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Original Article

Changing epidemiology and prognosis of nosocomial bloodstream infection: A single-center retrospective study in Taiwan

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Abstract *Background:* Nosocomial bloodstream infection (BSI) remains a significant cause of mortality and morbidity. We evaluate the trend of the pathogens of nosocomial BSI and investigate the distribution of the pathogens to demonstrate the risk factors of mortality.
Methods: In this retrospective study, we collected data from a 2076-bed tertiary referral center that offers a full range of clinical services in central Taiwan during January, 2016 to December, 2017.
Results: Five hundred and eighty-four patients were identified with nosocomial BSI. Among the comorbidities of nosocomial BSI patients with, the most frequent were hypertension, in 294 patients (50.3%), malignancy, in 279 patients (47.8%); diabetes, in 278 patients (47.6%); chronic kidney disease, in 171 patients (29.3%); and liver cirrhosis, in 132 patients (22.6%). Gram-positive organisms caused 22.9% of these nosocomial BSIs, gram-negative organisms caused 69.2%, and fungi caused 6.8%. The most common organism causing nosocomial BSIs were *Klebsiella* spp. (14%), *E coli*. (14%), and *Enterococcus* spp. (11%). Multivariate analysis of risk factors for mortality displayed that comorbidity with low body weight, liver cirrhosis, and malignancy, high CRP level, high Charlson Comorbidity Index and internal medicine and hematology/oncology distribution were strikingly associated with mortality ($P = 0.0222$, 0.0352, 0.0008, 0.0122, <0.001, and 0.041; [OR] = 1.8097, 1.9268, 2.7156, 2.7585, 3.5431, and 2.2449, respectively).

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Conclusion: *K.* spp. and *E coli*. became the most common pathogens of nosocomial BSI in recent years. Comorbidities could be important roles to predictive the outcome of nosocomial BSI. The modifiable risk factors of nosocomial BSI may be investigated further to improve the outcome.

Introduction

Nosocomial infections remain a major issue of patient care and mortality.[1] Nosocomial infections are frequently associated with drug-resistant micro-organisms, which can pose therapeutic problems.[2] The prevalence of nosocomial infections was 5%—10% and 5.7%—19.1% in developed countries and in developing countries, respectively.[3,4] Nosocomial bloodstream infection (BSI) continues to be a severe, life-threatening infectious disease, and remains a significant cause of mortality and morbidity.[5] Nosocomial BSI increases the difficulties of treatment for primary diseases, lengths of stay in an intensive care unit (ICU) as well as in the hospital, hospital mortality, and expands extra costs.[6,7]

According to Nosocomial Infections Surveillance Report in 2016 from Centers for Disease Control (CDC) Taiwan, all the healthcare-associated infections (HAI) in ICU of medical center, nosocomial BSI accounts for the largest proportion of HAI and the rate of occurrence was 31%—44% of HAI during 2007—2016.[8] During the period, the incidence of nosocomial BSI kept increasing from 1574 cases in 2007—2202 cases in 2015.[8] During the past decades, changes in health care, infection-control practices, and antimicrobial use and resistance may have influenced the hospital-acquired infection. The SENTRY Program performed global surveillance in the first 2 decades in this century and showed the predominance of *Staphylococcus aureus* (*S. aureus*) and *Escherichia coli* (*E. coli*) BSI pathogens worldwide.[9] The rank order of BSI pathogens varied over time and by regions. The *S. aureus* is the most common pathogen of BSI during the both first period of the SENTRY study, but *E. coli* has become the top major pathogen during the last period.

The appropriate empirical antimicrobial therapy is vital, because it can decrease mortality in severely ill patients.[10] Initial broad-spectrum therapy should be prescribed to septic patients in whom the microorganism is unknown. Inappropriate use of antibiotics for the treatment of suspected pneumonia is widely prevalent.[11] Empiric antibiotic therapy is often continued despite negative culture results. One study reported patients who received inappropriate empiric antibiotics more than 4 days had increased mortality.[12] To know the trend of BSI microorganisms and pattern of antimicrobial resistance is import.

