RESEARCH ARTICLE

Predictors of Bacteremia in Children Hospitalized With Community-Acquired Pneumonia

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ABSTRACT

BACKGROUND AND OBJECTIVES: The yield of blood cultures in children hospitalized with community-acquired pneumonia (CAP) is low. Characteristics of children at increased risk of bacteremia remain largely unknown.

METHODS: We conducted a secondary analysis of a retrospective cohort study of children aged 3 months to 18 years hospitalized with CAP in 6 children's hospitals from 2007 to 2011. We excluded children with complex chronic conditions and children without blood cultures performed at admission. Clinical, laboratory, microbiologic, and radiologic data were assessed to identify predictors of bacteremia.

RESULTS: Among 7509 children hospitalized with CAP, 2568 (34.2%) had blood cultures performed on the first day of hospitalization. The median age was 3 years. Sixty-five children with blood cultures performed had bacteremia (2.5%), and 11 children (0.4%) had bacteremia with a penicillin-nonsusceptible pathogen. The prevalence of bacteremia was increased in children with a white blood cell count $>20 \times 10^3$ cells per μL (5.4%; 95% confidence interval 3.5%–8.1%) and in children with definite radiographic pneumonia (3.3%; 95% confidence interval 2.4%–4.4%); however, the prevalence of penicillin-nonsusceptible bacteremia was below 1% even in the presence of individual predictors. Among children hospitalized outside of the ICU, the prevalence of contaminated blood cultures exceeded the prevalence of penicillin-nonsusceptible bacteremia.

CONCLUSIONS: Although the prevalence of bacteremia is marginally higher among children with leukocytosis or radiographic pneumonia, the rates remain low, and penicillin-nonsusceptible bacteremia is rare even in the presence of these predictors. Blood cultures should not be obtained in children hospitalized with CAP in a non-ICU setting.

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Consensus guidelines from the Pediatric Infectious Diseases Society (PIDS) and the Infectious Diseases Society of America (IDSA) recommend obtaining blood cultures in children hospitalized with moderate to severe (particularly those with complicated) community-acquired pneumonia (CAP),[1] although the term "moderate to severe" is not strictly defined. The guidelines state that identification of a pathogen allows for targeted antimicrobial therapy and may inform future vaccination efforts. Although the recommendation for blood cultures was labeled as strong, the quality of the evidence supporting this recommendation was rated as low.[1] Nonetheless, after the publication of these guidelines, efforts were implemented to increase blood culture use among children hospitalized with CAP.[2]

In studies of children hospitalized with CAP, authors have reported a prevalence of bacteremia ranging from 1.4% to 11.4%,[3–13] with higher percentages in children with parapneumonic effusion.[6,11,12] However, most of these studies were performed before widespread use of pneumococcal conjugate vaccines (PCVs). Authors of several studies conducted in the post-PCV era have suggested that the prevalence of bacteremia is on the lower end of this range.[5,6,13]

Our group recently reported a prevalence of bacteremia of 2.5% in a cohort of generally healthy children hospitalized with CAP who had blood cultures obtained, with only 0.4% harboring a pathogen not susceptible to penicillin.[9] Additionally, the prevalence of contaminant blood cultures in the cohort was more than double the prevalence of bacteremia from a pathogen not susceptible to penicillin. These findings argue against the routine performance of blood cultures in all children hospitalized with CAP. Given our finding of the low yield of blood culture in children hospitalized with CAP, we conducted a secondary analysis to identify the characteristics of children at higher risk of bacteremia. Our overarching goal was to determine if blood cultures were warranted in specific subsets of children hospitalized with CAP.

METHODS

Study Design

This was a retrospective cohort study using the Pediatric Health Information System Plus (PHIS+) database, which includes data from 6 institutions: Boston Children's Hospital (Boston, MA), Children's Hospital of Philadelphia (Philadelphia, PA), the Children's Hospital of Pittsburgh (Pittsburgh, PA), Cincinnati Children's Hospital Medical Center (Cincinnati, OH), Primary Children's Hospital (Salt Lake City, UT), and Seattle Children's Hospital (Seattle, WA). PHIS+ augmented the administrative and billing data available in PHIS with laboratory, microbiologic, and radiographic results data.[14] This study was approved by the institutional review board at 1 of the participating institutions.

