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ORIGINAL ARTICLE

Clinical predictors of *Stenotrophomonas maltophilia* bacteremia in adult patients with hematologic malignancy

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Abstract *Stenotrophomonas maltophilia* (SM) has emerged as an important nosocomial pathogen with high morbidity and mortality. Because of its unique antimicrobial susceptibility pattern, appropriate antimicrobial therapy for SM bacteremia is still challenging, especially in immunocompromised patients. The present study was performed to assess clinical predictors of SM bacteremia in adult patients with hematologic malignancy. From 2006 through 2016, a case-control study was performed at a tertiary-care hospital. Case patients were defined as SM bacteremia in patients with hematologic malignancy. Date- and location-matched controls were selected from among patients with gram-negative bacteremia (GNB) other than SM. A total of 118 cases of SM bacteremia were identified and compared to 118 controls. While pneumonia was the most common source of SM bacteremia, central line-associated infection was most common in the controls. The overall 30-day mortality rate of cases with SM bacteremia was significantly higher than that of the controls (61.0 and 32.2%, respectively; $P < 0.001$). A multivariable analysis showed that polymicrobial infection, previous SM isolation, the number of antibiotics previously used ≥ 3, and breakthrough bacteremia during carbapenem therapy were significantly associated with SM bacteremia (all $P < 0.01$). Previous use of trimethoprim/sulfamethoxazole (TMP/SMX) was negatively association with SM bacteremia ($P = 0.002$). Our data suggest that SM is becoming a significant pathogen in patients with hematologic malignancy. Several clinical predictors of SM bacteremia can be used for appropriate antimicrobial therapy in hematologic patients with suspected GNB.

Keywords *Stenotrophomonas maltophilia* · Hematologic malignancy · Bacteremia · Predictor

Introduction

Stenotrophomonas maltophilia has emerged as an important nosocomial pathogen with high morbidity and mortality, reflecting the increases in antimicrobial agent use and the immunocompromised population including cancer patients [1–3]. *S. maltophilia* was reported to be one of the most common multi-drug-resistant (MDR) gram-negative bacilli isolated from respiratory specimens, and it has a unique pattern of antimicrobial susceptibility originating from its intrinsic resistance against aminoglycoside and beta-lactams [1–4]. Trimethoprim/sulfamethoxazole (TMP/SMX) is the drug of choice for *S. maltophilia* infection, although levofloxacin may be considered an alternative drug which shows non-inferiority [5, 6]. Its unique antimicrobial susceptibility patterns compared to other gram-negative bacilli make it difficult to administer the appropriate antimicrobial agents for an *S. maltophilia* infection. According to previous studies, crude mortality rates of *S. maltophilia* bacteremia are high, ranging from 14 to 69% depending on the patient population [1]. Furthermore, when limited to patients with hematologic malignancy, mortality rates have been reported 32 and 64.5%, respectively [7, 8].

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Several previous studies were conducted to differentiate *S. maltophilia* bacteremia from other gram-negative bacteremia (GNB) with the aim of administering proper antibiotics [8–13]. However, the numbers of enrolled cases with *S. maltophilia* bacteremia were relatively small (from 12 to 54 cases), and they compared *S. maltophilia* with only restricted population, such as patients with non-fermentative GNB (e.g., *Pseudomonas* and/or *Acinetobacter*) [8, 12, 13], *Escherichia coli* bacteremia [9, 11], or non-bacteremia [10, 11]. This may be quite different from the real clinical situation, given that physicians are usually first informed of the results of gram-staining. In addition, few studies have focused on clinical predictors of *S. maltophilia* bacteremia in adult patients with hematologic malignancy, which are likely to be the most vulnerable patient group. Thus, we performed a case-control study to identify clinical predictors of *S. maltophilia* bacteremia in adult patients with hematologic malignancy compared with other GNB.

