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Full Length Research Paper

Changing trends in frequency and antimicrobial susceptibility of pathogens causing catheter related infections in children

Muhammad Qasim[1,2]*, Aizza Zafar[1], Hasan Ejaz[1], Hazir Rahman[2], Abdul Malik Tareen[3], Jafar Khan[2] and Attia Bari[4]

[1]Department of Microbiology, Children's Hospital and Institute of Child Health, Lahore, Pakistan.
[2]Department of Microbiology, Kohat University of Science and Technology, Kohat, Pakistan.
[3]Department of Microbiology, University of Baluchistan, Quetta, Pakistan.
[4]Department of Paediatric Medicine, Children's Hospital and Institute of Child Health, Lahore, Pakistan.

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Catheter-related infections (CRIs) by bacterial pathogens are the frequent cause of nosocomial infections in hospitalized pediatric patients. The undertaken study was carried out at two different time duration in 2005 and 2011 to determine the changing trend in bacterial pathogens isolated from catheters and their antimicrobial susceptibility in children. Patients implanted with endotracheal tube (ETT), peritoneal dialysis catheter (PDC), urinary catheters (UC) and central venous catheters (CVC) were included in this study. The prevalence of the organism causing CRI and its antibiotic susceptibility was determined using standard microbiological assay. In the present study, the most frequent catheter colonizing bacteria in 2005 were *Pseudomonas* spp. 30% (n = 30) followed by *Klebsiella* spp. 27% (n = 27) and *Escherichia coli* 27% (n = 27). In contrast, the most frequently isolated pathogens in 2011 were found to be *Klebsiella* spp. 34.7% (n = 40), followed by *E. coli* 25.2% (n = 29) and *Pseudomonas* spp. 15.6 % (n = 18). Beside these commonly isolated pathogens, we have also isolated *Acinetobacter* spp. 9.57% (n = 11), *Enterobacter* spp. 5.21% (n = 6) and *Citrobacter* spp. 0.86% (n = 1) in 2011. A significant increase in the resistance of Gram negative bacteria to amikacin, co-amoxiclav, cefixime and cefpriome was documented from 2005 to 2011. On the other hand, in 2011, the resistance of Gram positive bacteria to amikacin, co-amoxiclav, fusidic acid and teicoplanin was significantly increased. The isolation of causative agents of CRIs and the antibiogram of these pathogens may be helpful for a more appropriate and optimized treatment with potential benefits for the patients as well as for the rationale antibiotic policy.

Key words: Catheter related infections, antimicrobial susceptibility, pediatric, nosocomial infection.

INTRODUCTION

Catheter-related infections (CRIs) are the significant cause of morbidity, prolonged hospital stay and increased health care expenses (Leonidou and Gogos, 2010; Foster and Sabella, 2011). CRIs include infections in skin exit site and microbiologically proven device-related infections (Eggimann et al., 2004). Most CRIs are prevalent in the urinary tract, respiratory tract, bloodstream and surgical wound sites (Bigham et al., 2009; Frasca et al., 2010). Several risk factors identified which are associated with CRIs include prolonged catheterization, type of device used, presence of a genetic syndrome, gender, malnutrition, absence of systemic antibiotics and disconnection of the catheter-collecting tube junction (Bigham et al., 2009; Frasca et al., 2010; Sofianou et al., 2000; Vilela et al., 2007; Gould

*Corresponding author. E-mail: qasim89@gmail.com. Tel: +92-922-560376.

et al., 2010; Safdar et al., 2001). The use of catheters can evade normal host defenses of the body, especially skin and mucosal barriers which facilitate microbial invasion to the implant site (Safdar et al., 2001). CRIs are mainly caused by bacterial pathogens including Gram positive and negative bacteria (Donlan, 2001; Donlan and Costerton, 2002). *Pseudomonas aeruginosa, Escherichia coli, Klebsiella* and *Staphylococcus aureus* have been reported as frequent isolates from catheters (Tullu et al., 1998; Nseir et al., 2009). These pathogens form biofilm by excreting polymers that facilitate adhesion, matrix formation and alteration of the organism's phenotype (Donlan, 2001). The physical and genetic profile of microorganisms in protected biofilm is profoundly different from unprotected independent cells (Donlan and Costerton, 2002). Biofilm-related infections cause dramatic resistance to antimicrobial agents and host defense. Prevention of CRIs is challenging for clinician due the availability of narrow choice of antibiotics (Costerton et al., 2003). The increased incidence of CRIs have drawn considerable attention towards investigating epidemiology of infection, etiology and understanding of associated pathogens with the ultimate aim of developing more effective strategies to control device-related infections (Sabella, 2011; Safdar et al., 2001; Rewa and Muscedere, 2011).

The increased rate of antimicrobial resistance in health care-associated pathogens has mounted a serious public health concern among hospitalized patients (McDonald, 2006; Sande-Bruinsma et al, 2008; Lockhart et al, 2007).

