

Bacteremia in children at the University Hospital in Riyadh, Saudi Arabia

Fahad Abdullah Al-Zamil

Riyadh, Saudi Arabia

Background: Bacteremia is a major pediatric health care problem despite the availability of new modalities in the management of this disease. The aim of the present study was to determine the incidence and pattern of bacteremia in pediatric group at a tertiary hospital in Riyadh, Saudi Arabia.

Methods: This retrospective study was conducted at the Department of Pediatrics, College of Medicine, King Khalid University Hospital, Riyadh in the period of January 2003 to January 2005. Positive culture was found in 259 patients aged below 15 years with a total of 8244 admissions in the period.

Results: The highest incidence of bacteremia was found in patients aged less than 1 year (57.9%), and the majority of patients (30.5%) were infants aged less than 1 month. *Staphylococcus aureus* was the most common isolated pathogen (18.7%). Prematurity was associated with 13.2% of the cases, and respiratory tract infection (10.1%) and fever (76.1%) were chief complaints.

Conclusions: *Staphylococcus aureus* is the most common isolated pathogen. The most common primary infections are respiratory tract infection and septic meningitis. *Klebsiella pneumoniae* and *E. coli* are the most common isolated Gram-negative organisms.

World J Pediatr 2008;4(2):118-122

Key words: bacteremia;
incidence;
Staphylococcus aureus

Introduction

Bloodstream infection has been a primary concern of physicians for over 80 years. Blood cultures are usually done for the evaluation of sick children with or without evidence of a focus of infection.^[1] Many serious infections are associated with bacteremia and the blood culture may be positive even when cultures of the specimens taken from the local area of infection (cerebrospinal fluid, tissue aspirate, synovial fluid) are negative. A report of a positive blood culture without apparent site of infection usually prompts a clinical re-evaluation and search for a primary focus.

Septicemia is a pathological condition with a mortality rate varying from 30% to 70% depending on virulence of the pathogen and host factors.^[2,3] Bloodstream infection is an important cause of death, giving a rate of 25%-50%.^[4] More recently Blomberg et al (2007)^[5] reported a mortality of 40% in pediatric patients with laboratory confirmed bacteremia. Bacterial isolation from blood specimen is often associated with high morbidity and mortality particularly among children.^[6] In recent years, bloodstream infections due to Gram-positive cocci have increased in frequency and antimicrobial resistance. *Staphylococcus aureus* bacteremia is a clinical problem with a particularly high incidence and mortality.^[7] The majority of bacteremia cases are caused by *Staphylococcus spp.*, *Streptococcus spp.*, *Enterobacter spp.*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas*.^[8]

Children who are younger than 36 months are at increased risk for bacteremia or sepsis secondary to the immaturity of their immune system. Furthermore, children in this age group may be febrile for 1 of 4 major reasons: fever of unknown reason, occult bacteremia, serious bacterial infections, and sepsis. Serious bacterial infection includes bacteremia, sepsis, infections of the soft tissues or joints, meningitis, bacterial enteritis, bacterial pneumonia, and urinary tract infections. Since the growing health care problems are related to bacteremia in children, we attempted to investigate the incidence and pattern of bacteremia

in pediatric group at the University Hospital, Riyadh, Saudi Arabia. In addition, the study also aimed to provide information to the community and health officials about the main causes of bacteremia and its associated microorganism in pediatric patients.

Methods

This present retrospective study was conducted in the Department of Pediatrics, College of Medicine, King Khalid University Hospital, Riyadh during the period of January 2003 to January 2005. Included were 259 patients aged 1-180 months (less than 15 years) with positive blood culture.

All positive blood cultures were reported by the Bacteriology Laboratory of King Khalid University Hospital in the same period. The case records of all patients less than 15 years old were reviewed. The King Khalid University Hospital is a tertiary hospital that receives patients from the central region of the country. Clinical, microbiological data and other information such as temperature, immunodeficiency, central line and antibiotic therapy were obtained from the patient's medical record. A questionnaire concerning the demographic data, age, sex, clinical symptoms and signs was completed by the parents or guardians. Blood cultures were performed with an automated blood culture machine (Bact Alert, Organon Teknik). The organisms were identified by standard bacteriologic techniques.

