Original Article

http://dx.doi.org/10.3349/ymj.2015.56.2.348
pISSN: 0513-5796, eISSN: 1976-2437

Yonsei Med J 56(2):348-354, 2015

YMJ

Risk Factors for Mortality in Patients with *Serratia marcescens* Bacteremia

Sun Bean Kim,[1,2] Yong Duk Jeon,[1] Jung Ho Kim,[1] Jae Kyoung Kim,[1] Hea Won Ann,[1] Heun Choi,[1] Min Hyung Kim,[1,2] Je Eun Song,[1,2] Jin Young Ahn,[1,2] Su Jin Jeong,[1,2] Nam Su Ku,[1,2] Sang Hoon Han,[1,2] Jun Yong Choi,[1,2] Young Goo Song,[1,2] and June Myung Kim[1,2]

[1]Division of Infectious Disease, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul; [2]AIDS Research Institute, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea.

Received: March 18, 2014
Revised: May 14, 2014
Accepted: May 27, 2014
Corresponding author: Dr. Nam Su Ku,
Division of Infectious Disease,
Department of Internal Medicine,
Severance Hospital,
Yonsei University College of Medicine,
50-1 Yonsei-ro, Seodaemun-gu,
Seoul 120-752, Korea.
Tel: 82-2-2228-2277, Fax: 82-2-393-6884
E-mail: smileboy9@yuhs.ac

· The authors have no financial conflicts of interest.

Purpose: Over the last 30 years, *Serratia marcescens* (*S. marcescens*) has emerged as an important pathogen, and a common cause of nosocomial infections. The aim of this study was to identify risk factors associated with mortality in patients with *S. marcescens* bacteremia. **Materials and Methods:** We performed a retrospective cohort study of 98 patients who had one or more blood cultures positive for *S. marcescens* between January 2006 and December 2012 in a tertiary care hospital in Seoul, South Korea. Multiple risk factors were compared with association with 28-day all-cause mortality. **Results:** The 28-day mortality was 22.4% (22/98 episodes). In a univariate analysis, the onset of bacteremia during the intensive care unit stay (p=0.020), serum albumin level (p=0.011), serum C-reactive protein level (p=0.041), presence of indwelling urinary catheter (p=0.023), and Sequential Oran Failure Assessment (SOFA) score at the onset of bacteremia (p<0.001) were significantly different between patients in the fatal and non-fatal groups. In a multivariate analysis, lower serum albumin level and an elevated SOFA score were independently associated with 28-day mortality [adjusted odds ratio (OR) 0.206, 95% confidential interval (CI) 0.044–0.960, p=0.040, and adjusted OR 1.474, 95% CI 1.200–1.810, p<0.001, respectively]. **Conclusion:** Lower serum albumin level and an elevated SOFA score were significantly associated with adverse outcomes in patients with *S. marcescens* bacteremia.

Key Words: *Serratia marcescens*, bacteremia, mortality, risk factors

INTRODUCTION

Serratia marcescens (*S. marcescens*) is a Gram-negative *Enterobacteriaceae* species, initially considered non-pathogenic due to its low virulence in healthy populations.[1] Over the last 30 years, however, this species has emerged as an important pathogen, and a common cause of nosocomial infections.[2] *S. marcescens* has been shown to cause a wide range of infectious diseases, including urinary, respiratory, and biliary tract infections, peritonitis, wound infections, and intravenous catheter-related infections, which can also lead to life-threatening bacteremia.[1,2] Risk fac-

tors associated with these infections include prolonged immunosuppressive therapy, previous antimicrobial agents, indwelling catheterization, and underlying diseases such as chronic pulmonary disease and diabetes mellitus.[3]

Recent epidemiologic analyses have shown an increase in the rate of antimicrobial resistance among *S. marcescens* isolates.[4-6] Furthermore, multidrug-resistant (MDR) strains of *S. marcescens* have been associated with serious outcomes.[7-9] The overall mortality rate of *S. marcescens* bacteremia remains high, ranging from 25–58%.[2,9,10] However, despite this high mortality rate, the risk factors associated with mortality in *S. marcescens* bacteremia have not been well established since 2008 regardless of MDR strains.[10-13]

Therefore, we aimed to identify the risk factors associated with mortality in patients with *S. marcescens* bacteremia during the last 6 years.

