

BLOOD STREAM INFECTIONS: MICRO-ORGANISMS, RISK FACTORS AND MORTALITY RATE IN QATIF CENTRAL HOSPITAL

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Blood stream infections (BSI) lead to sepsis and septic shock, which continue to be important causes of morbidity and mortality. A vast body of literature has been devoted to this. Worldwide studies about the epidemiology, microbiological etiology and prognosis of BSI have been performed over the last six decades. These have shown changing patterns of the pathogens involved, namely the emergence of gram-negative pathogens as a major cause of bacteremia after the beginning of the antimicrobial era,^{1,2} and the recent re-emergence of gram-positive pathogens and fungi, especially among the growing population of immunocompromised patients.^{3,4}

While many studies are available from Western countries, mostly conducted in major teaching or research institutions, little work has been published from the developing countries. Extrapolation of data to hospitals in developing countries may be misleading because of the differing effects of factors such as endemic pathogens, underlying diseases, and antimicrobial prescribing habits.

The present study aims to define the pattern of blood stream infections over a five-year period in a general referral hospital in a developing country, to compare it with previously published work from Saudi Arabia and other countries, to point out differences in the spectrum of micro-organisms, community-acquired and hospital-acquired BSI, and to determine the case fatality rate in relation to different micro-organisms and patient age groups.

Materials and Methods

This study was carried out in Qatif Central Hospital (QCH). Qatif is located on the Gulf in the Eastern Province of Saudi Arabia, and the hospital is a 400-bed referral facility that provides all medical services. Data from the hospital's Department of Microbiology and from patients' records were reviewed. Patients with bacteremia and

fungemia diagnosed by blood culture from May 1990 through May 1995 were identified and included in the study. The course of each episode of bacteremia or fungemia was followed until its conclusion.

Ten and 3 mL of blood samples were drawn aseptically from adult and pediatric patients with suspected BSI, respectively. Each blood sample was divided into two bottles: NR6A (enriched soybean casein digest broth with CO₂) for aerobic cultures, and NR7A (prereduced enriched soybean casein digest broth with CO₂) for anaerobic cultures. Both bottles were incubated for seven days (eight weeks for brucella) at 37°C, and read daily on a Bactec NR 660 (Becton Dickinson). Subcultures on blood agar, chocolate agar and MacConkey agar were incubated aerobically with CO₂, and subcultures on blood agar were also incubated anaerobically for 48 hours. A total of 23,704 paired bottles were processed during the study period.

The significance of isolates was judged according to the growth in different blood cultures, the clinical findings and the isolates obtained from other body sites. Micro-organisms isolated were identified by standard techniques⁵ or by API 20 E system.

An episode of bacteremia was defined by the isolation of one (unimicrobial) or more (polymicrobial) micro-organisms from blood culture(s), together with clinical evidence of systemic infection. Bacteremia which developed before or within three days of admission and which was not related to medical procedures undertaken after admission, was designated as community acquired, and that with late onset or indirect relation to medical procedures undertaken in the hospital was considered to be hospital acquired. To calculate the case fatality rate, an attempt was made to establish an association between BSI and patient mortality based upon clinical evidence and cultural results.

Results

During the five years of study, 84,400 patients were admitted to Qatif Central Hospital. These included 1324 cases of blood stream infections (BSI), giving an overall rate of 15.7 per 1000 admissions. Of these, 703 cases (53.1%) were male and 621 (46.9%) were female. Most cases of BSI (97.5%) were caused by a single organism,

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TABLE 1. Blood stream infections of gram-positive and gram-negative organisms.

	No. of isolates	%
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Gram-positive organisms (460)		
<i>Staphylococcus aureus</i>	176	38.3
Coagulase-negative <i>Staphylococci</i>	75	16.3
<i>Strept. pneumoniae</i>	53	11.5
<i>Enterococci</i>	42	9.1
Beta hemolytic <i>Streptococci</i>	42	9.1
<i>Strept. viridans</i> and other <i>Streptococci</i>	61	13.3
Other gram-positive bacteria	11	2.4
Gram-negative organisms (853)		
<i>Escherichia coli</i>	151	17.8
<i>Klebsiella</i> spp.	144	16.9
<i>Salmonella</i> spp.	124	14.5
<i>Salmonella typhi</i>	45	5.3
<i>Pseudomonas</i> spp.	106	12.4
<i>Enterobacter</i> spp.	61	7.1
<i>Proteus-Morganella</i> spp.	44	5.2
<i>Acinetobacter</i> spp.	25	3.0
<i>Serratia</i> spp.	22	2.6
<i>Hemophilus</i> spp.	22	2.6
<i>Brucella</i> spp.	22	2.6
<i>Shigella</i> spp.	5	0.6
<i>Bacteroids</i> spp.	36	4.2
Other gram-negative bacteria	46	5.4
<i>Candida</i> spp.	46	-

while 32 cases had polymicrobial blood infections. In three of the 32 cases, three organisms were isolated, while in the remaining 29, two different organisms were isolated. All 1359 organisms recovered were composed of 460 gram-positive, 853 gram-negative and 46 *Candida* species (Table 1).