Furthermore, antibiotic susceptibility testing was done by the Modified Kirby-Bauer Method. Antimicrobial test was done with ampicillin/amoxicillin, amoxicillin/clavulamic acid, aztreonam, ciprofloxacin, ampicillin, imipenem, aztreonam, cefepime, cefixime, cefotaxime, ceftazidime, ceftriaxone, cefuroxime, cephalexin, gentamicin, meropenem, piperacillin/tazobactam and cotrimoxazole.

Data analysis

Univariate analysis was performed using Epi-Info version 6.0 (Centers for Disease Control and Prevention, Atlanta, USA). The means and proportions were compared by the Chi-square test and Student's *t* test. Statistical significance was considered at a value of $P < 0.05$.

Results

During the study period, the medical records of the 259 patients with bacteremia were reviewed. The age of the patients ranged from 1 to 180 months (mean 27.3, median 7; SD 42.33). Of the 259 patients, 152 (58.7%)

were male and 107 (41.3%) female. Bacteremia was documented in 150 patients (57.9%) of less than 1 year, of whom 79 (30.5%) were less than 1 month. Fifty (19.3%) of children were between 5 and 15 years old (Table 1). Infections and associated clinical conditions in these children are shown in Table 1 and Fig. 1. They included septicemia (16%), respiratory tract infection (10.1%), surgical repair (7.0%), osteomyelitis (5.4%), prematurity (13.2%), meningitis (8.2%), gastroenteritis (4.7%), cellulitis (3.5%), sickle cell disease (2.7%), and

Table 1. Characteristics of patients with bacteremia

Characteristics	Number of patients (%)
Age group (mon)	
0-1	79 (30.5)
2-12	71 (27.4)
13-60	59 (22.8)
61 and above	50 (19.3)
Sex	
Male	152 (58.7)
Female	107 (41.3)
Causes according to the site of infection	
Septicemia	41 (16)
Prematurity	34 (13.2)
Respiratory tract infection	26 (10.1)
Surgical repair	18 (7.0)
Meningitis	21 (8.2)
Osteomyelitis	14 (5.4)
Gastroenteritis	12 (4.7)
Cellulitis	9 (3.5)
Sickle cell disease	7 (2.7)
Nephrotic syndrome	4 (1.6)
Others (necrotising enterocolitis, cystic fibrosis, malignancy, pneumonia, burn, etc)	73 (28.18)

Table 2. The different types of isolated micro-organisms

Organisms isolated	Number of organisms (%)
<i>Staphylococcus aureus</i>	48 (18.7)
<i>Diphtheroids</i>	17 (6.6)
<i>Escherichia coli</i>	16 (6.2)
<i>Haemophilus influenzae</i>	16 (6.2)
<i>Klebsiella pneumoniae</i>	17 (6.6)
<i>Streptococcus spp</i>	42 (16.3)
<i>Salmonella typhi</i>	11 (4.3)
<i>Brucella</i>	9 (3.5)
<i>Enterobacter taylora</i>	9 (3.5)
<i>Acinetobacter</i>	10 (3.9)
<i>Pseudomonas aeruginosa</i>	9 (3.5)
MRSA	8 (3.1)
<i>Moraxella cat</i>	4 (1.6)
<i>Bacillus spp</i>	7 (2.7)
<i>Candida</i>	2 (0.8)
<i>Yeast</i>	2 (0.8)
<i>Polymicrobial</i>	13 (5.2)
Others	19 (7.34)

nephrotic syndrome (1.6%).

Gram-negative bacteria were predominant in 131 (50.6%) patients, while Gram-positive ones in 128 (49.4%) (Table 2, Fig. 2). The most common causative agents of bacteremia in these children were *Staphylococcus aureus* (48 patients, 18.7%), *Streptococcus spp* (42, 16.3%) (mainly group A *beta*-hemolytic streptococci), and *Klebsiella pneumoniae* (17, 6.6%). *Escherichia coli* and *Haemophilus influenzae* accounted for 16 (6.2%) patients respectively, *Diphtheroids* 17 (6.6%), *Salmonella* 11 (4.3%), *Acinetobacter* 10 (3.9%), and *Brucella*, *Enterobacter* and *Pseudomonas aeruginosa* 9 (3.5%) respectively. Methiciline resistance *Staphylococcus aureus* (MRSA) accounted for 8 (3.1%) patients, *Bacillus spp* 7 (2.7%), *Yeast* and *Candida* 2 (8%) respectively and *Polymicrobial* 14 (5.6%) (Table 2).

