

PREVALENCE AND PREDICTORS OF BACTEREMIA AMONG CHILDREN HOSPITALIZED WITH PNEUMONIA

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Abstract. National guidelines from many countries recommend obtaining blood culture from children with pneumonia upon hospitalization if the case is moderate to severe. However, etiological, microbes, and health systems vary by country and factors associated with bacteremia may also vary. We aimed to determine the prevalence and identify factors associated with bacteremia among children hospitalized with community-acquired pneumonia (CAP) in Thailand. We conducted a prospective descriptive study. The study population was children aged 60 days to 15 years hospitalized with CAP at King Chulalongkorn Memorial Hospital, Bangkok, Thailand from June 2014 to April 2015. We compared subject with positive and negative blood cultures. One hundred fifty-two children with CAP were recruited. Thirteen cases (8.6%) had a positive blood culture; 7 cases (4.6%) with a positive blood culture were considered contamination, leaving 6 (3.9%) true positive cases. The isolated organisms were *Streptococcus pneumoniae*, *Escherichia coli*, and *Salmonella* group B. Five factors were found to be associated with bacteremia: 1) body temperature $>38.5^{\circ}\text{C}$ [odds ratio (OR) = 9], 2) severe sepsis status (OR = 27), 3) severe respiratory distress requiring mechanical ventilation (OR = 145), 4) leukocytosis $>17,000/\mu\text{l}$ (OR = 6), and 5) patchy infiltration (OR=13). Children hospitalized with community acquired pneumonia have a low rate of bacteremia. The prevalence of subjects in our study with bacteremia was 3.9% and there were 3 clinical and 2 laboratory factors significantly associated with bacteremia. This study shows that hemoculture do not need to be routinely performed in all children hospitalized with CAP.

Keywords: pneumonia, hemoculture, children

INTRODUCTION

Blood cultures are often performed on children hospitalized with community-

acquired pneumonia (CAP). Bacteremia is a serious complication of pneumonia. Some studies have found the prevalence of bacteremia in children with CAP to be 1.4-2.7% among outpatients and emergency room patients (Bonadio, 1988; Hickey *et al*, 1996; Shah *et al*, 2003) and 3-7% (Esposito *et al*, 2012; Heine *et al*, 2013; Mendoza-Paredes *et al*, 2013; Myers *et al*, 2013). Latest systematic review

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found the prevalence of positive blood culture in pediatric CAP was 5% (Tam *et al*, 2015). *Streptococcus pneumoniae* was the most common pathogen isolated from positive blood cultures among children with CAP (Resti *et al*, 2010; Myers *et al*, 2013). Several factors have been found to be associated with positive blood cultures among children with CAP including toxic appearance, pleural effusion or empyema and leukocytosis (Bonadio, 1988; Hickey *et al*, 1996; Heine *et al*, 2013).

Studies from developing countries, including Thailand, show higher prevalence (7.9-29.7%) of bacteremia in CAP patients and some different pathogens compared with developed countries such as *Salmonella* spp, and *Burkholderia pseudomallei* (Banya *et al*, 1996; Ekalaksananan *et al*, 2001; Asih *et al*, 2011). In Thailand, only two studies have been conducted to identify incidences and etiology of CAP among children aged less than 5 years (Ekalaksananan *et al*, 2001; Hasan *et al*, 2010), none have evaluated factors associated with positive blood culture among children with CAP.

Some guidelines recommend obtaining blood cultures from children with severe pneumonia, such as those with high grade fever or severe respiratory distress (Bradley *et al*, 2011; Harris *et al*, 2011). However, genetic susceptibility of hosts, types and virulence of microbes and health care systems may vary by region and even communities, possibly affecting the prevalence and factors associated with positive blood cultures among children with CAP; therefore, we aimed to determine these in this study among children hospitalized with CAP in Thailand.