MATERIALS AND METHODS

Study population and design

A retrospective cohort study was conducted to investigate risk factors associated with mortality in *S. marcescens* bacteremia at Severance Hospital, a 2000-bed, tertiary-care teaching hospital, Seoul, South Korea. Inclusion criteria for this study included patients with 18 years of age or older, identified as having one or more blood cultures positive for *S. marcescens* between January 2006 and December 2012. For subjects reporting more than one episode of *S. marcescens* bacteremia, only the first episode was accepted. Demographic and clinical variables were evaluated using microbiological laboratory records and clinical data gained from electronic medical records; these included age, gender, length of hospital stay, underlying diseases, predisposing conditions, portal of entry, appropriateness of antimicrobial agents, appropriateness of definitive therapy, results of antimicrobial susceptibility testing, laboratory data at the time of bacteremia onset, Sequential Organ Failure Assessment score (SOFA),[14] and 28-day all-cause mortality. This study was approved by our Institutional Review Board. Informed consent was exempt from our local ethics committee because this study was concerned to cause minimal harm on persons.

Definitions

Significant *S. marcescens* bacteremia was defined as *S. marcescens* isolates cultured from one or more blood samples obtained from a patient, combined with clinical symptoms compatible with systemic inflammatory response syndrome.[15] Hospital-acquired bacteremia was defined as a positive blood culture taken from a patient no sooner than 48 h after hospital admission, whereas healthcare-associated bacteremia was defined as a positive blood culture taken from a patient receiving home and/or ambulatory intravenous therapy, hemodialysis, wound care, chemotherapy, or nursing care, or who had attended a hospital clinic within the last 30 days; patients hospitalized in an acute care hospital for ≥2 days within the last 90 days; or those living in a nursing home or long-term care facility.[16] The primary site of infection was presumed to be the source of bacteremia if *S. marcescens* was identified from any culture specimens at the time of bacteremia onset; if *S. marcescens* was not identified from any culture other than the blood, the source was presumed to be primary bacteremia. Polymicrobial bacteremia was defined as bacteremia where more than one organism were isolated from the same blood culture specimen. Septic shock was defined as sepsis-induced organ hypo-perfusion, combined with either a systolic blood pressure <90 mm Hg or <40 mm Hg less than baseline, or a mean arterial pressure <65 mm Hg after a fluid resuscitation, eventually leading to require the vasopressor use.[17] Underlying chronic diseases included hemato-oncological disease, chronic renal disease, chronic liver disease, chronic lung disease, cardiovascular disease, and cerebrovascular disease, as defined by the International Classification of Disease, 10th Revision.[18] Prior use of antimicrobial agent was defined as receipt for at least 48 h within 1 month prior to the bacteremic episode. Appropriateness of initial empirical antimicrobial agents was defined as the use of at least one *in vitro* susceptible antimicrobial agent within 24 h of positive blood culture before the susceptibility was known.[19] Definitive therapy was defined as antibiotic therapy given properly according to the results of final blood culture.[20] Hypoalbuminemia was defined as a serum albumin of less than 3.0 g/dL at the time of bacteremia.[21,22] Twenty-eight-day all-cause mortality was investigated to confirm the primary outcome.

Microbiological tests

Clinical isolates were evaluated using either conventional techniques or the ATB 32 GN system (bioMérieux, Marcy l' Etoile, France). Antimicrobial susceptibility testing was performed by microbiology laboratory staff using the disk-diffusion method or a VITEK-2 N131 card (bioMérieux,

Hazelwood, MO, USA). Results were interpreted using the guidelines set forth by the Clinical and Laboratory Standards Institute.[23]

Statistical analyses

Student's t-test was used to compare continuous variables; and categorical variables were analyzed using either a χ^2 or Fisher's exact test as appropriate. Nonparametric variables were analyzed using the Mann-Whitney U test. Univariate and multivariate analyses to evaluate independent risk factors for all-cause mortality in *S. marcescens* bacteremia were performed through the logistic regression models. Statistical analyses were performed using the SPSS software, version 20 (SPSS Inc., Chicago, IL, USA). *p*-values <0.05 were considered to indicate statistical significance; all values reported are for two-tailed analyses.

