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Original Article

Etiology of blood culture isolates among patients in a multidisciplinary teaching hospital in Kuala Lumpur

Rina Karunakaran, Nadeem Sajjad Raja, Kee Peng Ng, Parasakthi Navaratnam

Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

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Background and Purpose: Bloodstream infections are an important cause of morbidity and mortality among hospitalized patients and the surveillance of etiological agents in these infections is important for their prevention and treatment. Data on common organisms isolated from blood cultures from Malaysia are limited, and our aim was to identify the common bloodstream isolates in hospitalized patients at the University of Malaya Medical Centre (UMMC), Kuala Lumpur, Malaysia.
Methods: A retrospective analysis was conducted over a 1-year period from January to December 2004 by reviewing laboratory reports of patients from the UMMC. The clinical significance of the isolates was not analyzed.
Results: Coagulase-negative staphylococci were the most common organisms isolated, accounting for 33.0% of the total blood culture isolates, followed by *Staphylococcus aureus* (10.4%) and *Escherichia coli* (9.7%). The incidence of methicillin-resistant *S. aureus*, and extended-spectrum beta-lactamase-producing *E. coli* and *Klebsiella* spp. bacteremia was low (2.3% and 1.8% of total isolates, respectively). Non-albicans *Candida* were the most common fungal isolates.
Conclusions: The high number of coagulase-negative staphylococci should motivate clinicians and microbiologists to re-examine blood culture techniques in our institution. We recommend that further studies be carried out to establish the true significance of this organism among blood culture isolates.

Key words: Bacteremia; Etiology; Hospitals; Retrospective studies

Introduction

The surveillance of bloodstream pathogens in a hospital is important in monitoring the spectrum of microorganisms that invade the bloodstream and the types of organisms associated with a particular clinical discipline. Such data are often used to determine empiric antibiotic therapy and also to alert clinicians to emerging pathogens that may pose a threat to the community.

Bloodstream bacterial infections have been shown to have mortality rates of between 20% and 50% [1]. An association between the type of bloodstream organism and prognosis of the patient has been shown, with the isolation of enterococci, Gram-negative bacteria, and fungi being associated with increased mortality [2].

Corresponding author: Dr. Rina Karunakaran, Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Kuala Lumpur 50603, Malaysia.
E-mail: rinakarunakaran@yahoo.com; rina@ummc.edu.my

As there are limited published data on common etiological agents in bloodstream infections from Malaysia, we conducted this study to determine the microbial distribution of isolates from positive blood cultures at the University of Malaya Medical Centre (UMMC), Kuala Lumpur.

Methods

Collection and analysis of data

The microbiology laboratory at the UMMC (a 900-bed multidisciplinary teaching hospital) uses the BACTEC™ (BD Diagnostics, Becton Dickinson and Company, Sparks, MD, USA) blood culture system for routine blood cultures, and isolates are identified using standard microbiological tests or the API system (bioMérieux, Marcy l'Etoile, France) when necessary. Extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella* spp. are routinely identified using the double disk synergy method for all *Klebsiella* spp. and *E. coli* using the ceftazidime 30 μg, cefotaxime 30 μg and amoxicillin-clavulanate 20 μg/10 μg disks, based on the method described by Jarlier et al [3].

Data were collected retrospectively from laboratory records and included all organisms obtained from positive blood cultures and those obtained from inpatients at the UMMC over a 1-year period from January to December 2004. Repeat isolates from the same patient were excluded if isolation was within 14 days of a previous positive blood culture with the same isolate, as it was considered the same episode. An inhouse biphasic media consisting of brain heart infusion broth and brain heart agar is used for the specific isolation of fungi from blood cultures when fungal infection is thought likely. All positive fungal isolates from these cultures were also included in the study using the same criteria, i.e., if the isolate was obtained from the same patient within 2 weeks of a previous similar isolate, it was not included. No attempt was made to determine the clinical significance of any of the isolates.

Positive blood cultures were grouped according to various disciplines as follows: surgical, medical, general pediatric, special care nursery (the neonatal unit), hematological, various intensive care units (ICUs), and the obstetric and gynecology wards. The isolates were also analyzed according to the clinical discipline of the patient.

