ORIGINAL ARTICLE

Bacteraemia caused by Escherichia coli in cancer patients at a specialist center in Pakistan

Azra Parveen,[1] Faisal Sultan,[2] Aun Raza,[3] Waleed Zafar,[4] Summiya Nizamuddin,[5] Amjad Mahboob,[6] Saliha Saleem,[7] Syed Hammad Nazeer[8]

Abstract

Objective: To analyse the antimicrobial susceptibility patterns of Escherichia coli bacteraemia among cancer patients, and to assess the risk factors and outcomes of multidrug-resistant Escherichia coli bacteraemia.

Methods: The retrospective study was conducted at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, and comprised medical records of patients with Escherichia coli bacteraemia presenting between December 2012 and November 2013. Multivariable logistic regression analyses were used to determine the factors associated with the development and 30-day mortality of multidrug-resistant Escherichia coli bacteraemia.

Results: Out of 1603 episodes of bacteraemia, 227(35.6%) were caused by E.coli, of which 98(43.2%) were multidrug-resistant. In multivariable analysis, age less than 18 years (adjusted odds ratio 3.92; 95% confidence interval 1.43-10.68), presence of central venous catheter (adjusted odds ratio 2.12; 95% confidence interval 1.04-4.33) and exposure to piperacillin/tazobactam within 90 days prior to infection (adjusted odds ratio 2.37; 95% confidence interval 1.15-4.86) were identified as independent risk factors for acquisition of multidrug-resistant Escherichia coli bacteraemia. The overall 30 day mortality rate was 35.2% (80/227). Risk factors for mortality were intensive care unit admission (adjusted odds ratio 3.95; 95% confidence interval 1.79-8.71) and profound neutropenia (adjusted odds ratio 4.03; 95% confidence interval 1.55-10.49).

Conclusion: Bloodstream infections with multidrug-resistant Escherichia coli were common in cancer patients. However it was not a predictor of mortality.

Keywords: Escherichia coli, Bacteraemia, Multidrug resistant, Cancer. (JPMA 65: 1271; 2015)

Introduction

Although there have been significant improvements in prevention and treatment of infectious complications in cancer patients, bloodstream infections are still a major cause of mortality and morbidity in these cases. Use of broad-spectrum antibiotics to treat such infections has contributed towards the emergence of multidrug-resistant (MDR) gram-positive and gram-negative organisms.[1] Recent studies have reported re-emergence of gram-negative infections as the predominant source of bacteraemia in cancer patients.[2] Escherichia coli (E.coli) is the most frequent gram-negative organism isolated from cancer patients with significant number of cases resulting from extended spectrum beta lactamase (ESBL)-producing strains. Increased resistance to trimethoprim/sulfamethoxazole, amoxicillin/clavulanic acid, quinolones and cefepime has been reported. No significant resistance has been observed against carbapenems in this subgroup of patients.[3,4] There has also been a recent dramatic increase in the detection rate of MDR gram-negative bacteraemia.[5] These infections are associated with poor clinical outcomes, and, among cancer patients, can cause delays in administration of chemotherapeutic agents leading to longer hospital stays, suboptimal treatment, higher mortality rates and increased healthcare costs.[6] Factors that have been identified to be associated with MDR bacteraemia include liver disease, use of immunosuppressant drugs, recent surgery and prior use of cephalosporins and quinolones.[7]

Limited data from Pakistan has also shown E.coli to be the most commonly isolated gram-negative organism[8,9] with high levels of significant resistance to ceftriaxone, quinolones and piperacillin/tazobactam.[10] A previous study at our institution reported E.coli to be the most common gram-negative organism among post-chemotherapy febrile neutropenic patients, with susceptibility to imipenem, amikacin and piperacillin/tazobactam, and resistance to quinolones and third-generation cephalosporins.[11] However, data about the prevalence of MDRE Colibacteraemia among cancer

[1,2,7,8]Department of Internal Medicine, [4]Department of Cancer Registry, [5]Department of Pathology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, [3]Department of Internal Medicine, Sharif Medical and Dental College, Lahore, [6]Department of Internal Medicine, Bacha Khan Medical Complex, Swabi, Pakistan.

Correspondence: Azra Parveen. Email: azrap@skm.org.pk

patients is scarce. The current study was planned to analyse the anti-microbial susceptibility patterns of E.coli bacteraemia among cancer patients, and to assess the risk factors and outcomes of MDR E.coli bacteraemia.