RESULTS

Epidemiology of *S. marcescens* bacteremia

A total of 98 episodes of *S. marcescens* bacteremia were identified between January 2006 and December 2012. The annual distribution of *S. marcescens* bacteremia is shown in Fig. 1. To confirm the outbreak, the trend was investigated and stratified by ward and period, but there were no outbreaks.

Characteristics of patients with *S. marcescens* bacteremia

Table 1 shows the demographics, clinical characteristics, and underlying conditions of all patients with *S. marcescens* bacteremia. Sixty patients (61.2%) were male, and the ages of patients ranged from 26 to 92 years (median age, 63.5 years). Of 98 bacteremic episodes, hospital-acquired bacteremia accounted for 73.5% of the episodes (72 patients), whereas healthcare-associated bacteremia accounted for 18.4% of the episodes (18 patients). The remaining 8 episodes (8.1%) were defined as community-acquired bacteremia. The most common underlying condition was malignancy (46.9%), which included conditions such as solid organ and hematologic malignancy; and diabetes mellitus (30.6%) were also common. The most frequent portal of entry was the lower respiratory tract (50%). Other portals of entry included the urinary tract (20.4%), abdomen (11.2%), skin and soft tissue (10.2%), and intra-venous catheter (5.1%). Half of the patients had central venous catheters (CVCs), including chemo-ports, and urinary catheters. 56.1% of the patients showed bacteremia during the intensive care unit (ICU) stay. Among them, the fatal group showed a greater incidence of bacteremia during the ICU stay (77.3%) than the non-fatal group (50%) (*p*=0.020). 46.9% of the episodes (46 patients) showed the 3rd cephalosporin resistance, but there was no statistically significant difference between the fatal and non-fatal group (*p*=0.744).

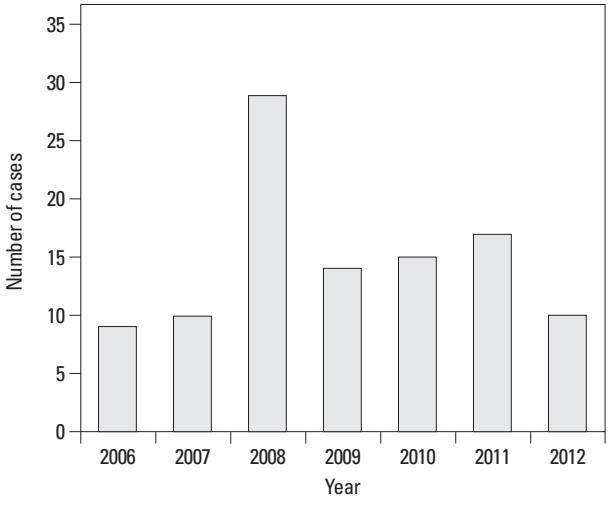

Fig. 1. Annual distribution of *S. marcescens* bacteremia in Severance Hospital between January 2006 and December 2012.

Antimicrobial susceptibilities

The antimicrobial susceptibilities of *S. marcescens* clinical isolates are characterized in Fig. 2. The majority of isolates were susceptible to ertapenem (100%), meropenem (99%), imipenem (93.4%), cefepime (87.8%), isepacin (81.8%), and ceftazidime (76.5%). A few isolates exhibited susceptibility to amoxicillin/clavulanic acid (1.1%), ampicillin (2.1%), and ampicillin/sulbactam (1.7%).

Risk factors for 28-day all-cause mortality

The 28-day all-cause mortality was 22.4% (22/98). Univariate analysis revealed significant differences in the number of important clinical covariates including the onset of bacteremia during the ICU stay (*p*=0.020), serum albumin level (*p*=0.011), serum C-reactive protein level (*p*=0.041), presence of indwelling urinary catheter (*p*=0.023), and SOFA score at the onset of bacteremia (*p*<0.001) between patients in the fatal and non-fatal groups (Table 1). In a multivariate analysis, lower serum albumin level [adjusted odds ratio (OR) 0.206, 95% confidential interval (CI) 0.044–0.960, *p*=0.040], and elevated SOFA score (adjusted OR 1.474, 95% CI 1.200–1.810, *p*<0.001) were all found to be inde-