Results

A total of 23,678 BACTEC blood culture bottles (12,015 aerobic bottles, 11,663 anaerobic bottles) were received during the study period. Of these, 3941 bottles had growth of at least 1 organism, giving a positive isolation rate of 16.7%. The total number of bloodstream isolates was 1795, and included both bacterial and fungal isolates. Overall, 56.7% of the blood culture isolates (excluding anaerobes) were Gram-positive organisms and 38.4% were Gram-negative organisms.

Table 1 shows the 10 most common organisms isolated from blood cultures of inpatients in the hospital. The 3 most common organisms were coagulase-negative staphylococci (CoNS), *Staphylococcus aureus*, and *E. coli*. Most of the fungi isolated were *Candida* spp. (47.8% of fungal isolates). Among the other fungi isolated were *Paecilomyces* spp. (10.1%), *Penicillium* spp. (8.7%), and *Cryptococcus neoformans* (8.7%). Among the *Candida* spp., *Candida tropicalis* predominated (48.5% of all *Candida* spp.), followed by *Candida albicans* (21.2%) and *Candida parapsilosis* (15.2%). Anaerobes accounted for only 1.1% of microorganisms. Table 2 lists the most common bacteria isolated according to clinical discipline. More than half of the bacterial isolates were from patients in the 2 major subspecialties, i.e., medical (40.3%) and surgical (19.3%), and isolates from the various ICUs accounted for another 15.6%. Among the general pediatric patients, CoNS, *S. aureus*, and *Klebsiella* spp. were the most common isolates; *Haemophilus influenzae* comprised only 2.3%.

Table 1. Ten most common bloodstream isolates

Organism	No. of isolates (n = 1795) [%]
Coagulase-negative staphylococci	593 (33.0)
Staphylococcus aureus	187 (10.4)
Escherichia coli	174 (9.7)
Klebsiella spp.	148 (8.2)
Pseudomonas aeruginosa	84 (4.7)
Acinetobacter spp.	78 (4.3)
All fungi	69 (3.8)
Enterococcus spp.	69 (3.8)
Other streptococci	55 (3.1)
Enterobacter spp.	54 (3.0)

The number of isolates of methicillin-resistant *S. aureus* (MRSA) from the various clinical disciplines were also compared (Table 3). The proportion of MRSA among all *S. aureus* bloodstream isolates and among all bloodstream isolates was 26.0% and 2.3%, respectively. The highest incidence of MRSA bloodstream isolates (18 isolates) was from the medical wards, accounting for 2.6% of the total number of bacterial bloodstream isolates. MRSA accounted for 3.3% of all bacterial isolates from the various ICUs and 3.0% of isolates from the surgical wards, although the number of MRSA isolates in each of these wards was lower than that in the medical wards. There were no MRSA isolates from the general pediatric, obstetric and gynecology, ear, nose and throat, and ophthalmology wards or from the 2 private wards of the hospital.

The distribution of ESBL-producing *E. coli* and *Klebsiella* spp. is shown in Table 4. ESBL-producing *E. coli* accounted for 9 isolates (5.2% of the total *E. coli* isolated or 0.5% of the total bloodstream isolates) and ESBL-producing *Klebsiella* spp. accounted for 23 isolates (15.5% of *Klebsiella* spp. isolated or 1.3% of bloodstream isolates).

Burkholderia pseudomallei accounted for only 0.4% of the isolates.

