Oman Medical Journal (2011) Vol. 26, No. 4: 240-247
DOI 10. 5001/omj.2011.59

Bloodstream Bacterial Pathogens and their Antibiotic Resistance Pattern in Dhahira Region, Oman

Prakash KP,[1] Vinod Arora,[2] Geethanjali PP[3]

Received: 02 May 2011/ Accepted: 06 Jul 2011

Abstract

Objectives: To describe the epidemiological, clinical, microbiological characteristics and antimicrobial resistance pattern of Bloodstream infections in Dhahira region, Oman.

Methods: Clinical data was collected from all patients with positive blood cultures for two years period. Standard laboratory methods were used for blood culture. Antibiotic sensitivity was tested using Kirby-Bauer disc diffusion method.

Results: Of the 360 bacterial pathogens isolated from 348 patients, 57.8% were gram-positive and 42.2% were gram-negative. The common isolates were: *Streptococcus* species 76 (21.1%), coagulase-negative *Staphylococci* 75 (20.8%), *Escherichia coli* 43 (11.9%), *Staphylococcus aureus* 41 (11.4%). Overall, mortality was 21.3% (74/348). *Staphylococcus* species (*Staphylococcus aureus* and CoNS) were more commonly resistant to Trimethoprim/ Sulphamethoxazole (35.3%) and Penicillin (25.9%). *Streptococcus* species were resistant to Trimethoprim/Sulphamethoxazole (39.1%) and Erythromycin (19.6%).

Conclusion: Bloodstream infections are important causes of morbidity and mortality in our patients, especially among chronically ill elderly adult males. Prescription of proven resistant antibiotics to suspected bacteremic patients needs attention in Dhahira region.

Keywords: Bloodstream infections; Antibiotic resistance; Bacterial pathogen; Epidemiology; Oman

Introduction

Identification of various organisms in a patient's blood is of immense diagnostic and prognostic importance. Blood cultures are essential in the diagnosis and treatment of the etiologic agents or sepsis. Bacteria and fungal pathogens remain an important cause of Bloodstream infections (BSI). Bacterial pathogens isolated from BSI are a leading cause of significant patient morbidity and mortality. BSI accounts for 10-20% of all nosocomial infections and is the eighth leading cause of mortality (15%) in the United States.[1-3]

The impact of specific etiologic agents on BSI patient outcome is tremendous; BSI increases the mortality rate, prolongs patient stay in an intensive care unit and in the hospital, and increased health care costs.[4,5] Furthermore, inadequate empirical therapy of bacteraemic infections is associated with adverse outcomes, including mortality.[6,7]

Researchers have observed significant changing trends in the microbiology, epidemiology and clinical as well as prognostic significance of positive blood cultures over a period of time.[3,5] For these reasons, surveillance of bloodstream infections from blood cultures and their antibiotic resistance patterns are vital to the care of patients and prevention of BSI. Several interventions have proven to be effective.[8-11]

The gradual increase in antimicrobial resistance among pathogens especially in developing countries is a cause of concern. In Dhahira region, most health institutions (especially primary health centers) where advanced laboratory facilities are limited, antibiotics are often used for empirical treatment. It has been observed that inadequate therapy is the common reason for antimicrobial resistance.[12] Hence, information on most likely causative organisms and their resistance patterns can increase the likelihood of selecting an effective antimicrobial drug for empirical treatment. Considering the current worldwide changes, information about the occurrence of pathogens and antibiotic resistance pattern are now seen as decisive for optimizing treatment.[13]

The prevalence and antibacterial resistance among bacterial pathogens among populations may vary at national or regional level. Appropriate surveillance data is critical to draw conclusions. Laboratory data of bacterial isolates from patients with BSI provide good setting for such resistance surveillance. The collection of additional information, such as the presumed focus of infection, demographic characteristics of patients and the treatment specialty enhances the usefulness of the microbiological data.[12]

Hospitalized patients are at high risk of infection for various reasons.[5] Hence, surveillance of BSI pathogens and their antimicrobial resistance pattern in the hospital is the key to its prevention.

Prakash Patel
Regional Epidemiologist, Directorate General of Health Services, Al Dhahira Region, Sultanate of Oman.
Email: drprakashkp@gmail.com

Vinod Arora
Department of Microbiology, Ibri Regional Referral Hospital, Al Dhahira Region, Sultanate of Oman.

Geethanjali P
Department of Biochemistry, Ibri Nursing Institute, Al Dhahira Region, Oman.

The evidence on epidemiology and resistance pattern among the Bloodstream bacterial pathogens are few in Dhahira region, hence, this study was carried out with the objective to illustrate the epidemiological, clinical and microbiological characteristics of bloodstream bacterial infections and to determine their antimicrobial resistance pattern in Dhahira region, Oman.

Methods

The fully integrated government health services system in Dhahira region virtually provides most medical care to the 207,015 residents. There are two major hospitals (IRRH - Ibri Regional Referral Hospital and BWH- Buraimi Wilayat Hospital) with a network of 17 other primary healthcare facilities in the region. The culture facility was available only in these two major hospitals. This study was a hospital-laboratory record based retrospective study. All patients with suspected septicemia for whom a blood culture test request was made by the different referring specialties were studied for 2 years period (1st March 2004 - 28th February 2006 in IRRH; 1st March 2005 - 28th February 2007 in BWH). This period was chosen because of the availability of the computerized Health Information Management System (HIMS) database during that period. The antimicrobial resistance pattern for the isolated bacterial pathogens from blood cultures was also studied.

