Blood Culture Sampling Rates at a German Pediatric University Hospital and Incidence of Invasive Pneumococcal Disease

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Abstract

Background: Recent pediatric surveillance studies suggest the incidence of pneumococcal bacteremia, but not meningitis, is lower in Germany than in most developed countries. Suboptimal case assessment in routine clinical practice has been suspected of contributing to this apparent discrepancy.

Methods: We aimed to assess the blood culture sampling rate at a German pediatric university hospital and the disease burden associated with pneumococcal bacteremia in children under 5 years of age. The study design was retrospective, based on data-linkage and chart review.

Results: Blood cultures were frequently obtained in sepsis (96%; CI 78–99%) and meningitis (95%; CI 77–99%), but less commonly in pneumonia (49%; CI 43–54%) and fever without focus (48%; CI 38–59%). Pneumococci were the most common source of clinically significant bacteremia in previously healthy children.

Conclusion: These blood culture sampling rates may be insufficient for the sensitive detection of pneumococcal bacteremia. Epidemiological surveillance based on poorly standardized diagnostic practices is prone to under-assessment.

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Introduction

Recent active surveillance of invasive pneumococcal disease (IPD) in German children under 5 years of age suggests an incidence of pneumococcal bacteremia of 6.9×10^{-5} and an overall incidence of IPD of 10.8×10^{-5} [1]. This is lower than in most other European countries [2] and considerably lower than in the United States before the introduction of routine vaccination with pneumococcal conjugate vaccines [3]. In contrast, pneumococcal meningitis rates in Germany (7.2×10^{-5} in children < 2 years) [1] compare to those reported from the United States (6.6×10^{-5} in the same age-group) [4].

Diagnostic practices for blood culture sampling in patients with potentially bacteremic conditions have frequently been suspected of being a factor in explaining the different reported rates of pneumococcal bacteremia in different healthcare settings. Data permitting such comparisons are scarce, but a British study supports the concept that variations in the incidence of invasive pneumococcal disease are largely due to variations in blood culture sampling rates. Significant regional differences in the incidence of pneumococcal bacteremia disappeared when correction for blood culture sampling rates was made [5].

We aimed to assess the local standard of data supplied to the national pneumococcal surveillance study and retrospectively analyzed blood culture sampling rates for various infectious disease conditions during the same time period at a pediatric tertiary care facility in Germany.

Methods

The study design was based on the data-linkage of electronic discharge diagnoses with electronic files on blood culture results from January 1996 through December 1999, backed up by chart review. The 120-bed pediatric department of the Heinrich Heine University, Düsseldorf, Germany, is a tertiary care facility that shares with other local hospitals the acute care and out-of-hours primary care for an urban population. The analysis was limited to children between 4 weeks and 5 years of age. Excluded from both databases were patients of the Department of Pediatric Hematology and Oncology, as the criteria for blood culture sampling in these children are markedly different.

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International Classification of Diseases, Ninth Revision (ICD-9) coded discharge diagnoses were filtered for the following groups (see Table 1 for ICD-9 codes): Sepsis/bacteremia, fever of unknown origin/fever without a source (FUO), meningitis, pneumonia, endocarditis, pyelonephritis, osteomyelitis/septic arthritis, erysipelas/ cellulitis, lymphadenitis and mastoiditis. These data were compared against the blood culture dataset for the presence of at least one blood culture (BC) during an admission period. In episodes without a BC record, the patient's hospital notes were reviewed to rule out data correlation or discharge diagnosis coding errors. In the case of pneumonia, a quasi-randomised subset of 207 cases without blood culture was analyzed (names were sorted alphabetically and every seventh case was reviewed). It was assumed the percentage would be the same in the pneumonia group as a whole and the estimated number of cases without a blood culture was adjusted accordingly. 95% confidence intervals (CI) for percentages with blood culture were calculated using Confidence Interval Analysis, Version 2.0 (University of Southampton, Hampshire, UK).

The records of all patients with positive blood cultures were reviewed and clinical information extracted. Isolates were interpreted as contaminants by predefined criteria. The blood culture system used throughout the study period was the BacT/Alert system, using either aerobic PediBact culture bottles or BacT/Alert-FA/FAN bottles, if anaerobic cultures were also taken. No information on the blood volume sampled or processing times was available.

Table 1
ICD-9 search terms.