Table 1. Clinical Characteristics of the Patients with *Serratia marcescens* Bacteremia

Characteristics	Total cases (n=98)	Fatal group (n=22)	Non-fatal group (n=76)	*p* value
Age, yr, median (range)	63 (26–92)	62.5 (26–92)	63 (26–88)	0.692
Age >65 yrs, n (%)	46 (46.9)	10 (45.5)	36 (47.4)	0.871
Male, n (%)	60 (61.2)	10 (50)	50 (64.1)	0.253
BMI (kg/m^2)	22.36 (12.17–40.09)	21.77 (12.17–40.09)	23.27 (14.79–33.42)	0.139
Polymicrobial, n (%)	27 (27.6)	5 (22.7)	22 (28.9)	0.573
Acquisition of bacteremia, n (%)				0.651
Hospital-acquired	72 (73.5)	18 (81.8)	54 (71.1)	
Healthcare-associated	18 (18.4)	3 (13.6)	15 (19.7)	
Community-acquired	8 (8.1)	1 (4.5)	7 (9.2)	
Underlying diseases, n (%)				
Malignancy				
Solid organ malignanacy	36 (36.7)	11 (50)	25 (32.9)	0.144
Hematologic malignancy	10 (10.2)	1 (4.5)	9 (11.8)	0.450
Diabetes mellitus	30 (30.6)	5 (22.7)	25 (32.9)	0.360
Chronic renal disease	26 (26.5)	4 (18.2)	22 (28.9)	0.308
Cerebrovascular disease	24 (24.5)	5 (22.7)	19 (25)	0.829
Cardiovascular disease	11 (11.2)	3 (13.6)	8 (10.5)	0.714
Chronic liver disease	6 (6.1)	3 (13.6)	3 (3.9)	0.132
Congestive heart failure	5 (5.1)	1 (4.5)	4 (5.3)	1.000
Neuromuscular disease	5 (5.1)	0 (0)	5 (6.6)	0.592
Chronic lung disease	4 (4.1)	0 (0)	4 (5.3)	0.571
Solid organ transplantation	3 (3.1)	1 (4.5)	2 (2.6)	0.540
Rheumatologic disease	3 (3.1)	0 (0)	3 (3.9)	1.000
Predisposing conditions, n (%)				
Prior anti-biotic use (within 1 month)	49 (50)	11 (50)	38 (50)	1.000
Immunosuppressive therapy	19 (19.4)	4 (18.2)	15 (19.7)	1.000
Inappropriate empirical antimicrobial therapy	17 (17.3)	4 (18.2)	13 (17.1)	1.000
Inappropriate definitive therapy	3 (3.1)	1 (4.5)	2 (2.6)	0.544
CVC indwelling	49 (50)	15 (68.2)	34 (44.7)	0.052
Urinary catheter indwelling	54 (55.1)	17 (77.3)	37 (48.7)	0.023
Onset of bacteremia during the ICU stay	55 (56.1)	17 (77.3)	38 (50)	0.020
Laboratory data				
Leukocyte count (×1000/uL) (range)	9.08 (0.45–60.95)	9.94 (0.45–60.95)	8.80 (0.71–51.96)	0.345
Serum CRP (mg/L) (range)	93.84 (4.19–346)	76.44 (4.19–346)	125.01 (12.1–335)	0.041
Serum albumin (g/dL) (range)	3.1 (2.0–4.4)	2.7 (2.0–4.1)	3.2 (2.1–4.4)	0.011
SOFA	4 (0–19)	3 (0–13)	9.5 (3–19)	<0.001
Portal of entry, n (%)				
Lower respiratory tract	49 (50)	14 (63.6)	35 (46.1)	0.152
Urinary tract	20 (20.4)	4 (21.1)	16 (18.2)	1.000
Abdomen	11 (11.2)	2 (9.1)	9 (11.8)	1.000
Skin and soft tissue	10 (10.2)	0 (0)	10 (13.2)	0.110
Biliary tract infection	5 (5.1)	2 (9.1)	3 (3.9)	0.314
Intra-venous catheter	5 (5.1)	1 (4.5)	4 (5.3)	1.000
Primary bacteremia	4 (5.8)	0 (0)	4 (5.3)	0.572
Presence of 3rd cephalosporin resistance	46 (46.9)	11 (50)	35 (46.1)	0.744

BMI, body mass index; CRP, C-reactive protein; CVC, central venous catheter; SOFA, Sequential Oran Failure Assessment; ICU, intensive care unit.
Values are given as n (%) or range.