MATERIALS AND METHODS

We conducted a prospective descrip-

tive study of patients aged 60 days to 15 years hospitalized with CAP at King Chulalongkorn Memorial Hospital, Thailand, from June 2014 to April 2015. The diagnosis of pneumonia was made by having lower respiratory tract symptoms and an infiltration on chest radiograph. Patients hospitalized during 2 weeks prior to admission at our hospital were excluded from our study to avoid hospital acquired pneumonia patients. Patients referred to our institution from other hospitals were also excluded.

The following data were obtained: demographic information, including age, sex, underlying diseases and vaccination status; clinical and laboratory data; body temperature, vital sign, respiratory signs, requiring mechanical ventilation, white blood cell count, blood culture results, pneumonia-associated complications and chest radiograph results. Chest radiographs were reviewed by pediatric pulmonologists. All radiographs were classified into patchy or perihilar infiltrations. Blood cultures were obtained from each patient. Severe sepsis status defined as sepsis-induced hypoperfusion or organ dysfunction according to international guideline for management of severe sepsis and septic shock 2012 (Dellinger *et al*, 2013). A contaminated blood culture was defined as a patient whose clinical status remained stable or improved without antibiotics, the first blood culture result was abnormal, and the repeated blood culture taken immediately after the first blood culture came back negative.

Blood cultures were obtained on admission using sterile technique. The blood was inoculated into a pediatric blood culture bottle (VersaTREK™ REDOX™). (Thermo Fisher Scientific, Waltham, MA).

Statistical analysis

Characteristics of the study population were described overall and by

Table 1
Demographic data of 152 patients with community acquired pneumonia.

Variables	Total (N=152)	Negative blood cultures (n=146)	Positive blood cultures (n=6)	p-value
Median (IQR) age of study subjects in years	1.9 (0.8-3.8)	1.9 (0.8-3.8)	2.5 (0.5-5)	0.82
Age group in years, n (%)				0.85
< 1	46 (30.3)	44 (30.1)	2 (33.3)	
1-5	87 (57.2)	84 (57.5)	3 (50)	
6-10	13 (8.6)	12 (8.2)	1 (16.7)	
> 10	6 (3.9)	6 (4.1)	0 (0)	
Sex, n (%)				0.35
Male	73 (48)	69 (47)	4 (67)	
Female	79 (52)	77 (53)	2 (33)	
Median weight (IQR) in kilograms	10.6 (7.7-13.4)	10.5 (7.7-13.3)	11.2 (5-15.4)	0.92
Weight group, n (%)				0.37
Normal	110 (72.4)	107 (73.3)	3 (50)	
Underweight	39 (25.6)	36 (24.7)	3 (50)	
Overweight	3 (2)	3 (2.1)	0 (0)	
Median height (IQR) in centrimeters	81.5 (70-95.3)	81 (70-95)	90 (60-106)	0.68

groups. Continuous data were analyzed using median and interquartile ranges (IQR). Comparisons of medians between two groups were made with the Wilcoxon rank-sum test and proportions were compared between categorical variables with the chi-square test. We calculated percentages and 95% confident intervals for positive hemoculture based on binomial distribution. Odds ratios (OR) were calculated of significant variables to determine strength of association.

Ethical considerations

Institutional review board of the Faculty of Medicine, Chulalongkorn University, Bangkok approved the project protocol, information sheet and informed consent form (COA NO. 300/2014, IRB No. 035/57). Written informed consent was obtained from the parents or caretakers of all participants.

RESULTS

One hundred fifty-two children were included in the study; 73 (48%) were male. The median age was 1.9 [Interquartile range (IQR) = 0.8-3.8] years. Eighty-seven point five percent of subjects were aged less than 5 years (Table 1). Ten patients (6.6%) had a history of a pneumococcal vaccine and 17 (11%) had a history of a hemophilus B vaccine (Table 2). Fifty-seven subjects (63%) had a history of underlying disease; the majority being chronic lung or neurological disease.