Physicians ordered blood culture tests based on the patient's presenting symptoms, typically of septicemia. Blood samples were collected before antibiotic administration and bacterial cultures were done by applying standard microbiology laboratory method. For patients with positive blood culture tests; information on age, gender, bacterial result and antibiotic resistance details was obtained from the HIMS at the two hospitals. Bloodstream infection was defined as isolation of one or more recognized bacteria from blood culture. Death was considered as attributable to BSI if it occurred during the phase of active infection or antibiotic treatment. *Klebsiella* spp. represents *Klebsiella* spp. other than *Klebsiella pneumoniae*. *Streptococcus* spp. represents *Streptococcus* spp. other than *Streptococcus pneumoniae*.

The required blood sample was collected aseptically before the commencement of antibiotic treatment. The Bactec Fluorescent series 9240 (Becton Dickinson, USA) instruments were used for rapid detection of microorganisms from blood samples. The samples were collected in Bactec standard 10 aerobic/F and Bactec plus+/ anaerobic/ F culture vials for aerobic and anaerobic cultures respectively. The bottles were loaded in the Bactec machine within 30 minutes of sample collection. Whenever the machine gave an alert signal, the specific bottle was removed and gram stain and subculture was done on blood agar and MacConkey's agar. The organism was identified by routine bacteriological methods. In case of negative or no alarm; the bottles were kept in the machine for seven days. The negative bottles were subjected to gram stain and subculture before discarding them.[14]

Antibiotic sensitivity was done by Kirby Bauer disc diffusion method using Diagnostic Sensitivity Test (DST) agar. This method is more suitable for routine testing in a clinical laboratory where a large number of isolates are tested for susceptibility to numerous antibiotics. An agar plate is uniformly inoculated with the test organism and a paper disk impregnated with a fixed concentration of an antibiotic is placed on the agar surface. Growth of the organism and diffusion of the antibiotic commence simultaneously resulting in a circular zone of inhibition in which the amount of antibiotic exceeds inhibitory concentrations. The diameter of the inhibition zone is a function of the amount of drug in the disk and susceptibility of the microorganism. Standardization and quality control tests were performed using standard strains of *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27953 and *S. aureus* ATCC 25923 as per the recommendation of National Committee for Clinical Laboratory Standards (NCCLS).[15]

Susceptibilities of the following antibiotics were tested; Amoxicillin/Clavulanic acid (Augmentin), Fusidic acid, Penicillin, Methicillin/Oxacillin, Gentamicin and Trimethoprim/ Sulphamethoxazole at 20, 10, 10, 5/1, 10 and 1.25/23.75 µgms concentration respectively for *Staphylococcus* species. For *Streptococcus* and *Haemophilus influenzae*: Ampicillin, Amoxicillin/ Clavulanic acid (Augmentin), Cefotaxime, Cefuroxime, Erythromycin, Oxacillin and Trimethoprim/ Sulphamethoxazole at 10, 20, 30, 30, 15, 1 and 1.25/23.75 µgms concentration was tested. For pseudomonas: Amikacin, Ceftazidime, Ciprofloxacin, Gentamicin, Imipenem, Piperacillin/Tazobactam at 10, 30, 5, 10, 10 and 110 µgms concentration was tested. For all the other organisms: First line, Amoxicillin/Clavulanic acid (Augmentin), Ampicillin, Cepharadine, Cefuroxime, Gentamicin and Trimethoprim/Sulphamethoxazole at 20, 10, 30, 30, 10 and 1.25/23.75 µgms concentration and second line, Amikacin, Ceftrioxone, Cefotaxime, Ciprofloxacin, Imipenem and Ceftazidime at 30, 30, 10, 5, 10 and 30 µgms concentration was tested. The results were recorded as either sensitive or resistant in this study.

The data was collected from the hospital database (HIMS). The data was computed in Microsoft Excel 7.0 software and analyzed using Statistical Package for Social Sciences (SPSS version 9). Frequencies and proportions in categorical data were calculated. Appropriate 95% Confidence Intervals (CI) were calculated for prevalence proportional data. Associations between pairs of categorical variables were assessed using chi-squared (X^2) tests or Fisher's exact tests, as appropriate. A p value of <0.05 was considered significant.

Results

A total of 7,579 blood cultures were done in Dhahira region during the study period. Approximately 5% (382/7579) of the total samples from 370 patients examined showed positive results for one or more microorganism. Nearly 6% (22/382) of the positive results was contaminants and 94% (360/382) had bacterial pathogens, hence, 360 positive cultures from 348 patients were available for further analysis. Three hundred and thirty seven

patients had single (96.8%), 10 had 2 (2.9%) and one had 3 (0.3%) bacterial pathogens isolated from blood culture.

Table 1 depicts the general characteristics of blood culture positive patients during the study period. Majority of the patients were from IRRH and adult males admitted in general medicine department. The mean age was 43.5 with wide (31.8) Standard Deviation (SD) and the median age were found to be 49.0 years (range 3 months to 101 years). Nearly 22% of the patients died during the current episode of BSI.

Table 1: General characteristics of blood culture positive patients (N=348).