Changes in surveillance in hospitals may provide a limitation in interpreting these shifting trends. We herein presented a 2-year retrospective data in a tertiary referral center and concluded that the most common nosocomial BSI pathogens. The surveillance was conducted to discover the latest distribution of microorganism, antimicrobial susceptibility of pathogens, and patient outcome.

Materials and methods

Study population

We retrospectively analyzed the patients with nosocomial bloodstream infection in a tertiary hospital, which is a 2076-bed referral center in central Taiwan between 2016 and 2017. Adult patients (≥18 years) fulfilling the criteria for nosocomial BSI, were included in this study (Fig. 1).

Definition of nosocomial primary BSI (PBSI)

Nosocomial PBSI was defined according to the surveillance criteria published by the centers of disease control (CDC) in

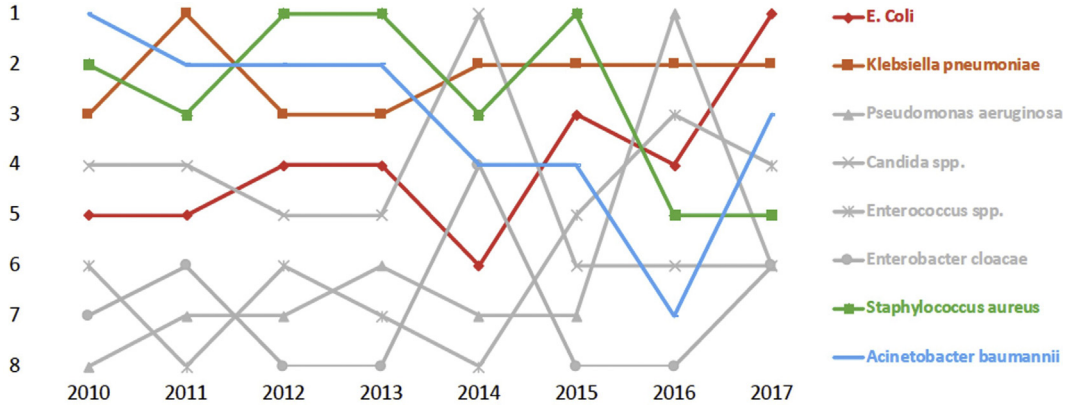

Figure 1. The ranking trend of nosocomial bloodstream infection between 2010 and 2017.

Taiwan, subject to the 2 following conditions: 1) one or more culture of blood drawn at least 48 h after hospital admission yielded a pathogenic organism; and 2) microbiologic diagnosis of nosocomial BSI: required one of the following: a) recognized pathogen in the blood and pathogen not related to an infection at another site; b) a potential skin contaminant was isolated from at least two blood cultures drawn on separate occasions and not related to infection at another site, as well as the presence of fever, chills, or hypotension.[13]

Data collection

Patient baseline characteristics included age, gender, body weight, comorbidities [e.g. hypertension (HTN), heart failure, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), liver cirrhosis, chronic kidney disease (CKD), malignancy and cerebral vascular accident (CVA)] were collected. The clinical data that were routinely collected included presence of intravascular catheters (i.e. central lines, arterial catheters, Hickman catheter or Port-A-Cath), location at the onset of nosocomial BSI, clinical service at the onset of BSI and days between admission and onset of nosocomial BSI. Microbiologic data, susceptibility profile and C-reactive protein (CRP), white blood cell count (WBC) and neutrophil percentage, simultaneously collected at the onset of nosocomial BSI were retrieved.

In vitro susceptibility test and Definition multiple-drug resistance and inadequate antibiotic therapy: Inadequate antibiotic therapy was defined as absence of antibiotic therapy with bacteriostatic or bactericidal activity against the pathogen empirically within 1 day after the onset of nosocomial BSI. The prognostic data including in-hospital mortality and hospital stay were also collected.

Statistical analysis

Means and standard deviations (SD) or median and interquartile range (IQR) for continuous variables, and frequencies and percentages for categorical variables, were used to summarize the demographic and clinical characteristics. The pattern of distribution of continuous variables was evaluated using Kolmogoro-Smirnov test. Univariate predictors of in-hospital mortality with p value less than 0.2 were included in the multivariate logistic regression analysis. A P value less than 0.05 was considered statistically significant. All data were analyzed using the Medcalc statistical software.