Table 2. Common bloodstream bacterial isolates according to clinical discipline

Discipline	Bloodstream bacterial isolates (n = 1726) No. (%)	Most common isolates	Incidence in the ward (%)
Medical	696 (40.3)	Coagulase-negative staphylococci	31.6
		Staphylococcus aureus	14.7
		Escherichia coli	14.7
Surgical[a]	333 (19.3)	Coagulase-negative staphylococci	35.1
		Staphylococcus aureus	10.5
		Acinetobacter spp.	9.6
Various ICUs	269 (15.6)	Coagulase-negative staphylococci	43.9
		Klebsiella spp.	8.2
		Staphylococcus aureus	7.8
Hematological[b]	229 (13.3)	Coagulase-negative staphylococci	26.6
		Escherichia coli	14.4
		Klebsiella spp.	11.8
General pediatric	98 (5.7)	Coagulase-negative staphylococci	42.9
		Staphylococcus aureus	10.2
		Klebsiella spp.	8.2
Gynecology	39 (2.19)	Coagulase-negative staphylococci	25.6
		Escherichia coli	20.5
		Pseudomonas aeruginosa	12.8
		Klebsiella spp.	12.8
Special care nursery	32 (1.9)	Coagulase-negative staphylococci	50.0
		Klebsiella spp.	34.4
		Group B *Streptococcus*	6.3
Other wards[c]	16 (0.9)	Coagulase-negative staphylococci	18.8
		Staphylococcus aureus	18.8
		Escherichia coli	12.5
		Pseudomonas aeruginosa	12.5
Obstetric	14 (2.3)	Coagulase-negative staphylococci	35.7
		Group B *Streptococcus*	21.4
		Escherichia coli	7.1
		Proteus	7.1
		Citrobacter	7.1
		Staphylococcus aureus	7.1
Total	1726 (100)		

Abbreviation: ICU = intensive care unit

[a]Includes both general and orthopedic surgeries.

[b]Includes both adult and pediatric hematology wards.

[c]Includes ear, nose and throat ward, ophthalmology ward, and 2 private wards of the hospital.

Discussion

This study reveals the most common bloodstream isolates among inpatients, and provides surveillance information which can be useful during the decision-making process when the clinician has to choose empirical antimicrobial therapy while awaiting culture results.

Overall, Gram-positive organisms predominated among bloodstream isolates, with CoNS being the most common organism, followed by *S. aureus* and *E. coli*. The isolation of organisms from blood cultures does not necessarily equate with true bacteremia, as blood culture contamination rates have been known to vary from 2-6% [4]. The clinical significance of CoNS when isolated from blood cultures should always be evaluated. However, in this study, no attempt was made to exclude contaminants or determine contamination rates and some of the CoNS isolated may have been skin contaminants. Some studies have reported that up to 85% of CoNS represent contamination rather than true bacteremia [5,6], although at times it might be difficult to determine their true clinical significance [1]. However, in recent years, CoNS have become an important nosocomial pathogen partly because of the

Table 3. Distribution of methicillin-resistant *Staphylococcus aureus* (MRSA) among bacterial isolates from blood in the various clinical disciplines

Discipline	No. of MRSA isolates	Incidence in the ward (%)
Medical	18	2.6
Surgical[a]	10	3.0
Various ICUs[b]	9	3.3
Hematological[c]	3	1.3
Special care nursery	1	3.1

Abbreviation: ICU = intensive care unit

[a]Includes both general and orthopedic surgeries.

[b]Includes the general ICU, pediatric ICU, other ICUs, and the bone marrow transplant unit.

[c]Includes both adult and pediatric hematology wards.

increasing use of medical devices such as long-term indwelling catheters, vascular grafts, and prosthetic heart valves and joints [1,7]. Studies have reported that although *S. aureus* and *E. coli* were the most common causes of clinically significant bacteremia in 1992-1993 and 1975-1977, there has been a dramatic increase in the incidence of clinically significant CoNS and it was the third most common pathogen in the 1992-1993 study [2,5,6]. Others have also reported this increase of true bacteremia by CoNS in recent years [4].

In the present study, MRSA bacteremia accounted for 2.3% of the total bloodstream isolates, with the highest rates being in the various ICUs. However, the prevalence of MRSA bacteremia cases was highest in the medical wards. Collignon et al [8] reported that out of 12,771 bloodstream infections in 17 hospitals in Australia, 3192 episodes were due to *S. aureus* bacteremia with MRSA accounting for 26.0% of the *S. aureus*, or about 6.5% of the total bloodstream infections. Although in the present study the percentage of MRSA bacteremia appears lower in comparison (2.3%), our data did not exclude CoNS that might have been contaminants, and it is likely that the true proportion of MRSA bacteremia may have been higher. In the present study, MRSA accounted for 21.9% of *S. aureus* isolated from the bloodstream, which is in contrast to trends in Spain, Portugal, Italy, France, and the UK, where MRSA was reported to comprise 30-45% of *S. aureus* bacteremia [9].