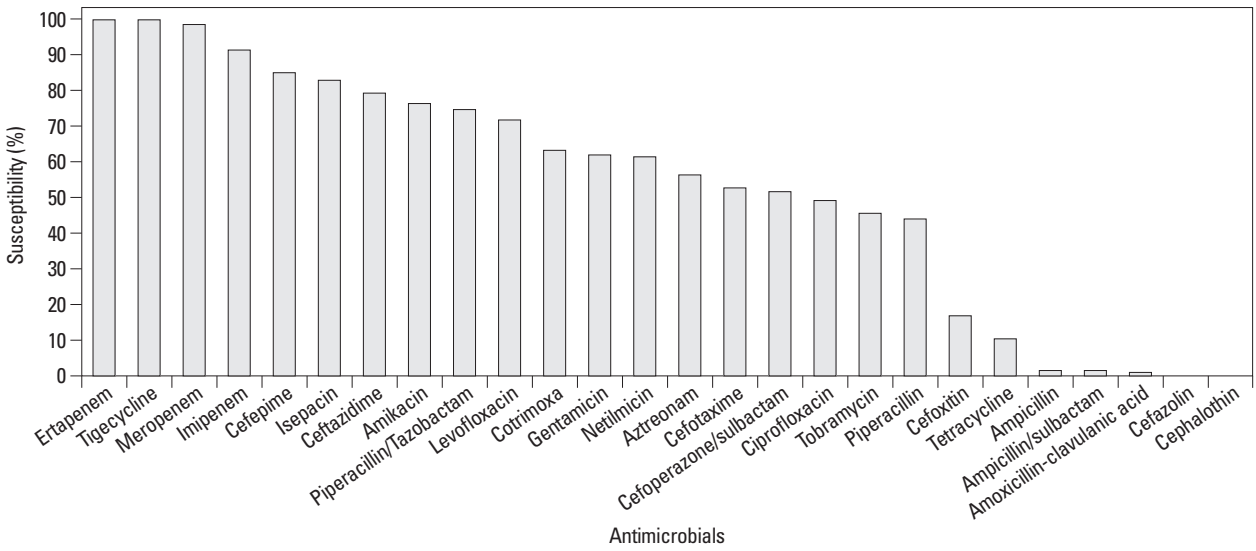

Fig. 2. *In vitro* antibiotic susceptibility tests for *S. marcescens* isolates cultured from blood.

Table 2. Risk Factors for the Mortality in Patients with *S. marcescens* Bacteremia

Variables	OR	95% CI	*p* value
Age	0.964	0.917–1.014	0.164
ICU stay	0.939	0.140–6.289	0.950
Serum albumin	0.206	0.044–0.960	0.040
SOFA	1.474	1.200–1.810	<0.001
Presence of indwelling urinary catheter	0.886	0.176–4.447	0.880
Presence of 3rd cephalosporin resistance	0.896	0.211–3.804	0.882

ICU, intensive care unit; SOFA, Sequential Oran Failure Assessment; OR, odds ratio; CI, confidential interval.
Multivariate logistic regression analyses were performed with all statistically significant variables of less than 0.05 of *p*-value obtained from univariate analyses.

pendent risk factors for mortality in patients with *S. marcescens* bacteremia (Table 2).

