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ARTICLE

Bacteremia in previously healthy children in Emergency Departments: clinical and microbiological characteristics and outcome

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Abstract A blood culture (BC) is frequently requested in both patients with a suspected occult bacteremia/invasive infection as well as those with certain focal infections. Few data are available on the characteristics of patients in whom a bacteremia is identified in the Pediatric Emergency Department (PED). A prospective multicenter registry was established by the Spanish Pediatric Emergency Society. Epidemiological data, complementary test results, clinical management, and final outcome were recorded. Data from the first three years of the registry were analyzed. A true bacterial pathogen grew in 932 of 65,169 BCs collected [1.43 %; 95 % confidence interval (CI) 1.34–1.51 %], with 711 of them collected in patients without previously known bacteremia risk factors. Among them, 335 (47.1 %) were younger than 1 year old and 467 (65.7 %) had a normal Pediatric Assessment Triangle (PAT) on admission. Overall, the most frequently isolated bacterial species was *Streptococcus pneumoniae* (27.3 %; 47.6 % among patients with an altered PAT). The main pathogens were *Escherichia coli* (40.3 %) and *S. agalactiae* (35.7 %) among patients younger than 3 months, *S. pneumoniae* among patients 3–60 months old (40.0 %), and *S. aureus* (31.9 %) among patients over 60 months of age. *Neisseria meningitidis* was the leading cause of sepsis in patients older than 3 months. Eight patients died; none of them had a pneumococcal bacteremia and all had abnormal PAT findings on admission. *S. pneumoniae* is the main cause of bacteremia in patients without bacteremia risk factors who attended Spanish PEDs. Age and general appearance influence the frequency of each bacterial species. General appearance also influences the associated mortality.

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Introduction

Blood culture (BC) is the gold standard for the diagnosis of bacteremia and one of the most often requested microbiological tests in Pediatric Emergency Departments (PEDs). It is mainly used first in children with a clinical suspicion of sepsis or bacterial meningitis and second in children who appear well but are considered to be at a higher risk for occult bacteremia (OB). Nevertheless, even in these latter patients, the indications for BC are not completely defined and, in clinical practice, different age and body temperature cut-off points are used to select patients with a higher risk of OB. Moreover, the introduction of the 7-valent pneumococcal conjugate vaccine (PCV) and, more recently, the 13-valent PCV has decreased the incidence of OB [1–3] and other invasive pneumococcal infections [4, 5], probably reducing the performance of BC in this clinical situation. Accordingly, nowadays, different guidelines also include vaccination status as one of the factors to estimate the risk of a well-appearing patient with fever without source having a pneumococcal OB [6, 7].

On the other hand, BC is frequently included among the complementary tests performed when evaluating certain focal infections, such as urinary tract infections (UTIs), pneumonias,

and cellulitis. However, the usefulness of this culture is not clearly defined in most of these clinical situations.

We established a prospective multicenter registry of the positive BCs collected at the participating PEDs. Our objectives were to identify the bacteria isolated, as well as patient characteristics and outcomes.

Materials and methods

Setting and subjects

In 2010, the Infectious Diseases Working Group of the Spanish Society of Pediatric Emergencies (SEUP) proposed the establishment of a prospective multicenter registry of all the positive BCs collected at the included Spanish PEDs. Patients were prospectively enrolled starting from 1st January 2011. For the purpose of this study, we analyzed the patients included during the three first years of the registry.

Exclusion criteria

(a) BCs in which a bacterial species classically considered a contaminant was isolated (including *Staphylococcus epidermidis*, *Propionibacterium acnes*, *Streptococcus viridans*, *Corynebacterium* spp., and other diphtheroids), if the samples had been collected in otherwise healthy patients. When any doubt was raised related to the potential pathogenicity of one of the species isolated, the research coordinator reviewed the case, requesting further information from the researcher who registered that patient, in order to decide whether the corresponding BC should be included in the registry.
(b) BCs collected from patients with previously known bacteremia risk factors (see definition below).
(c) A second and any subsequent positive BCs for the same bacterial species were not registered in cases in which multiple cultures were taken for a patient during the same infectious episode.

