Empyema and bacteremic pneumococcal pneumonia in children under five years of age*,**

Empiema e pneumonia pneumocócica bacterêmica em menores de cinco anos de idade

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Abstract

We compared bacteremic pneumococcal pneumonia (BPP) and pneumococcal empyema (PE), in terms of clinical, radiological, and laboratory findings, in under-fives. A cross-sectional nested cohort study, involving under-fives (102 with PE and 128 with BPP), was conducted at 12 centers in Argentina, Brazil, and the Dominican Republic. Among those with PE, mean age was higher; disease duration was longer; and tachypnea, dyspnea, and high leukocyte counts were more common. Among those with BPP, fever and lethargy were more common. It seems that children with PE can be distinguished from those with BPP on the basis of clinical and laboratory findings. Because both conditions are associated with high rates of morbidity and mortality, prompt diagnosis is crucial.

Keywords: Empyema, pleural; Pneumonia, pneumococcal; Pneumococcal infections.

Resumo

Comparamos crianças menores de cinco anos com pneumonia pneumocócica bacterêmica (PPB) àquelas com empiema pneumocócico (EP) quanto aos achados clínicos, radiológicos e laboratoriais. Um estudo de coorte aninhado transversal, com 102 crianças com EP e 128 com PPB, foi realizado em 12 centros na Argentina, no Brasil e na República Dominicana. Nas crianças com EP, a média de idade e a duração da doença foram maiores. Taquipneia, dispneia e contagem de leucócitos alta foram mais comuns nas crianças com EP; febre e letargia foram mais comuns naquelas com PPB. Parece possível distinguir crianças com EP de crianças com PPB a partir de achados clínicos e laboratoriais. Como essas duas doenças estão associadas a altas taxas de morbidade e mortalidade, o diagnóstico rápido é crucial.

Descritores: Empiema pleural; Pneumonia pneumocócica; Infecções pneumocócicas.

Streptococcus pneumoniae is widely recognized as the leading cause of community-acquired pneumonia (CAP)-related mortality during hospitalization, as well as being the most common cause of empyema in children. The incidence of complicated pneumococcal CAP (CP-CAP) has been reported to be increasing worldwide.[1] In Scottish children in the 1-4 year age bracket, there was a tenfold increase in empyema admissions in the period between the 1980s and the year

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2005.[2] This increase might be related to host susceptibility, individual characteristics, and pathogen virulence.

Few studies have investigated the characteristics of CP-CAP, especially those of CP-CAP associated with pleural empyema or bacteremia—although few cases of pneumococcal pneumonia are bacteremic—in children under 5 years of age, who are at the highest risk of death from CAP. Bacteremic pneumococcal pneumonia (BPP) is considered an advanced stage of severe pneumococcal pneumonia, in which early recognition and appropriate management can have a favorable impact on the outcome.[3] Given that pleural empyema and BPP are potentially severe, it is important to recognize their clinical peculiarities in order to provide early and appropriate management.

In a recent study of hospitalized CAP patients, the prevalence rates of pleural effusion and empyema were reported to be 27% and 17%, respectively.[3] In another study, empyema was found in 83 (11%) of 767 children hospitalized with CAP; in comparison with the children with CAP without empyema, those with empyema were older, had longer symptomatic periods, and were more likely to receive nonsteroidal anti-inflammatory drugs.[4] The objective of the present study was to compare children under 5 years of age with BPP and those with pneumococcal empyema (PE) in terms of their clinical, radiological, and laboratory features.

A cross-sectional nested cohort study was conducted at 12 centers in Argentina, Brazil, and the Dominican Republic and included 2,536 children 3-59 months of age hospitalized with severe CAP, the results having been published elsewhere.[5] On admission, blood cultures and, when appropriate, pleural fluid cultures were performed. S. pneumoniae was isolated from 283 children by standard procedures used in local referral laboratories. Most (90%) of the children lived in urban settings, and none had received the conjugate pneumococcal vaccine or steroidal/nonsteroidal anti-inflammatory drugs. Cases of BPP were defined as those in which S. pneumoniae was isolated from blood culture. Cases of PE were defined as those in which S. pneumoniae was isolated from pleural fluid culture.

The exclusion criteria were as follows: showing signs of very severe pneumonia (including severe malnutrition, stridor in a calm child, unconsciousness, convulsions, nasal flaring, and central cyanosis); and presenting with concurrent infections. Patients with concomitant PE and BPP (n = 3) and those with pleural effusion of unknown cause (n = 50) were also excluded.

A favorable response to the initial treatment (i.e., conventional doses of intravenous ampicillin or penicillin G for BPP and PE patients alike) was defined as unequivocal clinical improvement within the first 48 h after hospital admission; conversely, treatment failure was defined as no improvement (persistent fever—body temperature being measured at least every 6 h—tachypnea, difficulty breathing, or hypoxemia) after at least 48 h of antibiotic therapy or deterioration during antimicrobial therapy.[5] Demographic, clinical, radiological, and laboratory data were obtained on admission. In addition, the length of hospital stay and the treatment outcome were recorded. Descriptive statistics were calculated, and two multiple logistic regression models were used, both of which were controlled for age. One of the models included variables obtained on admission and the other included variables obtained during hospitalization.