Inappropriate use of broad spectrum antibiotics has led to emergence of antibiotic resistance which could be a contributing factor of mortality in developing and underdeveloped countries (Sande-Bruinsma et al., 2008; Lockhart et al., 2007; World Health Organization, 2000).

The antibiotic resistance profile of the catheter associated pathogens can differ by geographic location so care must to taken in selecting optimal antimicrobial regimen which could be vital for proper treatment (Rello et al., 1999; Schaefer et al., 2007). There is a continual change in microbial pathogens and their antibiotics resistance over time (Manjunath et al., 2011). In this context, the present study was conducted to identify the changing etiological trends of catheter associated infections in the pediatric patients, and to determine their antibiotic susceptibility pattern which will be helpful in the management of patients and framing the hospital antibiotic policy.

MATERIALS AND METHODS

MacConkey´s agar, blood agar, Mueller Hinton agar, motility test medium, tryptone water, urease base agar, Simmon citrate agar, triple sugar iron, antimicrobial discs of amikacin (30 µg), amoxicillin (20 µg), ampicillin (10 µg), co-amoxiclav (30 µg), ceftriaxone (30 µg), ciprofloxacin (5 µg), flucloxacillin (30 µg), fusidic acid (10 µg), gentamycin (10 µg), teicoplanin (10 µg), vancomycin (30 µg), cefixime (5 µg), cefotaxime (30 µg), cefpirome (5 µg), ceftazidime (30 µg) and meropenem (10 µg) were purchased from Oxoid, UK.

Clinical samples

The study was conducted on hospitalized patients suspected to have catheter-related infection in the Children's Hospital and Institute of Child Health Lahore, Pakistan, at two different time duration, from June to December 2005 and January to June 2011. All patients with endotracheal tubes, peritoneal dialysis catheters, urinary catheters and central venous catheters were included in the study. A total of 194 patients in 2005 and 153 patients in 2011, with suspected CRI were subjected to bacterial identification and antimicrobial susceptibility profiling.

Microbial culturing

The tips of the contaminated catheters were cut and incubated in the nutrient broth for 18 h at 37°C along with gentle shaking, followed by inoculation on MacConkey's and blood agar plates. Culture plates were incubated overnight at 37°C.

Bacterial identification

After examining colony cultural characteristics (colony shape, size, color, elevation and pigment production), a single colony was selected for Gram staining. Gram staining was performed as described by Robert Austrian (Schaefer et al., 2007). Further identification was done by using catalase test, coagulase test, DNase test, oxidase test, motility assay, indole production test, urease, citrate and triple sugar iron tests as described by Monica (1984).

Antimicrobial sensitivity

All isolated pathogens were examined for their antibiotic sensitivity pattern on Mueller- Hinton agar plates using standardized Kirby-Bauer disc diffusion method and the results were interpreted as per National Committee for Clinical Laboratory Standards (NCCLS), 2005 guidelines.

RESULTS

A total of 194 catheter samples in 2005 and 153 catheter samples in 2011 from suspected CRI patients were included in the study. The overall culture positivity was 51.54 % (n = 100) in 2005 and 75.16 % (n = 115) in 2011 (Figure 1). The culture positivity in various catheters is given in Figure 2. Endotracheal tube (ETT) catheters from CRI suspects were found to be the most frequently colonized among all the catheters, and represents 65 and 56.52% positive culture in 2005 and 2011, respectively (Figure 2). Bacterial distribution among all the catheters is shown in Table 1. Bacterial isolates from various catheters and their susceptibility to the antimicrobial agents are shown in Tables 2 to 5. Gram positive bacteria were isolated at frequency of 12 and 8.69% in 2005 and 2011, respectively, while Gram negative bacteria were frequently isolated in both 2005 (88%) and 2011 (91.30%) (Table 1).

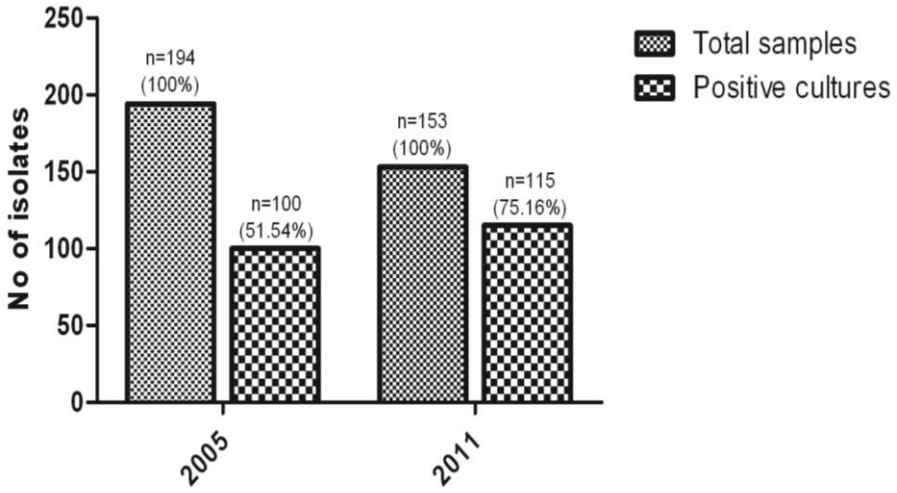

Figure 1. Culture positivity of various catheters in 2005 and 2011.

