Appropriateness of Testing for Serious Bacterial Infection in Children Hospitalized With Bronchiolitis

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KEY WORDS
bacteremia, bacterial infections, bronchiolitis, meningitis, urinary tract infection

ABBREVIATIONS
AAP: American Academy of Pediatrics
CBC: complete blood count
CSF: cerebral spinal fluid
LOS: length of stay
RSV: respiratory syncytial virus
SBI: serious bacterial infection
UA: urinalysis
UTI: urinary tract infection

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abstract

OBJECTIVE: The goal of this study was to evaluate provider practice patterns for evaluation of serious bacterial infection (SBI) in patients hospitalized with bronchiolitis and to assess the association of SBI testing with length of stay and antibiotic use.

DESIGN: This was a retrospective chart review of hospitalized patients <24 months of age with a discharge diagnosis of bronchiolitis from 2 separate study sites during 2004 to 2008. Patient characteristics, laboratory testing, antibiotic use, and clinical outcomes were assessed in relation to SBI testing.

RESULTS: A total of 1233 charts met inclusion criteria. The incidence of urinary tract infections in patients who underwent urine testing was 2.3%. Of the 367 patients undergoing blood culture testing, all 13 positive-result blood cultures were contaminated specimens. There were no cases of meningitis. In total, 64.5% of patients tested for SBI had a blood culture obtained, 45.0% had an urinalysis or urine culture, and 16.3% had a cerebral spinal fluid culture obtained. Of those patients who underwent SBI testing, 53.8% received antibiotics versus 19.1% who did not ($P < .0001$). Length of stay for patients undergoing SBI testing was 3.4 days versus 2.3 days for those without SBI testing ($P < .0001$). There was no significant difference in readmission rates.

CONCLUSIONS: SBI is uncommon in children hospitalized for bronchiolitis, and urinary tract infection is the most common diagnosis. In the evaluation of SBI in bronchiolitis, providers more frequently obtain blood cultures than urinalysis and/or urine cultures. Evaluation for SBI is associated with increased antibiotic use and increased LOS.

Bronchiolitis remains a leading cause of hospitalization for children. Between 1997 and 2006, an estimated 200 000 children were hospitalized for bronchiolitis annually.[1] The American Academy of Pediatrics (AAP) released clinical practice guidelines for the diagnosis and management of bronchiolitis in 2006 that do not recommend the routine use of laboratory or radiographic tests.[2] Younger infants, especially if febrile, however, can present a diagnostic dilemma given the perceived risk of serious bacterial infections (SBIs). Previous research has reported that the risk of SBI in children and infants with bronchiolitis is low, and urinary tract infection (UTI) is the most common concurrent bacterial infection.[3–11] The literature also supports a significantly lower risk of SBI specifically in younger infants, 0 to 3 months of age with bronchiolitis, including those with documented respiratory syncytial virus (RSV).[6–8,10,11] Despite these findings, patients routinely undergo evaluation for bacterial infection.[11–14] The objective of the current study was to evaluate provider practice patterns in SBI testing and to assess the potential association of SBI testing with antibiotic use, length of stay (LOS), and clinical outcomes.