Group Characteristics	Isolates		95% CI
	No.	%	
Hospital			
Ibri Hospital	297	85.3	
Buraimi Hospital	51	14.7	
Location			
Accident and Emergency	52	14.9	
ICU/SCBU	69	19.8	
General Medicine	150	43.1	
Pediatrics	58	16.7	
Others	19	5.5	
Age (years)			
<1	46	13.2	10.0 – 17.1
1-4	31	8.9	6.3 – 12.3
5-24	44	12.6	9.5 – 16.5
25-44	43	12.4	9.3 – 16.2
45-64	66	19.0	15.2 – 23.4
65-84	82	23.6	19.4 – 28.3
≥85	36	10.3	7.5 – 13.9
Gender			
Male	198	56.9	51.6 – 62.0
Female	150	43.1	38.0 – 48.3
Outcome			
Died	74	21.3	17.2 – 25.8
Recovered	274	78.7	74.1 – 82.7

Of the total isolated bacteria, 57.8% were gram-positive, 42.2% were gram-negative bacteria. Among the bacterial pathogens, the most common 10 bacterial isolates were: *Streptococcus* species 76 (21.1%), coagulase-negative *Staphylococci* (CoNS) 75 (20.8%), *Escherichia coli* (*E. coli*) 43 (11.9%), *Staphylococcus aureus* (*S. aureus*) 41 (11.4%), *Klebsiella* spp. 19 (5.3%), *Streptococcus pneumoniae* (*S. pneumoniae*) 16 (4.4%), *Pseudomonas aeruginosa* (*P. aeruginosa*) and *Proteus* spp. 11 (3.1%) each, *Salmonella* spp. 10 (2.8%) and *Klebsiella pneumoniae* (*K. pneumoniae*) 9 (2.5%). (Table 2)

Table 3 demonstrates the commonly encountered bacterial isolates and clinical syndromes (according to discharge diagnosis). A large number of our patients were adults and elderly commonly suffering from chronic illnesses like cardiac, respiratory, diabetes, hypertension, hepatitis, central nervous system leading to septicemia. The sickle cell disease patients leading to septicemia were mainly young and *Salmonella* spp. and *S. aureus* were the common organisms isolated. Malignancy was associated with 2.8% of the cases and *E. coli*, *Klebsiella* spp. and *S. aureus* were the common organisms. Fever (9.2%) with no apparent source of infection was the most common clinical syndrome associated with *E. coli*, *Enterobacter* spp., *Klebsiella* spp., *Salmonella* spp. and *S. pneumoniae* infections. There was one *Haemophilus influenzae* (*H. influenzae*) and 2 *Neisseria meningitides* (*N. meningitides*) meningitis cases. *Acinetobacter* spp., *Klebsiella* spp., *P. aeruginosa* and *S. aureus* sepsis was common in 3.3% of the sepsis patients.

Table 2: Common bacterial pathogens isolated from blood culture (N=360).

Bacterial pathogen	Isolates		95% CI
	No.	%	
Gram Positive Bacteria	**208**	**57.8**	**52.6 – 62.7**
Staphylococcus aureus	41	11.4	8.5 – 15.1
Coagulase-negative *staphylococci*	75	20.8	16.9 – 25.3
Streptococcus pneumoniae	16	4.4	2.7 – 7.1
Streptococcus species	76	21.1	17.2 – 25.6
Gram Negative Bacteria	**152**	**42.2**	**37.2 – 47.3**
Acinetobacter species	7	1.9	0.9 – 3.9
Escherichia coli	43	11.9	8.9 – 15.7
Enterobacter species	7	1.9	0.9 – 3.9
Klebsiella pneumoniae	9	2.5	1.3 – 4.6
Klebsiella species	19	5.3	3.4 – 8.1
Pseudomonas aeruginosa	11	3.1	1.7 – 5.3
Aeromonas species	2	0.6	
Providencia species	1	0.3	
Moraxella species	2	0.6	
Serratia marcescens	1	0.3	
Chyseomonas species	1	0.3	
Proteus species	11	3.1	
Haemophilus influenzae	1	0.3	
Neisseria meningitides	2	0.6	
Salmonella species	10	2.8	
Other gram-negative*	25	6.9	

* *Other gram negative – gram-negative bacteria further not classified*

Table 4 shows the various characteristics of bacterial isolates associated with mortality. The overall mortality rate among the study group was 21.3% (74/348). Nearly 75% (55/74) patients who died during the current episode of BSI were elderly patients (≥60 years) and stayed in Hospital wards. Most of the patients who died had serious underlying chronic medical conditions such as diabetes, neoplasm, respiratory, and cardiac disease and stayed for long time in hospital. The mortality was same among patients with gram-positive (50%) and gram-negative organism (50%). Among the organisms associated with the highest mortality were *S. pneumoniae* (37.5%) and *S. aureus* (24.4%). Among gram-negative organisms, the following resulted in highest mortality: *H. influenzae* (100%), *N. meningitides* (50.0%), *Aeromonas* spp. (50.0%), *E. coli* (34.3%), *P. aeruginosa* (27.3%), *Klebsiella* spp. (26.3%) and *K. pneumoniae* (11.1%). *Acinetobacter* spp. and *Enterobacter* spp. did not cause any fatalities in our study subjects. There was no gender difference in mortality (X^2=0.06, p=0.81). Mortality among patients who were 60 years or more was significantly higher when compared to <60 years old patients (X^2=46.31, p<0.0001).