Results

Study population and patient characteristics

From January 2016 to December 2017, 584 patients developed nosocomial PBSI while reached further analysis. Patients had a mean age of 61 $\pm$ 16.0 years and median body weight of 60 kg. The percentage of male patients were 61.8%. The most comorbidities of patients with nosocomial BSI were HTN and malignancy, in both 294 patients (50.3%); diabetes, in 278 patients (47.6%); chronic kidney disease, in 171 patients (29.3%); and liver cirrhosis, in 132 patients (22.6%). The distribution of the patients was in department of internal medicine (46.2%), general surgery (20.5%), and hematology/oncology (18.5%), as shown in Table 1.

Of the potential risk factors for in-hospital mortality, inadequate antibiotic therapy had the highest ratio, in 321 patients (55.0%). Then followed with ICU/Respiratory care center (RCC) hospitalization, in 262 patients (44.9%); catheter-related infection, in 256 patients (43.8%); and multiple drugs resistance, in 142 patients (24.3%).

Table 1 Demographic and clinical characteristics of 584 patients with nosocomial bloodstream infection.

Parameter	Value
Age, mean (SD), y	61 (16)
Male, No. (%)	361 (61.8%)
Body weight, median (IQR), kg	60 (52—70)
Comorbidities, No. (%)	
Hypertension	294 (50.3)
Heart failure	84 (14.4)
Diabetes	278 (47.6)
COPD	25 (4.3)
Liver cirrhosis	132 (22.6)
Chronic kidney disease	171 (29.3)
Malignancy	279 (47.8)
CVA	90 (15.4)
Charlson Comorbidity Index, median (IQR)	6 (3—8)
Laboratory data	
WBC, median (IQR), 1000/ul	9.2 (5.4—13.6)
CRP, median (IQR), mg/dl	5.1 (1.9—12.5)
Microbiological organisms, No. (%)	
Fermentative Gram-negative	267 (45.7)
Non-fermentative Gram-negative	137 (23.5)
Gram-positive	134 (22.9)
Fungi	40 (6.8)
Anaerobes	6 (1.0)
Distribution, No. (%)	
Internal medicine	270 (46.2)
Hematology/oncology	108 (18.5)
General surgery	120 (20.5)
Others	86 (14.7)
Potential risk factors, No. (%) [95% CI]	
ICU/RCC hospitalization	262 (44.9) [40.8—48.9]
Catheter-related infection	256 (43.8) [39.8—47.9]
Inadequate antibiotic therapy	321 (55.0) [50.9—59.0]
Multiple drug resistance	142 (24.3) [20.8—27.8]
Days between admission and BSI, median (IQR), d	14 (7—26)
Days between BSI and discharge, median (IQR), d	18 (10—35)
Hospital stay, median (IQR), d	37 (22—62)
In-hospital mortality, No. (%) [95% CI]	181 (31.0) [27.2—34.8]

Abbreviations: BSI, bloodstream infection; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVA, cerebral vascular accident; ICU, intensive care unit; RCC, respiratory care unit; WBC, white blood cell.

Pathogen distribution and antimicrobial susceptibility: Fig. 1 showed the ranking trend of nosocomial BSI between 2010 and 2017. The ranking list of the pathogens found in the nosocomial BSI changed a lot from 2010 to 2017. In 2010, the frequent place of the pathogens incidence ranking were *S. aureus* and *Acinetobacter baumannii*, respectively. However, the ranking changed significantly within 8 years. In 2017, *Klebsiella* spp. and *Escherichia coli (E. coli)* took place of *S. aureus* and *A. baumannii* as the first and second common pathogens.

