Bacterial isolates from fatal cases of bloodstream infections at a university hospital in Central, Saudi Arabia

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ABSTRACT

Objective: To describe the microbiology, underlying medical conditions and risk factors contributing to bloodstream infection (BSI) and mortality at a University Hospital in Riyadh, Kingdom of Saudi Arabia.

Methods: We conducted this study at King Khalid University Hospital, Riyadh, Saudi Arabia, wherein clinical data from patients who died with BSI were collected. All isolates from these patients, from 1 January to 31 December 2004, were identified and antimicrobial susceptibilities were determined.

Results: Of the total 778 patients with BSI, 82 (10.5%) died. Among which 34 (41.5%) were elderly. Half of the patients were from the intensive care units (ICUs). Cardiovascular diseases were the most common diagnosis in 14 (17.1%) patient, followed by malignancy 13 (15.9%), and respiratory diseases 12 (14.6%). Eleven (13.4%) had chronic liver diseases, 6 (7.3%) with renal diseases, sepsis in 5 (6.1%), 4 (4.8%) were post- surgical cases, 3 (3.7%) cases had systemic lupus erythematosus (SLE) and 3 premature infants. The majority of BSI episodes were monobacterial, 71(86.5%). Over 90% of the isolates were hospital acquired. Coagulase negative *Staphylococci* (CoNS) were the most common organisms representing 25 (30.5%) of all organisms isolated, while Gram positive as a whole represented 50 (61%). Thirty one (38%) were Gram negative bacteria among which *Pseudomonas* species 6 (7.3%) and *Escherichia coli* (*E. coli*) 5 (6%) were the most common. Two (2.4%) of isolates were *Candida glabrata*.

Conclusion: Mortality in our patients with BSI was attributed to old age and underlying medical conditions. The risk factors for nosocomial BSI were ICU admission, intravascular catheterization and respiratory tract infections.

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Bloodstream infection (BSI) is a significant cause of morbidity and mortality. It accounts for 10-15% of hospital acquired infections.[1,2] Results of mortality tend to vary between different regions and countries. Mortality due to bacteremia has been reported to range from 17.5-85% and to be among the most frequent causes of death in the Unites States and Spain.[3] Almost all reported studies on mortality due to BSI came from hospitalized patients with pre-existing medical conditions and associated risk factors such as intensive care unit (ICU) admission, intravascular catheters, respiratory intubations, prolonged hospitalization and treatment by broad spectrum antimicrobial agents.[3-7] Mortality was also attributed to the causative organisms where *Candida albicans* was reported to have the highest mortality rate (58.5%) whilst Gram negative bacteria 17%.[8] Apart from mortality and morbidity and prolonged hospital stay, BSI is associated with significant cost and difficulty in choice of empirical antimicrobial therapy without knowledge of the causative organisms and its susceptibility patterns.

The aim of the current study is to describe the microbiology, underlying medical conditions and risk factors contributed to BSI and mortality at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia.

Methods. This study was conducted at the Microbiology Unit at KKUH over a one year period from 1 January to 31 December 2004. King Khalid University Hospital is 700-bedded with 5 different ICUs. It provides primary, secondary and tertiary health care. The clinical data collected from each patient medical record includes: age, gender, whether ICU or non ICU patient, clinical diagnosis, presence of vascular catheters or respiratory intubation and the antimicrobial therapy.

Initially, 10 ml of blood were aseptically collected from adults and for pediatric cases, 2-5 ml of blood were collected. Patients having fever (temperature greater than 39°C (102.2°F), chills, hypotension

with no apparent infection at other site and febrile patients with intravascular devices consisted the criteria in taking blood for culture in our hospital. In neonates, the criteria include; toxic appearance, lethargy, hypotension, hypoventilation, hyperventilation or cyanosis. Blood was inoculated into blood culture bottles (aerobic and anaerobic bottles for adults and standard pediatric bottle for children) (Biomerieux, S.A. 69280 Marcy-l'Etoile, France). Blood culture bottles were then incubated in BacT/Alert 3D (Organon Teknika, USA). Aerobic bottles were vented before incubation. Bottles showing positive growth index were Gram stained and subcultured on 2 sheep blood agar plates (aerobic and anaerobic), chocolate agar and MacConkey agar plates. One of the blood agar and chocolate agar plates were then incubated aerobically for 24-48 hours. The other blood agar was incubated anaerobically for 48 hours. MacConkey agar plates were incubated aerobically for 24 hours. Identification and susceptibility testing were carried out by MicroScan Walk Away 96 (Dade Behring Inc., West Sacramento, CA95691, USA). Colonies from MacConkey plates were inoculated into MicroScan rapid negative Combo Panel types 30, 31 and negative MIC Panel types 20, 21 and positive MIC Panel type 20. Specimens that grew more than one organism were also subcultured, organisms separated and identified similarly. Only one isolate was considered from each patient with recurrent BSI with the same bacterial species. The same species identified within the previous 30 days were excluded. All aerobic and facultative anaerobic bacteria were identified by the MicroScan except *Bacteroides* species, yeasts as well as any bacteria that failed to be identified by the MicroScan. These were identified by standard methods. Our laboratory criteria for considering CoNS or other skin organisms as contaminant includes isolation from single blood culture or multiple blood cultures of different strains and if the organism is not related to infection at another site.