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METHODS

Study Population and Setting

We used data from an existing database designed to assess potential differences in practice behavior among physicians treating children aged 0 to 24 months hospitalized with bronchiolitis before and after the release of the 2006 AAP guidelines.[15] These data were gathered from a retrospective cohort chart review of children hospitalized at 2 academic children's hospitals, Hasbro Children's Hospital at Rhode Island Hospital and University of Missouri Women and Children's Hospital. Data were gathered on children admitted to Hasbro Children's Hospital from calendar years 2005 and 2008. Due to the difference in annual patient census between the 2 participating hospitals, we included children from University of Missouri Children's Hospital from calendar years 2004–2005 and 2007–2008. This addition allowed for a better balance of patient numbers from the 2 institutions. All charts with a primary discharge diagnosis of *International Classification of Diseases, Ninth Revision*, code 466.19 (nonrespiratory syncytial virus bronchiolitis), 466.11 (RSV bronchiolitis), 786.03 (apnea), 465.9 (acute upper respiratory infection), 493.9 (asthma, unspecified), or V73.99 (unspecified viral illness) were screened for inclusion by reviewers. All charts abstracted included a combination of paper-based and electronic medical record data. Charts were excluded if the patient was initially admitted to the ICU. Finally, reviewers excluded patients without either a primary or secondary discharge diagnosis of bronchiolitis (codes 466.11 or 466.19) or documentation of symptoms and clinical findings consistent with bronchiolitis. Clinical findings and symptoms were reviewed from emergency department documentation, admission notes, progress notes from the day of discharge, and, when available, the patient's discharge summary. Clinical findings supporting the diagnosis of bronchiolitis could include: respiratory distress, tachypnea, retractions, wheezing, cough, fever, poor feeding, and associated upper respiratory symptoms including rhinorrhea or nasal congestion. Formal bronchiolitis guidelines before and after 2006 in both hospitals, when present, were not routinely used, were not comprehensive, and did not reflect recommendations of the AAP 2006 guidelines. None of the reviewers were blinded to the nature of the study, and all were supervised directly by the primary researcher at each study site. The study was approved by the institutional review boards at both study sites.

Data Collected

Baseline characteristics assessed included age, gender, history of prematurity, fever present, history of wheeze /reactive airway disease, and tobacco and day care exposures. Researchers also collected data on diagnostic testing for SBI, including complete blood count (CBC), urinalysis (UA), urine culture, blood culture, and cerebral spinal fluid (CSF) testing. Antibiotic use, ICU admission, LOS, and readmission rates were also obtained.

We defined patients who underwent SBI testing as those who had any of the following diagnostic tests performed: CBC, UA, urine culture, blood culture, or CSF culture. We chose to include CBC in the SBI evaluation because we posited that the only reason to decide to obtain a CBC in a child presenting with symptoms consistent with bronchiolitis would be to evaluate for leukocytosis or the immature neutrophils to total neutrophils ratio as a potential indication of infection. SBI was defined as UTI, bacteremia, or meningitis based on microbiologic culture data. Patients were considered positive for UTI if cultures grew a single organism >10 000 CFU/mL. Patients were considered bacteremic if a blood culture result was positive for a definite pathogen (eg, *Escherichia coli, Streptococcus pneumoniae, Staphylococcus aureus*), if blood culture results from 2 separate sites were positive for a low-virulence organism (eg, coagulase-negative staphylococci), or if a sole blood culture result was positive for a low-virulence organism and the patient was <60 days old. All positive blood culture results were reviewed by the principal investigators at each site (Dr McCulloh for site 1 and Dr Koehn for site 2) and differences resolved by consensus. Meningitis was defined as a positive result on CSF culture.

Statistical Analysis

Patient characteristics, laboratory testing, antibiotic use, and clinical outcomes were assessed in relation to SBI testing. χ^2 testing was performed on categorical variables; Mann-Whitney *U* testing was used for continuous variables. Multivariate analysis was performed by using multiple logistic regression. Statistical analysis was performed by using Stata version 11.1 (StataCorp, College Station, TX).

RESULTS

Patient Characteristics of Children Undergoing SBI Testing

A total of 1233 charts met inclusion criteria. Baseline characteristics of patients evaluated for SBI compared with those not evaluated for SBI are listed in Table 1. Patients undergoing SBI evaluation were more likely to be younger. Sixty-one percent of

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TABLE 1 Characteristics of Children Hospitalized for Bronchiolitis According to SBI Evaluation Status