Of 584 microbial episodes, a total of 267 episodes (45.7%) were caused by fermentative Gram-negative organisms, 137 (23.5%) by non-fermentative gram-negative organisms, and 134 (22.9%) by gram-positive organisms. Fungi were isolated in a total of 40 episodes (6.8%). Anaerobes accounted for 1.0% of nosocomial BSI (Table 1). The rank order of the major microbiological organisms isolated in patients with nosocomial BSI were *Klebsiella* spp. (14%), *E. coli* (14%), *Enterococcus* spp. (11%), *Acinetobacter* spp. (10%), *Enterobacter* spp. (9%), *S. aureus* (9%) and *Pseudomonas* spp. (8%), and, as shown in Fig. 2. The most frequently isolated organism during the shortest time interval between admission and onset of BSI are *Enterobacter* spp., *E. coli*., and *Acinetobacter* spp. which occurred within two weeks of admission. *Candida* spp., *and Stenotrophomonas maltophilia* frequently occurred more than two weeks after admission, as show in Fig. 3.

Antimicrobial resistance levels for the most common gram-negative organisms causing nosocomial BSI are shown in Table 2. *Enterobacter* species had high proportions displaying resistance to ampicillin, cefazolin, ampicillin-sulbactam, cefazolin, and cefmetazole (100%, 98%, 94.1%,

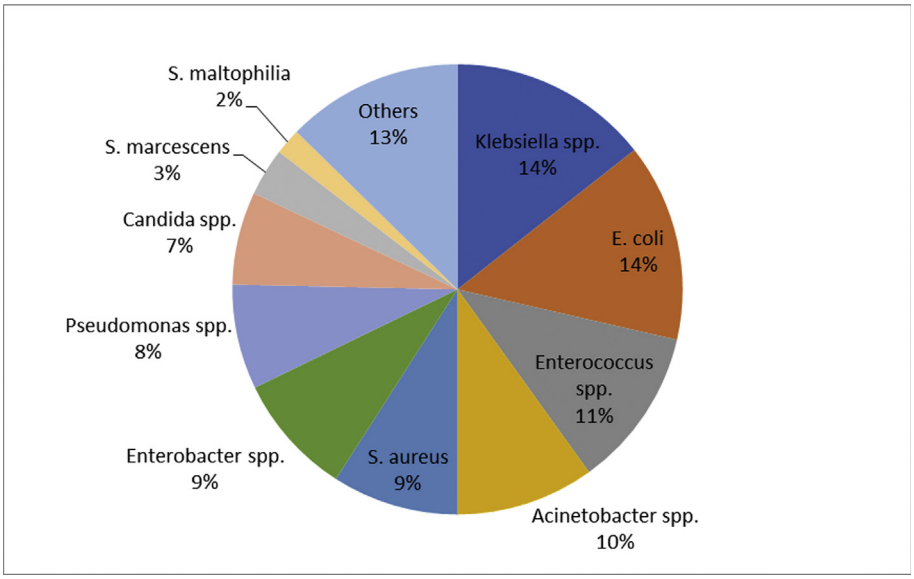

Figure 2. Microbiological organisms isolated in patients with nosocomial bloodstream infection (with percentages).