DISCUSSION

A number of recent reports have shown that *S. marcescens* bacteremia may arise from both community-acquired as well as healthcare-associated exposures.[10,12,13,24,25] Furthermore, an increase in the number of multidrug-resistant *S. marcescens* strains has been reported worldwide.[26-28] As these factors can substantially influence the outcome of *S. marcescens* bacteremia, we sought to identify the risk factors associated with *S. marcescens*-related mortality during recent 6 years. In our study, the 28-day all-cause mortality rate was 22.4%, similar to that in a previous report from South Korea.[12]

In previous studies, a wide array of independent risk factors have been found to be associated with mortality in patients with *S. marcescens* bacteremia, including old age (>65 years), pneumonia, hemorrhage, shock, inappropriate treatment, leukocytosis (leukocyte count >20000/mm^3), thrombocytopenia (platelet count <50000/mm^3), hyperbilirubinemia (serum total bilirubin >18 μmol/L), ICU stay, rapidly fatal or ultimately fatal disease, existence of poly-microorganisms, and unknown portal of entry.[7,12,29-31] Previous studies reports have directly investigated the association between chronic, fatal conditions and *S. marcescens*-associated bacteremia.[12,31] Watanakunakorn reported that both rapidly fatal and ultimately fatal diseases influenced the rate of mortality in *S. marcescens* bacteremia-related patients with no underlying conditions. Similar results were obtained by Choi, et al.[12] with rapidly fatal or ultimately fatal diseases serving as independent prognostic factors for *S. marcescens* bacteremia-associated fatality. However, in our study, underlying diseases were not significantly different between the fatal and the non-fatal group.

Herein, we identified significant associations between 28-day all-cause mortality and decreased serum albumin, and elevated SOFA score. Serum albumin level was significant-

ly associated with mortality in *S. marcescens* bacteremia. Hypoalbuminemia was shown in the fatal group although both groups showed evidence of decreased albumin level. Serum albumin levels are used to gauge the general health of a patient, since significant fluctuations are seen during acute illnesses due to changes in vascular permeability and redistribution of fluids.[32,33] Moreover, hypoalbuminemia can alter pharmacokinetics (PK) and pharmacodynamics of certain antimicrobial agents.[34] Hypoalbuminemia influences PK as a result of decreased binding of the antimicrobial compound to albumin, leading to an increase in the unbound fraction. The relationship between hypoalbuminemia and mortality in acutely ill patients is well established.[32,33] Herrmann, et al.[32] found that subjects with low serum albumin levels had a higher rate of mortality than the subjects with normal concentrations. The impact of these changes has since been quantified, with mortality risk increasing 137% with each 1 mg/dL decline in serum albumin level.[33]

Elevated SOFA score was also found to be an independent risk factor for mortality in *S. marcescens* bacteremia. The SOFA score is a grading system that describes the severity of a patient's illness based on the degree of organ dysfunction, and serves as a useful tool for predicting mortality in bacteremic patients.[35] An elevated SOFA score is indicative of severe organ dysfunction and poor prognosis. Several studies demonstrated correlations between SOFA score and clinical outcomes, such as severe sepsis and septic shock, in patients with bacteremia.[35-37]

In our study, the fatal group showed a poorer general condition, including a greater presence of indwelling CVC, urinary catheter, and the onset of bacteremia during the ICU stay than the non-fatal group. These conditions might result in decreased serum albumin level and low SOFA score.

The rate of resistance to cefotaxime (46.9%) during this study period was slightly lower than previous investigations in South Korea.[12,38] In our study, there was no statistically significant difference between the fatal and non-fatal group for the presence of 3rd cephalosporin resistance. Most of the patients received appropriately definitive therapies, which could have affected the result.

Our study has some limitations. First, patients with *S. marcescens* bacteremia included in this study were enrolled from a single center. Second, there is potential for bias and inaccurate data collection due to retrospective nature of this study. Moreover, evidence of a high proportion (>20%) of polymicroorganisms other than *S. marcescens* may create a bias when analyzing the data. Further prospective studies, conducted in larger patient populations involving multiple centers, are necessary to more accurately identify the risk factors associated with mortality in *S. marcescens* bacteremia. Finally, the small sample size of those with *S. marcescens* bacteremia may possibly influence our results.

In conclusions, lower serum albumin level and an elevated SOFA score were significantly associated with adverse outcomes in patients with *S. marcescens* bacteremia.