Characteristic	Evaluated for SBI (n = 569)	Not Evaluated for SBI (n = 664)	P
History/admission data			
Mean age, mo (range)	5.29 (0.26–23.9)	5.94 (0.23–23.8)	<.0001
Age ≤30 d	73/569 (12.8%)	47/664 (7.1%)	.001
Age 31–60 d	136/569 (23.9%)	105/664 (15.8%)	<.0001
Female gender	309/569 (54.3%)	396/664 (59.6%)	.06
History of prematurity	114/569 (20.0%)	118/664 (17.8%)	.31
Mean gestational age, wk (range)	32.1 (24–36)	32.2 (23–36)	.98
History of day care exposure	79/569 (13.9%)	126/664 (19.0%)	.02
History of tobacco exposure	197/569 (34.6%)	230/664 (34.6%)	1.00
History of wheeze/RAD	73/569 (12.8%)	106/664 (16.0%)	.12
Fever at/during admission	329/569 (57.8%)	210/664 (31.6%)	<.0001
Patient management			
Influenza tested	246/569 (43.2%)	193/664 (29.1%)	<.0001
Influenza positive	7/246 (2.8%)	10/193 (5.2%)	.81
RSV tested	499/569 (87.7%)	575/664 (86.6%)	.57
RSV positive	291/499 (58.3%)	396/575 (68.9%)	.0004
CXR performed	488/569 (85.8%)	367/664 (55.3%)	<.0001

CXR, chest radiograph; RAD, reactive airway disease.

infants aged 0 to 30 days and 56% of infants aged 31 to 60 days underwent SBI testing. In addition, 85% of infants aged 0 to 30 days and 79.7% of infants aged 31 to 60 days presenting with fever underwent SBI testing. Overall, patients not undergoing SBI evaluation were more likely to have exposure to day care and be RSV positive. Patients incurring SBI testing more commonly had a fever present at or during their admission, were more likely to have influenza tested for, and have a chest radiograph performed. All other measured baseline characteristics were similar between the 2 groups.

Rates of SBI

Microbiologic testing results are listed in Table 2. The incidence of UTI in patients who underwent urine testing was 2.3% (6 of 259). Of the 367 patients who underwent blood culture testing, there were 13 positive blood culture results. Of these, 10 patients' cultures grew coagulase-negative staphylococci, 2 patients' cultures grew diphtheroids, and 1 patient's culture results were positive for coagulase-negative staphylococci in 1 set and α-hemolytic streptococci in another. All were deemed to be contaminants; therefore, there were no cases of bacteremia. There were no cases of meningitis.

SBI Testing and Antibiotic Use

Table 2 also lists the incidence of microbiologic testing in patients admitted with bronchiolitis. Of the 569 patients undergoing SBI testing, 27.1% (n = 154) had only a CBC obtained, 45.0% (n = 256) had a UA and/or urine culture obtained, 64.5% (n = 367) had a blood culture obtained, and 16.3% (n = 93) had CSF cultures obtained. Of the 367 patients who underwent blood culture testing, only 210 (57.2%) also underwent urine testing.

TABLE 2 SBI Testing and Results Among Children Hospitalized for Bronchiolitis (n = 569)

Microbiologic Testing	No. Tested/Total Tested (%)	Positive/No. Tested (%)
UA/urine culture	256/569 (45.0%)	6/256 (2.3%)
Blood cultures	367/569 (64.5%)	0/367 (0%)[a]
CSF cultures	93/569 (16.3%)	0/94 (0%)

[a] All 13 positive blood cultures were positive for a contaminant.

In total, 53.8% of patients undergoing evaluation for SBI received antibiotics whereas only 19.1% of patients not undergoing SBI evaluation were treated with antibiotics (P < .0001). Table 3 lists antibiotic use associated with SBI testing. Of those patients with UA/urine culture obtained, 62.1% received antibiotics; 62.1% of patients with blood cultures obtained received antibiotics; and 91.4% of patients with CSF cultures obtained received antibiotics. Logistic regression analysis of factors associated with antibiotic use is listed in Table 4. SBI testing was independently associated with increased antibiotic use (odds ratio: 3.19 [95% confidence interval: 2.42–4.20]; P < .0001).

Length of Stay

Clinical outcomes of patients undergoing SBI testing are listed in Table 5. LOS for patients undergoing SBI testing was 3.4 days (range: 1–25 days) versus 2.3 days (range: 0–35 days) for patients not undergoing SBI evaluation (P < .0001). There was no significant difference in the readmission rate within 4 weeks between the 2 groups.