Definitions

- Patients with bacteremia risk factors: the following factors were considered as increasing the risk of having a bacteremia: (a) immunosuppression (oncological illness, chronic renal failure, transplant patient, sickle cell disease); (b) the presence of a mechanical device (indwelling catheter, ventriculoperitoneal shunt, auditory prostheses); and (c) an invasive diagnostic or therapeutic procedure in the previous 10 days. These patients were excluded from the analysis. For the purpose of this study, patients without any of these risk factors were considered as previously healthy patients
- Pediatric Assessment Triangle (PAT): a rapid tool recommended by the American Academy of Pediatrics (AAP) to assess the first general impression of any child [8]. The appearance, the work of breathing, and the circulation to the skin are evaluated using specific predefined physical, visual, or auditory findings. If any of these three components is abnormal, the patient is considered unstable.
- OB: presence of pathogenic bacteria in the blood of a well-appearing febrile child in the absence of an identifiable focus of infection [9].
- Sepsis: for the purpose of this study, we adapted the sepsis criteria published by Goldstein et al. [10]. A patient with a positive BC was diagnosed with sepsis if presenting with any of the following signs:

  – Tachycardia (>180 bpm) not due to external or painful stimuli, or long-term medication.
  – Bradycardia (<100 bpm) not due to external vagal stimulus, β-blocker drugs, or congenital heart disease (only applicable in infants younger than 1 year old).
  – Tachypnea (>50 rpm).
  – Signs of organ dysfunction as listed in the aforementioned publication [10].

Data collection

Two forms were created to be completed online using the Google Drive® application:

- A patient registration form for each positive BC collected, with epidemiological and clinical data, including the results of tests performed, final diagnosis, and outcome.
- A second form to provide the following additional data monthly: total number of patients attended, of BCs taken, and of positive BCs obtained.

Only the research coordinator had access to the two resulting online databases, being responsible for downloading regular backups of both databases and reviewing them for possible errors in data entry. The participating researcher in each center was responsible for reviewing the episodes with potential errors.

This study was approved by the Ethical Committee of the Basque Country. Approval for the study and for data sharing with the coordinating institution and with the centralized data center was granted by the institutional review board at each participating institution. To maintain patient confidentiality, the forms did not include any data that would have allowed the identification of any patient. Since identities remained

anonymous and no intervention was performed on patients, informed consent was not required.

The procedures performed in this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008, as well as the national law.

Blood culture technique

BCs were obtained at the discretion of the physician in charge, according to the protocols used in each center. No standard guideline was established for the purpose of this study to be used across the participating centers. Researchers in each center were surveyed in order to ascertain the recommendations for obtaining a BC established in each institution. All of them include obtaining a BC in the following clinical situations:

- Patients with clinical suspicion of invasive bacterial infection: sepsis, bacterial meningitis, meningococcemia, toxic shock syndrome.
- Infants less than 90 days old with fever without source.
- Infants 3–36 months with fever without source: in these patients, different criteria for obtaining a BC are used. Upper age limit varies across the participating centers (24 vs. 36 months) and also temperature over which obtaining a BC is recommended (>39.5 °C, >40 °C, >40.5 °C) and whether the antipneumococcal vaccination status is included or not in the protocol of management.
- Immunosuppressed patients with fever.
- Patients diagnosed with a focal infection who are admitted with parenteral antibiotic treatment; however, criteria for administering parenteral antibiotic treatment vary across the participating centers for several focal infections (UTI, pneumonia,…).

Other recommendations for obtaining a BC are only established in some of the participating centers, such as patients with febrile UTI who are managed as outpatients with oral antibiotics or patients admitted with focal infections not requiring parenteral antibiotics (for instance, acute gastroenteritis).