ESBL-producing *E. coli* and *Klebsiella* spp., which are reported to cause increased mortality among bacteremic patients [10], only accounted for 1.8% of the total bloodstream isolates; the incidence was highest in the medical wards, followed by the various ICUs and hematological wards. A study from the Seoul National University Children's Hospital between 1993 and 1998 found the prevalence of ESBL producers among all *E. coli* and *Klebsiella* spp. to be 17.9% and 52.9%, respectively [10]. In another study from Italy over a 5-year period, ESBL-producing *Klebsiella pneumoniae* accounted for 32.7% of total *K. pneumoniae* bloodstream isolates [11]. Although the percentage of ESBL producers among *E. coli* and *Klebsiella* spp. in this study was much less (5.2% and 15.5%, respectively) for the 1-year study period, we used only the double disk synergy method for the detection of ESBLs, and so may not have detected all ESBL strains present. The difference in rates could also have been due to different patient populations in the respective hospitals (the Korean study [10] was in children). The rates of ESBL found among total hospital isolates (1.8%) may also have been higher if CoNS contaminants had been excluded.

The most common organisms isolated from the bloodstream in the general pediatric and adult populations do not seem to be very different; CoNS was the most common isolate, followed by *S. aureus*, and while *E. coli* was third most common isolate in adults, *Klebsiella* spp. was the third most common in children. According to a review article on the detection of bacteremia and fungemia [1], microorganisms causing

Table 4. Distribution of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella* spp. among bloodstream bacterial isolates according to clinical discipline

Discipline	No. of ESBL-producing *E. coli* and *Klebsiella* spp.	Incidence in the ward (%)
Medical	11	1.6
Various ICUs[a]	10	1.5
Hematological[b]	6	2.6
Surgical[c]	5	1.5

Abbreviation: ICU = intensive care unit

[a]Includes the general ICU, pediatric ICU, other ICUs, and the bone marrow transplant unit.

[b]Includes both adult and pediatric hematology wards.

[c]Includes both general and orthopedic surgeries.

bacteremia and fungemia in children are similar to those in adults, although anaerobic bacteremia tends to be less common in children, and staphylococcal, streptococcal, and meningococcal infections are more likely to occur in non-immunosuppressed children. Gram-negative bacteremia was more likely in neonates, and *H. influenzae* bacteremia had nearly vanished from many centers due to widespread immunization [1]. In our study, we also found more bacteremic isolates of *Klebsiella* spp. among patients in the special care nursery (neonatal ward) as compared to the general pediatric wards, and it was the second most common isolate there after CoNS. However, we did not analyze all neonates as a group; some neonates may have been admitted to other general pediatric wards, and therefore not all were represented in the special care nursery. *H. influenzae* accounted for only 2.3% of pediatric bacteremic isolates and there were no isolates of *N. meningitidis* in both children and adults in the year of this study.

Anaerobic bacteremia has been reported to be on a decreasing trend [6]; Sharp reported a rate of 1.5% of all positive blood cultures [12], and the high number of possible contaminants again may have influenced the rate of 1.1% found in this study.

The incidence of fungal blood infections has reportedly increased in recent years, with rates of 5.4% in 1980 and 9.9% in 1990, as reported by the National Nosocomial Infection Surveillance System for the United States Hospitals [13]. In this study, fungi accounted for 3.8% of the total isolates. Most of the fungi were various spp. of *Candida*, of which the majority were non-albicans *Candida*, with a predominance of *C. tropicalis*. Several studies continue to report *C. albicans* as the most common cause of candidemia [14-16]. However, trends towards increasing numbers of non-albicans *Candida* among bloodstream pathogens have also been reported [14]. The preponderance of non-albicans candidemia is important to note, as empirical therapy with fluconazole, while appropriate against *C. albicans*, may not be adequate to cover other spp. of *Candida*.

B. pseudomallei, the causative agent of melioidosis, a disease that is endemic in Malaysia, was responsible for only 0.4% of the total blood isolates; however, non-septicemic forms of the disease are common and are detected by culture from infected sites.

In conclusion, the high incidence of CoNS alerts us of the need to re-examine blood culture techniques in the hospital. Further studies are required to determine the true significance of this organism among septicemic patients in UMMC.

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