DISCUSSION

The results of the current study reveal a low incidence of SBI in children hospitalized with bronchiolitis. The only SBI we identified was UTI (2.3% of patients). There were no cases of bacteremia or meningitis. Due to the fact our study was designed to evaluate provider practices and excluded patients admitted to the PICU, the

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TABLE 3 Antibiotic Use According to SBI Testing Among Children Hospitalized for Bronchiolitis (n = 569)

Microbiologic Testing	% Tested Who Received Antibiotics	% Not Tested Who Received Antibiotics	*P*
UA/urine culture	159/256 (62.1%)	274/977 (28.0%)	<.0001
Blood cultures	228/367 (62.1%)	205/866 (23.7%)	<.0001
CSF culture	85/93 (91.4%)	348/1140 (30.5%)	<.0001

incidence of SBI reported in this article may not be a true reflection of the overall incidence of SBI in patients with bronchiolitis. Nevertheless, our findings are similar to previous studies that have shown a low incidence of concurrent SBI in patients with bronchiolitis.[3–14] A recent literature review reported on occult SBI in young infants with bronchiolitis.[11] In the review of 11 included studies, the weighted rate of UTI was 3.3% (95% confidence interval: 1.9–5.7). There were no cases of bacteremia in 8 of the 11 studies and no cases of meningitis in any of the studies. This evidence further supports our findings of the potential low yield of SBI testing in patients with bronchiolitis.

Concern for SBI in the setting of clinical bronchiolitis may be higher for those patients in high-risk age groups such as younger children or children with a history of prematurity, relative immune immaturity, and susceptibility to perinatal pathogens. We found that a significantly larger percentage of the total patient population undergoing SBI testing were aged <60 days, and in an adjusted multivariate analysis, age <60 days was associated with SBI testing. Interestingly, we found that of those patients undergoing SBI evaluation, only 12.8% and 23.9% were in the <30-day and 31- to 60-day age groups, respectively; thus, ~63% of patients with bronchiolitis undergoing testing were >2 months old.

Despite knowledge that UTI is the most common concurrent SBI in bronchiolitis, we found that a larger percentage of patients undergoing SBI evaluation were evaluated with a blood culture. Many of these patients were only tested for bacteremia without any urine testing. The fact that all of the blood cultures in this study were contaminated further suggests blood culture testing has low utility. In addition, increased false-positive findings have the potential to lead to other adverse consequences, which have been demonstrated in other studies. Antonow et al[12] found that 142 of 282 patients aged 0 to 60 days with bronchiolitis underwent a sepsis evaluation, with a resulting 31 positive culture results. Twenty-seven of those cultures were found to be contaminants (4 CSF, 5 blood, and 18 urine). This outcome was associated with increased antibiotic use, LOS, and costs. Purcell et al[5] also found that of the 2396 children they studied who were hospitalized with RSV, 12 had positive blood culture results, all of which were found to be contaminants. Although determining the reasoning behind provider practices in diagnostic testing is beyond the scope of the current study, we speculate that when blood is collected at intravenous placement or other diagnostic testing is being sent, providers often order a blood culture without fully thinking through the ramifications of a false-positive finding.

In addition, in evaluating provider practices in SBI testing, we found that approximately one-quarter of patients had only a CBC obtained. As stated earlier, CBC testing was included in our definition of SBI testing because it is most likely that this diagnostic test was used for the evaluation of white blood cell count as a marker of potential bacterial infection. It is unlikely that an appreciable rate of provider concern exists for anemia and/or thrombocytopenia in patients presenting with clinical bronchiolitis. CBC testing alone would not be a thorough evaluation for SBI, therefore it could be considered low utility when done in isolation. This finding again highlights additional low-yield diagnostic testing being performed for patients with bronchiolitis.