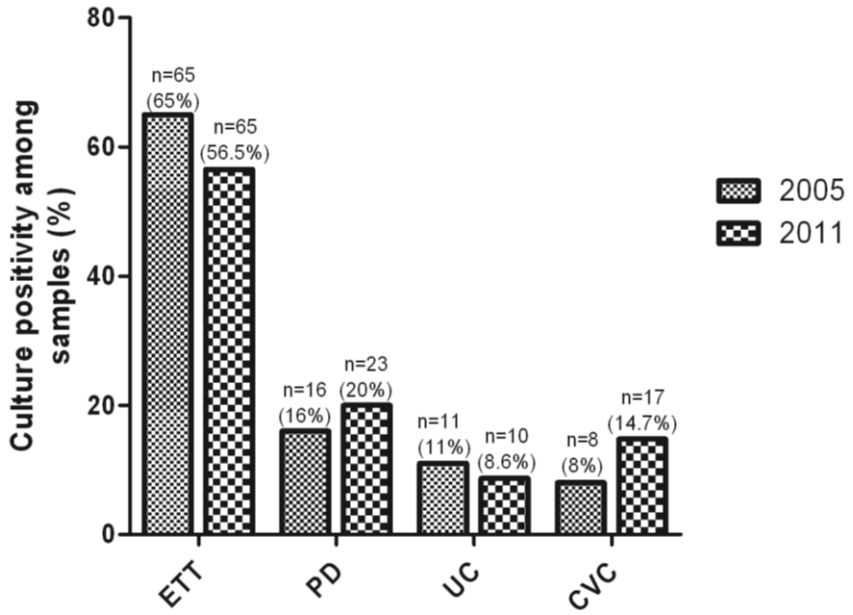

Figure 2. Sample distribution of positive cultures in 2005 (n=100) and 2011 (n=115).

Table 1. Bacterial isolates from various catheters in 2005 (n = 100) and 2011 (n = 115).

Gram's positive bacteria					Gram's negative bacteria				
	2005		2011			2005		2011	
	n	%	n	%		n	%	n	%
Total	12	12	10	8.69		88	88	105	91.30
Staphylococcus aureus	6	6	9	7.82	*Pseudomonas* spp.	30	30	18	15.65
CoNS	4	4	0	0	*Klebsiella* spp.	27	27	40	34.78
Streptococcus pyogenes	1	1	0	0	*Escherichia coli*	27	27	29	25.21
Staphylococcus saprophyticus	0	0	1	0.869	*Proteus*	4	4	0	0
Non haemolytic *Streptoocci*	1	1	0	0	*Acinetobacter* spp.	0	0	11	9.56
					Enterobacter spp.	0	0	6	5.21
					Citrobacter spp.	0	0	1	0.86

Table 2. *In-vitro* susceptibility of bacterial isolates recovered from ETT to commonly used antibiotics.

Antibiotics	*S. aureus*		*CoNS*		*Proteus* spp.		*Pseudomonas* spp.		*Klebsiella* spp.		*Escherichia coli*		*Acinetobacter* spp.		*Enterobacter* spp.	
	2005	2011	2005	2011	2005	2011	2005	2011	2005	2011	2005	2011	2005	2011	2005	2011
	n=1	n=2	n=2	n=0	n=4	n=	n=21	n=9	n=20	n=28	n=17	n=18	n=0	n=6	n=0	n=2
Amikacin	1 (100)	2 (100)	2 (100)	nt	3 (75)	nt	16 (76.2)	3 (33.3)	15 (75)	10 (35.7)	15 (88.3)	11 (61.1)	nt	2 (33.3)	nt	0 (0)
Co-amoxiclav	1 (100)	2 (100)	2 (100)	nt	3 (75)	nt	8 (38.1)	1 (11.1)	11 (55)	8 (28.5)	6 (35.2)	2 (11.1)	nt	0 (0)	nt	0 (0)
Ceftriaxone	0 (0)	2 (100)	0 (0)	nt	1 (25)	nt	1 (4.8)	2 (22.2)	1 (5)	2 (7.14)	1 (6)	2 (11.1)	nt	0 (0)	nt	0 (0)
Ciprofloxacin	0 (0)	2 (100)	0 (0)	nt	0 (0)	nt	0 (0)	3 (33.3)	0 (0)	13 (46.4)	1 (6)	5 (27.7)	nt	1 (16.7)	nt	0 (0)
Gentamycin	1 (100)	2 (100)	2 (100)	nt	0 (0)	nt	2 (9.5)	3 (33.3)	2 (10)	9 (32.14)	5 (29.5)	7 (38.8)	nt	1 (16.7)	nt	0 (0)
Ampicillin	0 (0)	2 (100)	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Amoxicillin	0 (0)	2 (100)	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Flucloxacillin	1 (100)	2 (100)	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Fusidic acid	1 (100)	2 (100)	1 (50)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Teicoplanin	1 (100)	2 (100)	2 (100)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Vancomycin	1 (100)	2 (100)	1 (50)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Cefotaxime	nt	nt	nt	nt	1 (25)	nt	1 (4.8)	2 (22.2)	1 (5)	4 (14.2)	1 (6)	4 (22.2)	nt	1 (16.7)	nt	0 (0)
Ceftazidime	nt	nt	nt	nt	0 (0)	nt	2 (9.5)	3 (33.3)	2 (10)	4 (14.2)	3 (17.6)	5 (27.7)	nt	1 (16.7)	nt	0 (0)
Cefpriome	nt	nt	nt	nt	1 (25)	nt	1 (4.8)	1 (11.1)	1 (5)	1 (3.57)	2 (11.7)	1 (5.5)	nt	0 (0)	nt	0 (0)
Cefixime	nt	nt	nt	nt	1 (25)	nt	8 (37.1)	0 (0)	3.8 (19)	1 (3.57)	1 (6)	1 (5.5)	nt	0 (0)	nt	0 (0)
Meropenem	nt	nt	nt	nt	4 (100)	nt	18 (85.7)	8 (88.8)	17 (85)	27 (96.4)	11 (65.7)	18 (100)	nt	6 (100)	nt	2 (100)