Study Population

We included children aged 3 months to 18 years hospitalized with CAP between January 1, 2007, and December 31, 2011, in whom a blood culture was obtained on the initial or second day of hospitalization. CAP was defined by a primary *International Classification of Diseases, Ninth Revision* (ICD-9) discharge diagnosis code for pneumonia (480–483, 485–487) or a primary ICD-9 discharge diagnosis code for pleural effusion (510.0, 510.9, 511.0, 511.1, 511.9) with a secondary diagnosis code for pneumonia.[9,15,16] We did not require radiographic evidence of pneumonia for inclusion in the study. We excluded children transferred into the study institution, because these children may have undergone laboratory and radiographic testing before transfer. We also excluded children with complex chronic conditions on the basis of a previously described algorithm.[16,17]

Patient Characteristics and Laboratory Testing

We recorded patient age (≤1, 2–4, 5–9, 10–18 years), sex, and race and/or ethnicity (non-Hispanic white, non-Hispanic African American, Hispanic, Asian American, other); comorbid diagnoses of asthma (ICD-9 code: 493.x), bronchiolitis (487.0, 487.1, or 488.11) and influenza (079.6, 466.19, 466.11, 480.1); and laboratory data for white blood cell (WBC) count, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) using standardized units across institutions.

Radiographic Pneumonia

The PHIS+ database includes final radiograph interpretations by radiologists as part of routine clinical care. One of 4 study investigators reviewed each radiograph report to determine the presence or absence of radiographic pneumonia, presence or absence of pleural effusion, and size of pleural effusion (small or trivial or medium or large). The presence of radiographic pneumonia was determined by using a previously defined classification scheme and categorized as definite radiographic pneumonia, equivocal for pneumonia, no pneumonia, or unclear on the basis of the radiographic report.[18,19] For radiographs revealing definite radiographic pneumonia, the pattern of pneumonia was ascertained (focal or lobar, interstitial or diffuse, or not specified). Pleural effusion was determined by radiologist declaration of effusion presence, and size (small or trivial or moderate or large) if described in the report. Radiographs with reports describing blunting of the costophrenic angle or reports stating "cannot rule out pleural effusion" were considered to have a small pleural effusion present. Any effusion with a description of layering or loculation was considered to be a moderate or large size. Ambiguous cases of pneumonia, effusion presence, or subtype were resolved by group consensus. We classified a child as having complicated pneumonia at presentation if there was a moderate or large pleural effusion on the admission chest radiograph or if the patient underwent a surgical chest drainage procedure on the initial or subsequent day of hospitalization. We defined a chest drainage procedure by an ICD-9-CM procedure code for thoracentesis (34.91), chest tube placement (34.03), video-assisted thoracoscopic surgery (34.21), or thoracotomy (34.02, 34.09).

Outcome Measure

The primary outcome was the presence of bacteremia based on pathogen detection in the initial blood culture. Bacteria were labeled as pathogens or contaminants

according to a previously defined classification scheme.[5,9] Blood cultures with growth of only a contaminant were classified as being negative for pneumonia. For each case of bacteremia, we assessed whether the pathogen was susceptible or nonsusceptible to penicillin, including "intermediate susceptibility" as nonsusceptible.[5,9] We classified *Streptococcus pneumoniae* isolates as penicillin susceptible if the minimum inhibitory concentration was <2 μg/mL.[1,9] We chose penicillin as our susceptibility measure because ampicillin is recommended by the PIDS and IDSA guideline as first-line treatment of uncomplicated CAP in children.[1]

Our goal was to identify factors associated with bacteremia at the time of hospital admission because this is often when clinicians make the decision to obtain or not obtain a blood culture. Thus, we limited our analyses to diagnostic studies and procedures performed on the initial or second calendar day, and within this period, we limited our analyses to the first instance of each study performed. We included the second hospital day as representative of testing performed at admission given the fact that the PHIS+ database contains data delineated by date but not time, and some patients present to the hospital in evening hours. We applied the same timing restriction to the definitions of performance of pleural drainage procedures and ICU admission.