Staphylococcus aureus was by far the most frequently isolated organism (176, or 13%), and it was also most common (38.4%) among the gram-positive group. Others frequently reported among the gram-positive group were coagulase-negative *Staphylococci* (16.3%), *Streptococcus pneumoniae* (11.5%), *Enterococci* (9.1%), and beta hemolytic *Streptococcus* (9.1%) isolates. Other less frequent gram-positive organisms included *Clostridium* spp., *Peptostreptococci*, group *J.K. corynebacterium* and *Listeria monocytogenes*. On the other hand, *Salmonella* spp. were the most frequently isolated (19.8%) of all gram-negative bacteria. Out of a total of 169 *Salmonella* isolates, 45 (26.6%) were *Salmonella typhi*. Other frequently encountered gram-negative bacteria were *E. coli* (11.1%), *Klebsiella* spp. (10.6%), *Pseudomonas* spp. (7.8%) and *Enterobacter* spp. (4.5%). *Candida* spp. was the cause of BSI in 46 cases, representing 3.4% of all encountered organisms.

With regard to the place of acquisition, 57% of BSI were acquired in the community, as compared to 43% acquired in the hospital (Table 2). Almost all cases of *Streptococcus pneumoniae*, *Salmonella* spp., *Brucella* spp., *Haemophilus* spp. and *Shigella* spp. were community acquired, while coagulase-negative *Staphylococci* and *Candida* spp. were all predominantly hospital acquired. Polymicrobial blood infections were hospital acquired.

The age of the patients with BSI ranged from newborn to more than 90 years old (Table 3). Approximately 25% of cases were children under one year of age, and the incidence decreased to 7.4% in the 5-12-year age group, but then markedly increased to 31% in patients over 50 years of

age. In considering organisms involved with the different age groups, it was obvious that *S. aureus* and *Pseudomonas* spp. were frequent in all ages, while beta-hemolytic *Streptococci* and *E. coli* were predominant among neonates and those over 50 years of age.

The overall case fatality rate (CFR) was 14.1% (Table 3), being highest in the over 50-year age group (23.4%), followed by neonates (17.1%). There were no significant gender differences. The CFR among patients with community-acquired BSI was 9.7%, as compared to 21% among patients with hospital-acquired infection. The CFR caused by gram-positive organisms was 14%, compared to 15.6% caused by gram-negative organisms. Among the organisms associated with the highest CFR were beta-hemolytic *Streptococci* (26%), *S. aureus* (17%), coagulase-negative *Staphylococci* (16%), and *Enterococci* (11.9%). Among gram-negative organisms, the following produces the highest CFR: *Serratia* spp. (31.8%), *Proteus-Morganella* spp. (31.8%), *Pseudomonas* spp. (22.6%), and *Acinetobacter* spp. (20%). The CFR with *Candida* spp. was 28.3%, but only 3% with *Salmonella* spp., while *Brucella* spp. did not cause any fatalities.

Discussions

Blood stream infection rates vary in reports from different countries. For example, the incidence in European and US hospitals has ranged from 4.3-21/1000 admissions,⁶⁻⁸ whereas in Zaria, Northern Nigeria, it reached 96/1000 admissions.⁹ However, our data showed an incidence of 15.7/1000 admissions, which is comparable to the 16.1/1000 admissions reported at the University of the West Indies,¹⁰ but higher than the 7/1000 admissions reported from Abu Dhabi.¹¹

Gram-negative organisms have been encountered more often from blood cultures than gram-positive organisms. *E. coli*, *Klebsiella* spp. and *Salmonella* spp. have accounted for more than 54% of gram-negative isolates. These findings are similar to those reported in other Gulf countries.¹¹ *Pseudomonas* spp. was recovered from 7.8% of blood cultures at Qatif Central Hospital, which is similar to the 7.2% reported by Weinstein et al.¹²

Other gram-negative organisms encountered were *Enterobacter* spp., *Proteus-Morganella* spp., and *Acinetobacter* spp., which were predominantly hospital-acquired pathogens, probably related to advanced invasive medical technology at our hospital. Reports from developed countries point increasingly to hospital-acquired BSI.^{12,13} On the other hand, reports from developing countries have indicated community-acquired pathogens as the predominant cause of BSI.¹⁴ In the present study, 57%

TABLE 2. Incidence and acquisition of blood stream infections and micro-organisms.