BCs were collected by PED nurses following the standard procedures of each center. BC processing methods varied slightly between the participating hospitals. In most cases, blood was inoculated into BACTEC Plus Aerobic/F culture bottles (Becton Dickinson) and blood samples were normally delivered to the laboratory within 1 h of collection through a pneumatic tube system. BCs were then processed in a BACTEC 9240 instrument, which monitors carbon dioxide production within each bottle every 10 min, 24 h a day, and incubated using a 7-day incubation protocol. Alternatively, in the other hospitals, blood was inoculated into BacT/ALERT PF bottles (bioMérieux), processed in a BacT/ALERT 3D instrument and incubated using a 5-day incubation protocol.

Bottles identified as positive by the instrument were immediately removed by a technician to perform a Gram stain and subculture. Based on the Gram stain results, aliquots of the bottles were subcultured onto appropriate media and incubated by standard procedures.

Statistical analysis

Normally distributed data were expressed as mean±standard deviation and non-normally distributed data as median and interquartile range (IQR), while categorical variables were reported as percentages. Comparisons were performed with Mann–Whitney *U*-tests for non-normally distributed data and with independent samples *t*-tests for normally distributed data. For categorical data, the χ^2 test was used. A *p*-value of<0.05 was considered statistically significant. The statistical analysis was carried out using IBM SPSS Statistics for Windows (version 21, Armonk, NY).

Results

Fifteen PEDs participated during 2011, 22 during 2012, and 21 during 2013. Overall, all but four of the PEDs attend patients less than 14 or 15 years of age; three of the remaining PEDs attend patients less than 18 years old and the fourth one attends patients less than 11 years old. A total of 2,043,252 patients were attended and BCs were collected in 65,169 of them [3.18 %, 95 % confidence interval (CI): 3.16–3.21 %]. Overall, 932 BCs were positive according to the study criteria (1.43 % of the BCs collected; 95 % CI 1.34–1.51 %) and 711 of them were collected in patients without any bacteremia risk factor.

Among the 711 studied patients with a positive BC, 334 (46.9 %) were younger than 1 year old and 573 (80.5 %) were younger than 5 years old. Upon arrival at the PED, 467 (65.7 %) had a normal PAT. Table 1 reports descriptive statistics for the main epidemiological variables, the complementary tests performed, and the initial management that patients received.

Six bacteria accounted for 84 % of the episodes of bacteremia. The most frequently isolated bacterial pathogen was *S. pneumoniae* (194 cases; 27.3 %), followed by *Escherichia coli* (147; 20.6 %), *S. aureus* (90; 12.6 %), *S. agalactiae* (72; 10.1 %), *Neisseria meningitidis* (51; 7.1 %), and *S. pyogenes* (46; 6.5 %). Twenty-five different species accounted for the remaining 16 %. Except for *Salmonella* species (*n*=31), *Enterococcus faecalis* (*n*=18), *Haemophilus influenzae* (*n*=15), and *Moraxella catarrhalis* (*n*=7), the rest of them were anecdotically isolated in up to three patients each. The distribution

Table 1 Epidemiological and clinical characteristics, complementary tests, and management of patients with positive blood cultures

Age (months; median and interquartile range)	14 (3–44)
Sex (male; %)	57.0 %
Evolution time of fever (h; median and interquartile range)[a]	24 (6–72)
Temperature upon arrival to the PED (°C; mean ± standard deviation)[b]	38.0 ± 1.1
Normal Pediatric Assessment Triangle (%)	65.7 %
No findings in the physical examination (%)	37.1 %
Lumbar puncture performed (%)	27.4 %
Urine culture performed (%)	49.2 %
Chest X-ray performed (%)	36.9 %
Antibiotic received in the Emergency Department (%)	52.3 %
Initially managed as outpatients (%)	23.9 %
- without antibiotic treatment (%)	14.7 %
Finally managed as outpatients (%)	15.6 %
Length of stay for those admitted patients (days; mean ± standard deviation)	11 ± 9.5