Data Analysis

Demographic, clinical, laboratory, and radiographic characteristics were compared between children with and without bacteremia by using χ^2 and Wilcoxon rank-sum tests as appropriate. Receiver operating characteristic (ROC) curves were generated for the evaluation of the performance of laboratory tests (WBC, ESR, CRP) for the identification of bacteremia, and the area under the curve (AUC) calculated.

After identifying characteristics associated with bacteremia on bivariate testing at a level of $P < .10$ and limiting our analysis to children with complete data for all candidate predictors, we constructed a multivariable model for the prediction of bacteremia using generalized linear mixed-effects models with random intercepts for each hospital. For the WBC count, we used recursive partitioning (ie, classification and regression trees) to identify the best discriminatory value to differentiate children with and without bacteremia. We calculated the prevalence of bacteremia, penicillin-nonsusceptible bacteremia, and contaminated blood cultures in the presence of each candidate predictor. All analyses were performed by using SAS version 9.4 (SAS Institute, Inc, Cary, NC).

RESULTS

During the 5-year study period, 14 166 children were hospitalized with CAP at the participating institutions. After excluding patients with complex chronic conditions ($n = 5376$) and those transferred from another institution ($n = 1281$), 7509 children remained. A total of 2568 children (34.2%) had a blood culture obtained on the initial or second day of hospitalization. The median age of children in the cohort was 3 years (interquartile range [IQR]: 1–6 years) (Table 1).

As reported in our previous study, 65 (2.5%) of the 2568 children with blood cultures obtained on admission had bacteremia.[9] The

TABLE 1 Characteristics of Children Hospitalized With CAP Stratified by the Presence or Absence of Bacteremia

	Overall ($N = 2568$)	Bacteremia ($n = 65$; 2.5%)	No Bacteremia ($n = 2503$; 97.5%)	*P*
Age, median (IQR), y	3 (1–6)	3 (1–5)	3 (1–6)	.54
≤1	795 (31.0)	19 (29.2)	776 (31.0)	—
2–4	887 (34.5)	29 (44.6)	858 (34.3)	—
5–9	579 (22.5)	12 (18.5)	567 (22.7)	—
10–18	307 (12)	5 (7.7)	302 (12.1)	—
Female, *n* (%)	1254 (48.8)	32 (49.2)	1222 (48.8)	.95
Race and/or ethnicity, *n* (%)				
Non-Hispanic white	1374 (58.7)	35 (59.3)	1339 (58.7)	.73
Non-Hispanic African American	556 (23.8)	17 (28.8)	539 (23.6)	—
Hispanic	287 (12.3)	5 (8.5)	282 (12.4)	—
Asian American	103 (4.4)	2 (3.4)	101 (4.4)	—
Other	21 (0.9)	0 (0.0)	21 (0.9)	—
Comorbid conditions, *n* (%)				
Asthma[a]	650 (25.3)	13 (20)	637 (25.4)	.32
Bronchiolitis[b]	320 (12.5)	3 (4.6)	317 (12.7)	.05
Influenza[c]	48 (1.9)	2 (3.1)	46 (1.8)	.47

—, not applicable.
[a] ICD-9 code 493.x.
[b] ICD-9 codes 487.0, 487.1, and 488.11.
[c] ICD-9 codes 079.6, 466.19, 466.11, and 480.1.

most common penicillin-susceptible blood pathogen isolated was *S pneumoniae* ($n = 47$), followed by *Haemophilus influenzae* ($n = 2$), β-hemolytic streptococcus ($n = 2$), *Streptococcus pyogenes* ($n = 2$), and *Moraxella* species ($n = 1$). Eleven children (0.4%) had bacteremia with a pathogen not susceptible to penicillin (Supplemental Table 5). The most common penicillin-nonsusceptible pathogens were *S pneumoniae* ($n = 4$), methicillin-resistant *Staphylococcus aureus* ($n = 3$), methicillin-susceptible *S aureus* ($n = 2$), *Enterobacter aerogenes* ($n = 1$), and *H influenzae* ($n = 1$). Of the 4941 children who did not have blood cultures sent on the first or second day of hospitalization, 96 had blood cultures sent later in their hospital course. Two of these cultures were positive for bacterial growth, both with growth of penicillin-nonsusceptible pathogens.

