, 7 (27%) of 26 were narrowed and 9 (34.6%) of 26 had no change based on culture results (Table, Supplemental Digital Content 1, <http://links.lww.com/INF/B562>). Of the patients for whom susceptibilities were available, 6 (26.1%) of 23 received a narrower spectrum of antibiotic therapy at discharge, although the narrowest effective antibiotic was not used in 1 case (ie, case 12 in which the patient could have been discharged with amoxicillin instead of a third-generation cephalosporin for a penicillin susceptible pneumococcus; Table, Supplemental Digital Content 1, <http://links.lww.com/INF/B562>). Blood culture–directed changes in therapy occurred in 37.5% (all broadened) of patients who were determined to have a contaminated culture ($n = 8$). Of the 6 patients with contaminated culture results who received an antibiotic at discharge, only one-third received narrowest therapy possible.

DISCUSSION

We determined the prevalence of bacteremia in children hospitalized with CAP across 4 children's hospitals in the conjugate vaccine era. Blood cultures were obtained in only slightly more than half of the study population. Bacteremia was identified in 3.9% overall, and 7.1% of those who had a blood culture obtained, which is higher than previously reported from single-center studies of children in the hospital and outpatient settings.^{4,6,17} *Pneumococcus* was the predominant pathogen identified in this study, consistent with previous studies in both the pre- and postvaccine eras.^{10,12} Pleural fluid examination identified an additional 6 organisms that were not found on blood culture, increasing the yield to 8.7% in patients who had a blood culture obtained.

While the prevalence of bacteremia was low overall, it was higher in children with a longer duration of fever, elevated C-reactive protein, complicated pneumonia and metastatic complications, adding data to the current evidence that patients with moderate-to-severe disease are more likely to have a positive blood culture than children with mild disease and have the potential to benefit from pathogen-directed therapy. In addition, there were 6 (23.1%) patients with bacteremia whose pneumonia was uncomplicated at admission that evolved to become complicated over time. This highlights the difficulty in determining risk of bacteremia in the patient who appears to have a simple pneumonia at admission. Interestingly, only 1 of these patients had the pathogen identified on pleural fluid. This finding underscores the importance of obtaining a blood culture at admission, as these patients were initially classified as uncomplicated. If blood cultures were only directed at those with complicated pneumonia at presentation, the causative pathogen for 5 of these patients would have been missed.

Contamination rates were low across institutions with a mean of 2% (range: 1–3.8%), which is consistent with other studies that have examined the contamination rates in outpatient settings. Herz et al¹⁸ reported a blood culture contamination rate of 1.8% in their study evaluating the prevalence of bacteremia before and after the pneumococcal vaccine era using a large outpatient database. Conversely, contamination rates have been reported to be as high as 8%, making a false-positive result more likely than a true positive result in some studies.^{6,17,19} However, in this study, the positive blood culture rate was higher than the contamination rate in those who had a blood culture obtained.

One-quarter of patients for whom a pathogen was identified and susceptibility results were available had a change in management, with narrowing of antibiotic therapy at hospital discharge. While these changes were typically made to target therapy based on the culture result, 1 of these could have been narrowed even further. Furthermore, an additional 10 patients could have safely been narrowed by either decreasing the number of agents used (eg, case 2: clindamycin alone instead of clindamycin plus a third-generation cephalosporin for methicillin-resistant *Staphylococcus aureus*) or by using the most narrow agent available (eg, case 5: amoxicillin instead of amoxicillin-clavulanate for a susceptible pneumococcus). These findings provide information regarding optimal narrowing and further opportunities to narrow therapy for patients with bacteremia in the inpatient setting. While previous work has suggested that positive blood culture results have had little or no impact on clinical management due to few positive cultures, these studies were performed in the emergency department or outpatient setting, and as such may not be easily generalized to the inpatient population.^{4–6,17}

Variability in patient management was noted across hospitals in percentage of patients with a blood culture obtained, method of antibiotic delivery and antibiotic spectrum at hospital discharge. These findings are consistent with other studies that have found significant variation among practitioners and across sites.^{15,20} This highlights not only the importance of national guideline development but also the value of monitoring guideline adherence.