Materials and Methods

The retrospective study was conducted at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan.

After approval by the institutional review board, the in-house information system database was used to identify all cancer patients with E.coli bacteraemia during the 12 months from December 2012 to November 2013. The medical records were reviewed to collect data regarding patient's age, gender, type of cancer, history of cancer treatment, blood culture results with anti-microbial susceptibilities, absolute neutrophil count (ANC), history of prior antibiotic use within 90 days, and mortality within 30 days of index E.coli bacteraemia. During the study period all blood cultures had processed by the BACTEC 9240 system (Becton Dickinson), with an incubation period of 7 days. Isolates were identified by standard techniques[12] and anti-microbial susceptibility testing was performed and interpreted according to Clinical Laboratory Standards Institute (CLSI) criteria using the disk diffusion methodology.[13]

Source of bacteraemia was determined either by isolation of E.coli from different specimens (urine, sputum, tracheal aspirate, wound) or was based on the treating physician's clinical evaluation. The date of the first positive culture was regarded as the date of onset of infection. Empiric antibiotic was considered appropriate if it was in vitro active against E.coli. MDR E.coli was defined as isolate resistant to three or more classes of anti-microbial agents, including fluoroquinolones, third- generation cephalosporins, anti-pseudomonal penicillins + beta-lactamase inhibitors, and carbapenems.[14] Neutropenia was defined as ANC of less than 500 cells/mm^3 and profound neutropenia as ANC of less than 100 cells/mm^3 at the onset of bacteraemia.[15]

The clinical data extracted using a structured questionnaire was analysed using statistical software Stata version 11.0 (College Station, Texas, US). Standard descriptive summary statistics were used to characterise the sample. Associations between categorical variables were evaluated using Chi Square test or Fisher's exact test, as appropriate. All tests were 2-sided, with a type 1 error level of 0.05. Multivariable logistic regression (MLR) analyses were used to test the association with outcomes identified a priori.

Results

A total of 1603 episodes of bacteraemia were identified, with gram-negative bacteria being the cause of infection in 636(39.6%). Out of them, 227(35.6%) were caused by E.coli, of which 98(43.2%) were MDR E.coli.

Baseline characteristics of these 227 episodes showed that 171(75%) happened in patients 18 years or older, 135(59.5%) with solid organ malignancy, 174(76.7%) hospitalised within 30 days prior to infection, 145(63.9%) receiving chemotherapy within 30 days prior to infection, and 104(45.8%) with profound neutropenia (Table-1).

Intra-abdominal infections, including neutropenic colitis and hepatobiliary infections, were the most common sources of E.coli bacteraemia 83 (36.6%) followed by urinary tract (UTI) infections 49 (21.6%). In 48(21.1%) patients, no source of bacteraemia could be identified. Overall, 218(96%) isolates were susceptible to amikacin, followed by 168(74%) to chloramphenicol, and resistant to penicillins and 2nd and 3rd generation cephalosporins. Piperacillin/tazobactam was the most common empiric antibiotic prescribed in 132(60%)patients, and initial

Table-1: Baseline characteristics.

Characteristic	N (%)
Age (years)	
Less than 18	56 (24.7)
18 and above	171 (75.3)
Gender	
Male	148(65.2)
Female	79 (34.8)
Type of malignancy	
Haematological	92 (40.5)
Solid organ	135 (59.5)
Hospitalisation within 30 days prior to infection	
Yes	174 (76.7)
No	53 (23.3)
Admission to intensive care unit	
Yes	39 (17.2)
No	188 (82.8)
Central venous catheter placed	
Yes	67 (29.5)
No	160 (70.5)
Treatment received within 30 days prior to infection	
Chemotherapy	145 (63.9)
Surgery	28 (12.3)
Radiation	15 (6.6)
Absolute neutrophil count	
Less than 100	104 (45.8)
100-500	4 (1.8)
501-1900	10 (4.4)
1901-8000	48 (21.1)
More than 8000	61 (26.9)

Table-2: Antimicrobial susceptibilities.

Antibiotics to which E. coli was susceptible	N (%)
Amikacin	218 (96.0)
Ampicillin	8 (3.5)
Cefixime	45 (19.8)
Ceftriaxone	45 (19.8)
Cefuroxime	47 (20.7)
Chloramphenicol	168 (74.0)
Ciprofloxacin	49 (21.6)
Coamoxiclav	18 (7.9)
Colistin	9 (not checked in all strains)
Cotrimoxazole	41 (18.1)
Gentamicin	118 (52.0)
Imipenem	211 (93.0)
Meropenem	211(93.0)
Piperacillin/Tazobactam	128 (56.4)
Tetracycline	36 (15.9)

empiric antibiotic was appropriate in 128(56.4%).