There were no significant differences between the children with bacteremia and those without with respect to age, sex, race, or codiagnoses (Table 1). Candidate clinical, laboratory, and radiographic predictors of bacteremia are shown in Table 2. Children with bacteremia had a higher median admission WBC count than those without bacteremia (17.5×10^3 cells per μL vs 12.4×10^3 cells per μL, respectively; $P < .01$). CRP and ESR were also higher in

TABLE 2 Univariate Predictors of Bacteremia

	Overall ($N = 2568$)	Bacteremia ($n = 65$; 2.5%)	No Bacteremia ($n = 2503$; 97.5%)	*P*
Laboratory results				
WBC obtained, *n* (%)	2392 (93.1)	60 (92.3)	2332 (93.2)	.79
WBC, median $\times 10^3$ cells per μL (IQR)	12.5 (8.4–18.4)	17.5 (10–23.9)	12.4 (8.4–18.2)	<.01
CRP obtained, *n* (%)	905 (35.2)	32 (49.2)	873 (34.9)	.02
CRP, median mg/dL (IQR)	8.4 (3.4–22.1)	23.5 (17.8–30.8)	8 (3.2–21.6)	<.01
ESR obtained, *n* (%)	393 (15.3)	12 (18.5)	381 (15.2)	.47
ESR, median mm/h (IQR)	59 (34–87)	75 (67.5–93)	58 (32–86)	.05
Radiographic findings, *n* (%)				
CXR obtained on d 1	1956 (76.2)	49 (75.4)	1907 (76.2)	.88
CXR report available	1953 (76.1)	49 (75.4)	1904 (76.1)	.89
Radiographic findings, *n* (%)				<.01
Definite pneumonia	1300 (66.5)	44 (89.8)	1256 (65.9)	
Equivocal for pneumonia	442 (22.6)	2 (4.1)	440 (23.1)	
No pneumonia	204 (10.4)	3 (6.1)	201 (10.5)	
Unclear from report	10 (0.5)	0 (0.0)	10 (0.5)	
Pattern of definite pneumonia ($n = 1300$), *n* (%)				.88
Focal or lobar	1165 (89.6)	41 (93.2)	1124 (89.5)	
Interstitial or diffuse	2 (0.2)	0 (0.0)	2 (0.2)	
Not specified	133 (10.2)	3 (6.8)	129 (10.3)	
Pleural effusion present, *n* (%)				<.01
Yes	456 (23.3)	19 (38.8)	437 (23.0)	
No	1479 (75.7)	28 (57.1)	1451 (76.2)	
Unclear	18 (0.9)	2 (4.1)	16 (0.8)	
Pleural effusion size ($n = 456$), *n* (%)				.69
Small or trivial	269 (59.0)	13 (68.4)	256 (58.6)	
Medium or large	153 (33.6)	5 (26.3)	148 (33.9)	
Unspecified	34 (7.5)	1 (5.3)	33 (7.6)	
Hospital course				
Length of stay, median (IQR), d	2 (2–4)	4 (3–10)	2 (2–4)	<.01
Admitted to ICU, *n* (%)	293 (11.4)	14 (21.5)	279 (11.1)	<.01
Chest tube drainage procedure,[a] *n* (%)	148 (5.8)	8 (12.3)	140 (5.6)	.02
Complicated pneumonia,[b] *n* (%)	226 (8.8)	10 (15.4)	216 (8.6)	.06
Died, *n* (%)	1 (0)	1 (1.5)	0 (0.0)	<.01

CXR, chest radiograph.

[a] ICD-9-CM procedure code for thoracentesis (34.91), chest tube placement (34.03), video-assisted thorascopic surgery (34.21), or thoracotomy (34.02, 34.09) occurring on initial or second hospital d.

[b] Composite definition including moderate or large pleural effusion on initial CXR and/or chest drainage procedure on initial or second hospital d.