''nt'' Indicate that antibiotics are not tested, and numbers in ''parentheses'' indicate percent values.

Among the Gram positive isolates, the frequent pathogens were found to be *S. aureus* (6%) and Coagulase negative *Staphylococci* (CoNS) (4%) in 2005, while in 2011, *S. aureus* (7.82%) was the main causative agent in CRIs. In Gram negative isolates, the frequent causative agents were found to be *Pseudomonas* spp. (30%), followed by *Klebsiella* spp. (27%) and *E. coli* (27%) in 2005, while in 2011, *Klebsiella* spp. (34.78%) was found to be the frequent isolate followed by *E. coli* (25.21%) and *Pseudomonas* spp. (15.65%) (Table 1). The antimicrobial agents with the highest level of activity against Gram positive bacteria in 2005 were amikacin (100%), teicoplanin (83.3%), co-amoxiclav (75%), fusidic acid (75%), vancomycin and gentamycin (66.66% each). However, lowest susceptibility was shown to ampicillin (8.33%), amoxicillin (16.66%), ciprofloxacilin (16.66%), ceftriaxone (25%) and flucloxacillin (33.3%) (Figure 3). In comparison to 2005 data, the Gram positive isolates from 2011 showed highest susceptibility to vancomycin (100%), amikacin (90%), ceftriaxone, ciprofloxacin and gentamycin (80% each), while least susceptibility was shown to ampicillin and flucloxacin (30% each) (Figure 3). Moreover, Gram negative bacterial isolates from all catheters in 2005 exhibited greater sensitivity to amikacin (80.68%) and meropenem (77.27%) while least antibiotics susceptibility was shown to ciprofloxacin (4.54%), gentamycin (11.36%), cefotaxime and ceftriaxone (9.09% each). In comparison to Gram negative isolates in 2005, meropenem (97.14%) and amikacin (45.71%) showed high antimicrobial activity while least activity was shown by cefixime (3.80%), cefpriome (5.71%) and ceftriaxone (14.28%) against Gram negative isolates in 2011 (Figure 4).

DISCUSSION

Nosocomial infections associated with CRIs are the leading cause of morbidity and mortality in hospitalized patients (Eggimann et al., 2004). Several risk factors are associated with CRIs which include patient health status, prolonged

Table 3. *In vitro* susceptibility of bacterial isolates recovered from PDC to commonly used antibiotics.