Methods

Study population

A case-control study was designed to identify clinical predictors of *S. maltophilia* bacteremia among hematologic patients with suspected GNB. The electronic medical records were reviewed for individuals diagnosed with *S. maltophilia* bacteremia during the period of January 2006 through December 2016 at Samsung Medical Center, Seoul, South Korea. This is a 1950-bed tertiary-care university hospital and referral center combined with the 700-bed Samsung Comprehensive Cancer Center. Cases were defined as *S. maltophilia* bacteremia in adult patients with hematologic malignancy. Bacteremia was defined as either the isolation of *S. maltophilia* from more than two separate blood samples or the isolation of *S. maltophilia* from a single blood sample in patients with clinical symptoms and a concomitant focus of infection [14]. Each patient was included only once during the study period. The control group consisted of patients with hematologic malignancy that experienced other GNB caused by frequently isolated gram-negative bacilli as a bloodstream infection in prior study in South Korea: *Escherichia coli*, *Klebsiella* species, *Acinetobacter* species, *Pseudomonas* species, and *Enterobacter* species [15]. We matched the cases with the controls by location (whether events occurred in the general ward or in the intensive care unit) and date (GNB other than *S. maltophilia* bacteremia that occurred at the date closest to the case).

Variables and definition of clinical information

We collected the following data from electronic medical records: age, gender, length of hospital stay, polymicrobial infection, previously isolated pathogens, breakthrough infection during carbapenem therapy, underlying diseases, history of hematopoietic stem cell transplantation, Charlson comorbidity index (CCI) [16], neutropenia, administration of chemotherapy, use of mechanical ventilation, use of central venous catheter, history of renal replacement therapy, history of operation, Sequential Organ Failure Assessment (SOFA) score [17], previous antibiotic use, and appropriate empirical antibiotic use. Polymicrobial infection was defined as the isolation of two or more bacterial or fungal pathogens in a blood culture sample collected within 72 h. Breakthrough infection during carbapenem therapy was defined as new-onset gram-negative bacteremia after receiving more than 48 h of administration of carbapenem (e.g., imipenem, meropenem, and doripenem), and some of the data included in this study have already been described in our previous study [18]. Every antibiotic administered for more than 48 h within a 30-day period via an intravenous route was recorded as previous antibiotic use. If *S. maltophilia* or an identical causative pathogen was isolated from a patients' clinical specimen (including contaminated blood culture) within 30 days before the onset of bacteremia, it was recorded as a previous isolation of *S. maltophilia* or previous isolation of an identical pathogen. Empirical antimicrobial agents were considered appropriate, if administered within 72 h after obtaining the blood culture sample, and if they were appropriate compared to the in vitro susceptibility test results [12].

Microbiological tests

All blood samples were taken from peripheral veins and/or a central line. A Bactec-9240 system (Becton Dickinson, Sparks, MD) or a BacT/Alert 3D system (bioMérieux Inc., Marcy l'Etoile, France) was used for blood cultures. A Vitek II automated system (bioMérieux Inc.) was used to identify microbes and their antimicrobial agent sensitivity, with a standard identification card and the modified broth microdilution method.

Statistical analysis

All statistical analyses were performed using SPSS 23.0 for Window (IBM Corp., 2015). To determine the predictive factors for *S. maltophilia* bacteremia, a Student's *t* test or Mann-Whitney test was used to compare continuous variables and the Chi-square test or Fisher's exact test was used to compare categorical variables. We used a logistic regression model to control for confounding variables and to identify clinical predictors of *S. maltophilia* bacteremia. Variables with $P < 0.1$ in the univariate analysis were candidates for multivariable analysis and were included in the forward stepwise logistic regression model. All *P* values were two-tailed and *P* values < 0.05 were considered to be statistically significant.