Results. *Clinical results.* Over the 12 months period, a total of 778 patients had BSIs but of whom 82 died. **Table 1** summarizes the characteristics, underlying medical conditions and microorganisms isolated from the patients that died with BSI. Thirty-four (41.5%) of the patients were elderly (age range 65-92 years) and 13 (15.8%) were children (age range 3 days-15 years). Forty six (56.1%) were males. Half of the patients were from ICUs with respiratory intubations and intravascular catheters for more than 48 hours and on antimicrobial chemotherapy. Cardiovascular diseases were the most common diagnosis, 14 (17.1%); 12 of these were elderly, one was a 15-year-old patient with rheumatic fever and

Table 1 - Risk factors, underlying diseases and distribution of microorganisms isolated from the bloodstream of patients and who died with blood stream infection (BSI) (total no. of positive BSI=778).

Risk factors	Number	(%)
Age		
3 days- 15 years	13	(15.8)
16 – 45 years	15	(18.3)
46 – 64 years	20	(24.4)
65 – 92 years	34	(41.5)
Gender		
Males	46	(56.1)
Females	36	(43.9)
Intensive care unit admission	41	(50)
Underlying diseases & conditions		
Cardiovascular diseases	14	(17.1)
Malignancy	13	(15.9)
Respiratory diseases	12	(14.6)
Liver diseases	11	(13.4)
Renal failure	6	(7.3)
Sepsis/septic shock	5	(6.1)
Post surgery	4	(4.8)
Systemic lupus erythematosus	3	(3.7)
Prematurity	3	(3.7)
Others	11	(13.4)
Microorganisms		
Monomicrobial isolates	71	(86.5)
Polymicrobial isolates*	11	(13.4)
Gram positive bacteria		
CoNS	25	(30.5)
Staphylococcus aureus	7	(8.5)
Methicillin susceptible	4	(57.1)
Methicillin-resistant	3	(42.8)
Enterococcus species	7	(8.5)
Diphtheroids	4	(4.8)
Gram negative bacteria		
Pseudomonas species	6	(7.3)
Escherichia coli	5	(6)
Pseudomonas aeruginosa	4	(4.8)
Acinetobacter species	4	(4.8)
Klebsiella pneumoniae	3	(3.6)
Enterobacter species	3	(3.6)
Stenotrophomonas maltophilia	2	(2.4)
Serratia marcescens	2	(2.4)
Bacteroides fragilis	2	(2.4)
Candida glabrata	2	(2.4)
Other bacterial isolates	6	(7.3)
No. of death	**82**	(10.5)

Polymicrobial BSI isolates include*: Coagulase negative *Staphylococci* (CoNS) + *Enterococcus* species, *Pseudomonas* species + CoNS, *Staphylococcus aureus* + *Streptococcus agalactiae*, *Acinetobacter* species + *E. coli*, *Enterococcus* species + *Pseudomonas* species, and *Acinetobacter* species + *Enterococcus* species

the other patient had endocarditis and renal failure. Thirteen (15.9%) patients had malignancy distributed as follows: 5 (6%) colon carcinoma, 4 (5%) non-Hodgkin lymphoma, 2 (2.4%) acute leukemia, a case of neuroblastoma and another patient with hepatocellular carcinoma. Regarding respiratory diseases; 9 elderly patients died with aspiration pneumonia, the rest were patients with pulmonary tuberculosis and viral pneumonia and pulmonary embolism. Chronic liver diseases accounted for 11 (13.4%) of the causes. Five elderly patients had end stage renal failure and one child had nephritic syndrome. Seventeen (20.7%) of the elderly patients who died had diabetes mellitus or hypertension or both. Among the patients who died following surgical procedures; 2 underwent coronary artery by-pass, one had perforated duodenal ulcer and associated gastrointestinal bleeding and another had peri-anal fistulectomy.