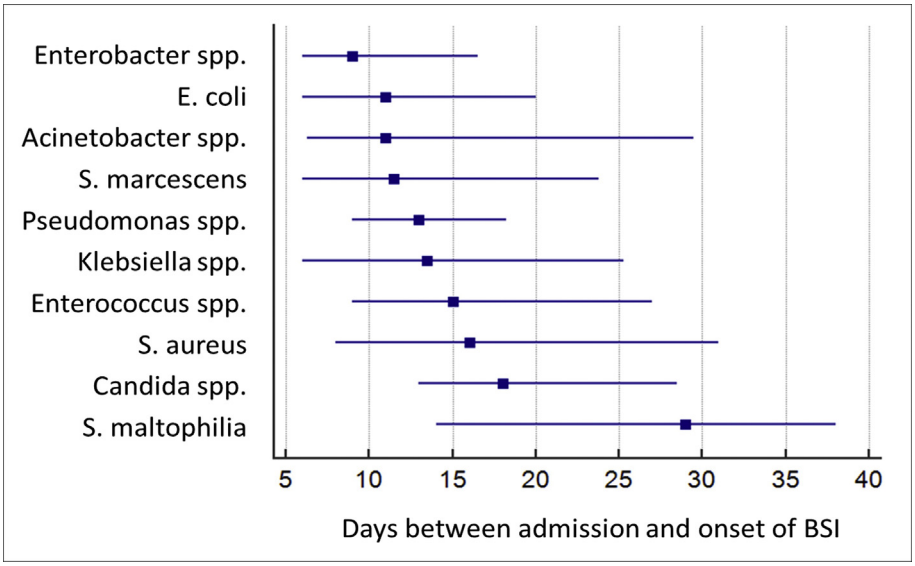

Figure 3. Time interval between admission and onset of infection for the most frequently isolated organisms.

and 88.0%, respectively). For *E. coli*, 72.3%, 55.4%, and 51.8% were resistant to ampicillin, ampicillin-sulbactam, and trimethoprim/sulfamethoxazole (TMP-SMX), respectively. Resistance to amikacin, ertapenem, and imipenem was seen in 6.0%, 4.9%, and 2.4% of the isolates. Of the *Klebsiella* species isolates, the resistance to ampicillin was 100%. Amikacin and tigecycline were 3.6% and 14.3%. As for the resistance rate of *Acinetobacter* species, tigecycline and gentamicin were 61.5% and 43.9%. A high percentage of *Serratia marcescens* showed resistance to ampicillin, cefazolin, and ampicillin-sulbactam (100%, 100%, and 95%, respectively).

Table 3 showed penicillin resistance in 90.6% *S. aureus* isolates, and 74.6% in *Enterococcus* species isolates. The proportion of *S. aureus* with penicillin resistance was significantly higher among all of the antimicrobial resistance rates of gram-positive organisms. *S. aureus* had no resistance (0%) to vancomycin, teicoplanin, linezolid. The resistant rate to daptomycin, and fusidic acid were 3.8% and 1.9%. And 60.4% of the isolates was resistant to oxacillin. *Enterococcus* species displayed no resistance (0%) to linezolid and daptomycin, and was resistant to streptomycin, vancomycin, and teicoplanin (71.7%, 56.7%, and 56.7%, respectively).

The most frequently isolated causative pathogens of nosocomial BSI were *Klebsiella* spp., *E. coli*, and *C.* spp. in internal medicine ward, hematology/oncology ward, and general surgery ward respectively, as showed in Table 4.

In-hospital mortality: One hundred and eighty-one patients died during hospitalization, accounting for a crude mortality rate of 31%. The main characteristics of the survivor and non-survivor subgroups are presented in Table 5. Univariate analysis revealed differences between each subgroup. Non-survivor patients had higher CRP levels (7.3 mg/dl, IQR 4.3–16.7; the former 4.0 mg/dl, IQR 1.5–10.5) ($P < 0.001$; odds ratio [OR] = 1.0600) and Charlson Comorbidity Index (CCI) (7, IQR 5–9) ($P < 0.0001$; odds ratio [OR] = 1.1603). The rate of comorbidities also varied.

Multivariate analysis of risk factors for mortality (Table 6) displayed that low body weight, comorbidity with malignancy and liver cirrhosis, high CRP level, high CCI, and internal medicine and hematology/oncology distribution were strikingly associated with mortality ($P = 0.0222$,

Table 3 Rates of antimicrobial resistance among Gram-positive organisms most frequently isolated from patients with nosocomial bloodstream infection.

	Staphylococcus aureus	*Enterococcus* species
Oxacillin	60.4	ND
Erythromycin	52.8	ND
Penicillin	90.6	74.6
Vancomycin	0	56.7
Teicoplanin	0	56.7
Tetracycline	50.9	ND
Clindamycin	43.4	ND
Linezolid	0	0[a]
TMP-SMX	32.1	ND
Ciprofloxacin	50.9	ND
Daptomycin	3.8	0[a]
Fusidic acid	1.9	ND
Doxycycline	6.7[a]	ND
Gentamicin	ND	56.7
Streptomycin	ND	71.7

[a] Susceptibility testing not performed in all cases.