Table 3: Bacterial isolates from commonly encountered clinical syndromes (N=360).

Clinical syndrome - n (%)	Bacterial isolates †
Fever 33(9.2)	*E. coli, Enterobacter spp., Klebsiella spp., Salmonella spp., S. pneumoniae*
Respiratory tract infection 51(14.2)	*E. coli, Enterobacter spp., K. pneumoniae, Klebsiella spp., P. aeruginosa, Salmonella spp., S. aureus, S. pneumoniae*
Sepsis 12 (3.3)	*Acinetobacter spp., Klebsiella spp., P. aeruginosa, S. aureus*
Cardiac diseases 53(14.7)	*E. coli, Enterobacter spp., K. pneumoniae, Klebsiella spp., P. aeruginosa, S. aureus, S. pneumoniae,*
Renal diseases 34(9.4)	*E. coli, K. pneumoniae, Klebsiella spp., P. aeruginosa, S. aureus*
Gastrointestinal tract diseases 14 (3.9)	*K. pneumoniae, Salmonella spp., S. aureus, S. pneumoniae*
Malignancy 10(2.8)	*E. coli, Klebsiella spp., S. aureus*
Surgical intervention 12(3.3)	*E. coli, Enterobacter spp., K. pneumoniae, Klebsiella spp., P. aeruginosa, S. aureus*
Sickle cell disease 21 (5.8)	*Salmonella spp., S. aureus*
Hepato-Biliary 13(3.6)	*Acinetobacter spp., E. coli, K. pneumoniae, S. aureus, S. pneumoniae*
Trauma leading to sepsis 18(5.0)	*Acinetobacter spp., E. coli, S. aureus*
Central nervous system 20(5.6)	*Aeromonas spp., E. coli, Haemophilus influenzae, K. pneumoniae, Klebsiella spp., Neisseria meningitides, S. aureus, S. pneumoniae*
Diabetes 39(10.8)	*Aeromonas spp., E. coli, Acinetobacter spp., K. pneumoniae, Klebsiella spp., P. aeruginosa, Salmonella spp., S. aureus, S. pneumoniae*
Hypertension 13(3.6)	*Acinetobacter spp., P. aeruginosa, S. aureus*
Other* 17 (4.7)	*Klebsiella spp., P. aeruginosa, S. aureus*

** includes preterm, bone and joint infections, congenital anomalies, birth asphyxia and brought dead.*

† other gram-negative bacteria, CoNS and Streptococcus spp. were isolated from all the clinical syndromes.

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

Table 4: Number of blood culture positive patients died during the current episode of bloodstream infection according to gender, age, location and bacteria isolated (N=74).

Gender	Age (Years)			Location		Bacteria isolated
	<60	60-80	≥80	Non-ICU	ICU	
Male	11	21	11	35	8	*E. coli, K. pneumoniae, Klebsiella* spp., *Pseudomonas aeruginosa, S. aureus,* CoNS, *S. pneumoniae, Streptococcus* spp.
Female	8	10	13	20	11	*E. coli, Enterobacter* spp., *Klebsiella* spp., *Pseudomonas aeruginosa, Aeromonas* spp., *Salmonella* spp., *Haemophilus influenzae, Neisseria meningitides, S. aureus,* CoNS, *S. pneumoniae, Streptococcus* spp.

CoNS - Coagulase-negative staphylococci, E. coli - Escherichia coli, K. pneumoniae - Klebsiella pneumoniae, S. aureus - Staphylococcus aureus, S. pneumoniae - Streptococcus pneumoniae

Male vs. Female mortality - X^2=0.06, p=0.81, Age ≥60 Vs <60 years - X^2=46.31, p<0.0001

Staphylococcus species (*S. aureus* and CoNS) were more commonly resistant to Trimethoprim/Sulphamethoxazole (35.3%), Penicillin (25.9%), Fusidic acid (22.4%), and Gentamicin (15.5%). Only one (2.4%) of the *S. aureus* isolates was resistant to Methicillin/Oxacillin (MRSA). All *Streptococcus* species (*Streptococcus* spp. and *S. pneumoniae*) showed frequent antibiotic resistance to Trimethoprim/Sulphamethoxazole (39.1%), Erythromycin (19.6%) and Cefuroxime (9.8%). (Table 5)

Table 5: Antimicrobial resistance of gram-positive bacteria isolated from blood culture during 2 year study period.

Antibiotic Tested	Bacterial Pathogen- Gram-positive					
	Staphylococcus aureus (N=41)		Coagulase-negative *staphylococci* (N=75)		Total (N=116)	
	No.	%	No.	%	No.	%
AMC	4	9.8	1	1.3	5	4.3
FUS	2	4.9	24	32.0	26	22.4
GEN	4	9.8	14	18.7	18	15.5
MET/OXA	1	2.4	3	4.0	4	3.4
PEN	16	39.0	14	18.7	30	25.9
SXT	11	26.8	30	40.0	41	35.3
	Streptococcus pneumoniae (N=16)		*Streptococcus* species (N=76)		Total (N=92)	
AMC	0	0.0	1	1.3	1	1.1
AMP	1	6.3	4	5.3	5	5.4
CTX	0	0.0	0	0.0	0	0.0
CXA	0	0.0	9	11.8	9	9.8
ERY	0	0.0	18	23.7	18	19.6
OXA	0	0.0	0	0.0	0	0.0
SXT	6	37.5	30	39.4	36	39.1

Antibiotic abbreviations: *AMC - Amoxicillin/Clavulanic acid (Augmentin), AMP - Ampicillin, CTX - Cefotaxime, CXA - Cefuroxime, ERY - Erythromycin, FUS- Fusidic acid, GEN - Gentamicin, OXA- Oxacillin, PEN- Penicillin, and SXT -Trimethoprim/ Sulphamethoxazole*

Table 6: Antimicrobial resistance of gram-negative bacteria isolated from blood cultures during 2 year study period.