Chief complaints in most of the patients were fever, i.e., 197 (76.1%) patients who complained of

fever and only 62 (23.7%) patients presented without fever. Symptoms recorded beside fever were dependent on the primary site of infection. They were rash (12, 4.7%), convulsions (32, 12.4%), vomiting (120, 46.3%), diarrhoea (46, 17.8%), cough (59, 22.8%), abdominal pain (38, 14.7%), chest pain (13, 5.1%), and bone pain (30, 11.6%).

Staphylococcus aureus was resistant to ampicillin/amoxicillin (95%), penicillin G (95%), cephalexin/cephradine (44%), and amoxicillin/clavulenic acid (24%). *Streptococcus pneumoniae* resistant to the above drugs accounted for 35%, 38%, 31% and 16%, respectively. Gram-negative isolates were resistant to ampicillin/amoxicillin, including *Klebsiella* 100%, *Acinetobacter* 95% and *E. coli* 65%, respectively. The resistance rates of *Klebsiella*, *Acinetobacter*, and *E.coli* to amoxicillin clavulanic acid were 21%, 70% and 37%, respectively. Those of *Klebsiella*, *Acinetobacter* and *E. coli* to cotrimoxazole were 27%, 71% and 50%, respectively.

Our treatment protocol for bacteremia cases was the third generation of intravenous cephalosporin combined with ampicillin. However, the antibiotics were modified according to the blood culture.

Discussion

Bloodstream infection still carries high morbidity and mortality in hospitalized patients despite the availability of current sophisticated therapeutic modalities.^[5,9] Over the last decade, the occurrence of bloodstream infection has increased in hospitalized patients.^[9] The detection of causative bacteria is essential to the proper treatment.

In this study, bacteremia was confirmed in the 259 patients with various diseases. Primary infection was the common cause giving a rate of 84%. The most common infections identified included respiratory tract infection (10.1%) and septic meningitis (8.2%). The findings of our study were not in agreement with those reported by Nimri et al (2001)^[10] that common infections were gastroenteritis (40.4%) and pneumonia or bronchopneumonia.^[11]

The most common causative bacteria were *Staphylococcus aureus* (48 cases, 18.7%) isolated by surgical repair from osteomyelitis cases, *Streptococcus spp* (42, 16.3%), and *Streptococcus pneumoniae* (15, 5.8%) isolated from cases of pneumonia. Similar to our study, *Streptococcus pneumoniae* was reported previously as the most common pathogen in children with bacteremia.^[12] In our study, group B *Streptococcus* was found as a causative pathogen in 11 neonates (4.3%). Unlike our study, group A *Streptococcus* was found in

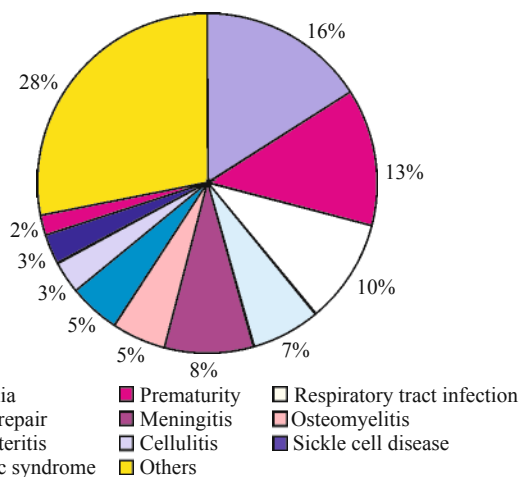


Fig. 1. Distribution of different types of primary cause of infection.

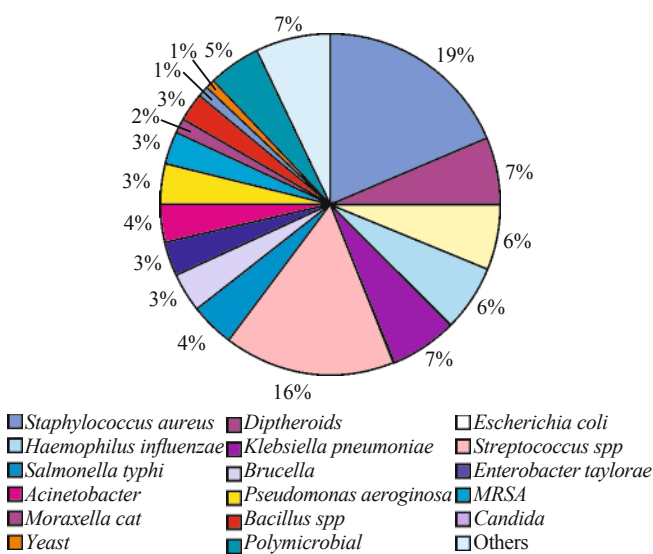


Fig. 2. Distribution of different types of micro-organism isolated.