In multivariable analyses, three variables were identified as significant risk factors for bacteraemia by MDR E.coli: age less than 18 years (adjusted odds ratio [AOR] 3.92; 95% confidence interval [CI] 1.43-10.68), presence of central venous catheter (AOR 2.12; 95% CI 1.04-4.33), and exposure to piperacillin/tazobactam within 90 days prior to infection (AOR 2.37; 95% CI 1.15-4.86) (Table-3).

In 98 patients with MDR E.coli bacteraemia, 44(44.9%) episodes resulted in death within 30 days of infection compared to 36(27.9%) episodes of death in patients with non-MDR bacteraemia. Risk factors for 30-days mortality were noted (Table-4). Multivariable analyses revealed two independent risk factors for mortality: intensive care unit (ICU) admission (AOR 3.95; 95% CI 1.79-8.71) and profound neutropenia (AOR 4.03; 95% CI 1.55-10.49). Having received chemotherapy 30 days prior to infection

Table-4: Adjusted association of risk factors with mortality within 30 days of index E.coli bacteraemia using multiple logistic regression.

Risk factor	Adjusted OR (95%CI)	p value
Male gender	1.26 (0.58-2.72)	0.56
Age less than 18 years	2.04 (0.90-4.61)	0.09
Haematological malignancy	0.94 (0.41-2.11)	0.88
Hospitalisation within 30 days prior to infection	0.77 (0.34-1.74)	0.54
Admission to intensive care unit	3.95 (1.79-8.71)	<0.01
Previous chemotherapy within 30 days	0.30 (0.11-0.80)	0.02
Previous surgery within 30 days	0.53 (0.17-1.59)	0.26
Previous radiation within 30 days	2.53 (0.78-8.17)	0.12
ANC less than 100 cells/mm^3	4.03 (1.55-10.49)	<0.01
Charlson score	1.11 (0.94-1.32)	0.19
MDR E.coli	1.85 (0.89-3.86)	0.10
Inappropriate empiric antibiotic therapy	1.44 (0.72-2.87)	0.30

MDR: Multidrug resistant
OR: Odds ratio
CI: Confidence interval
ANC: Absolute neutrophil count.

Table-3: Comparison of risk factors for multidrug resistant (MDR) E.coli bacteraemia and the adjusted association of factors with development of MDRE.coli bacteraemia using multiple logistic regressions.

Characteristic	Non-MDR E.coli N=129 n (%)	MDR E.coli N=98 n (%)	p	Adjusted OR for MDR E. coli bacteraemia (95%CI)	p
Male gender	75 (58.1)	73 (74.5)	0.01	1.05 (0.50-2.20)	0.88
Age less than 18 years	6.2 (5.6)	6.5 (5.2)	<0.01	3.92 (1.43-10.68)	<0.01
Haematological malignancy	35 (27.1)	57 (58.1)	<0.01	1.54 (0.74-3.23)	0.25
Hospitalization within 30 days prior to infection	92 (71.3)	82 (83.7)	0.04	0.59 (0.25-1.43)	0.25
ICU admission	16 (12.4)	23 (23.5)	0.03	1.58 (0.67-3.74)	0.29
Charlson score				0.89 (0.74-1.08)	0.26
Central venous catheter use	27 (20.9)	40 (40.8)	<0.01	2.12 (1.04-4.33)	0.04
Previous chemotherapy within 30 days	69 (53.5)	76 (77.5)	<0.01	1.15 (0.45-2.91)	0.76
Previous surgery within 30 days	22 (17)	6 (6.1)	0.01	0.32 (0.11-9.1)	0.03
Previous radiation within 30 days	10 (7.7)	5 (5.1)	0.59	0.99 (0.17-5.54)	0.97
ANC less than 100 cells/mm^3			<0.01	0.95 (0.44-2.08)	0.90
Use of quinolones within 90 days of index sampling	55 (61.1)	35 (38.9)	0.34	1.04 (0.50-2.18)	0.13
Use of third generation cephalosporins within 90 days of index sampling	29 (47.5)	32 (52.5)	0.10	1.50 (0.70-3.21)	0.29
Use of Piperacilin/Tazobactamwithin 90 days of index sampling	52 (42.3)	71 (57.7)	<0.01	2.37 (1.15-4.86)	0.02
Use of carbapenems within 90 days of index sampling	20 (40)	30(60)	<0.01	1.47 (0.68-3.15)	0.31

OR: Odds ratio
CI: Confidence interval
ICU: Intensive care unit
ANC: Absolute neutrophil count.

had a significant protective effect (AOR 0.3; 95% CI 0.11-0.80).