The present study included 230 children under 5 years of age (102 children with PE and 128 children with BPP). There was no significant difference between the two groups in terms of antibiotic use prior to hospital admission ($p = 0.23$). Table 1 displays the frequency distribution and the comparison (multivariate analysis) of the two groups of children on admission and during hospitalization.

In brief, our logistic regression analysis showed that, on hospital admission, children with PE were older and presented with a longer symptomatic period before hospitalization. In addition, tachypnea, difficulty breathing, and a leukocyte count > 15,000 cells/mm^3 were more common in those children. Persistent fever was one of the most common findings during the first days of hospitalization, requiring further investigation (chest X-ray, chest ultrasound, or both). Fever (axillary temperature > 37.5°C) and lethargy at diagnosis/baseline tended to be more common in the children with BPP. The hospital stay tended to be longer for the children with PE ($p < 0.001$; data not shown).

In the children with PE, the most common serotypes were 14, 1, 6B, 3, 9V, 19A, and 5,

Table 1 - Comparison (multivariate analysis) of children with pneumococcal empyema and those with bacteremic pneumococcal pneumonia on admission and during hospitalization.

Characteristic	PE (n = 102)	BPP (n = 128)	Adjusted OR (95% CI)	p
On admission				
Age (months)[a]	19 (12-33)	13 (9-22)	1.03 (1.00-1.05)	0.01
Duration of disease[b]				
≤ 3 days	17.7	34.4	1	0.013
4-6 days	39.2	35.1	2.84 (1.23-6.58)	
≥ 7 days	43.1	30.5	3.12 (1.35-7.20)	
Tachypnea[b,c]	91.2	75.6	4.16 (1.54-11.22)	0.005
Difficulty breathing[b]	87.9	70.9	3.61 (1.51-8.63)	0.004
Body temperature > 37.5°C on admission[b]	42.4	68.2	0.32 (0.17-0.63)	0.001
Lethargy[b]	53.5	67.7	0.35 (0.17-0.71)	0.004
Leukocyte count > 15,000 cells/mm^3[b]	48.5	29.8	2.13 (1.10-4.13)	0.02
During hospitalization				
Difficulty breathing on the 3rd day[b]	57.6	27.0	2.9 (1.52-5.56)	0.001
Body temperature (°C) on the 3rd day[a]	37.6 (37.0-38.8)	37.0 (36.6-38.0)	1.65 (1.05-2.59)	0.028
Treatment failure[b]	17.6	12.5	0.39 (0.14-1.07)	0.06
Length of hospitalization[a]	11 (7-15)	7 (5-10.5)	1.09 (1.02-1.17)	0.004

PE: pneumococcal empyema; and BPP: bacteremic pneumococcal pneumonia. [a]Values expressed as median (interquartile range). [b]Values expressed as %. [c]RR > 50 breaths/min in the children 3-11 months of age and > 40 breaths/min in those ≥ 12 months of age.

accounting for 92.4% of all serotypes in those children. In the children with BPP, the most common serotypes were 14, 6B, 5, 1, 6A, 9V, and 19F, accounting for 84.9% of all serotypes in those children. In other words, serotypes 1, 5, 6B, and 14 were found in both PE and BPP, whereas serotypes 6A, 9V, 19A, and 19F were found in either PE or BPP. It is of note that serotypes 6A and 19A are not included in the 10-valent pneumococcal conjugate vaccine currently used in Brazil.

To the best of our knowledge, the present study is the first to have focused specifically on BPP and PE in children under 5 years of age. Therefore, the results presented herein cannot be compared with those of other studies. In fact, our analyses showed that demographic characteristics, clinical features, and hematologic findings (i.e., leukocyte counts) are likely to be quite different between children with BPP and those with PE.

Although our objectives and methods were different from those of François et al.,[4] some of the results were similar between the two studies. François et al. studied 767 children with CAP and found that 83 (11%) had empyema.[4] The children with CAP and empyema were older and had a longer symptomatic period in comparison with those with CAP without empyema.[4] Interestingly, the length of hospital stay found in the present study was quite similar to that reported in a study involving 33 Brazilian children with empyema (i.e., 12 days).[6] In addition, serotype 1 was one of four serotypes found in both PE and BPP (i.e., 14, 1, 6B, and 5), a finding that is consistent with those of the study by François et al.,[4] which was conducted in a developed country.

In conclusion, our study investigated CAP patients under 5 years of age and showed clinical and laboratory findings at admission and during the first three days of hospitalization. Our findings can help clinicians and pediatricians to distinguish children with PE from those with BPP. Because these two critical conditions are associated with high rates of morbidity and mortality, prompt clinical, laboratory, and radiological diagnosis is crucial for appropriate management.

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