There are several limitations to this study. First, the data are retrospective and subject to availability in the medical record. Second, it is possible that the prevalence of bacteremia was overestimated because culture collection was at the discretion of the provider and may have been preferentially obtained in patients who were more ill at presentation, and thus more likely to have bacteremia. The reasons for blood cultures being obtained in slightly over half of the population are unclear, but may be related to more ill appearance, or in some cases pretreatment with antibiotics and a common thought process that bacteremia is unlikely in the pre-treatment setting. Third, decisions regarding appropriateness of blood culture–directed changes in management were based solely on spectrum of antibiotic coverage relative to *S. pneumoniae* and *Staphylococcus aureus*, thus excluding a determination of broadening or narrowing of anaerobic (eg, clindamycin) or Gram-negative coverage (eg, ceftriaxone) in that context. However, as nearly all pathogens were identified as either *S. pneumoniae* or *Staphylococcus aureus*, decisions about the coverage provided against other pathogens are less relevant. Finally, the data from this study were obtained from large children’s hospitals that provide tertiary care, and as such may not be able to be generalized to smaller community-based hospitals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE 1

Prevalence of Bacteremia in Patients With Blood Culture Obtained

	N	Percent Bacteremia (95% Confidence Interval)	P
All patients	369	7.1 (4.4–9.7)	
Age (yr)			
<1	63	4.9 (1.2–14.6)	0.66
1–5	195	8.2 (4.3–12.1)	
>5–12	92	4.4 (0.1–8.5)	
>12	19	5.3 (0.0–15.3)	
Initial chest radiograph			
No radiograph	2	0.0 (0.0–0.0)	
No infiltrate	60	11.7 (3.5–19.8)	0.13
Infiltrate present	307	6.2 (3.4–8.9)	
Pneumonia complications			
Uncomplicated	325	5.9 (3.3–8.4)	<0.01
Complicated*	40	10.0 (0.7–19.3)	
Metastatic complication [†]	4	75.0 (32.5–100.0)	
Pleural drainage procedure			
No	336	5.7 (3.1–8.1)	<0.01
Yes	33	21.2 (8.9–38.9)	
Pleural fluid culture [‡]			
Negative	24	16.7 (1.7–31.6)	0.30
Positive	9	33.3 (2.5–64.1)	

* Patients with complicated pneumonia at presentation including those with or without extrapulmonary complications: systemic inflammatory response syndrome, cardiovascular dysfunction, neurologic dysfunction, hematologic dysfunction, renal dysfunction and hepatic dysfunction.

[†] Metastatic complications included pyomyositis, septic arthritis, osteomyelitis and abscess with or without complicated pneumonia.

[‡] Pathogens include *S. pneumoniae*, *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus*.

TABLE 2

Blood Culture, Pneumonia Complications and Pleural Drainage Rates by Hospital

	Hospital 1	Hospital 2	Hospital 3	Hospital 4	P
N (%)	181 (27.5)	167 (25.4)	167 (25.4)	143 (21.7)	
No blood culture performed (N = 289)	75 (41.4)	96 (57.5)	68 (40.7)	50 (35.0)	<0.01
Blood culture performed (N = 369)					
Bacteremia	5 (4.7)	5 (7.0)	10 (10.1)	6 (6.5)	0.637
Contaminated	4 (3.8)	1 (1.4)	1 (1.0)	2 (2.2)	
Negative	97 (91.5)	65 (91.6)	88 (88.9)	85 (91.4)	
Pneumonia complications					
Uncomplicated	172 (95.0)	152 (91.0)	153 (91.6)	124 (86.7)	0.143
Complicated*	8 (4.4)	13 (7.8)	14 (8.4)	16 (11.2)	
Metastatic complication [†]	1 (0.6)	2 (1.2)	0 (0.0)	3 (2.1)	
Pleural drainage procedure	11 (6.1)	8 (4.8)	7 (4.2)	15 (10.5)	0.101
Discharge antibiotic					
None	5 (2.8)	18 (10.8)	11 (6.6)	11 (7.7)	
Enteral	175 (96.7)	137 (82.0)	153 (91.6)	126 (88.1)	0.004
Parenteral	1 (0.6)	12 (7.2)	3 (1.8)	6 (4.2)	
Discharge antibiotic					
None	5 (2.8)	18 (10.8)	11 (6.6)	11 (7.7)	<0.001
Broad	50 (27.6)	72 (43.1)	130 (77.8)	107 (74.8)	
Narrow	126 (69.6)	77 (46.1)	26 (15.6)	25 (17.5)	

* Patients with complicated pneumonia at presentation including those with or without extrapulmonary complications: systemic inflammatory response syndrome, cardiovascular dysfunction, neurologic dysfunction, hematologic dysfunction, renal dysfunction and hepatic dysfunction.

[†] Metastatic complications included pyomyositis, septic arthritis, osteomyelitis and abscess with or without complicated pneumonia.