REFERENCES

1. Eisenstein BI, Zaleznik DF. Enterobacteriaceae. In: Mandell GL, Douglas RG, Bennett JE, Dolin R, editors. Principles and practice of infectious diseases. 5th ed. Philadelphia: Churchill Livingstone; 2000. p.2297-310.
2. Yu VL. Serratia marcescens: historical perspective and clinical review. N Engl J Med 1979;300:887-93.
3. Henjyoji EY, Whitson TC, Oashi DK, Allen BD. Bacteremia due to Serratia marcescens. J Trauma 1971;11:417-21.
4. Luzzaro F, Perilli M, Migliavacca R, Lombardi G, Micheletti P, Agodi A, et al. Repeated epidemics caused by extended-spectrum beta-lactamase-producing Serratia marcescens strains. Eur J Clin Microbiol Infect Dis 1998;17:629-36.
5. Bonnet R, Sampaio JL, Chanal C, Sirot D, De Champs C, Viallard JL, et al. A novel class A extended-spectrum beta-lactamase (BES-1) in Serratia marcescens isolated in Brazil. Antimicrob Agents Chemother 2000;44:3061-8.
6. Ivanova D, Markovska R, Hadjieva N, Schneider I, Mitov I, Bauernfeind A. Extended-spectrum beta-lactamase-producing Serratia marcescens outbreak in a Bulgarian hospital. J Hosp Infect 2008; 70:60-5.
7. Saito H, Elting L, Bodey GP, Berkey P. Serratia bacteremia: review of 118 cases. Rev Infect Dis 1989;11:912-20.
8. Wong WW, Wang LS, Cheng DL, Lin SJ, Chin TD, Hinthorn DR, et al. Serratia marcescens bacteremia. J Formos Med Assoc 1991;90:88-93.
9. Yu WL, Lin CW, Wang DY. Serratia marcescens bacteremia: clinical features and antimicrobial susceptibilities of the isolates. J Microbiol Immunol Infect 1998;31:171-9.
10. Shih HI, Lee HC, Lee NY, Chang CM, Wu CJ, Wang LR, et al. Serratia marcescens bacteremia at a medical center in southern Taiwan: high prevalence of cefotaxime resistance. J Microbiol Immunol Infect 2005;38:350-7.
11. Cheong HS, Ko KS, Kang CI, Chung DR, Peck KR, Song JH. Clinical significance of infections caused by extended-spectrum β-lactamase-producing Enterobacteriaceae blood isolates with inducible AmpC β-lactamase. Microb Drug Resist 2012;18:446-52.
12. Choi SH, Kim YS, Chung JW, Kim TH, Choo EJ, Kim MN, et al. Serratia bacteremia in a large university hospital: trends in antibiotic resistance during 10 years and implications for antibiotic use. Infect Control Hosp Epidemiol 2002;23:740-7.
13. Engel HJ, Collignon PJ, Whiting PT, Kennedy KJ. Serratia sp. bacteremia in Canberra, Australia: a population-based study over 10 years. Eur J Clin Microbiol Infect Dis 2009;28:821-4.
14. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, et al. Use of the SOFA score to assess the incidence of

organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. Crit Care Med 1998;26:1793-800.
15. Kang CI, Kim SH, Park WB, Lee KD, Kim HB, Oh MD, et al. Bloodstream infections caused by Enterobacter species: predictors of 30-day mortality rate and impact of broad-spectrum cephalosporin resistance on outcome. Clin Infect Dis 2004;39:812-8.
16. Friedman ND, Kaye KS, Stout JE, McGarry SA, Trivette SL, Briggs JP, et al. Health care--associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. Ann Intern Med 2002;137:791-7.
17. Marik PE, Lipman J. The definition of septic shock: implications for treatment. Crit Care Resusc 2007;9:101-3.
18. World Health Organization. International statistical classification of diseases and related health problems. 10th revision. 2nd ed. Geneva: World Health Organization; 2004.
19. Harbarth S, Garbino J, Pugin J, Romand JA, Lew D, Pittet D. Inappropriate initial antimicrobial therapy and its effect on survival in a clinical trial of immunomodulating therapy for severe sepsis. Am J Med 2003;115:529-35.
20. McGregor JC, Rich SE, Harris AD, Perencevich EN, Osih R, Lodise TP Jr, et al. A systematic review of the methods used to assess the association between appropriate antibiotic therapy and mortality in bacteremic patients. Clin Infect Dis 2007;45:329-37.
21. Song SW, Kim KT, Ku YM, Park SH, Kim YS, Lee DG, et al. Clinical role of interstitial pneumonia in patients with scrub typhus: a possible marker of disease severity. J Korean Med Sci 2004;19:668-73.
22. Carratalà J, Rosón B, Fernández-Sabé N, Shaw E, del Rio O, Rivera A, et al. Factors associated with complications and mortality in adult patients hospitalized for infectious cellulitis. Eur J Clin Microbiol Infect Dis 2003;22:151-7.
23. Clinical and Laboratory Standards Institue. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Second Informational Supplement M100-S21. Wayne, PA, USA: CLSI; 2012.
24. Haddy RI, Mann BL, Nadkarni DD, Cruz RF, Elshoff DJ, Buendia FC, et al. Nosocomial infection in the community hospital: severe infection due to Serratia species. J Fam Pract 1996;42:273-7.
25. Laupland KB, Parkins MD, Gregson DB, Church DL, Ross T, Pitout JD. Population-based laboratory surveillance for Serratia species isolates in a large Canadian health region. Eur J Clin Microbiol Infect Dis 2008;27:89-95.
26. Park YJ, Park SY, Oh EJ, Park JJ, Lee KY, Woo GJ, et al. Occurrence of extended-spectrum beta-lactamases among chromosomal AmpC-producing Enterobacter cloacae, Citrobacter freundii, and Serratia marcescens in Korea and investigation of screening criteria. Diagn Microbiol Infect Dis 2005;51:265-9.
27. Nordmann P, Naas T, Poirel L. Global spread of Carbapenemase-producing Enterobacteriaceae. Emerg Infect Dis 2011;17:1791-8.
28. Kim SY, Shin J, Shin SY, Ko KS. Characteristics of carbapenem-resistant Enterobacteriaceae isolates from Korea. Diagn Microbiol Infect Dis 2013;76:486-90.
29. Arribas JR, Dominguez A, Folgueira MD, Peña P, Luengo S, Peña JM, et al. Prognostic factors in Serratia bacteremia. Rev Infect Dis 1990;12:563-4.
30. Ho PL, Shek RH, Chow KH, Duan RS, Mak GC, Lai EL, et al. Detection and characterization of extended-spectrum beta-lactamases among bloodstream isolates of Enterobacter spp. in Hong Kong, 2000-2002. J Antimicrob Chemother 2005;55:326-32.
31. Watanakunakorn C. Serratia bacteremia: a review of 44 episodes. Scand J Infect Dis 1989;21:477-83.
32. Herrmann FR, Safran C, Levkoff SE, Minaker KL. Serum albumin level on admission as a predictor of death, length of stay, and readmission. Arch Intern Med 1992;152:125-30.
33. Vincent JL, Dubois MJ, Navickis RJ, Wilkes MM. Hypoalbuminemia in acute illness: is there a rationale for intervention? A meta-analysis of cohort studies and controlled trials. Ann Surg 2003; 237:319-34.
34. Ulldemolins M, Roberts JA, Rello J, Paterson DL, Lipman J. The effects of hypoalbuminaemia on optimizing antibacterial dosing in critically ill patients. Clin Pharmacokinet 2011;50:99-110.
35. Routsi C, Pratikaki M, Sotiropoulou C, Platsouka E, Markaki V, Paniara O, et al. Application of the sequential organ failure assessment (SOFA) score to bacteremic ICU patients. Infection 2007;35: 240-4.
36. Anami EH, Grion CM, Cardoso LT, Kauss IA, Thomazini MC, Zampa HB, et al. Serial evaluation of SOFA score in a Brazilian teaching hospital. Intensive Crit Care Nurs 2010;26:75-82.
37. Ku NS, Han SH, Kim CO, Baek JH, Jeong SJ, Jin SJ, et al. Risk factors for mortality in patients with Burkholderia cepacia complex bacteraemia. Scand J Infect Dis 2011;43:792-7.
38. Kim BN, Lee SO, Choi SH, Kim NJ, Woo JH, Ryu J, et al. Outcome of antibiotic therapy for third-generation cephalosporin-resistant Gram-negative bacteraemia: an analysis of 249 cases caused by Citrobacter, Enterobacter and Serratia species. Int J Antimicrob Agents 2003;22:106-11.