few cases of bacteremia.^[13]

Staphylococcus epidermidis exists in the normal skin and mucosal flora and their presence in blood might indicate contamination of blood culture.^[14] In this study, we found 192 *Staphylococcus epidermidis* isolates, and in the same period, researchers from King Faisal Specialist Hospital, Riyadh found 124 cases of *Staphylococcus epidermidis* infection.^[15] They considered the majority of these isolates as possible skin contaminants. The number of positive blood cultures and sepsis symptoms encourage clinicians to decide antimicrobial therapy.

In this study, *E. coli* was isolated from 6.2% of the cases, the same number of cases of *Haemophilus influenza* (6.2%). *Klebsiella pneumoniae* was isolated from 6.6% of the cases. A study reported that *E. coli*, *Pseudomonas aeruginosa* and *Klebsiella spp* were the most common isolated Gram-negative organisms.^[16] Our findings in the present study were also consistent with those that *E. coli* were the most frequent Gram-negative bacterial species recovered from blood culture.^[17] The incidence of bacteremia caused by *Klebsiella pneumoniae* was 6.6% of the cases in this study; the rate was similar to that reported previously (7.4%).^[12]

We found *Haemophilus influenzae* in 16 cases (6.2%), including 15 cases (93.7%) under the age of 5 years. This is in agreement with the rate of 92% for cases of *Haemophilus influenzae* below 5 years.^[18]

Pseudomonas aeruginosa was isolated from 3.5% of cases by positive blood culture in this study. This concurs with Wendt et al^[16] who found that this organism was the commonest Gram-negative pathogen. Similarly, a study of children undergoing transplantation found *Pseudomonas aeruginosa* as a major pathogen causing blood infection.^[8]

Polymicrobial bacteremia was found in 13 cases (5.2%) in this study. The isolates included *E. coli*, MRSA, *Klebsiella*, *Pseudomonas*, *Acinetobacter*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Candida*, and *Streptococcus*. Polymicrobial bacteremia was previously reported to be caused by *E. coli*, *P. aeruginosa*, *K. pneumoniae*, *K. oxytica*, *S. marcescens*, *E. cloacal*, and *A. caumannii*.^[11]

In addition, occult bacteremia was detected in 13 patients (31%) and the mean age of children was 21 months.^[19] Similarly, 78.6% of the isolates were Gram-positive bacteria including the *Staphylococcus epidermidis* (55.4%), *Staphylococcus aureus* (9.5%) *Streptococcus pneumoniae* (4.5%) and *Enterococcus faecalis* (4%).^[20] Furthermore, Gram-negative bacteria in 44 cases (20%) included *Escherichia coli* and *Klebsiella pneumoniae* (*K. pneumoniae*) (3.6% respectively). Three isolates (1.3%) were *Candida glabrata*.

High rates of resistance to common antibiotics for mild and moderate infection are potentially a serious problem in hospitalized patients. Since particular concern is given to the number of non-susceptible isolates, the overall high rates of resistance to available antibiotics in this study may not reflect the actual rates in the community, because those patients with more susceptible organisms may be successfully treated at home or at a local health center. Multiple drug resistance of isolates from bacteremic children is also reported.^[21,22]

We conclude that the highest incidence of bacteremia may be present in patients below 1 year and most of them are infants under 1 month old. Considering the whole study population, we find *Staphylococcus aureus* is the most common isolated pathogen. The most common primary infections are respiratory tract infection and septic meningitis. *Klebsiella pneumoniae* and *E. coli* are the most common isolated Gram-negative organisms.

Acknowledgements

The author would like to thank Dr. Muslim Al Saadi (assistant Prof. & Consultant Pediatric Respirologist) for critical review of the manuscript and Mr. Nabeel Abdulqader for his collection of the data.

Funding: None.

Ethical approval: Ethical Committee of the College of Medicine approved the study.

Competing interest: I declare that in the present study there is no conflict of interest with any institution or organization.

Contributors: This manuscript is a sole work of Dr. Fahad Al Zamil.