Thirteen patients (8.6%) had a positive blood culture; 7 (4.6%) were considered to be a contaminant and 6 (3.9%) were considered to have true bacteremia. The blood culture specimens considered to be contaminated were coagulase negative *Staphylococcus*, *Corynebacterium*, and *Micrococcus*. The specimens considered

Table 2
Variables among study subjects with and without a positive blood culture.

Variables	Total (N=152)	Negative blood culture (n=146)	Positive blood culture (n=6)	p-value	Odd ratio (95% CI)
History of underlying disease, n (%)					
Yes	57 (37.5)	55 (37.7)	2 (33.3)	0.83	
No	95 (62.5)	91 (62.3)	4 (66.67)		
History of vaccines, n (%)					
Pneumococcal	10 (6.6)	10 (6.9)	0 (0)	0.55	
Haemophilus influenza type B	17 (11.2)	16 (11)	1 (16.7)	0.66	
Influenza	37 (24.3)	35 (24)	2 (33.3)	0.60	
Median duration (IQR) of fever in days	1 (1-3)	1 (1-3)	1.5 (1-3)	0.70	
Median duration (IQR) of URI symptoms in days	3 (1-5)	3 (1-5)	2 (1-3)	0.34	
Body temperature, n (%)				0.03	9.2
≤38.5°C	122 (80.3)	120 (82.2)	2 (33.3)		(1.6-53.2)
>38.5°C	30 (19.7)	26 (17.8)	4 (66.7)		
Severe sepsis ^a , n (%)				<0.001	27.2
No	148 (97.4)	145 (99.3)	3 (50)		(4.1-167)
Yes	4 (2.6)	1 (0.7)	3 (50)		
Mechanical ventilation, n (%)				0.001	145
No	138 (90.8)	136 (93.2)	2 (33.3)		(11.5-1,830)
Yes	14 (9.2)	10 (6.9)	4 (66.7)		
Respiratory distress ^b , n (%)				0.79	
No	32 (21.1)	31 (21.2)	1 (16.7)		
Yes	120 (79.5)	115 (78.8)	5 (83.3)		

^aSevere sepsis defines as sepsis-induced hypoperfusion or organ dysfunction.

^bRespiratory distress defines as presenting sign of increased work of breathing: chest retractions, nasal flaring.

URI, upper respiratory tract infection.

to be true infections were *Streptococcus pneumoniae*, *Escherichia coli*, and *Salmonella* group B (two patients each). Two subjects had a parapneumonic effusion (Table 1).

There were no statistically significant differences in age, sex, weight, height, underlying disease, vaccination history, history of fever or respiratory symptom duration between children with positive and negative blood cultures. Significantly more patients with bacteremia had a body temperature > 38.5°C (OR = 9.2; 95% CI: 1.6-53.2). Severe sepsis (OR = 27.2; 95%

CI: 4.4-167) and severe respiratory distress requiring endotracheal intubation and mechanical ventilation (OR = 145; 95% CI: 11.5-1,830) were significantly more common in bacteremic group (Table 2).

Significantly more subject with bacteremia had a white blood cell count > 17,000/μl (OR = 6.1; 95% CI: 1.1-34.7). Hemoglobins and platelets did not differ between the two groups. Significantly, more subjects with bacteremia had an initial chest radiograph showing patchy infiltration (OR = 12.8; 95% CI: 1.5-113).

Table 3
Test results among study subjects with and without a positive blood culture.

Variables	Total (N=152)	Negative blood culture (n=146)	Positive blood cultures (n=6)	p-value	Odds ratio (95% CI)
WBC per μ l: n (%)					
≤17,000	112 (73.6)	110 (75)	2 (33.3)	0.04	6.1 (1.1-34.7)
>17,000	40 (26.4)	36 (25)	4 (66.7)		
Median (IQR) ANC per μ l	7,140 (4,562-11,418)	7,075 (4,400-11,330)	16,420 (5,600-19,911)	0.05	
Median (IQR) Hb level (g/dl)	12 (10.9-13)	12 (11-13)	10.3 (9.6-12.1)	0.16	
Median (IQR) platelet count $\times 10^3$ per μ l	311 (237-401)	308 (237-402)	363 (234-389)	0.83	
Chest radiograph findings, n (%)					
Perihilar/interstitial infiltration	106 (69.7)	105 (71.9)	1 (16.7)	0.01	12.8 (1.5-113)
Patchy infiltration	46 (30.3)	41 (28.1)	5 (83.3)		
Pleural effusion, n (%)					
No	150 (98.7)	145 (99)	5 (83.3)	0.08	
Yes	2 (1.3)	1 (0.7)	1 (16.7)		

WBC, white blood cell; ANC, absolute neutrophil count; Hb, hemoglobin.