Sepsis (038 septicaemia; 790.7 bacteremia, unspecified)

FUO (780.6 pyrexia of unknown origin)

Meningitis (036.0 meningococcal meningitis; 320 bacterial meningitis; 322 meningitis of unspecified cause)

Pneumonia (480 viral pneumonia; 481 pneumococcal pneumonia; 482 other bacterial pneumonia; 483 pneumonia due to other specified organism; 485 bronchopneumonia, organism unspecified; 486 pneumonia, organism unspecified)

Osteomyelitis/septic arthritis (730.0 acute osteomyelitis; 730.2 unspecified osteomyelitis; 711.0 pyogenic arthritis; 711.9 unspecified infective arthritis)

Pyelonephritis (590.1 acute pyelonephritis and acute pyonephrosis; 590.8 other pyelonephritis or pyonephrosis, not specified as acute or chronic; 590.9 infection of kidney, unspecified)

Endocarditis (421 acute and subacute endocarditis; 424.9 endocarditis, valve unspecified)

Cellulitis (035 erysipelas; 682 other cellulitis and abscess)

Mastoiditis (383.0 acute mastoiditis)

Lymphadenitis (683 acute lymphadenitis; 289.3 lymphadenitis, unspecified, except mesenteric)

Results

During the study period, a total of 6,845 inpatient episodes and 1,716 blood cultures were identified in children between 4 weeks and 5 years of age. Of these inpatient episodes, 620 had one of the previously mentioned diagnoses. Chart review of cases without evidence of blood cultures led to the exclusion of 83 cases because of incorrectly coded diagnoses. This comprises an estimated 44 incorrectly coded pneumonia cases, based on 21% (6/28) miscoded discharge diagnoses identified on selective chart review (28 out of 217 cases reviewed). In most cases, misclassification was either due to an event of the past medical history or an unconfirmed admission diagnosis being coded as an active discharge diagnosis.

The percentage of cases with blood cultures obtained was: sepsis 96% (21/22); FUO 48% (44/91); meningitis 95.2% (20/21); pneumonia 49% (154/317); pyelonephritis 90% (9/10); osteomyelitis 100% (4/4); erysipelas/cellulitis 62% (21/34); endocarditis 100% (5/5); lymphadenitis 58% (18/31); mastoiditis 50% (1/2). Figure 1 shows these percentages with confidence intervals. The number of confirmed cases with mastoiditis (n = 2, one with blood culture), endocarditis (n = 5, all with blood culture) and septic arthritis/osteomyelitis (n = 4, four with blood culture) was insufficient to allow meaningful estimation of the percentage of cases with blood cultures. They are therefore not included in the figure.

During the study period, 11 cases of pneumococcal bacteremia were observed. Two of these had pneumonia, nine had primary bacteremia without an apparent focus of infection. Other diagnostic tests performed in these patients were chest X-ray (8/9), lumbar puncture (3/9) and urine culture (8/9). Six of them appeared systemically unwell. Five children had underlying medical conditions (congenital heart disease, n = 2; AIDS, n = 1; bronchopulmonary dysplasia, n = 1; neurodegenerative disease, n = 1). All pneumococcal blood culture isolates were penicillin-sensitive. Intensive care admission was required in one case (a 3-month-old infant born prematurely). No fatalities were observed.

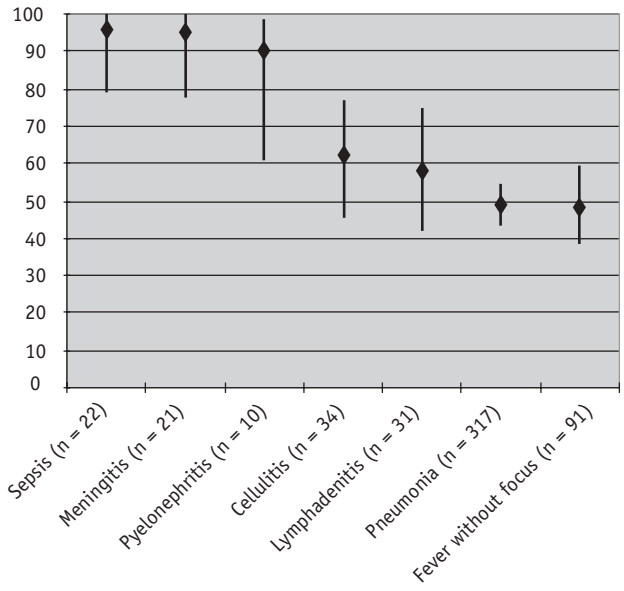

Figure 1. Percentage of cases with blood cultures, with 95% confidence intervals.

Table 2
BC isolates classified as contaminants.

Classified as contaminants in all cases	*Actinobacillus*, spore-forming aerobes, *Corynebacterium*, *Gemella morbillorum*, *Propionibacterium*, *Acinetobacter* in immunocompetent patients not receiving intensive care. *Ochrobactrum anthropi*, micrococci, apathogenic *Neisseria*
Classified as contaminants in most cases	Coagulase-negative staphylococci except in patients with indwelling vascular catheters or VP-shunt in situ. *Staphylococcus aureus* if mixed growth or identified in non-septic patient. α-hemolytic streptococci (except in patients with cardiac abnormality and/or endocarditis). Mixed growth except: Growth of at least one isolate in subsequent culture or one isolate having high likelihood to explain clinical picture and patient was treated for it.