Discussion

In this study of bloodstream infections due to E.coli in cancer patients, 43.2% episodes of bacteraemia were caused by MDR E.coli. It is difficult to compare the results with previously published data because very few studies in literature have focused exclusively on MDR E.coli bacteraemia in cancer patients. Most of the available data discusses extended-spectrum beta-lactamase (ESBL)-producing E.coli.[4,7] Moreover, there is no standardised definition for MDR organisms and variable definitions have been used in various studies.[14,16,17] One study described bacteraemia due to MDR gram-negative bacilli in cancer patients and found the incidence to be13.7% and out of these 49% episodes were due to MDR E.coli.[17]

About 58% patients with MDR E.coli bacteraemia in our study had underlying haematological malignancies. This is similar to results of previously published studies.[16,17] This highlights the possibility that patients with haematological malignancies receive more aggressive chemotherapies resulting in a profound immune-compromised state which may make them more prone to infections with resistant organisms.

The rates of resistance of E.coli to third-generation cephalosporins have risen substantially. Similarly, increasing resistance to fluoroquinolones has been reported in several studies.[4,7,8] In our study the resistance to cephalosporins and quinolones was considerably higher compared to the previously published literature. A significant number of patients (40%) were exposed to ciprofloxacin in the 90 days prior to onset of infection.

Resistance of E.coli to piperacillin/tazobactam has also increased significantly. This has been observed both in cancer and non-cancer patients. One study conducted in ICU setting and including non-cancer patients demonstrated that 19.25% E.coli isolates were resistant to piperacillin/tazobactam.[18] Studies in cancer patients have reported piperacillin/tazobactam-resistant E.coli rates ranging from 12.9% to 41.6%.[4,7]

The proportion of piperacillin/tazobactam resistance was much higher in our study population (43.6%). A significant number of patients were neutropenic and had received empiric piperacillin/tazobactam for neutropenic fever. Many patients had recurrent admissions due to chemotherapy-induced febrile neutropenia and had received multiple courses of piperacillin/tazobactam which may have promoted resistance. However, in a previous study from our centre, the rate of resistance was only 11%.[11] It points towards presence of additional factors that may be responsible for the emergence of MDR E.coli bacteraemia.

We attempted to analyse risk factors associated with MDR E.coli bacteraemia in cancer patients. Multivariable analysis revealed that treatment with piperacillin/tazobactam within 90 days prior to infection was an independent risk factor for MDR E.coli bacteraemia. Several studies have also reported antimicrobial exposures as risk factors for infection with MDR organisms.[17,19]

In the present study, patients less than 18 years of age were more likely to have MDR E.coli bacteraemia compared to adults. This finding had not been observed in prior studies. Most of the patients in this age group had haematological malignancies. Such patients receive more aggressive and myelosuppressive chemotherapies which result in significant dysfunction of mucosal barrier, with alteration in the intestinal microflora which can in turn promote infections with resistant organisms.[20]

Another risk factor identified was the presence of central venous catheters, including both short-term and long-term catheters. Long-term catheters are frequently used in cancer patients for administration of chemotherapeutic agents and these can be a potential source of infection. A recent retrospective analysis conducted in elderly patients with cancer and long-term catheters demonstrated significantly increased risk of infection. Other studies have shown gram-negative organisms to be the predominant aetiological agents in catheter-related blood stream infections. Implementation of adequate infection control measures can reduce the incidence of these infections.[21,22]

Factors influencing mortality in our study were admission to an ICU and ANC less than 100. Previous studies have also reported that patients with E.coli bacteraemia who are critically ill and are admitted to ICU have significantly increased mortality.[4] This increased mortality in ICUs has been attributed to comorbid illnesses like liver disease and immunosuppression.[19]

An additional risk factor for worse outcomes in our study was ANC of less than 100/mm^3. This finding had not been observed previously.[7,17] However, subgroup analysis of one study showed that neutropenic patients with ESBL E.coli bacteraemia had a higher overall mortality rate compared to non-neutropenic patients.[4] In the present study about half of the

patients had ANC count of less than 100/mm^3 and 63% of these had haematological malignancies. Prophylactic administration of granulocyte colony-stimulating factor can shorten the duration of neutropenia and reduce the incidence of infectious complications in patients with lympho-proliferative disorders and solid tumours.