Antibiotic Tested	Bacterial Pathogen – Gram-negative									
	Acinetobacter spp. (N=7)		*Escherichia coli* (N=35)		*Enterobacter* spp. (N=7)		*Klebsiella* spp. including *Klebsiella pneumoniae* (N=28)		*Pseudomonas aeruginosa* (N=11)	
	No.	%	No.	%	No.	%	No.	%	No.	%
AMC	5	71.4	6	17.1	0	0.0	1	3.6	Not Tested	
AMP	6	85.7	19	54.3	1	9.1	20	71.4	Not Tested	
CXA	4	57.1	4	11.4	1	9.1	2	7.1	Not Tested	
CED	7	100.0	7	20.0	0	0.0	5	17.9	Not Tested	
GEN	5	71.4	2	5.7	7	63.6	3	10.7	0	0.0
SXT	3	42.9	21	60.0	7	63.6	10	35.7	Not Tested	
AMK	4	57.1	0	0.0	0	0.0	0	0.0	0	0.0
CTX	4	57.1	2	5.7	0	0.0	3	10.7	Not Tested	
CAZ	3	42.9	2	5.7	0	0.0	0	0.0	1	9.1
CRO	5	71.4	4	11.4	0	0.0	2	7.1	Not Tested	
CIP	4	57.1	6	17.1	0	0.0	1	3.6	1	9.1
IPM	1	14.3	6	17.1	2	28.6	4	14.3	7	63.6
PZP	Not Tested		Not Tested		Not Tested		Not Tested		7	63.6

Antibiotic abbreviations: *AMC - Amoxicillin/Clavulanic acid (Augmentin), AMP - Ampicillin, AMK- Amikacin, CAZ- Ceftazidime, CED- Cepharadine, CIP- Ciprofloxacin, CRO- Ceftrioxone, CTX - Cefotaxime, CXA - Cefuroxime, GEN - Gentamicin, IPM- Imipenem, PZP- Piperacillin/Tazobactam and SXT -Trimethoprim/ Sulphamethoxazole*

Antimicrobial resistance levels for the gram-negative organisms most commonly causing blood stream infections were relatively high. Gram-negative bacteria other than *P. aeruginosa* were frequently resistant to Ampicillin (59.7%), Trimethoprim/Sulphamethoxazole (53.2%), Cepharadine (24.7%), Gentamicin (22.1%), Imipenem (16.9%) and Ampicillin (15.6%). *Acinetobacter* spp. was resistant to Ampicillin (85.7%), Gentamicin and Amoxicillin/Clavulanic acid (71.4%) and Amikacin Cefuroxime, Cefotaxime and Ciprofloxacin (57.1%). This organism was 100% resistant to Cepharadine. *Enterobacter* spp. resistance rates to the antibiotics were; Trimethoprim/Sulphamethoxazole (60%), Ampicillin 54.3% and Cepharadine 20%. They were highly sensitive to Amikacin. *E. coli* were resistant to Trimethoprim/Sulphamethoxazole (63.6%), Gentamicin (63.6%) and Imipenem (28.6%). They were highly sensitive to Cephalosporins. *Klebsiella* species including *K. pneumoniae* were resistant to Ampicillin (71.4%), Trimethoprim/Sulphamethoxazole (35.7%) and Cepharadine (17.9%). *Pseudomonas aeruginosa* were mainly resistant to Piperacillin/Tazobactam (63.6%), Imipenem (63.6%), Ceftazidime (9.1%) and Ciprofloxacin (9.1%). This organism was highly sensitive to Gentamicin and Amikacin. (Table 6)

Discussion

The present study broadly illustrates the BSI bacterial spectrum and antimicrobial resistance pattern in Dhahira region, Oman. The observed blood culture positivity rate was 5% which is low compared to the range (10.2-37.1%) reported by other studies.[5,16-18] However, in children a still higher prevalence (48.2%) has been observed.[13] The varying proportions may be due to the different methodology used and the area of study, because of the regional variation known to occur.[19,20] The prevalence may be an underestimate because large number of bloodstream infections may be clinical sepsis and not microbiologically confirmed (blood culture positive).[21]

The BSI caused by gram-positive rods like *Diphtheroid* spp., *Bacillus* spp. and other gram-positive rods were considered contaminants in the absence of clinical features of sepsis. These could be due to skin contamination at the time of collection or due to contaminated bottles. The contamination of blood culture in our study was 6% which is low compared to studies conducted elsewhere (10.7 and 14.3% respectively).[17,22]

The range of microorganisms that invade the bloodstream has been systematically studied by several researchers. In our study, 57.8% of infections were caused by gram-positive and 42.2% by gram-negative bacteria. Several studies in USA (65 and 25%), Iran (72 and 28%) and UK (66.2 and 31.3%) have shown marginally higher prevalence of gram-positive and lower prevalence of gram-negative organisms respectively.[23-25] On the contrary, gram-negative organisms have been encountered more often from blood cultures than gram-positive organisms in studies conducted in Iran (42.3 and 42.3%) and Saudi Arabia (62.2 and 33.8%) in that order.[22,26]