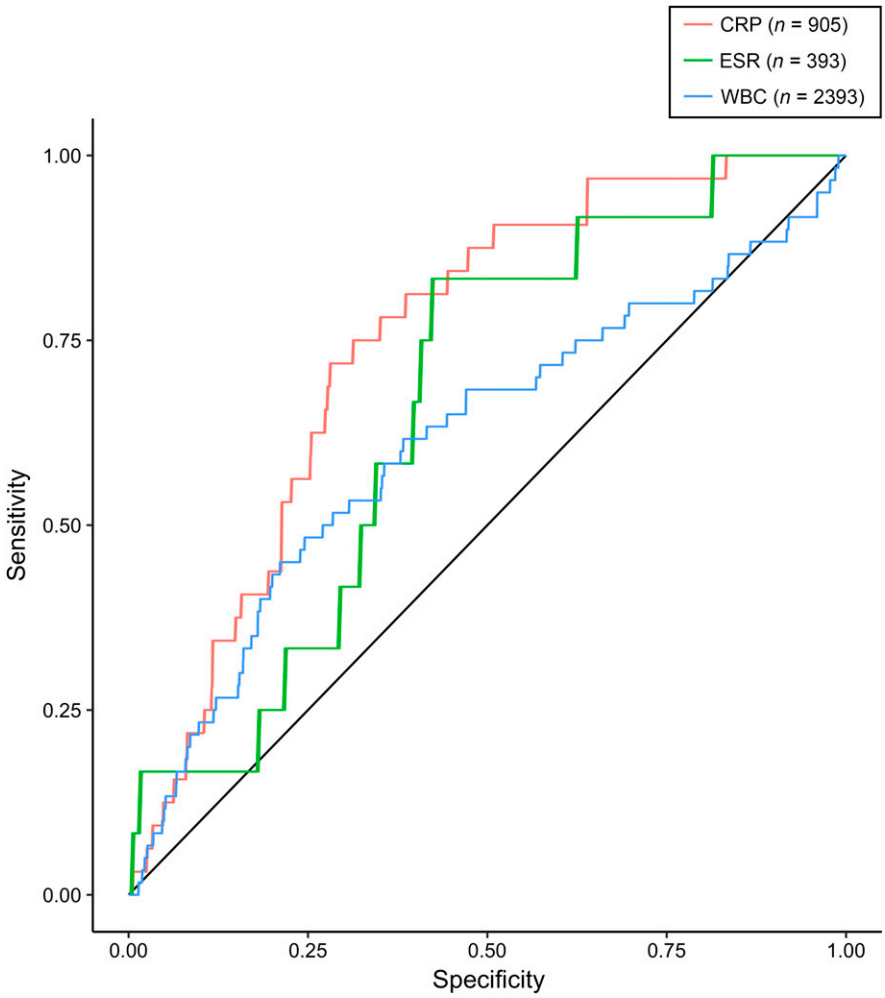

FIGURE 1 ROC curves for WBC (AUC: 0.62), CRP (AUC: 0.75), and ESR (AUC: 0.67) for the prediction of bacteremia.

children with bacteremia but were only obtained in 35% and 15% of patients, respectively. The area under the ROC curve was higher for CRP (AUC = 0.75) than for WBC (AUC = 0.62) and ESR (AUC = 0.67) (Fig 1). Children with bacteremia were more likely to have definite radiographic pneumonia on admission chest radiograph (89.8% vs 65.9%; $P < .01$) than children without bacteremia. Of children with definite radiographic pneumonia, 89.6% had a lobar infiltrate pattern (Table 2). Children with bacteremia had a higher prevalence of complicated pneumonia on admission (15.4% vs 8.6%; $P = .06$) than children without bacteremia. Children with bacteremia had longer lengths of stay (4 days vs 2 days; $P < .01$) and were more likely to be admitted to an ICU (21.5% vs 11.1%; $P < .01$) than children without bacteremia.

Radiographic data were available for 1953 patients (76.1% of the cohort) and WBC data for 2392 patients (93.1%); a total of 1849 patients (72.0%) had data for both. The prevalence of bacteremia in this cohort of 1849 patients with complete data was 2.4% (95% confidence interval [CI] 1.8%–3.2%). Using recursive partitioning, a WBC threshold of 20.0 $\times$ $10^3/\mu$L best discriminated children with and without bacteremia. Among children with a WBC >20, the prevalence of bacteremia was 5.4% compared to 1.6% among children with a WBC ≤20 ($P < .01$).