Even without positive results, SBI testing is associated with increased antibiotic use. In our study, more than one-half of patients undergoing any SBI testing received antibiotics at some point during their hospitalization compared with 19.1% of those not

TABLE 4 Analysis of Factors Associated With Receiving Antibiotics (n = 1233)

Factor	Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Age ≤60 d	0.89 (0.69–1.15)	NS	—	—
History of prematurity	1.01 (0.75–1.36)	NS	—	—
Fever at/during admission	3.37 (2.64–4.30)	<.0001	2.58 (1.98–3.35)	<.0001
Admitted to the ICU	2.66 (1.90–3.72)	<.0001	1.84 (1.27–2.67)	.001
Influenza tested	1.84 (1.44–2.34)	<.0001	1.43 (1.10–1.88)	.008
RSV tested	0.93 (0.66–1.32)	NS	—	—
CXR performed	3.11 (2.32–4.15)	<.0001	1.76 (1.28–2.44)	.001
Underwent SBI testing	4.92 (3.82–6.34)	<.0001	3.19 (2.42–4.20)	<.0001

CI, confidence interval; CXR, chest radiograph; OR, odds ratio.

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TABLE 5 Clinical Outcomes of Patients According to SBI Evaluation Status

Outcome Measure	Evaluated for SBI (*n* = 569)	Not Evaluated for SBI (*n* = 664)	*P*
Received antibiotics	306/569 (53.8%)	127/664 (19.1%)	<.0001
ICU admission	118/569 (20.7%)	42/664 (6.3%)	<.0001
LOS mean (range)	3.4 (1–25)	2.3 (0–35)	<.0001
Rehospitalized within 4 wk	39/569 (6.9%)	40/664 (6.0%)	.55

No deaths occurred in the studied cohort.

undergoing testing. Although we did not quantify duration of antibiotic use and included antibiotic doses administered in the emergency department, a previous study by Purcell et al[5] found that 97% of antibiotics started on admission in patients hospitalized with RSV were continued until discharge. Antibiotics are not a benign treatment; they have potential adverse effects and risk of potentiating resistance patterns.

Our study also found that children undergoing SBI evaluation had significantly longer LOS than those who did not. Because of our retrospective study design, we are unable to determine if there was a causal nature between SBI evaluation and LOS. The increase in LOS, however, may be partially explained by a prolongation of a patient's hospitalization while microbiologic cultures are observed for growth. Given the average difference in LOS of 1.1 days and a daily hospital cost of ~$2900 (per hospital billing data), SBI testing may result in as much as $3190 in excess costs per hospitalization. This translates to $1.8 million in costs for the cohort in adjusted 2013 dollars. Reduction of unnecessary SBI testing in this group may therefore result in significant cost savings.

A limitation of our study includes the retrospective nature of the analysis. Although we used both primary and secondary *International Classification of Diseases, Ninth Revision,* discharge codes for inclusion criteria, we run the risk of underreporting the incidence of SBI because they may have been coded differently once the diagnosis was made. It is also possible that SBI testing may have been overestimated. One potential scenario includes infants aged 0 to 60 days who may have been admitted initially for fever, who underwent neonatal fever evaluation (including SBI testing), and were subsequently found to be RSV-positive; these infants thus carried that discharge diagnosis. A large percentage of the patients in the study were also seen by an outside provider before admission. In these cases, we did not have those outside medical records to review. In addition, we cannot speak to the role of severity of illness as a confounder in the association between SBI evaluation and management of these patients. Strengths of the study include the large patient population and the multicenter study design.

CONCLUSIONS

Although there has been a lot of progress in developing best practice guidelines for bronchiolitis given previous research, there is still room for improvement. Our study demonstrated that providers continue to evaluate for SBI in the setting of clinical bronchiolitis despite evidence for the low utility of these tests. The results of this study provide additional evidence for a more selective approach to the evaluation of SBI in bronchiolitis. Ongoing education should be directed to those providers doing the initial evaluation of these children to help optimize recommended evaluation and treatment measures and minimize use of nonindicated diagnostic testing in patients with bronchiolitis.

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