Infections with MDR gram-negative bacilli have been reported to be associated with poor outcomes.[23] But in the current study MDR E.coli bacteraemia was not a predictor of mortality, when evaluated in a multivariable analysis, despite the fact that there were more deaths in this group of patients. This is in line with studies published recently which have shown that MDR is not associated with higher mortality provided that effective antibiotics are used for definitive therapy within appropriate time.[20,24]

Initial inappropriate antibiotic therapy in cancer patients with gram-negative bacteraemia has been reported in some studies to be associated with poor outcomes.[25] Others have shown contradictory results.[4,17] In our study a significant proportion of patients (43.6%) did not receive appropriate initial antibiotic therapy and this was not associated with increased mortality.

At our centre, piperacillin/tazobactam is the commonest empiric antibiotic in febrile neutropenic patients. Recently there have been concerns regarding its effectiveness in view of increasing number of E.coli isolates that are MDR. We suggest continuing its use, since initial inappropriate antibiotic was not a risk factor for mortality, but it should be changed to an appropriate agent once anti-microbial susceptibilities are known.

The study has several limitations. Firstly, it was a retrospective observational study and definite association between mortality and the various factors could not be deduced. Secondly, minimum inhibitory concentrations (MICs) of the antibiotics were not checked and molecular studies were not performed to determine the different types of beta lactamases. Finally, given the limitations of data, we were unable to perform time-to-event analyses or look for associations between receipt of antibiotic therapy and time to death.

Conclusion

Bloodstream infections with MDR E.coli were common in cancer patients. However, it was not a predictor of mortality. Rational use of antibiotics and adherence to infection-control measures during insertion and further manipulation of central venous catheters can prevent such infections.

References

1. Klatersky J. Management of fever in neutropenic patients with different risks of complications. Clin Infect Dis. 2004; 39: S32-7.
2. Gudiol C, Bodro M, Simonetti A, Tubau F, González-Barca E, Cisnal M, et al. Changing etiology, clinical features, antimicrobial resistance, and outcomes of bloodstream infection in neutropenic cancer patients. Clin Microbiol Infect 2013; 19: 474-9.
3. Ha Ye, Song JH, Kang WK, Peck KR, Chung DR, Kang CI, et al. Clinical factors predicting bacteraemia in low-risk febrile neutropenia after anti-cancer chemotherapy. Support Care Cancer. 2011; 19: 1761-7.
4. Gudiol C, Calatayd L, Vidal CG, Tamaya JL, Cisnal M, Duarte R, et al. Bacteraemia due to extended-spectrum Beta-lactamase-producing Escherichia coli (ESBL-EC) in cancer patients: clinical features, risk factors, molecular epidemiology and outcome. J Antimicrob Chemother. 2010; 65: 333-41.
5. Montassier E, Batard E, Gastinne T, Potel G, Cochetiere MFD. Recent changes in bacteraemia in patients with cancer: A systematic review of epidemiology and antibiotic resistance. Eur J Clin Microbiol Infect Dis 2013; 32: 841-850.
6. Arnold RJ, Gabrail N, Rat M, Kim R, Sung JC,Zohu Y. Clinical implications of chemotherapy induced diarrhea in patients with cancer. J Support Oncol.2005; 3:227-232.
7. Ha YE, Kang CI, Cha MK, Park SY, Wi YM, Chung DR, et al. Epidemiology and clinical outcomes of bloodstream infections caused by Extended-spectrum Beta-lactamase-producing Escherichia coli in patients with cancer. Int J Antimicrob Agents. 2013; 42: 403-9.
8. Irfan S, Idrees F, Mehraj V, Habib F, Adil, S, Hasan R. Emergence of carbapenem resistant gram negative and vancomycin resistant gram positive organisms in bacteremic isolates of febrile neutropenic patients: A descriptive study . BMC Infect Dis. 2008; 8: 80.
9. Saghir S, Faiz M, Saleem M, Yunus A, Aziz H. Characterization and antimicrobial susceptibility of gram-negative bacteria from blood stream infections of cancer patients on chemotherapy in Pakistan. Indian J Med Microbiol. 2009; 27: 341-7.
10. Khan MA, Siddiqui BK, Shamim A, Yusuf MA, Ahmed U, Zakiullah N, et al. Emerging bacterial resistance patterns in febrile neutropenic patients: Experience at a tertiary care hospital in Pakistan. J Pak Med Assoc. 2004; 54: 357-60.
11. Zahid KF, Hafeez H, Afzal A. Bacterial spectrum and susceptibility patterns of pathogens in adult febrile neutropenic patients: A comparison between two time periods. J Ayub Med Coll Abbottabad. 2009; 21: 146-9.
12. Murray RR, Baron EJ, Jorgensen JH, eds. Manual of Clinical Microbiology, 9thedition. Washington DC: ASM Press, 2007.
13. Clinical Laboratory Standards Institute, "Performance standards for antimicrobial susceptibility testing," Sixteen informational supplement, M 100-S16 (M7-A7), 2006.
14. Falgas ME, Karageorgpulos DE. Pandrug resistance (PDR), extensive drug resistance (XDR), and multidrug resistance (MDR) among gram-negative bacilli: need for international harmonization in terminology. Clin Infect Dis. 2008; 46: 1121-2.
15. Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA et al. Clinical practice guidelines for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by infectious diseases society of America-93. Clin Infect Dis. 2011; 52: e56-93.
16. Vigil KJ, Adachi JA, AboufaycalH, Hachem RY, Reitzel RA, Jiang Y, et al. Multidrug-resistant Escherichia coli bacteraemia in cancer patients. Am J Infect control 2009; 37: 741-45.
17. Gudiol C, Tubau F, Calatayaud L, Vidal CG, Cisnal M, Sanchez Ortega I et al. Bacteraemia due to multidrug resistance Gram negative bacilli in cancer patients: risk factors, antibiotic therapy and outcomes. J Antimicrob Chemother. 2011; 66: 657-63.