Table 2 Rates of antimicrobial resistance among Gram-negative organisms most frequently isolated from patients with nosocomial bloodstream infection.

	Klebsiella species	*Escherichia coli*	Acinetobacter species	Enterobacter species	Pseudomonas species	*Serratia marcescens*
Cefmetazole	42.9	14.5	ND	88.0	ND	15.0
Amp-Sulb	57.1	55.4	33.9	94.1	ND	95.0
Gentamicin	40.5	34.9	43.9	9.8	6.8	5.0
Ampicillin	100	72.3	ND	100	ND	100
Cefazolin	58.3	48.8	ND	98.0	ND	100
Amikacin	3.6	6.0	31.6	0	0	5.0
Cefotaxime	36.9	33.7	ND	29.4	ND	5.0
Ertapenem	25.0	4.9	ND	10.0	ND	10.0
Ciprofloxacin	27.4	49.4	36.8	9.8	4.5	5.0
TMP-SMX	53.6	51.8	40.4	9.8	90.9	0
Cefepime	29.8	31.3	38.6	13.7	4.5	5.0
Imipenem	28.6	2.4	29.8	25.5	11.6	15.0
Levofloxacin	25.0	47.0	32.1	7.8	6.8	5.0
Pip-Tazo	28.6	13.3	35.1	21.6	4.5	5.0
Meropenem	47.1[a]	ND	30.9	33.3[a]	11.9	0[a]
Ceftazidime	ND	ND	40.0	ND	4.7	ND
Aztrenam	ND	ND	ND	ND	20.5	ND
Tigecycline	14.3[a]	0[a]	61.5[a]	13.3[a]	ND	33.3[a]
Colistin	ND	ND	0	ND	ND	ND

[a] Susceptibility testing not performed in all cases.
Abbreviations: Amp-Sub, ampicillin-sulbactam; Pip-Tazo, piperacillin tazobactam.

Table 4 Distribution of nosocomial bloodstream infection and most frequently isolated causative pathogens by clinical service.

Clinical service, class of BSI, pathogen	No. (%) of BSIs
Internal medicine	
All BSIs	270 (46.2)
Monomicrobial BSIs	
Klebsiella species	35 (12.9)
Acinetobacter species	34 (12.6)
Escherichia coli	32 (11.9)
Hematology/oncology	
All BSIs	108 (18.5)
Monomicrobial BSIs	
Escherichia coli	27 (25.0)
Klebsiella species	18 (16.7)
Enterococcus species	16 (14.8)
General surgery	
All BSIs	120 (20.5)
Monomicrobial BSIs	
Candida species	16 (13.3)
Staphylococcus aureus	15 (12.5)
Escherichia coli	14 (11.7)
Klebsiella species	14 (11.7)
Others	
All BSIs	86 (14.7)
Monomicrobial BSIs	
Klebsiella species	17 (19.8)
Enterobacter species	13 (15.1)
Escherichia coli	10 (11.6)
Enterococcus species	10 (11.6)

Abbreviations: BSI, bloodstream infection.

0.008, 0.0352, <0.001, 0.0122, and 0.041; [OR] = 1.8091, 2.7156, 1.9268, 3.5431, 2.7585, and 2.2449, respectively).

Discussion

The surveillance in a tertiary referral center nosocomial BSI demonstrated the increasing microorganism incidence of *E. coli* and *Klebsiella pneumonia* and decreasing microorganism incidence of *A. baumannii* and *S. aureus* in nosocomial BSI in 2016—2017. The nosocomial BSI patients who had liver cirrhosis, malignancy, high CRP, high CCI, and Internal medicine and hematology/oncology distribution scores were associated with higher hospital mortality.