The prevalence of bacteremia, penicillin-nonsusceptible bacteremia, and contaminated blood cultures in children with individual and combined predictors are shown in Table 3. Bacteremia was more common among children with a WBC >20 $\times$ 10^3 cells per μL (prevalence of bacteremia: 5.4%; 95% CI 3.5%–8.1%) and among children with definite radiographic pneumonia (prevalence of bacteremia: 3.3%; 95% CI 2.4%–4.4%). The prevalence of bacteremia was highest among children with a combination of a WBC >20 $\times$ 10^3 cells per μL and definite radiographic pneumonia (prevalence of bacteremia: 6.1%; 95% CI 4.0%–9.4%) and among children with a combination of a WBC >20 $\times$ 10^3 cells per μL and ICU admission (prevalence of bacteremia: 6.0%, 95% CI 3.2%–11.1%). The prevalence of penicillin-nonsusceptible bacteremia ranged from 0% to 2.1% and the prevalence of contaminated cultures from 0% to 1.6% across groups.

In multivariable analysis, the presence of definite radiographic pneumonia (adjusted odds ratio [aOR]: 4.8; 95% CI 2.1–10.9) and WBC >20 $\times$ 10^3 cells per μL (aOR: 3.2; 95% CI 2.0–5.2) were independently associated with bacteremia (Table 4). When the multivariable analysis was restricted to patients with definite radiographic pneumonia, children with a WBC >20 $\times$ 10^3 cells per μL were more likely to have bacteremia (aOR: 3.6; 95% CI 1.9–6.5) (Supplemental Table 6).

Among the subset of children hospitalized in a non-ICU setting ($n = 1597$), the prevalence of bacteremia was 2.2% (95% CI 1.6–3.0); 4 children (0.25%) had growth of a pathogen not susceptible to penicillin, and 19 children (1.2%) had growth of a contaminant.

DISCUSSION

In this large multicenter study of generally healthy children hospitalized with CAP, we identified several factors associated with a higher prevalence of bacteremia, including a WBC >20 $\times$ 10^3 cells per μL, definite radiographic pneumonia (predominantly lobar), complicated pneumonia, and ICU admission. However, leukocytosis and definite radiographic pneumonia were the only factors independently associated with the presence of bacteremia in

TABLE 3 Prevalence of Bacteremia, Penicillin-Nonsusceptible Bacteremia, and Contaminated Blood Cultures Among Children Hospitalized With CAP

Predictor	Prevalence, *n*	Bacteremia, *n*, % (95% CI)	Penicillin-Nonsusceptible Bacteremia, *n*, % (95% CI)	Contaminated Blood Culture, *n*, % (95% CI)
Single predictor				
WBC >20	390	21, 5.4 (3.5–8.1)	3, 0.77 (0.26–2.2)	2, 0.51 (0.14–1.9)
ICU admission	252	9, 3.6 (1.9–6.7)	3, 1.2 (0.41–3.4)	4, 1.6 (0.62–4.0)
Definite radiographic pneumonia	1227	40, 3.3 (2.4–4.4)	7, 0.57 (0.28–1.2)	14, 1.1 (0.68–1.9)
Complicated pneumonia[a]	175	5, 2.9 (1.2–6.5)	1, 0.57 (0.1–3.2)	1, 0.57 (0.10–3.2)
Two predictors				
WBC >20 + ICU admission	45	3, 6.7 (2.3–17.9)	0, 0 (0–7.9)	0, 0 (0–7.9)
Complicated pneumonia + ICU admission	47	3, 6.4 (2.2–17.2)	1, 2.1 (0.38–11.1)	0, 0 (0–7.6)
Definite radiographic pneumonia + WBC >20	310	19, 6.1 (4.0–9.4)	3, 0.97 (0.33–2.8)	2, 0.65 (0.18–2.3)
Definite radiographic pneumonia + ICU admission	149	9, 6.0 (3.2–11.1)	3, 2.0 (0.69–5.8)	2, 1.3 (0.37–4.8)
Definite radiographic pneumonia + complicated pneumonia	159	5, 3.1 (1.4–7.1)	1, 0.63 (0.11–3.5)	1, 0.63 (0.11–3.5)
WBC >20 + complicated pneumonia	59	1, 1.7 (0.3–9.0)	0, 0 (0–6.1)	0, 0 (0–6.1)
Three predictors				
WBC >20 + definite pneumonia + complicated pneumonia	55	1, 1.8 (0.32–9.6)	0, 0 (0–6.5)	0, 0 (0–6.5)
WBC >20 + definite pneumonia + ICU admission	32	3, 9.4 (3.2–24.2)	0, 0 (0–10.7)	0, 0 (0–10.7)
WBC >20 + complicated pneumonia + ICU admission	17	0, 0 (0–18.4)	0, 0 (0–18.4)	0, 0 (0–18.4)
Definite pneumonia + complicated pneumonia + ICU admission	43	3, 7.0 (2.4–18.6)	1, 2.3 (0.41–12.1)	0, 0 (0–8.2)
Four predictors				
WBC >20 + ICU admission + definite radiographic pneumonia + complicated pneumonia	16	0, 0 (0–19.4)	0, 0 (0–19.4)	0, 0 (0–19.4)