In our study, CoNS, *Streptococcus* spp., *S. aureus*, *E. coli*, *Klebsiella* spp., *S. pneumoniae* *P. aeruginosa*, *K. pneumoniae*, *Acinetobacter* spp., and *Enterobacter* spp. were the 10 most common noteworthy bacterial pathogens causing BSI. More or less similar observations have been made in cases of bacteraemia in different countries, however, the proportion and predominance of the organisms varied.[5,12,16,19,20,22,23,26-28] The role of CoNS in bacteraemia is divisive. Until the 1970's, coagulase-negative *Staphylococci* were mainly recognized as a contaminant. Since then, several studies have reported increasing incidence of infections due to CoNS.[29-31]

Similar to our study (4.4%), *S. pneumoniae* was isolated from 4.0% of blood cultures in an Iranian hospital. This organism is a major and well-known cause of community-acquired infections, but there is increasing interest in its role in the epidemiology of hospital-acquired infection.[32] The *P. aeruginosa* (3.1%) and *K. pneumoniae* (2.5%) were less commonly isolated from BSI patients in our study. However, in others, it was commonly witnessed.[16,27,28] Only one case of *H. influenzae* and 2 cases *N. meningitides* were isolated from blood cultures. Wide use of *H. influenzae* and *N. meningitides* vaccine has probably limited their spread in our community.

Chronic disease like cardiac diseases, respiratory diseases and diabetes were the most common presentations (discharge diagnosis) of BSI followed by renal diseases in our study. However, these are the underlying conditions and may not be directly responsible for the infection. Hence, studies to ascertain the cause and origin of infection are needed in our region, which was a limitation of this study. Fever was associated with 9.2% of BSI in our study. However, fever was the most common presentation (26%) among children suffering from BSI.[33] Similar to a Brazilian study the commonly isolated organisms were *E. coli*, *S. aureus* and *Klebsiella* spp. among cancer patients.[34]

The resistance of *S. aureus* and CoNS to commonly used antibiotics such as Penicillin and Gentamicin was low, but Trimethoprim/Sulphamethoxazole resistance was high compared to other studies.[22] Fortunately, *S. pneumoniae* were highly sensitive to most of the antibiotics tested except Trimethoprim/Sulphamethoxazole.[26] *Staphylococcus aureus* was the third most significant isolate constituting 11.4%, and 2.4% of them were due to Methicillin/Oxacillin resistant *S. aureus* (MRSA) in our study. In opposition, a higher increasing resistance of *S. aureus* and CoNS to Methicillin, Oxacillin or Nafcillin was observed and the percentage of MRSA rose from 2.4% in 1975 to 29% in 1991 in USA,[35] similarly, Methicillin resistance of *S. aureus* increased from 4% in 1990 to 42% in 2000 in England and Wales.[12] The MRSA resistance has also been reported to be as high as 56% in Turkey.[17]

In this study, *Acinetobacter* was resistant to most of the tested antibiotics with varying degrees. This organism was 100% resistant to Cepharadine. The antimicrobial resistance levels to Ampicillin, Trimethoprim/Sulphamethoxazole Gentamicin and Imipenem for the gram-negative bacteria like *E. coli*, *Enterobacter* spp., and *Klebsiella* spp., were relatively high. *P. aeruginosa* were highly resistant to Imipenem and Piperacillin/Tazobactam. Varying degrees of resistance to a range of gram-positive and gram-negative

organisms to the commonly used and tested antibiotics have been studied across the world.[12,16-20,22-24,28,33] A wider multicentre study in Oman is considered essential to know the exact range of BSI, their resistance pattern and their trend among Omani population.

In our study, 74 (21.3%) patients died during the current episode of illness. The case fatality varies from country to country, a case fatality of 6%,[36] 14.1%,[26] 23.4%,[26] 25.4%,[17] and 27%,[23] have been reported across the world. This variation can be explained by the characteristics of patients, place of acquisition of infection, microorganism isolated and severity of underlying disease. Underlying diseases, severity of illness and adequate treatment has been significantly associated with death.[17] Similarly, severity of underlying illness was an intrinsic risk factor in another study.[5] Similar to our study, there was no gender difference in the mortality,[26] however, adults >50 years,[26] and age ≤1 or ≥60 years have been significantly associated with case fatality.[5] BSI mortality varies from the place of acquisition of infection and the focus of Infection, hence, studies to describe these parameters are considered necessary in the region. Since BSI is multi-factorial and the exact cause of death was not determined in our study, the mortality data among our study subjects should be interpreted cautiously.