Nosocomial infection has a lot of negative impacts on hospitalized patients. It can not only deteriorate the disease and even lead to permanent disability but also result in higher mortality.[14] The mean additional cost of nosocomial bacteremia is also high.[15] Although many strategies were studies to reduce the incidence of nosocomial infection, nosocomial BSI still is the critical problem in hospital care.[16]

From 1990 through 1992, Gram-positive bacterial pathogens are most frequently associated with BSIs. During 1997—2004, *S. aureus* is still the most common microorganism causing bloodstream infection.[9] In the early 2000's, *A. baumannii* was increasingly reported as an important nosocomial pathogen and became low incident of BSI microorganism in recent years.[9,17] The trend of bloodstream infections with Gram-negative *Enterobacterales* developed in recent years.[9]

In addition, nosocomial BSIs prolong patients' length of stay and increases both expenditure and waste of medical resources, which can easily increase burden on the families with nosocomial BSI patients.[18,19] The extensive use of antibiotics can contribute to mutation and natural selection, and further cause problems with massive increase of multidrug-resistant bacteria.[18,20]

In our studies, the incidence of gram-negative bacteria (GNB) is 69.2%, while gram-positive bacteria stand only 22.9%, and the remaining 6% were anaerobic organisms or fungus. Compared to other studies,[21] the percentage of GNB is much higher than we expected, and this might result in e risks at treatment for giving inadequate empirical antibiotic therapy. The most common isolates are *E. coli*, *Klebsiella species* and *Acinetobacter species*. *E. coli* has increased in these years, *Enterococcus* spp. is even doubled in our unit, which contribute to a different decision of empiric antibiotics.

The antimicrobial resistance of the organism is an important effect on therapy. During the period of this study, the strategy of empirical antibiotic choice for patients with bloodstream infections in our unit is mostly according to experiences of physicians and the situations of the patients, which make the information important for physicians. From our data, many patients with bloodstream infections are infected with multidrug-resistant bacterial pathogens that add difficulties to initial empirical antimicrobial therapy. Much nosocomial GNBs are relatively highly resistant to ampicillin, cefazolin, ampicillin-sulbactam, and cefmetazole, such as *Enterobacter* species, *Klebsiella* species, and *S. marcescens*. Therefore, empirical broad-spectrum antimicrobials should be used due to the increased successful chance to treat resistant organisms.[22] According to our susceptibility test, amikacin and imipenem seems to be the better solution in GNB BSIs. However, according to our study (Table 4) and others,[9,21] different patient group had different dominant BSI pathogens. Empirical antibiotic for BSI should be individualized and consider patients' prior antibiotic use, underlying disease and epidemiology of current ward status.

In our study, CRP level can predict the mortality rate in nosocomial BSI patients. From Table 5, we could demonstrate that the risk factors of mortality are associated with heart failure, liver cirrhosis, malignancy, and high CCI scores. There had been literatures about the association between infection related mortality and some underlying illness causing patients possess poor functional status and extensive frailty.[23] Our patients who had heart failure, liver cirrhosis and malignancy are relatively fragile, and often acquired longer duration of intravenous catheters, which may bring them more risk of developing nosocomial BSI. Other studies reported the major risk factor of mortality of nosocomial BSI was the severity of illness.[24] Our study also validates that high CCI scores were associated with higher hospital mortality. Therefore, measuring the severity of each nosocomial BSI patients gives us the hint of prognosis.

Table 5 Univariate analysis of factors associated with mortality among patients with nosocomial bloodstream infection.