Limited to the 1849 children with complete data available. Overall prevalence of bacteremia in the cohort was 2.4% (44 of 1849).

[a] Composite definition including moderate or large pleural effusion on initial chest radiograph and/or chest drainage procedure on initial or second hospital d.

TABLE 4 Multivariate Prediction Model of Bacteremia

Patient Characteristic	Unadjusted OR (95% CI)	aOR[a] (95% CI)
Definite radiographic pneumonia	5.2 (1.9–14.6)	4.8 (2.1–10.9)
Complicated pneumonia[b]	1.2 (0.5–3.2)	0.7 (0.3–1.5)
WBC >20	3.6 (1.9–6.5)	3.2 (2.0–5.2)
ICU admission	1.7 (0.8–3.5)	2.0 (0.8–5.0)

Limited to the 1849 patients with complete data available for all candidate predictors.
[a] Model included variables present on admission and significant in bivariate testing at the level of $P < .10$.
[b] Composite definition including moderate or large pleural effusion on initial chest radiograph and/or chest drainage procedure on initial or second hospital d.

a multivariable analysis. Furthermore, the prevalence of bacteremia with penicillin-nonsusceptible pathogens was below 1% in the presence of any individual predictor, and in some groups, it was lower than the prevalence of contaminated blood cultures.

PIDS and IDSA guidelines recommend obtaining blood cultures in children hospitalized with moderate to severe CAP. This recommendation is classified as strong, although it is based on low-quality evidence.[1] Publication of these guidelines led to efforts to increase the proportion of children hospitalized with CAP who have blood cultures obtained.[2] However, authors of multiple recent studies suggest that the yield of blood cultures in children hospitalized with CAP is low.

Many of the previous studies examining the prevalence of bacteremia in children with CAP were conducted before widespread use of PCVs. In those studies, the prevalence of bacteremia ranged from 1% to 11% and was as high as 27% in children with empyema.[3,4,8,12] In a study of 877 children diagnosed with CAP in the emergency department between 2006 and 2007, blood cultures were obtained in 291 children, of whom 2.1% had bacteremia.[6] The prevalence of bacteremia was 2.6% in the subset of children with an infiltrate on chest radiograph and 13% in the subset of children with complicated pneumonia, defined as lung abscess, empyema, lung necrosis, or bronchopleural fistula.[6] The observed prevalence of bacteremia among children with complicated pneumonia was lower in our study, which may relate to our assessment of complicated pneumonia only at the time of at admission (correlating to the timing of the blood culture), to our definition of complicated pneumonia (inclusion of moderate or large effusion without chest tube drainage), or to changes in the epidemiology of bacterial pneumonia over time.