18. Mohammedi I, Ploin D, Duperret S, Chapuis F, Petit P. Risk factors for Piperacillin/tazobactam-resistant Escherichia coli in ICU patients: a clinical study. Intensive Care Med. 2003; 29: 1164-8.
19. Patel SJ, Oliveira AP, Zhou JJ, Alba L, Furuya EY, Weisenberg SA et al. Risk factors and outcomes of infections caused by extremely drug-resistant gram-negative bacilli in patients hospitalized in intensive care units. Am J Infect Control. 2014; 42: 626-31.
20. Van Vliet MJ, Tissing WJ, Dun CA, Meessen NE, Kamps WA, de Bont ES et al. Chemotherapy treatment in pediatric patients with acute myeloid leukemia receiving antimicrobial prophylaxis leads to a relative increase of colonization with potentially pathogenic bacteria in the gut. Clin Infect Dis. 2009; 49: 262-70.
21. Lipitz-Snyderman A, Sepkowitz KA, Elkin EB, Pinheiro LC, Sima CS, Son CH et al. Long-term central venous catheter use and risk of infection in older adults with cancer. J Clin Oncol. 2014; 32: 2351-6.
22. Braun E, Hussein K, Geffen Y, Rabino G, Bar-Lavie Y, Paul M. Predominance of gram negative bacilli among patients with catheter-related bloodstream infections. Clin Microbiol Infect. 2014; 20: 627-29.
23. Schwaber MJ, Navon-Venezia S, Kaye KS, Ben-Ami R, Schwartz D, Carmeli Y. Clinical and economic impact of bacteraemia with extended-spectrum-beta-lactamase-producing Enterobacteriaceae. Antimicrob Agents Chemother. 2006; 50: 1257-62.
24. Kim SH, Kwon JC, Choi SM, Lee DG, Park SH, Choi JH et al. Escherichia coli and klebsiellapneumoniaebacteraemia in patients with neutropenic fever: factors associated with extended-spectrum beta-lactamase production and its impact on outcome. Ann Hematol. 2013; 92: 533-41.
25. Peralta G, Sanchez MB, Garrido JC, De Benito I, Cano ME, Martinez-Martinez L, et al. Impact of antibiotic resistance and of adequate empirical antibiotic treatment in the prognosis of patients with Escherichia coli bacteraemia. J Antimicrob Chemother. 2007; 60: 855-63.