Antibiotics	*S. aureus*		*CoNS*		*Pseudomonas* spp.		*Klebsiella* spp.		*Escherichia coli*		*Acinetobacter* spp.		*Enterobacter* spp.	
	2005	2011	2005	2011	2005	2011	2005	2011	2005	2011	2005	2011	2005	2011
	n=3	n=4	n=2	n=0	n=6	n=3	n=3	n=5	n=2	n=5	n=0	n=4	n=0	n=2
Amikacin	3 (100)	3 (75)	2 (100)	nt	5 (83.3)	2 (66.6)	2 (66.6)	2 (40)	2 (100)	3 (60)	nt	3 (75)	nt	1 (50
Co-amoxiclav	1 (33.3)	2 (50)	1 (50)	nt	3 (50)	1 (33.3)	2 (66.6)	0 (0)	0 (0)	1 (20)	nt	1 (25)	nt	0 (0)
Ceftriaxone	1 (33.3)	4 (100)	0 (0)	nt	1 (16.7)	0 (0)	1 (33.3)	0 (0)	0 (0)	1 (20)	nt	2 (50)	nt	0 (0)
Ciprofloxacin	1 (33.3)	4 (100)	1 (50)	nt	1 (16.7)	3 (100)	0 (0)	4 (80)	0 (0)	2 (40)	nt	2 (50)	nt	2 (100)
Gentamycin	2 (66.6)	3 (75)	0 (0)	nt	1 (16.7)	2 (66.6)	0 (0)	2 (40)	0 (0)	1 (20)	nt	2 (50)	nt	1 (50)
Ampicillin	1 (33.3)	1 (25)	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Amoxicillin	2 (66.6)	2 (50)	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Flucloxacillin	1 (33.3)	1 (25)	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Fusidic acid	2 (66.6)	2 (50)	1 (50)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Teicoplanin	2 (66.6)	2 (50)	1 (50)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Vancomycin	2 (66.6)	4 (100)	2 (100)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Cefotaxime	nt	nt	nt	nt	2 (33.7)	0 (0)	0 (0)	0 (0)	0 (0)	2 (40)	nt	2 (50)	nt	0 (0)
Ceftazidime	nt	nt	nt	nt	1 (16.7)	1 (33.3)	0 (0)	1 (20)	0 (0)	2 (40)	nt	2 (50)	nt	0 (0)
Cefpriome	nt	nt	nt	nt	2 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	nt	0 (0)	nt	0 (0)
Cefixime	nt	nt	nt	nt	2 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	nt	0 (0)	nt	0 (0)
Meropenem	nt	nt	nt	nt	4 (66.6)	3 (100)	1 (33.3)	5 (100)	1 (50)	5 (100)	nt	4 (100)	nt	2 (100)

‘‘nt’’ Indicate that antibiotics are not tested, and numbers in ‘‘parentheses’’ indicate percent values.

catheterization, type of device used and disconnection of the catheter-collecting tube junction (Bigham et al., 2009; Sofianou et al., 2000; Frasca et al., 2010). Though several reports have been documented the prevalence of CRIs (Leonidou and Gogos, 2010; Eggimann et al., 2004; Deep et al., 2004; Thongpiyapoom et al., 2004; Gikas et al., 2010; Timsit, 2007; Worthington and Elliott, 2005), however few reports are available on the shift in antimicrobial susceptibility of microorganisms associated with CRIs (Fridkin et al., 2002; Al-Hasan et al., 2011). This study has documented the distribution of catheter associated bacterial pathogens from pediatric patients and their antimicrobial susceptibility patterns in 2005 and 2011.

Among all culture of positive samples, most of the cases were from ETT tips followed by PD catheters (Figure 2). One reason for increased number of ETT positive culture could be its frequent insertion in ICUs. In ICUs patients, the risk of nosocomial infections is greater than for those in general medical wards (Tullu et al., 1998). Increased risk factors include age, immunosuppression and the use of medical devices itself (Brown et al., 1985). The incidence of nosocomial pneumonia was significantly higher in intubated patients who were mechanically ventilated as compared to those who were not mechanically ventilated (Legras et al., 1998). Previous studies also revealed ventilator associated pneumonia (VAP) as the most frequent nosocomial infection (Thongpiyapoom et al., 2004; Raymond and Aujard, 2000), while others reported blood stream infections as common paediatric nosocomial infections (Urrea et al., 2003; Grohskopf et al., 2002; Jordan et al., 2011). It was found that all patients who have developed nosocomial pneumonia were ETT colonized. We found that the frequent colonizing agent of ETT in 2005 was *Pseudomonas* spp. (32.3%) followed by *Klebsiella* spp. (30.76%). Similar findings were also previously reported in which 80% of ETT related infections were caused by *Pseudomonas* spp. (Becerra et al., 2010). In 2011, the most

Table 4. *In vitro* susceptibility of bacterial isolates recovered from UC to commonly used antibiotics.