Microbiological results. In 71 (86.5%) of the episodes, BSI was monobacterial while 11 (13.4%) were polymicrobial BSI (**Table 1**). Over 90% of these isolates were hospital acquired. Gram positive bacteria were the most common isolates accounting for 50 (61%) of the total isolates whilst 31 (38%) were Gram negative bacteria. Twenty-five (30.5%) of the Gram positive were CoNS and the majority were isolated from single occasions, patients had no related infection at another site. *Pseudomonas species* 6 (7.3%) and *E. coli* 5 (6%) were the most common Gram negative bacteria. *Bacteroides fragilis* was isolated from 2 cardiac patients with central venous catheters and *Stenotrophomonas maltophilia* from a premature infant and an adult with sepsis. Two isolates (2.4%) were *Candida glabrata* isolated from one patient with aspiration pneumonia and another from a patient with perforated duodenal ulcer. Other bacterial isolates 1 (1.2%) each included; *Streptococcus pyogenes* from an elderly patient with aspiration pneumonia, *Streptococcus agalactiae* from hepatocellular carcinoma patient, *Streptococcus* species from a 7-month-old child with nephritic syndrome, *Mycobacterium fortutum* from a patient with immune deficiency, *Brucella* species from SLE patient and *Proteus mirabilis* from an elderly patient with cerebrovascular accident and atrial fibrillation (**Table 2**). Three out of 7 *Staphylococcus aureus* (*S. aureus*) (42.8%) were methicillin resistant *S. aureus* (MRSA) and isolated from a case of colon carcinoma, a post coronary artery-bypass and post arrest patients. The methicillin susceptible *S. aureus* were isolated from hepatocellular carcinoma, neuroblastoma, a patient with septic shock and another post arrest patient. All the *Enterococcus* species isolated were susceptible to ampicillin. None of the Gram positive isolates were resistant to vancomycin. Nine patients had multi-resistant Gram negative bacteria (such as resistant to 3 or more classes of antimicrobial agents) that included: 3 *E. coli;* one from preterm infant, one from an elderly patient with aspiration pneumonia and one from post-cardiac surgery patient. One *Klebsiella pneumoniae* (*K. pneumoniae*) was isolated from a leukemic patient, one *Pseudomonas* species from a patient with cerebrovascular accident, one *Enterobacter* species from a patient with liver disease and obstructive jaundice and 3 of 4 *Acinetobacter* species

All these patient were admitted to general hospital wards or ICUs for a period ranges from 14-45 days, had indwelling vascular catheters, respiratory intubation and on broad-spectrum antimicrobial therapy including: ceftriaxone, ceftazidime cefepime, amikacin, ciprofloxacin, imipenem, meropenem or piperacillin -tazobactam.

Discussion. In the present study, the overall mortality among patients with BSIs was 10.5%, which is slightly lower than reported from another local study.[9]

Table 2 - Blood culture isolates from different underlying medical conditions.

Underlying diseases/conditions	N	Bacterial isolates
Cardiovascular diseases	14	*Enterococcus* species, CoNS, *P. aeruginosa*, *Acinetobacter* species, *Proteus mirabilis*, *Bacteroides fragilis*, diphtheroids
Malignancy	13	
Leukemia	2	*K. pneumoniae*, *Enterobacter* species
Solid tumors	11	*S. aureus*, CoNS, *Streptococcus agalactiae*, *Pseudomonas* species, *Enterobacter* species, *Acinetobacter* species
Respiratory diseases	12	*Streptococcus pyogenes*, CoNS, diphtheroids, *E. coli*, *P. aeruginosa*, *Pseudomonas* species, *Candida glabrata*
Liver diseases	11	*K. pneumoniae*, *Enterobacter* species, *Aeromonas hydrophilia*, *Enterococcus* species, CoNS
Renal failure	6	*Enterococcus* species, CoNS, *Pseudomonas* species, *Acinetobacter* species
Sepsis / septic shock	5	*S. aureus*, CoNS, *E. coli*, *P. aeruginosa, Stenotrophomonas maltophilia*
Post-surgery	4	CoNS, *K. pneumoniae, E. coli, Pseudomonas* species, *Acinetobacter* species, *Enterococcus* species, *Candida glabrata*
Prematurity	3	*E. coli*, *Stenotrophomonas maltophilia,* CoNS
Systemic lupus erythematosus	3	*Pseudomonas* species, *Brucella* species, CoNS

P. aeruginosa - Pseudomonas aeruginosa, K. pneumoniae - Klebsiella pneumoniae, S. aureus - Staphylococcus aureus, E. coli - Escherichia coli, P. aeruginosa - Pseudomonas aeruginosa,