References

- 1 Wald ER, Minkowski JM. Bacteremia in childhood. South Med J 1980;70:904-905.
- 2 Wenzel RP, Pinsky MR, Ulevitch RJ, Young L. Current understanding of sepsis. Clin Infect Dis 1996;22:407-412.
- 3 Wheeler AP, Bernard GR. Treating patient with severe sepsis. N Engl J Med 1999;340:207-214.
- 4 Gill J, Kumar R, Todd J, Wiskin C. Methicillin-resistance *Staphylococcus aureus*: awareness and perceptions. J Hosp Infect 2006;62:330-337.
- 5 Blomberg B, Manji KP, Urassa WK, Tamim BS, Mwakagile DS, Jureen R, et al. Antimicrobial resistance predicts death in Tanzanian children with bloodstream infections: a prospective cohort study. BMC Infect Dis 2007;7:43.
- 6 Orrett FA, Changoor E. Bacteremia in children at a regional hospital in Trinidad. Int J Infect Dis 2007;11:145-151.
- 7 Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality

- associate with Methicillin susceptible *Staphylococcus aureus* bacteremia: a meta analysis. *Clin Infect Dis* 2003;36:53-59.
- 8 Weinstein MP, Mirrett S, Reimer LG, Wilson ML, Smith-Elekes S, Chuard CR, et al. Controlled evaluation of BacT/Alert standard aerobic and FAN aerobic blood culture bottles for detection of bacteremia and fungemia. *J Clin Microbiol* 1995;33:978-981.
 - 9 Weinstein MP, Towns ML, Quartey SM, Mirrett S, Reimer LG, Parmigiani G, et al. The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. *Clin Infect Dis* 1997;24:584-602.
 - 10 Nimri LF, Rawashdeh M, Meqdam MM. Bacteremia in children: etiologic agents, focal sites, and risk factors. *J Trop Pediatr* 2001;47:356-360.
 - 11 Emori TG, Gaynes RP. An overview of nosocomial infections, including the role of the microbiology laboratory. *Clin Microbiol Rev* 1993;6:428-442.
 - 12 Haddon RA, Barnett PL, Grimwood K, Hogg GG. Bacteremia in febrile children presenting to a pediatric emergency department. *Med J Aust* 1999;170:475-478.
 - 13 Moses AE, Beerl M, Engelhard D. Group A streptococcal meningitis: report of two cases. *J Infect* 1998;36:116-118.
 - 14 Kloos WE, Bannerman TL. Update on clinical significance of coagulase-negative staphylococci. *Clin Microbiol Rev* 1994;7:117-140.
 - 15 Hussain QS, Khalil SH, Johnson S, Flourney DJ. Etiology of bacteremia in a referral hospital in Saudi Arabia. *Ann Saudi Med* 1987;7:51-55.
 - 16 Wendt C, Messer SA, Hollis RJ, Pfaller MA, Herwaldt LA. Epidemiology of polyclonal gram-negative bacteremia. *Diagn Microbiol Infect Dis* 1998;32:9-13.
 - 17 Anthony RM, Brown TJ, French GL. Rapid diagnosis of bacteremia by universal amplification of 23S ribosomal DNA followed by hybridization to an oligonucleotide array. *J Clin Microbiol* 2000;38:781-788.
 - 18 Lee HJ. Epidemiology of systemic hemophilus influenzae disease in Korean children. *Pediatr Infect Dis J* 1998;17(Suppl 9):S185-189.
 - 19 Abdullah AM, Chowdhury MN, al Mazrou A, Al-Zamil F, Peds AB, Kambal AM. Spectrum of *Haemophilus influenzae* type b disease in children at a university hospital in Riyadh, Saudi Arabia. *J Trop Pediatr* 1997;43:10-12.
 - 20 Babay HA, Twum-Danso K, Kambal AM, Al-Otaibi FE. Bloodstream infections in pediatric patients. *Saudi Med J* 2005;26:1555-1561.
 - 21 Silverstein M, Bachur R, Harper MB. Clinical implications of penicillin and ceftriaxone resistance among children with pneumococcal bacteremia. *Pediatr Infect Dis J* 1999;18:35-41.
 - 22 Totapally BR, Walsh WT. Pneumococcal bacteremia in childhood: a 6-year experience in a community hospital. *Chest* 1999;113:1207-1214.

Received May 21, 2007

Accepted after revision February 15, 2008