Age and evolution time are expressed as median and interquartile range, and temperature and length of stay are expressed as mean±standard deviation

[a] Fever was present in 668 patients (93.9 %)

[b] No patient presented a temperature<35 °C

of the different bacterial species varied related with the age of the patients and the PAT findings upon arrival at the PED (Table 2). The prevalence of *E. coli* among patients younger than 3 months old increased during the study period, becoming the leading cause of bacteremia in this age group in 2013. The frequency of *S. aureus* increased with the age, being the most frequently isolated bacterium among patients older than 5 years.

The global prevalence of *S. pneumoniae* decreased during the study period: 30.5 % of the positive BCs in 2011; 28 % in 2012, and 23.3 % in 2013, although without reaching statistical significance (p=0.09). No significant variation was identified in the relative prevalence of any serotype during the study period. The three leading serotypes were: 1 (36 cases; only three in infants younger than 2 years old), 19A (20 cases; nine of them in infants younger than 2 years old), and 14 (13 cases; eight of them in infants younger than 2 years old). The most frequent serotypes identified in patients with pneumonia (n=90) were serotypes 1 (32 cases), 19A (16 cases), and 7 F (8 cases). No predominant serotype was identified among patients diagnosed with OB (n=65), bacterial meningitis (n=16), or sepsis (n=12). Serotypes included in PCV13 comprised 68.3 % in 2011, 50.0 % in 2012, and 61.2 % in 2013. Pneumococcal vaccination status was known in 95 of the 101 patients with a pneumococcal bacteremia by a serotype included in PCV13. Among them, only 5 (5.2 %) had received two or more doses of any of the PCVs that include that serotype.

The most common final diagnosis was OB (204 cases; 28.6 %) and the most common focal infections diagnosed were UTI (128; 18.0 %) and pneumonia (104; 14.6 %). The main diagnoses for each age group are shown in Table 3. Overall, 170 patients (23.9 %) were initially managed as outpatients after being assessed in the PED in the visit during which the BC was obtained. The main initial diagnoses for these patients were fever without source (73 patients), pneumonia (21), UTI (21), and gastroenteritis (11). Among them, 59 patients (34.5 %) were subsequently admitted once the BC result was known (47 cases) or in an unscheduled visit before receiving the result (12 cases). One of them was a 6-year-old girl initially diagnosed with tonsillitis and discharged with oral antibiotics, who developed a sepsis due to *S. pyogenes*. She did well.

Table 2 Main bacteria isolated according to age and the Pediatric Assessment Triangle (PAT)

	Bacteria						
	S. pneumoniae	*E. coli*	*S. aureus*	*S. agalactiae*	*N.meningitidis*	*S. pyogenes*	Other bacteria
Globally (n=711)	194 (27.3 %)	147 (20.6 %)	90 (12.6 %)	72 (10.1 %)	51 (7.1 %)	46 (6.5 %)	111 (15.6 %)
Age							
<3 months (n=176)	3 (1.7 %)[a]	71 (40.3 %)[a]	14 (7.9 %)	63 (35.7 %)[a]	2 (1.1 %)[a]	1 (0.5 %)[a]	22 (12.5 %)
3–23 months (n=259)	95 (36.7 %)	62 (23.9 %)	15 (5.8 %)	7 (2.7 %)	30 (11.5 %)	10 (3.9 %)	40 (15.4 %)
24–59 months (n=138)	64 (46.3 %)	3 (2.1 %)[a]	16 (11.5 %)	2 (1.4 %)	11 (7.9 %)	20 (14.4 %)[a]	22 (15.9 %)
>59 months (n=138)	32 (23.2 %)[a]	10 (7.2 %)[a]	44 (31.9 %)[a]	0	8 (5.7 %)	15 (10.9 %)	29 (21.0 %)
Pediatric Assessment Triangle (≥3 months)							
Normal (n=348)	102 (29.3 %)	62 (17.8 %)	64 (18.3 %)	5 (1.4 %)	18 (5.1 %)	33 (9.4 %)	64 (18.3 %)
Altered (n=187)	89 (47.6 %)[b]	13 (7.0 %)[b]	11 (5.9 %)[b]	4 (2.1 %)	31 (16.5 %)[b]	12 (6.4 %)	27 (14.4 %)