Parameter	Non-survivor (n = 181)	Survivor (n = 403)	P value	OR (95% CI)
Age, mean (SD), y	65 (15)	60 (16)	0.0010	1.0194 (1.0078–1.0312)
Male, No. (%)	109 (60.2)	252 (62.5)	0.5952	0.9071 (0.6332–1.2996)
Body weight, median (IQR), kg	57 (50–66)	61 (52–72)	0.0013	0.9789 (0.9662–0.9917)
Comorbidities, No. (%)				
Hypertension	75 (41.4)	219 (54.3)	0.0041	0.5945 (0.4169–0.8476)
Heart failure	33 (18.2)	51 (12.7)	0.0772	1.5390 (0.9541–2.4824)
Diabetes	97 (53.6)	181 (44.9)	0.0526	1.4163 (0.9961–2.0138)
COPD	9 (5.0)	16 (4.0)	0.5808	1.2656 (0.5485–2.9205)
Liver cirrhosis	56 (30.9)	76 (18.9)	0.0014	1.9276 (1.2895–2.8815)
Chronic kidney disease	63 (34.8)	108 (26.8)	0.0498	1.4583 (1.0003–2.1261)
Malignancy	112 (61.9)	167 (41.4)	<0.0001	2.2938 (1.6011–3.2863)
CVA	24 (13.3)	66 (16.4)	0.3354	0.7805 (0.4715–1.2922)
Charlson Comorbidity Index, median (IQR)	7 (5–9)	5 (3–8)	<0.0001	1.1603 (1.0975–1.2266)
Laboratory data				
WBC, median (IQR), 1000/ul	8.7 (3.9–13.5)	9.3 (5.9–13.7)	0.4422	0.9901 (0.9651–1.0156)
CRP, median (IQR), mg/dl	7.3 (4.3–16.7)	4.0 (1.5–10.5)	<0.0001	1.0600 (1.0325–1.0883)
Microbiological organisms, No. (%)				
Gram-negative	118 (65.2)	286 (71.0)	0.1628	0.7662 (0.5272–1.1136)
Gram-positive	44 (24.3)	90 (22.3)	0.5994	1.1170 (0.7393–1.6876)
Fungi	16 (8.8)	24 (6.0)	0.2047	1.5313 (0.7927–2.9582)
Internal medicine and hematology/oncology, No. (%)	141 (77.9)	237 (58.8)	<0.0001	2.4690 (1.6496–3.6954)
Potential risk factors, No. (%)				
ICU/RCC hospitalization	97 (53.6)	165 (40.9)	0.0046	1.6657 (1.1700–2.3713)
Catheter-related infection	89 (49.2)	167 (41.4)	0.0820	1.3671 (0.9610–1.9447)
Inadequate antibiotic therapy	107 (59.1)	214 (53.1)	0.1771	1.2770 (0.8953–1.8214)
Multiple drug resistance	56 (30.9)	86 (21.3)	0.0128	1.6513 (1.1123–2.4515)
Days between admission and BSI, median (IQR), d	16 (9–30)	13 (7–25)	0.2125	1.0041 (0.9977–1.0105)

Abbreviations: BSI, bloodstream infection; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVA, cerebral vascular accident; ICU, intensive care unit; RCC, respiratory care unit; WBC, white blood cell.

Table 6 Multivariate analysis of risk factors for mortality in patients with nosocomial bloodstream Infection.

Variable	P value	OR (95% CI)
Low weight (≤59)	0.0222	1.8097 (1.0887–3.0083)
Comorbidity with hypertension	0.0386	0.5603 (0.3237–0.9700)
Comorbidity with liver cirrhosis	0.0352	1.9268 (1.0467–3.5469)
Comorbidity with malignancy	0.0008	2.7156 (1.5115–4.8788)
High Charlson comorbidity index (>3)	0.0122	2.7585 (1.2480–6.0973)
High CRP level (>3.68)	<0.0001	3.5431 (2.0280–6.1900)
Internal medicine and hematology/ oncology distribution	0.0041	2.2449 (1.2925–3.8992)

Abbreviations: CRP, C-reactive protein

Several limitations should be considered. First, the epidemiological result of nosocomial BSI is only in a tertiary hospital in central Taiwan, but the result was similar to the data of Healthcare-associated infection and Antimicrobial resistance Surveillance (THAS). We also reported the clinical manifestations and risk factors of mortality of nosocomial BSI patients. Second, we couldn't survey the reports of all the nosocomial BSI patients, so we couldn't compare the detailly clinical characteristics during these years. Third, our study was a retrospective study, so we couldn't evaluate the relationship of intervention and prognosis and the antibiotics prescriptions in the period of the time.

In conclusion, the study demonstrated the changing epidemiology of nosocomial BSIs. *K.* spp. and *E coli.* became the most common pathogens of nosocomial BSI in recent years. Comorbidities could be important roles to predictive the outcome of nosocomial BSI. The modifiable risk factors of nosocomial BSI may be investigated further to improve the outcome.

Declaration of competing interest

No actual or potential conflicts of interest were associated with this study.

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