One subject with bacteremia and one without had a parapneumonic effusion (Table 3).

DISCUSSION

The prevalence of bacteremia among subjects in our study (3.9%) is similar to 3-7% reported in other studies. (Esposito *et al*, 2012; Heine *et al*, 2013; Mendoza-Paredes *et al*, 2013; Myers *et al*, 2013; Tam *et al*, 2015). Pneumococcus, *E. coli* and Salmonella were found in blood cultures among our subjects similar to several studies from developing countries. (Banya *et al*, 1996; Ekalaksananan *et al*, 2001; Hasan *et al*, 2010; Asih *et al*, 2011). The percentage of contaminants in our study (4.6%) was higher than the 1-3% reported in other studies (Herz *et al*, 2006; Myers *et al*, 2013). The reason for our higher contamination rate requires further study.

Positive blood cultures have an impact on clinical management of CAP. Previous studies conducted among pediatric populations with CAP found positive culture results led to changes in management (Shah *et al*, 2003; Mayers *et al*, 2013); we found the same thing in our study as well. Four of the 6 bacteremic patients in our study were treated with cephalosporins and two patients were changed from cefotaxime to meropenem.

We found no differences in baseline characteristics be-

tween the bacteremic and non-bacteremic patients in our study. Five factors were significantly associated with bacteremia in our study subjects: body temperature $>38.5^{\circ}\text{C}$, severe sepsis, mechanical ventilation, a white blood cell count $>17,000/\mu\text{l}$ and a patchy infiltration of chest radiograph. The association between bacteremia and mechanical ventilation was reported previously (Tam *et al*, 2015). In our study, bacteremic patients were more likely to have leukocytosis similar to other studies (Hickey *et al*, 1996; Resti *et al*, 2010).

A high fever was also associated with bacteremia in our study, similar to previous studies (Banya *et al*, 1996; Shah *et al*, 2003; Myers *et al*, 2013). C-reactive protein (CRP) has also been found to be associated with a positive culture (Myers *et al*, 2013) but at our institution CRP is not routinely examined in CAP patients. Severe CAP, defined requiring endotracheal intubation or an ICU admission, was associated with a positive blood culture in our study, similar to a recent meta-analysis (Tam *et al*, 2015). Unlike previous studies (Asih *et al*, 2011; Heine *et al*, 2013), we did not find a history of a chronic medical conditions or pleural effusion being associated with bacteremia in our study.

Three clinical and two laboratory factors were associated with bacteremia in our study. Forty percent of patients in our study had at least one of the five factors associated with bacteremia. Obtaining a hemoculture in these 40% would increase the predictive value from 3.9% to 10.2%. The more the number of associated factors the subjects had, the more likely the subjects had bacteremia. Heine *et al* (2013) found similar factors to be associated with bacteremia and used them as institutional guideline for when to obtain a blood culture.

In summary, the prevalence of bacteremia among subjects with CAP in our study was 3.9%. The clinical factors associated with bacteremia in our study were a body temperature of $>38.5^{\circ}\text{C}$, the presence of severe sepsis and requiring mechanical ventilation and the test results associated with bacteremia were having a white blood cell count $>17,000/\mu\text{l}$ and having a chest radiograph showing a patchy infiltrate. This study supports that blood cultures do not need to be routinely obtained in all children hospitalized with CAP. However, some patients who have a factor associated with bacteremia, hemoculture should be obtained.

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