Of 150 positive blood cultures, 84 were interpreted as contaminants upon chart review (Table 2). The remaining 66 positive cultures represented 52 distinct clinical episodes. *Escherichia coli* and *Streptococcus pneumoniae* were the leading causes of clinically significant bacteremia (Table 3). *S. pneumoniae* was the single most common isolate in previously healthy children (6/16 clinically significant episodes), followed by *Neisseria meningitidis*, *E.coli* and *Haemophilus influenzae* type b (2/16 episodes each).

Table 3
Microbiological isolates from clinically significant episodes of bacteremia.

Bacteria	n = 55 [a]	% of total
Gram-positiv cocci	**32**	**58.2**
Streptococcus pneumoniae	11	20
Coagulase-neg. staphylococci	7	12.7
α-hemolytic streptococci	6	10.9
Enterococcus	4	7.3
Staphylococcus aureus	2	3.6
β-hemolytic streptococci (group A, group B)	2	3.6.
Gam-negative cocci	**2**	**3.6**
Neisseria meningitidis	2	3.6
Gram-negative rods	**20**	**36.4**
Escherichia coli	11	20
Klebsiella pneumoniae	3	5.5
Enterobacter sp.	2	3.6
Haemophilus influenzae	2	3.6
Proteus mirabilis	1	1.8
Salmonella	1	1.8
Fungi	**1**	**1.8**
Candida albicans	1	1.8

[a] 55 isolates in 52 blood cultures (three polymicrobial episodes)

Among children with underlying medical conditions, *E.coli* was the leading cause (9/37 episodes), followed by coagulase-negative staphylococci (7/37 episodes) and *S. pneumoniae* (5/37 episodes).

Discussion

Between 1996 and 1999, *S. pneumoniae* was the most common cause of bacteremia among previously healthy children in our study population. It was the third most common in children with underlying medical conditions, where coagulase-negative staphylococci and *E.coli* prevailed. Two of the 11 cases of pneumococcal bacteremia were associated with pneumonia, but the majority had no identifiable focus of infection. In contrast to appropriately high blood culture sampling rates in patients with meningitis or sepsis, only slightly less than 50% of patients with pneumonia or fever without a focus had blood cultures. These are the conditions most commonly associated with pneumococcal bacteremia; pneumonia has accounted for 26–37% of pneumococcal bacteremia in some United States studies and FUO for 33–50% [6–8]. Our data, therefore, suggest a potential for under-ascertainment of pneumococcal bacteremia associated with routine clinical practice.

Pneumococcal bacteremia produces a less distinct clinical picture than meningitis. A large proportion of cases is occult and resolves with oral antibiotics or even spontaneously [6, 9]. Physicians' index of suspicion is an unreliable predictor of bacteremia risk [10]. Thus, high blood culture rates in conditions with increased risk of invasive pneumococcal disease are key to an appreciation of the disease burden. This was shown in a United States study that documented a 2.2-fold increase in the incidence of pneumococcal bacteremia over a 10-year period, coincident with a 2.3-fold increase in the number of blood cultures [8].

Retrospectively, we could not establish what criteria clinicians used for obtaining blood cultures. In patients at risk of pneumococcal bacteremia, primary aims would be the identification of patients at risk from secondary complications of bacteremia [11], as well as the ascertainement of antibiotic sensitivities. As antibiotic resistance rates in Germany were among the lowest in Europe during the study period [12], the likely impact of a positive blood culture on clinical management may have been perceived as limited by clinicians.

Our data are of patients who were hospitalized for their presenting illness, however, information regarding the practices in relation to ambulatory patients at risk of occult bacteremia was unavailable. We believe the percentage of outpatients with blood cultures would be lower than described here. Observations about the serotype distribution in different countries have been interpreted as suggesting that occult bacteremia, in particular, might be underdiagnosed in countries with low IPD incidence figures [2]. In the United States, the detection of occult bacteremia is facilitated by widely accepted guidelines with criteria for blood culture sampling in patients with FUO, using either a tem-

perature of 39 °C or a white blood cell count of 15,000 as the pertinent cutoff [13]. Although some United States studies have suggested clinical practice does not universally adhere to these recommendations, especially in the primary care sector, the same data show that most patients who receive any blood test have a blood culture included [14]. There are no equally influential recommendations to guide a pediatrician's practice in Germany.

A lack of published data precludes comparison of our findings with practices in other German hospitals or European countries. However, our results suggest surveillance that relies on routine diagnostic practice for its primary data may underestimate IPD incidence. Enhanced surveillance with sensitive and standardized methods of case ascertainment may be required in order to provide estimates of IPD incidence that reflect the wide spectrum of clinical presentations and to allow international comparisons.

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