	Community acquired	Hospital acquired	Total isolates	% of all isolates
<i>Staphylococcus aureus</i>	113	63	176	12.9

Coagulase-negative <i>Staphylococci</i>	2	73	75	5.5
<i>Strept. pneumoniae</i>	52	1	53	3.9
<i>Enterococci</i>	19	23	42	3
<i>Beta hemolytic Streptococci</i>	30	12	42	3
<i>Strep. viridans</i> and other <i>Streptococci</i>	56	5	61	4.5
Other gram-positive bacteria	8	3	11	0.8
Subtotal gram-positive group	280 (60.9%)	180 (39.1%)	460	33.8
<i>Escherichia coli</i>	110	41	151	11.1
<i>Klebsiella</i> spp.	51	93	144	10.6
<i>Salmonella</i> spp. (other than <i>typhi</i>)	124	–	124	9.1
<i>Salmonella typhi</i>	44	1	45	3.3
<i>Pseudomonas</i> spp.	40	66	106	7.8
<i>Enterobacter</i> spp.	20	41	61	4.5
<i>Proteus-Morganella</i> spp.	17	27	44	3.2
<i>Acinetobacter</i> spp.	10	15	25	1.8
<i>Brucella</i> spp.	21	1	22	1.6
<i>Serratia</i> spp.	6	16	22	1.6
<i>Haemophilus</i> spp.	21	1	22	1.6
<i>Shigella</i> spp.	5	–	5	0.4
<i>Bacteroids</i> spp.	23	13	36	2.6
Other gram-negative bacteria	34	12	46	3.4
Subtotal gram-negative group	490 (57.4%)	363 (42.6%)	853	62.8
<i>Candida</i> spp.	4	42	46	3.4
Total micro-organisms	774 (57%)	585 (43%)	1359	

of BSI were community acquired, and this rate of incidence is comparable to that reported from other areas of the Gulf.¹⁴ The endemicity of certain bacterial pathogens in the community may have been significant in this respect. Previous studies have noted that *Salmonella* spp., *Haemophilus* spp. and *Streptococcus pneumoniae* were major community-acquired organisms causing BSI.¹⁰ In this study, a similar pattern was observed where almost all community-acquired BSI were caused by *Salmonella* spp., *Haemophilus* spp. and *Streptococcus pneumoniae*. *S. aureus* was also predominant in community-acquired BSI, and this is also consistent with the findings of other studies.^{1,10}

The presented data also revealed that BSI due to *E. coli* was community acquired in 73% of cases. This could be explained by the fact that *E. coli* is the major pathogen in community-acquired urinary tract infections, and so BSI caused by *E. coli* is secondary to bacteriuria. At Qatif Central Hospital, 15% of BSI were in neonates, and it was

also found that gram-negative organisms caused 60% of neonatal BSI, and that *Klebsiella* spp., *E. coli*, *Pseudomonas* spp., *Serratia* spp. and *Enterobacter* spp. were the most frequent isolates. This is in agreement with the results of other studies from Saudi Arabia,¹⁵ and other countries.^{16,17} Worthy of note is the complete absence of infection due to *Salmonella* spp. in the neonates, in contrast to an earlier study from a specialist hospital in Riyadh where *Salmonella* spp. were reported as the most common organism in neonatal BSI.¹⁸ Our data showed that 30% of all BSI were found in patients over 50 years, and that 65% of these were caused by gram-negative organisms. These findings are similar to those reported by Young.²¹ The present study shows that 9.5% of BSI were due to *Candida* spp., which is higher than 4.4% reported previously in this institution.¹⁹ A variety of factors could contribute to this alarming infection rate, including misuse of a broad spectrum of antibiotics, indwelling central venous or arterial catheters, often unavoidable procedures and the immature immune defence mechanisms of very low birthweight infants.²⁰