Although we observed that bacteremia was more common among children with leukocytosis and definite radiographic pneumonia, we recommend against the routine performance of a complete blood count and blood culture in the majority of children hospitalized with CAP, even those with lobar pneumonia. When faced with the decision of whether to obtain a blood culture in a child hospitalized with CAP, the clinician must consider 2 questions. First, how likely is it that blood culture results will lead to a change in management? Guidelines recommend the use of ampicillin as empirical therapy in children hospitalized outside of the ICU with uncomplicated CAP.[1] Identifying a blood pathogen susceptible to penicillin would not necessitate a change in management, and thus blood cultures in this group of children are of low utility unless they identify a penicillin-nonsusceptible pathogen. In our study, the prevalence of penicillin-nonsusceptible bacteremia was low; on the basis of our data, 400 blood cultures would need to be obtained from children admitted to a non-ICU setting to identify 1 child with penicillin-nonsusceptible bacteremia. The second question a clinician must consider is the potential harm associated with the performance of blood culture. In our cohort of children hospitalized in a non-ICU setting, the prevalence of contaminated blood cultures was 1.2%, whereas the prevalence of nonsusceptible bacteremia was 0.25%. This means that for every 1 child identified as harboring a penicillin-nonsusceptible pathogen, almost 5 additional children would have contaminated cultures. Authors of previous studies suggest that contaminated blood cultures are associated with longer lengths of hospital stay and increased costs.[20,21] Thus, we believe that blood cultures should not be routinely obtained in children hospitalized in a non-ICU setting and should be reserved for children who are not improving after empirical antibiotic therapy. This recommendation is strengthened by our finding that of the 4941 children who did not have cultures drawn initially, only 2 had bacteremia detected later in their hospital course.

Children admitted to the ICU, especially those with complicated pneumonia, still may benefit from the routine performance of blood cultures. In our cohort, the prevalence of bacteremia in children admitted to the ICU with complicated pneumonia was 6.4%, with 2.1% of children growing a pathogen not susceptible to penicillin. Given that these children are critically ill and are typically treated with empirical broad-spectrum antibiotics, a positive blood culture result may allow clinicians to tailor antibiotic therapy, in many cases narrowing coverage if a penicillin-susceptible organism is identified.[1]

Our study findings should be interpreted in the context of several limitations. First, children in this study were all hospitalized at tertiary-care children's hospitals, which care for a greater proportion of children with medical complexity.[22] However, we excluded children with chronic medical conditions, and thus our results are likely generalizable to the majority of children hospitalized with pneumonia in non–tertiary-care centers throughout the United States. Second, our study cohort consisted of children hospitalized for CAP regardless of radiographic findings, and thus children with equivocal radiographic pneumonia as well as those with negative chest radiograph results were included. However, when we restricted our multivariable analysis to children with definite radiographic pneumonia, our findings did not materially differ. Third, the classification of radiographic pneumonia

was based on written reports generated by radiologists during the clinical encounter rather than direct review of the radiographs themselves. However, radiologists generally have high interrater reliability when identifying the presence of alveolar infiltrate,[23] and we applied a systematic approach to our interpretation of radiograph reports. Fourth, although leukocytosis (WBC $\geq$ 20) was strongly associated with bacteremia, not all children hospitalized for CAP had a WBC or other markers such as CRP or ESR obtained. Because of the difficulty associated with the performance of phlebotomy in children, particularly in nonpediatric centers, as well as the discomfort associated with the procedure, clinicians most often obtain both a WBC and blood culture simultaneously. Thus, reliance on the WBC to determine the need for obtaining a blood culture may be limited. Furthermore, although CRP and ESR revealed better discrimination performance than WBC, they were uncommonly performed and thus could not be included as potential predictors of bacteremia. Fifth, our study cohort was restricted to children who had blood cultures obtained. We suspect that the prevalence of bacteremia would be lower among children in whom a blood culture was not performed. Sixth, our multivariable model was restricted to the 72% of children for whom data were available for all candidate predictors, including chest radiography and WBC, which may have introduced selection bias. However, the prevalence of bacteremia did not differ among children with (2.4%) and without (2.5%) data available for all candidate predictors. Finally, the PHIS+ data set spans the introduction of the 13-valent pneumococcal vaccine, and so the current prevalence of bacteremia in CAP may be lower than that found in this study.

CONCLUSIONS

The prevalence of bacteremia was low among a cohort of generally healthy children hospitalized with CAP, and no individual feature or combination of features strongly predicted the presence of bacteremia. The prevalence of bacteremia in children hospitalized in a non-ICU setting was low (2.2%), with only 1 in 400 children demonstrating bacteremia due to a penicillin-nonsusceptible pathogen. Thus, the practice of routine performance of blood cultures in children hospitalized with CAP in a non-ICU setting should be discouraged.

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