[a] p<0.05 when compared with the prevalence among patients aged 3–23 months

[b] p<0.05 when compared with the prevalence among patients with a normal Pediatric Assessment Triangle

Table 3 Main diagnosis received in the different age groups

Age group	Main diagnosis
<3 months (*n*=176)	UTI (64; 36.3 %)
	OB (49; 27.8 %)
	Sepsis ± focal infection (43; 24.4 %)
	Bacterial meningitis (9; 5.1 %)
3–23 months (259)	OB (73; 28.1 %)
	UTI (58; 22.3 %)
	Sepsis ± focal infection (36; 13.8 %)
	Pneumonia (32; 12.3 %)
24–59 months (*n*=138)	Pneumonia (42; 30.4 %)
	OB (33; 23.9 %)
	Sepsis ± focal infection (19; 13.7 %)
	Osteoarticular infection (10; 7.2 %)
>59 months (*n*=138)	Osteoarticular infection (31; 22.4 %)
	Pneumonia (29; 21.0 %)
	OB (14; 10.1 %)
	Sepsis ± focal infection (12; 8.6 %)

UTI urinary tract infection; *OB* occult bacteremia

Overall, 109 patients (15.3 %) met the criteria for sepsis. The median age was 5.5 months (IQR: 1–31.5 months) vs. 15 months for those without criteria for sepsis (IQR: 3–47 months). The evolution time of fever was also lower, with a median of 12 h (IQR: 4–46 h) vs. 24 h (IQR: 6–72 h) for those without criteria for sepsis. Eleven patients (10.0 %) presented a normal PAT upon arrival to the PED, with clinical worsening after admission. The bacterial species most frequently isolated among patients meeting criteria for sepsis were *N. meningitidis* (39.3 %) among those older than 3 months and *S. agalactiae* (76.7 %) among those younger than 3 months (Table 4). Eight patients died (1.1 % of the global sample; 95 % CI 0.1–2.2 %). Their characteristics are detailed in Table 5. All of them had an altered PAT when admitted. The mortality rate was 3.2 % (95 % CI 1.0–5.5 %) among patients with an altered PAT upon arrival at the PED (vs. 0 % among those with a normal PAT; $p<0.01$).

Discussion

To our knowledge, this is the first prospective multicenter study describing the characteristics of pathogens isolated in BCs of patients presenting to the PED, as well as patients' clinical characteristics and outcome. According to our results, in the era of the PCV13, *S. pneumoniae* remains the leading cause of bacteremia among patients attended in this setting. However, the global prevalence of pneumococcal bacteremia during the three years of the study seems to decrease, although cases of bacteremia caused by one of the 13 serotypes included in this vaccine remain stable. It could be partially explained by the incomplete pneumococcal vaccine coverage existing in Spain, as it is not included among the routine immunizations in the Spanish vaccination schedule.

Despite the *S. pneumoniae* being the overall leading cause of bacteremia, the distribution of the bacterial species isolated varied with the age of the patients. Specifically, *S. agalactiae* and *E. coli* accounted for up to 75 % of the cases of bacteremia among infants younger than 3 months old. The use of intrapartum antibiotic prophylaxis has reduced the incidence of early-onset infections caused by *S. agalactiae* [11, 12]. Moreover, recent studies have shown that *E. coli* has replaced *S. agalactiae* as the leading cause of late-onset bacteremia among infants less than 90 days old [13, 14], mainly related to UTIs. It also explains that the presence of leukocyturia is reported to be the only known predictor of the presence of a positive blood culture besides general appearance in this age group [15]. In line with this, the prevalence of *E. coli* in this age group in our study increased during the study period.