Due to the diversity of clinical conditions, it was not possible to attribute BSI as a cause of mortality in all our patients. However, mortality could be attributed to different factors such as the causative organisms, age, underlying diseases and ICU admission. In relation to the organisms, the most commonly isolated organisms in patients who died of BSI in our study were CoNS, *S. aureus*, *Enterococcus* species followed by *Pseudomonas* species, *E. coli*, *Pseudomonas aeruginosa* (*P. aeruginosa*). CoNS and diphtheroids were considered as contaminants. Weinstein[10] reported that patients whose blood cultures grow contaminants usually have only a single positive blood culture. In contrast, other studies have shown that only a single blood culture positive for CoNS is necessary for identification of BSIs.[11,12] Mortality due to CoNS was reported to be 14%.[11] MRSA was associated with increased risk of death compared to methicillin susceptible isolates.[13] This is in contrast to our results. In relation to age, mortality was higher among old age patients compared to children and other age groups and the reason could be attributed to advanced age and serious underlying medical conditions, which probably requiring longer periods of hospitalization and increases the risk of acquisition of nosocomial infections among these patients. Kaoutar et al[7] reported that 60% of the patients had underlying diseases that were fatal in short time before nosocomial infections could set in. In this study, most patients with cardiovascular disorders were elderly and stayed for longer duration in ICU and required continuous use of intravascular and central venous catheterization. Central venous catheterization was reported to be the most common risk factor for BSI and attributed with 4-37% of mortality.[6] It has been reported that 1 to 20 of patients admitted to ICU acquired BSI and these infections were associated with a crude mortality rate of 40%.[14-16] Jamal et al[8] reported 58.5% mortality rate among ICU patients due to fungemia in contrast to only 2.4% in our study. *Stenotrophomonas maltophilia* was reported from 76% of hospitalized patients with central venous catheters.[17] This is in contrast to our results. *Enterococcus* species was noticed to be common in our patients with cardiac and renal diseases as well as in association with instrumentation and prior antimicrobial therapy and with polymicrobial BSI. This finding is consistent with other study.[18] Aspiration pneumonia was common in elderly patients with nasogastric tubes or percutaneous enterogastric tubes, in addition to poor oral hygiene and aspiration of gastric contents in acute respiratory distress.[19,20] Gram negative bacilli were more commonly isolated from these patients, which agreed with other reports.[19] Although anaerobic bacteria was reported to cause 45-58% of community acquired aspiration pneumonia, we did not isolate any anaerobic bacteria from these patients.[20] The majority of patients who died with malignancy had solid tumors compared to those with leukemia (13.4% versus 2.4%). This could be explained by the different types and stages of solid tumors and local conditions at the site of neoplasm predisposes to bacteremia such as: inflammation and local necrosis in the alimentary tract, intestinal lesions, portal hypertension, prolonged antimicrobial therapy and tumor necrosis.[21] In Egyptian pediatric patients with cancer, mortality was higher among those with polymicrobial infections and fungemia.[22] In this study, a patient with hepatocellular carcinoma had double infection with *S. aureus* and *Streptococcus agalactiae*. Mortality due to *S. aureus* was reported to be between 3.7-49% while 26% for *Streptococcus* species BSI.[9,23,24] In contrast, Dinkel et al[25] reported that the influence of nosocomial infections was small among patients with malignancy but greater for metabolic disorders and trauma.[25] Outcome of BSI caused by a member of the family *Enterobacteriaceae* depends on several factors such as the underlying diseases, the clinical severity at the time of administration of antimicrobials and the antibiotic regimen.[26] In contrast, Kang et al[4] reported that mortality among patients who received inappropriate antimicrobial therapy was not significantly higher than the mortality in those who received appropriate antimicrobial therapy such as carbapenem or ciprofloxacin, which are most effective for *E. coli* and *K. pneumoniae*. Risk factors for acquiring multi-resistant extended spectrum β-lactamases producing organisms is prior use of oximino-cephalosporins and ICU admission.[26] In our study, nosocomial multiresistant Gram negative single isolates such as *Pseudomonas* species, *Enterobacter* species, *K. pneumoniae* and *Acinetobacter* species probably contributed to mortality in our patients. However, *E. coli* monobacterial BSI was reported to have lower mortality (8.9%) compared with *E. coli* polymicrobial BSI (35%).[27] Advanced chronic liver diseases appeared to be common among those who died of BSI. Patients who died with sepsis were mainly young children. It has been reported that septic children usually present with no focus of infection especially neonates and BSI could be missed if blood culture was not performed.[28,29] Furthermore, *P. aeruginosa* BSI in

Related topics

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immunocompromised patients can lead to death within the first 72 hours.[30] This is similar to one of our pediatric patients who died with *P. aeruginosa* sepsis. Nosocomial BSI following major surgical procedures such as cardiac surgery also contributed to death in 4.9% in our study, which agrees with the finding of Kaoutar et al.[7]

In conclusion, mortality among our patients population is likely to be related to age and underlying medical diseases. Risk factors such as ICU admission with associated use of intravascular catheters and respiratory intubations and the development of hospital acquired BSI further complicated the underlying conditions of these patients and led to death.

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