Mortality due to gram-positive bacteria (50%) was similar to gram-negative organisms (50%). On the other hand, gram-positive organisms were less commonly associated with mortality than that of gram-negative organisms elsewhere.[17,26] The overall mortality was less (6.7%) among cancer patients compared to a study in Brazil (25%).[34]

It is apparent that surveillance programs are necessary to identify changes in the spectrum of microbial pathogens, risk factors causing them and to monitor trends in antimicrobial resistance patterns and to implement appropriate measures in nosocomial and community-acquired BSI.[20,28,37] Pathogen frequency and resistance patterns may vary significantly from country to country and also in different hospitals within a country. Thus, national or regional or at the hospital level surveillance programs are essential to guide therapy and infection control measures.[28,37,38]

The laboratory has an important role to play in detecting BSI and in infection control measures.[5] Proper identification and accurate reporting of identified organism and antibiotic sensitivity pattern is critical, since, nearly 16% antibiotic sensitivity identification errors and 38% judged inappropriate reporting episodes have been reported. Accurate reporting influences the clinician's choice of antimicrobial therapy and interns the patient's outcome.[39]

Thus, efforts should therefore be concentrated on training staff on collecting blood from patients using aseptic precautions. Antibiotic resistance bacteria will continue to challenge care for patients with BSI. Therefore, it is important to take infection control measures to limit the spread of resistance in microorganisms and to reduce the rate of infections through surveillance.

Conclusion

BSI was an important cause of morbidity and mortality in our patients especially among chronically ill elderly adult males. Coagulase-negative *staphylococcus*, *Streptococcus* spp., *S. aureus* and *E. coli* were the most important bacterial pathogens causing BSI in Dhahira region. Prescription of Trimethoprim/Sulphamethoxazole, Ampicillin, Cepharadine, Penicillin, Gentamicin and Amoxicillin/Clavulanic acid to bacteremia patients needs attention. It also necessitates establishment of BSI and antimicrobial resistance surveillance system in the region. Studies to determine the source of infection and risk factors associated with BSI are further considered necessary and the current study provides the baseline for such future studies.

Acknowledgments

We thank all the participating laboratory personnel for their excellent assistance in performing the diagnostic tests. We appreciate the administrative support of all the health facilities in the region. We thank the clinicians of various departments in both hospitals for their assistance. We express our deep gratitude to the health information department personnel in the two major hospitals for their data management. We thank the participating study subjects and the regional administrators for giving permission to publish the article. The authors declare that they have no competing interests and no financial support was provided

References

1. Wenzel RP, Edmond MB. The impact of hospital-acquired bloodstream infections. Emerg Infect Dis 2001 Mar-Apr;7(2):174-177.
2. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med 2003 Apr;348(16):1546-1554.
3. 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 Apr;24(4):584-602.
4. Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients. Excess length of stay, extra costs, and attributable mortality. JAMA 1994 May;271(20):1598-1601.
5. Emori TG, Gaynes RP. An overview of nosocomial infections, including the role of the microbiology laboratory. Clin Microbiol Rev 1993 Oct;6(4):428-442.
6. Ibrahim EH, Sherman G, Ward S, Fraser VJ, Kollef MH. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. Chest 2000 Jul;118(1):146-155.
7. Behrendt G, Schneider S, Brodt HR, Just-Nübling G, Shah PM. Influence of antimicrobial treatment on mortality in septicemia. J Chemother 1999 Jun;11(3):179-186.
8. Raad I, Darouiche R, Dupuis J, Abi-Said D, Gabrielli A, Hachem R, et al; The Texas Medical Center Catheter Study Group. Central venous catheters coated with minocycline and rifampin for the prevention of catheter-related colonization and bloodstream infections. A randomized, double-blind trial. Ann Intern Med 1997 Aug;127(4):267-274.
9. Eggimann P, Harbarth S, Constantin MN, Touveneau S, Chevrolet JC, Pittet D. Impact of a prevention strategy targeted at vascular-access