In this study, the overall case fatality rate attributed to BSI was 14.1%, which is comparable to that reported from the University of Minnesota Medical Center, but lower than the 42% reported in a study by Weinstein et al.¹² This could be explained by the types of patients and underlying conditions. On the other hand, the increased mortality documented among elderly patients conforms with similar findings by Myers et al.,²⁷ whereas the 17% mortality rate among neonates is slightly higher than that reported from other parts of Saudi Arabia.²⁸ In the latter study, coagulase-negative *Staphylococci* were the most common cause of BSI, and they are known to be accompanied by a lower mortality rate than infections with gram-negative bacteria.²⁹ At the same time, the present finding that hospital-acquired BSI caused significantly higher mortality than community-acquired infections is consistent with several previous reports.¹¹⁻³⁰ Moreover, our present findings, which indicate that the mortality rate of 14% due to gram-positive organisms is not much different from the 15.6% due to gram-negative organisms, do not support the findings of several earlier studies, which showed a higher mortality rate due to BSI caused by gram-negative organisms.^{10,12,13} This could be explained by the low mortality rate (3%) of *Salmonella* infections, which are endemic in Saudi Arabia. On the other hand, our data confirm the results of others that *Serratia* spp., *Pseudomonas* spp., *Enterobacter* spp. and *Klebsiella* spp. are associated with high mortality rates.¹²⁻³¹ Mortality from streptococcal BSI has been found to be 23%,³² which is similar to the 26% reported at this hospital. Mortality due to *S. aureus* has ranged from 3.7%¹⁰ to 49%.³³ The figure of 17% in the present study may be explained in part by the occurrence of more blood stream infections related to

TABLE 3. Blood stream infections: incidence of micro-organisms and mortality rate in relation to age of patients.

Organisms	Neonate	Infant	1-5	>5-12	>12-50	>50	Total isolates	Mortality	
								Cases	%

<i>Staphylococcus aureus</i>	21	15	16	23	41	60	176	30	17
Coagulase-negative <i>Staphylococci</i>	7	12	7	2	18	29	75	4	6
<i>Strept. pneumoniae</i>	4	10	16	5	10	8	53	6	11.3
<i>Strept. viridans</i> and other <i>Streptococci</i>	9	7	13	6	13	13	61	4	6.5
<i>Enterococci</i>	5	3	8	–	10	16	42	5	11.9
<i>Beta hemolytic Streptococci</i>	13	3	3	1	8	14	42	11	26
Other gram-positive bacteria	1	1	1	–	5	3	11	1	7.3
Subtotal gram-positive group	60	51	64	37	105	143	460	61	13.3
<i>Salmonella</i> spp. including <i>typhi</i>	–	15	21	30	94	9	169	5	3
<i>Escherichia coli</i>	17	6	6	2	38	82	151	23	15.2
<i>Klebsiella</i> spp.	56	17	10	5	18	38	144	22	15.3
<i>Pseudomonas</i> spp.	14	14	13	13	19	33	106	24	22.6
<i>Enterobacter</i> spp.	8	10	7	3	14	19	61	11	18
<i>Proteus-Morganella</i>	2	–	3	–	2	37	44	14	31.8
<i>Acinetobacter</i>	5	1	3	2	7	7	25	5	20
<i>Brucella</i> spp.	–	–	1	2	16	3	22	–	–
<i>Serratia</i> spp.	9	3	1	1	4	4	22	7	31.8
<i>Hemophilus</i> spp.	–	7	6	2	1	6	22	4	18.2
<i>Shigella</i> spp.	–	1	2	1	–	1	5	1	20
<i>Bacteroids</i> spp.	–	3	2	–	16	15	36	6	16.7
Other gram-negative bacteria	19	3	6	2	9	17	46	6	13
Subtotal gram-negative group	120	80	81	63	238	271	853	128	15
<i>Candida</i> spp.	19	11	5	1	6	4	46	13	28.3
Total micro-organisms	199	142	150	101	349	418	1359	202*	14.9*
Mortality									
Cases: 187 (14.1%)*	34	16	5	5	29	98			
% in age group	17%	11.3%	3.3%	5%	8.3%	23.4%			

*Difference due to polymicrobial cases.

the intravascular devices, and to skin and wound infections. This study confirms earlier reports^{34,35} that systemic candidiasis is a major cause of morbidity and mortality in very ill patients in NICU, and in chronically ill infants.

Blood stream infections continue to be life-threatening. Their incidence, the prevalence of causative organisms, and the case mortality rate tend to vary greatly between hospitals in the same area, between regions in the same country and between different countries.

Extrapolation of data from one hospital to another may sometimes be misleading. Treatment should as far as possible be based on local data, and since that may also vary from time to time even in the same hospital, regular surveillance of BSI is desirable.

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