Among patients older than 5 years, *S. aureus* was the most frequently isolated bacterial species. This is probably due to the fact that BCs are not taken to diagnose OB in this age group, as they are in younger children, but, rather, culture is mostly used for patients with focal infections. In this way, osteoarticular infections were the main diagnosis in this age group.

The type of bacteria isolated varied also related to the appearance of the patient. Specifically, the prevalence of *S. pneumoniae* was even higher when selecting patients classified as not well-appearing according to the PAT (47.6 % vs. 29.4 % among patients older than 3 months). Moreover, our results show that, among children with bacteremia, those with abnormal findings in the PAT in the PED (34.3 % of the patients in our sample) have a higher mortality rate than those with a normal PAT. Although the PAT has not yet been validated, it is an empiric tool promoted by the AAP that allows the severity of a child's condition and the urgency of potential interventions to be assessed [16].

Among the eight patients who died, two of them were neonates with septic shock due to *S. agalactiae*, one of them with a mother testing positive for *S. agalactiae* and who received complete antibiotic intrapartum prophylaxis, and the other with unknown maternal status and who did not receive prophylaxis against *S. agalactiae*. A third deceased patient was a non-immunized 6-month-old infant with a septic shock by *H. influenzae* type b. Standardizing the intrapartum antibiotic prophylaxis and strengthening the compliance with the national immunization schedule in those reluctant families could reduce the mortality related to infectious processes.

Although *S. pneumoniae* was the most frequently isolated bacterial species, it was only identified in 10 % of the patients meeting criteria for sepsis and no patient with a pneumococcal

Table 4 Main bacteria isolated in patients meeting the criteria for sepsis according to age

	Bacteria					
	S.agalactiae	*N.meningitidis*	*E. coli*	*S.pneumoniae*	*S.pyogenes*	*S. aureus*
Globally (n=109)	36 (33.0 %)	26 (23.8 %)	15 (13.7 %)	12 (11.0 %)	8 (7.3 %)	3 (2.7 %)
Age						
<3 months (n=43)	33 (76.7 %)	0	6 (14.0 %)	0	0	1 (2.3 %)
3–23 months (n=36)	3 (8.3 %)	15 (41.6 %)	6 (16.7 %)	5 (13.9 %)	3 (8.3 %)	1 (2.8 %)
24–59 months (n=18)	0	7 (38.9 %)	1 (5.6 %)	5 (27.8 %)	4 (22.2 %)	0
>59 months (n=12)	0	4 (33.3 %)	2 (16.7 %)	2 (16.7 %)	1 (8.3 %)	1 (8.3 %)

bacteremia died. *N. meningitidis* was the leading cause of sepsis in patients older than 3 months of age. This kind of national surveillance system will allow the identification of future changes in epidemiology, for instance, after the introduction of the meningococcal B vaccine.

More than 50 % of the BCs were from samples collected in patients who were not septic in whom a focal infection had been identified, such as UTIs, pneumonias, and osteoarticular or otorhinolaryngologic infections. Moreover, three-quarters of them were obtained in patients with normal PAT findings. Nowadays, there are no clear recommendations for BC collection in pediatric patients diagnosed with focal infections in order to identify those with concomitant bacteremia. Indeed, some studies have shown a poor performance of this tool when used in other populations. In this way, different studies performed in adult populations have identified subgroups of patients with UTI [17] or cellulitis [18] who are more likely to have concomitant bacteremia, but this finding rarely modifies the subsequent management of patients with UTIs [19], pneumonia [20, 21], or cellulitis [22, 23]. Other studies have validated these findings in pediatric populations, concluding that the presence of a positive BC seldom modifies the outcome of children with a UTI [24] or those with a community-acquired pneumonia [25]. According to these results, a more selective use of BC would probably be more efficient in the management of these patients without affecting their outcome. Curiously, previous studies have shown an increase over recent years in the use of BC during Emergency Department visits, even in patients without apparent indicators for bacteremia [26].