Antibiotics	*S. aureus*		*S. pyogenes*		*S. saprophyticus*		*Pseudomonas* spp.		*Klebsiella* spp.		*Escherichia coli*		*Citrobacter* spp.	
	2005	2011	2005	2011	2005	2011	2005	2011	2005	2011	2005	2011	2005	2011
	n=1	n=1	n=1	n=0	n=0	n=1	n=1	n=0	n=2	n=3	n=6	n=4	n=0	n=1
Amikacin	1 (100)	1 (100)	1 (100)	nt	nt	1 (100)	1 (100)	nt	2 (100)	0 (0)	6(100)	3 (75)	nt	0 (0)
Co-amoxiclav	1 (100)	0 (0)	1 (100)	nt	nt	0 (0)	0 (0)	nt	1 (50)	1 (33.3)	2 (33.3)	1 (25)	nt	0 (0)
Ceftriaxone	0 (0)	1 (100)	1 (100)	nt	nt	0 (0)	0 (0)	nt	0 (0)	0 (0)	1 (16.7)	0 (0)	nt	0 (0)
Ciprofloxacin	0 (0)	1 (100)	0 (0)	nt	nt	0 (0)	0 (0)	nt	0 (0)	0 (0)	0(0)	0 (0)	nt	1 (100)
Gentamycin	1 (100)	1 (100)	0 (0)	nt	nt	0 (0)	0 (0)	nt	0 (0)	0 (0)	0 (0)	1 (25)	nt	0 (0)
Ampicillin	0 (0)	0 (0)	0 (0)	nt	nt	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt
Amoxicillin	0 (0)	0 (0)	0 (0)	nt	nt	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt
Flucloxacillin	0 (0)	0 (0)	1 (100)	nt	nt	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt
Fusidic acid	1 (100)	0 (0)	1 (100)	nt	nt	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt
Teicoplanin	1 (100)	1 (100)	1 (100)	nt	nt	1 (100)	nt	nt	nt	nt	nt	nt	nt	nt
Vancomycin	1 (100)	1 (100)	0 (0)	nt	nt	1 (100)	nt	nt	nt	nt	nt	nt	nt	nt
Cefotaxime	nt	nt	nt	nt	nt	nt	0 (0)	nt	0 (0)	0 (0)	0(0)	0 (0)	nt	0 (0)
Ceftazidime	nt	nt	nt	nt	nt	nt	0 (0)	nt	1 (50)	0 (0)	2 (33.3)	0 (0)	nt	0 (0)
Cefpriome	nt	nt	nt	nt	nt	nt	0 (0)	nt	0 (0)	0 (0)	1 (16.7)	0 (0)	nt	0 (0)
Cefixime	nt	nt	nt	nt	nt	nt	0 (0)	nt	0 (0)	0 (0)	0 (0)	0 (0)	nt	0 (0)
Meropenem	nt	nt	nt	nt	nt	nt	1(100)	nt	2 (100)	3 (100)	4 (66.7)	3 (75)	nt	1 (100)

‘‘nt’’ Indicate that antibiotics are not tested, and numbers in ‘‘parentheses’’ indicate percent values.

frequent isolates were *Klebsiella* (43.07%) and *E. coli* (27.69%). *Pseudomonas* spp. and *Klebsiella* spp., isolated from the ETT in 2005 were found to be maximally susceptible to meropenam (85%) and amikacin (76%). In contrast, the antibiotics susceptibility of the *Pseudomonas* and *Klebsiella* spp. isolated from ETT in 2011 was significantly reduced to amikacin, cefixime and co-amoxiclav. Another study showed that 80% of *Pseudomonas* spp. from ETT were resistant to ceftazidime, amikacin, ciprofloxacin and meropenem (Becerra et al., 2010).

In the peritoneal dialysis catheter (PDC) related infections, Gram negative bacteria were commonly isolated in both 2005 and 2011 (Table 3), while others reported Gram positive bacteria being the common isolates (Bordador et al., 2010).

According to the global survey reports, a significant regional variation exists regarding the distribution of causative organisms of PDC related infections (Schaefer et al., 2007). Different factors like climate, humidity, age distribution and PDC practices of the patients may contribute to the geographical variation of the bacteriological profile (Szeto et al., 2003). In addition, among the urinary catheter-related infections, *E. coli* was the common causative agent, which showed maximum susceptibility to amikacin and meropenam in both 2005 and 2011 (Table 4). In addition, *E. coli* showed highest resistance to ciprofloaxacin, cefotaxime, cefixime, ceftriaxone, cefpriome and gentamycin. Similar studies have also reported *E. coli* as the most frequent causative agent of catheter related urinary tract infections and showed more susceptibility to ceftazidime (87.4%), cefuroxime (85.1%) and cefatrizine (76.6%) (Tullu et al., 1998; Bi et al., 2009).

In central venous catheters (CVC) related infections, Gram negative bacteria were the frequent causative pathogens (Table 5); however, a related study reported Gram positive organisms as frequent cause of nosocomial bloodstream infections (Wisplinghoff et al., 2003). In this study, *Pseudomonas* spp., *Klebsiella* spp and *E. coli*

Table 5. *In-vitro* susceptibility of bacterial isolates recovered from CVCs to commonly used antibiotics.