care on incidence of infections acquired in intensive care. Lancet 2000 May;355(9218):1864-1868.
10. Sherertz RJ, Ely EW, Westbrook DM, Gledhill KS, Streed SA, Kiger B, et al. Education of physicians-in-training can decrease the risk for vascular catheter infection. Ann Intern Med 2000 Apr;132(8):641-648.
11. Crnich CJ, Maki DG. The promise of novel technology for the prevention of intravascular device-related bloodstream infection. II. Long-term devices. Clin Infect Dis 2002 May;34(10):1362-1368.
12. Reynolds R, Potz N, Colman M, Williams A, Livermore D, MacGowan A; BSAC Extended Working Party on Bacteraemia Resistance Surveillance. Antimicrobial susceptibility of the pathogens of bacteraemia in the UK and Ireland 2001-2002: the BSAC Bacteraemia Resistance Surveillance Programme. J Antimicrob Chemother 2004 Jun;53(6):1018-1032.
13. Chang MR, Carvalho NC, Oliveira AL, Moncada PM, Moraes BA, Asensi MD. Surveillance of pediatric infections in a teaching hospital in Mato Grosso do Sul, Brazil. Braz J Infect Dis 2003 Apr;7(2):149-160.
14. Bactec fluorescent series users manual. Document number MA-0074, BD biosciences. Available at www.bd.com/ds/technicalCenter/clsi/9000bc2.pdf, accessed on 20-06-07.
15. National Committee for Clinical Laboratory Standards. Performance Standards for Antimicrobial Disk Susceptibility Tests: 11th informational supplement. Wayne PA: National Committee for Clinical Laboratory Standards, 2001 (Publication no. M100-S11).
16. Raveh D, Rudensky B, Schlesinger Y, Benenson S, Yinnon AM. Susceptibility trends in bacteraemias: analyses of 7544 patient-unique bacteraemic episodes spanning 11 years (1990-2000). J Hosp Infect 2003 Nov;55(3):196-203.
17. Esel D, Doganay M, Alp E, Sumerkan B. Prospective evaluation of blood cultures in a Turkish university hospital: epidemiology, microbiology and patient outcome. Clin Microbiol Infect 2003 Oct;9(10):1038-1044.
18. Obi CL, Mazarura E. Aerobic bacteria isolated from blood cultures of patients and their antibiotic susceptibilities in Harare, Zimbabwe. Cent Afr J Med 1996 Dec;42(12):332-336.
19. Biedenbach DJ, Moet GJ, Jones RN. Occurrence and antimicrobial resistance pattern comparisons among bloodstream infection isolates from the SENTRY Antimicrobial Surveillance Program (1997-2002). Diagn Microbiol Infect Dis 2004 Sep;50(1):59-69.
20. Pfaller MA, Jones RN, Doern GV, Kugler K. Bacterial pathogens isolated from patients with bloodstream infection: frequencies of occurrence and antimicrobial susceptibility patterns from the SENTRY antimicrobial surveillance program (United States and Canada, 1997). Antimicrob Agents Chemother 1998 Jul;42(7):1762-1770.
21. Hugonnet S, Sax H, Eggimann P, Chevrolet JC, Pittet D. Nosocomial Bloodstream Infection and Clinical Sepsis Emerging Infectious Diseases 2004;10(1):76-81.
22. Rahbar M, Gra-Agaji R, Hashemi S. Nosocomial blood stream infections in Imam Khomeini Hospital, Urmia, Islamic Republic of Iran, 1999-2001. East Mediterr Health J 2005 May;11(3):478-484.
23. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis 2004 Aug;39(3):309-317.
24. Mamishi S, Pourakbari B, Ashtiani MH, Hashemi FB. Frequency of isolation and antimicrobial susceptibility of bacteria isolated from bloodstream infections at Children's Medical Center, Tehran, Iran, 1996-2000. Int J Antimicrob Agents 2005 Nov;26(5):373-379.
25. Gray JW. A 7-year study of bloodstream infections in an English children's hospital. Eur J Pediatr 2004 Sep;163(9):530-535.
26. Elbashier AM, Malik AG, Knot AP. Blood stream infections: micro-organisms, risk factors and mortality rate in Qatif Central Hospital. Ann Saudi Med 1998 Mar-Apr;18(2):176-180.
27. Eykyn SJ, Gransden WR, Phillips I. The causative organisms of septicaemia and their epidemiology. J Antimicrob Chemother 1990 Apr;25(Suppl C):41-58.
28. Yinnon AM, Schlesinger Y, Gabbay D, Rudensky B. Analysis of 5 years of bacteraemias: importance of stratification of microbial susceptibilities by source of patients. J Infect 1997 Jul;35(1):17-23.
29. Boisson K, Thouverez M, Talon D, Bertrand X. Characterisation of coagulase-negative staphylococci isolated from blood infections: incidence, susceptibility to glycopeptides, and molecular epidemiology. Eur J Clin Microbiol Infect Dis 2002 Sep;21(9):660-665.
30. Thylefors JD, Harbarth S, Pittet D. Increasing bacteremia due to coagulase-negative staphylococci: fiction or reality? Infect Control Hosp Epidemiol 1998 Aug;19(8):581-589.
31. Marshall SA, Wilke WW, Pfaller MA, Jones RN. Staphylococcus aureus and coagulase-negative staphylococci from blood stream infections: frequency of occurrence, antimicrobial susceptibility, and molecular (mecA) characterization of oxacillin resistance in the SCOPE program. Diagn Microbiol Infect Dis 1998 Mar;30(3):205-214.
32. Paradisi F, Corti G. Is *Streptococcus pneumoniae* a nosocomially acquired pathogen? Infect Control Hosp Epidemiol 1998 Aug;19(8):578-580.
33. Babay HA, Twum-Danso K, Kambal AM, Al-Otaibi FE. Bloodstream infections in pediatric patients. Saudi Med J 2005 Oct;26(10):1555-1561.
34. Velasco E, Byington R, Martins CS, Schirmer M, Dias LC, Gonçalves VM. Bloodstream infection surveillance in a cancer centre: a prospective look at clinical microbiology aspects. Clin Microbiol Infect 2004 Jun;10(6):542-549.
35. In R, Emori TG, Gaynes RP. An Overview of Nosocomial Infections, Including the Role of the Microbiology Laboratory. Clin Microbiol Rev 1993;4(6):428-442.
36. Hill PC, Onyeama CO, Ikumapayi UN, Secka O, Ameyaw S, Simmonds N, et al. Bacteraemia in patients admitted to an urban hospital in West Africa. BMC Infect Dis 2007;7:2.
37. Department of Health. UK Antimicrobial Resistance Strategy and Action Plan. Department of Health 2000, London, UK. Available from http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4007783 accessed on 20-06-07.
38. Sader HS, Gales AC, Pfaller MA, Mendes RE, Zoccoli C, Barth A, et al. Pathogen frequency and resistance patterns in Brazilian hospitals: summary of results from three years of the SENTRY Antimicrobial Surveillance Program. Braz J Infect Dis 2001 Aug;5(4):200-214.
39. Diekema DJ, Lee K, Raney P, Herwaldt LA, Doern GV, Tenover FC. Accuracy and appropriateness of antimicrobial susceptibility test reporting for bacteria isolated from blood cultures. J Clin Microbiol 2004 May;42(5):2258-2260.