Our study has several limitations. First, criteria for BC are not homogeneous across the 22 participating hospitals. In fact, some of them do not have an established policy on when to collect the BC in different clinical situations. This is reflected by the fact that a BC was frequently obtained in patients already diagnosed with a focal infection, despite the evidence that the results do not usually modify the subsequent management. It does not seem a cost-effective approach in most of these types of cases and studies like this one could be a starting point for trying to establish appropriate indications to request BCs. As previously noted, to the best of our knowledge, little is known about the current yield of collecting a BC in pediatric patients presenting with different focal infections in terms of both the prevalence of associated bacteremia and the real

Table 5 Characteristics of the patients who died

	Age (months)	PAT upon arrival	Time of evolution of fever (h)	Bacterium isolated	Final diagnosis
1	<1	Cardiopulmonary failure	2	*S. agalactiae*	Septic shock+bacterial meningitis
2	<1	Decompensated shock	48	*S. agalactiae*	Septic shock
3	6	Respiratory failure	24	*H. influenzae* type b	Septic shock+bacterial meningitis
4	14	Decompensated shock	8	*S. pyogenes*	Streptococcal toxic shock syndrome
5	183	Respiratory distress	No fever	*S. aureus*	Bacteremia (patient with spastic quadriplegia, died due to respiratory worsening during admission)
6	21	Cardiopulmonary failure	10	Group B *N. meningitidis*	Septic shock
7	145	Decompensated shock	No fever	*E. coli*	Septic shock+hemolytic uremic syndrome
8	106	Respiratory distress	96	*P. aeruginosa*	Septic shock+acute myeloid leukemia[a]

PAT Pediatric Assessment Triangle

[a] This patient was diagnosed with an acute myeloid leukemia during admission, and, so, she was included as "previously healthy" for the purpose of this study

usefulness of identifying a bacteremia in relation to the outcome of the patient. Unfortunately, as only patients with a positive BC are registered in our study, we cannot offer data about these two topics. However, we consider it mandatory to unify as much as possible the management of these patients based on the existing evidence. Accordingly, the SEUP and the Spanish Society of Pediatric Infectious Diseases are currently developing a Clinical Practice Guideline on the use of BCs in the PED, including indications for requesting a BC.

Second, although PCV13 was commercialized in Spain in June 2010, it must be taken into account that PCV13 is not included on the list of child vaccinations covered by the Spanish Public Health System, and coverage with this vaccine varies widely across regions in Spain. It could explain the low impact observed on the rate of invasive pneumococcal infections. However, even with this partial coverage, a reduction in the OB rate has been observed in some Spanish regions [1].

Recent studies have shown that new polymerase chain reaction (PCR) techniques have a significant role in the microbiological confirmation of meningococcal and pneumococcal invasive infections, identifying cases of bacteremia that would be missed when using only BCs [27, 28]. As the PCR technique is not routinely used in all the participating centers, we only included those cases in which the bacteremia was identified by BC. The inclusion of cases identified only by a PCR technique could have increased the relative prevalence of these two pathogens, although the results would have to be treated with caution, as it is not a globally accepted method for diagnosing a bacteremia.

In conclusion, *S. pneumoniae* is the most frequently isolated pathogen from BCs obtained in children without bacteremia risk factors attending the PED in Spain. The prevalence of isolated pathogens showed specific age-related distribution patterns that have implications for empiric antibiotic treatment. In this population, an abnormal PAT on presentation is associated with an increase in the mortality.

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