	S. aureus		***Non-haemolytic Streptoocci***		***Pseudomonas* spp.**		***Klebsiella* spp.**		***Escherichia coli***		***Acinetobacter* spp.**		***Enterobacter* spp.**	
	2005	**2011**	**2005**	**2011**	**2005**	**2011**	**2005**	**2011**	**2005**	**2011**	**2005**	**2011**	**2005**	**2011**
	n=1	**n=2**	**n=1**	**n=0**	**n=2**	**n=6**	**n=2**	**n=4**	**n=2**	**n=2**	**n=0**	**n=1**	**n=0**	**n=2**
Amikacin	1 (100)	2 (100)	1 (100)	nt	1 (50)	3 (50)	2 (100)	2 (50)	1 (50)	2 (100)	nt	1 (100)	nt	0 (0)
Co-amoxiclav	1 (100)	1 (50)	1 (100)	nt	0 (0)	1 (66.6)	2 (100)	1 (25)	1 (50)	1 (50)	nt	1 (100)	nt	0 (0)
Ceftriaxone	0 (0)	1 (50)	1 (100)	nt	1 (50)	2 (33.3)	0 (0)	2(50)	0(0)	1 (50)	nt	1 (100)	nt	0 (0)
Ciprofloxacin	0 (0)	1 (50)	0 (0)	nt	1 (50)	3 (50)	0 (0)	3(75)	1(50)	1 (50)	nt	1 (100)	nt	0 (0)
Gentamycin	1 (100)	2 (100)	1 (100)	nt	0 (0)	2 (33.3)	0 (0)	1 (25)	0 (0)	1 (50)	nt	1 (100)	nt	0 (0)
Ampicillin	0 (0)	0 (0)	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Amoxicillin	0 (0)	0 (0)	0 (0)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Flucloxacillin	0 (0)	0 (0)	1 (100)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Fusidic acid	1 (100)	1 (50)	1 (100)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Teicoplanin	1 (100)	1 (50)	1 (100)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Vancomycin	1 (100)	2 (100)	1 (100)	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt
Cefotaxime	nt	nt	nt	nt	2 (100)	2 (33.3)	0 (0)	2 (50)	0(0)	1 (50)	nt	1 (100)	nt	0 (0)
Ceftazidime	nt	nt	nt	nt	1 (50)	2 (33.3)	0 (0)	2 (50)	0 (0)	0(0)	nt	1 (100)	nt	0 (0)
Cefpriome	nt	nt	nt	nt	1 (50)	2 (33.3)	0 (0)	1 (25)	0(0)	0 (0)	nt	0 (0)	nt	0 (0)
Cefixime	nt	nt	nt	nt	2 (100)	0 (0)	0 (0)	1(25)	0 (0)	0 (0)	nt	1 (100)	nt	0 (0)
Meropenem	nt	nt	nt	nt	1 (50)	6 (100)	2 (100)	4 (100)	2 (100)	2 (100)	nt	1 (100)	nt	2 (100)

‘‘nt’’ Indicate that antibiotics are not tested, and numbers in ‘‘parentheses’’ indicate percent values.

were among the common isolates from CVC. Another study reported *Candida* spp. as the common isolate in CVC related infections (41%), followed by coagulase negative *Staphylococci* (17%) (Becerra et al., 2010), while others found CoNS (31%), *S. aureus* (20%), *Enterococci* (9%) and *Candida* species as the frequent causative agent of CVC related infections (Wisplinghoff et al., 2004).

In the current study, Gram negative bacteria were more prevalent in 2005 (88%) and 2011 (91.3%) as compared to Gram positive pathogens in 2005 (12%) and in 2011 (8.69%) (Table 1). Schaefer et al. (2007) reported that Gram negative infections predominate in Asia and Argentina. Among the Gram negative pathogens, *Pseudomonas* spp. (30%) was the common pathogen causing CRIs in 2005, while *Klebsiella* spp. (34.78%) were frequently isolated in 2011. These finding are in line with the previous reports (Richet et al., 1990; Sreeramoju et al., 2008; Zingg et al., 2009).

Furthermore, the antimicrobial susceptibility trend in the CRIs associated pathogens in data collected from 2005 showed that most of the Gram positive bacteria isolated from catheter were found to be more sensitive to amakacin (100%), teicoplanin (83.33%), co-amoxiclav (75%) and fusidic acid (75%) (Figure 3), while in data from 2011, decrease in the susceptibility was observed in amikacin (90%), teicoplanin (70%), co-amoxiclav (50%) and fusidic acid (50%) (Figure 3). The increased bacterial resistance might be due to the misuse of these antibiotics in hospitals evolving multi-drug resistant bacterial strains (Peirano, 2008). Moreover, in 2005, Gram negative pathogens were more susceptible to amikacin (80.68%), meropenam (77.27%), and less susceptible to ciprofloxacin (4.54%), ceftriaxone, cefotaxime (9.09% each), cefpriome (10.22%) and gentamycin (11.36%) (Figure 4), which is in line with a previous study conducted in Pakistan (Mahmood et al., 2002). Gram negative bacteria in 2011 revealed a decrease in antimicrobial susceptibility for amikacin (45.71%), co-amoxiclav (19.04%) and cefixime (3.80%) (Figure 4). A previous study also reported amikacin resistance in Gram negative isolates (Wormser et al., 1983). In general, the overall trend of antimicrobial susceptibility pattern is different among the isolates. The possible

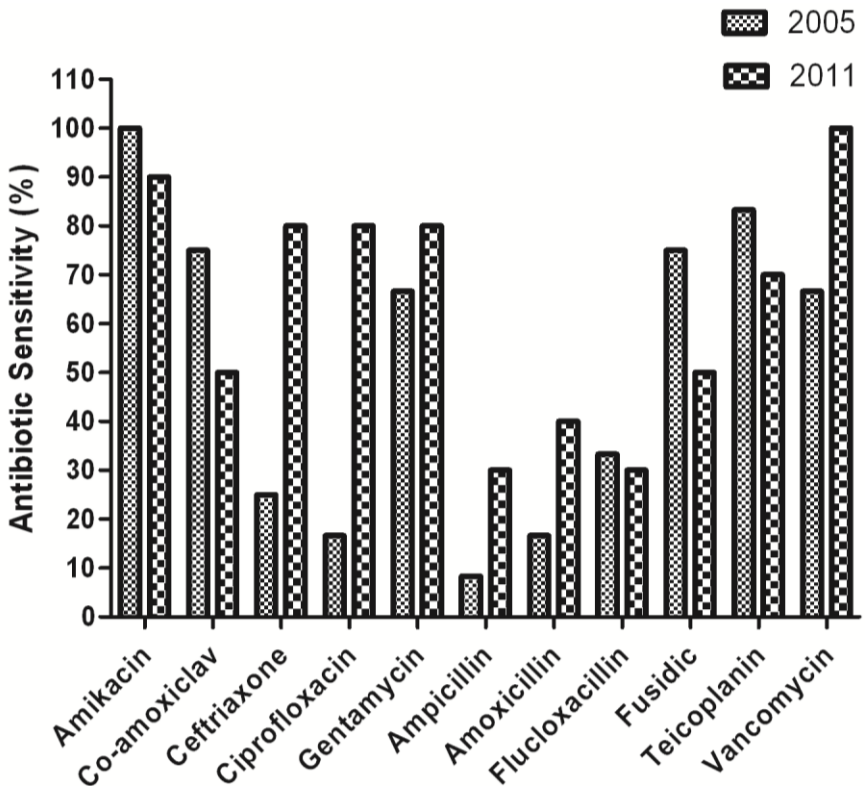

Figure 3. Antibiotics susceptibility pattern of Gram positive bacterial isolates (n=12 in 2005 and n=10 in 2011).

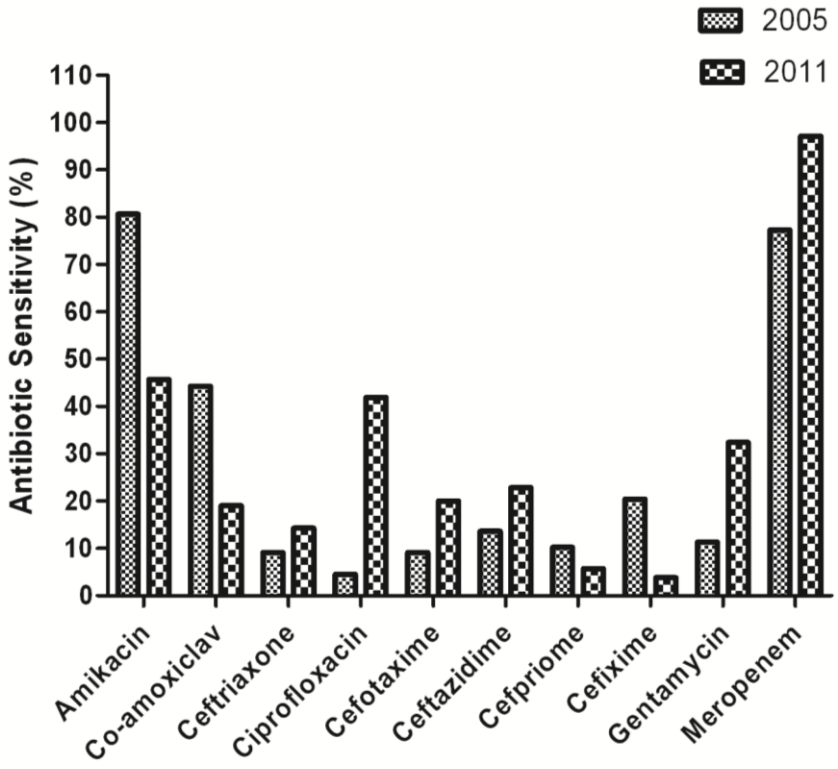

Figure 4. Antibiotics susceptibility pattern of Gram negative bacterial isolates (n=88 in 2005 and n=105 in 2011).

explanation of such trend might be the difference in the virulence and antibiotic resistance mechanisms operated in CRIs associated pathogens under stress conditions (Martinez and Baquero, 2002, 2000). The problem of changing resistance patterns will remain an ongoing threat to both developed and developing countries due to higher rates of antibiotic resistance gene transfer (World Health Organization, 2000; Frasca et al., 2010), which contributed to the current pandemic antibiotic resistance scenario for some bacterial factors (Deep et al., 2004). The rapid spread of antibiotics resistance in vulnerable populations is facilitated by carrying of resistant bacteria by the international travelers (Thongpiyapoom et al., 2004), worldwide distribution of food supply (Gikas et al., 2010), and poor hygienic conditions (Timsit, 2007). The growing antibiotics resistance has become an important cause of high rate of morbidity, mortality and cost of health care in the recent decades (Lockhart et al., 2007; Worthington and Elliott, 2005). An up to date knowledge of pathogens prevalence including their antibiotics resistance is needed to maintain appropriate and empirical usage of antibiotics, which will have profound impact on the patient life. In this context, the present study determined the frequency and antibiotic susceptibility profile of catheter-related infections which will be helpful in formulating appropriate antibiotic policies for the hospital infection control.

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