Results

Study population

During the study period, we identified 118 cases of *S. maltophilia* bacteremia and matched them to 118 control patients with other GNB. All cases were hospital-acquired or healthcare-associated infections. The control group consisted of 86 cases of bacteremia with *Enterobacteriaceae* and 32 cases of bacteremia with non-fermenters. Forty and 13 cases of polymicrobial infection were included in the *S. maltophilia* group and the control group, respectively. *E. coli* was most common in the control group ($n = 47$), followed by *Klebsiella* species ($n = 40$), *Pseudomonas* ($n = 17$), *Acinetobacter* ($n = 15$), and *Enterobacter* ($n = 7$). The distribution of frequency of each species was similar to that of the reported frequencies of GNB isolated in South Korea [6]. When we compared appropriate empirical therapy, only 31 (26.3%) of the cases with *S. maltophilia* bacteremia received appropriate antibiotics, while in the control group, 108 (87.3%) received appropriate antimicrobial therapy ($P < 0.001$). As for the antimicrobial susceptibility results of isolates in the study, 96.6% of *S. maltophilia* isolates were susceptible to TMP/SMX and 83.1% were susceptible to levofloxacin. 78.8% of GNB in the controls were susceptible to carbapenem; however, only 36.1% of non-fermenters in the controls were susceptible to carbapenem. The overall 14-day mortality rates of the case and control groups were 54.2 and 25.4%, respectively ($P < 0.001$), and the overall 30-day mortality rates were 61.0 and 32.2%, respectively ($P < 0.001$), demonstrating that *S. maltophilia* bacteremia resulted in significantly higher mortality than other GNB. When we reviewed the sources of bacteremia, pneumonia was the most common focus of bacteremia in the case group (55/118, 46.6%), while central line-associated bloodstream infection was the most common source of bacteremia in the control group (62/118, 52.5%). There were no cases of urinary tract infection (UTI) in the *S. maltophilia* bacteremia group, while 13 episodes (11.0%) with UTI occurred in the control group.

Clinical predictors for *S. maltophilia* bacteremia

Risk factors for the development of *S. maltophilia* bacteremia in adult patients with hematologic malignancy were analyzed and are summarized in Table 1. The univariate analysis showed a significant association of *S. maltophilia* bacteremia with length of hospital stay ≥ 30 days, polymicrobial infection, previous *S. maltophilia* or identical pathogen isolation within 30 days, breakthrough bacteremia during carbapenem therapy, UTI, pneumonia, leukemia, history of allogenic stem cell transplantation, use of mechanical ventilation, SOFA score ≥ 7, platelet ≤ 10,000/mm^3, previous receipt of antimicrobial agents, and the number of different antibiotics previously used ≥ 3 within 30 days (Table 1). In the multivariable analysis, polymicrobial infection ($P = 0.002$), previous *S. maltophilia* isolation within 30 days ($P < 0.001$), breakthrough bacteremia during carbapenem therapy ($P < 0.001$), and the number of previously used antibiotics ≥ 3 within 30 days ($P = 0.002$) were significantly associated with *S. maltophilia* bacteremia. In contrast, previous use of TMP/SMX showed a negative association with *S. maltophilia* bacteremia ($P = 0.002$) (Table 2).

In the subgroup analysis divided by fermenter and non-fermenter, two of five variables that showed an independent association with *S. maltophilia* bacteremia had inconsistencies of statistical significance between fermenters and non-fermenters: breakthrough bacteremia during carbapenem therapy ($P < 0.001$ in fermenter, $P = 0.224$ in non-fermenter) and previous TMP/SMX use ($P = 0.003$ in fermenter, $P = 0.122$ in non-fermenter). The other variables showed statistical consistencies of association with *S. maltophilia* bacteremia (Table 3).

Discussion

The present study identified potential risk factors for *S. maltophilia* bacteremia among GNB in adult patients with hematologic malignancy and revealed the high mortality from *S. maltophilia* bacteremia in these patients. In our review of previous studies, the mortality rates from *S. maltophilia* bacteremia in patients with hematologic malignancy were relatively high and have not changed substantially over 20 years [7, 8]. This finding is consistent with our finding that the overall 30-day mortality rate was 61.0% (72/118), and among these deaths, 88.9% (64/72) of patients died within 14 days. These findings suggest that early administration of appropriate empirical antibiotics for *S. maltophilia* bacteremia should be emphasized. Administration of appropriate empirical antibiotics improved the survival rate of patients with *S. maltophilia* bacteremia [8, 19], while inappropriate antimicrobial therapy was associated with a poor prognosis in previous studies [20, 21].

Several predictive factors for *S. maltophilia* bacteremia have been reported in previous studies [8–13] and summarized in Table 4. Previous use of carbapenem was the most frequently reported predictive factor for patient with *S. maltophilia* bacteremia and its association was also demonstrated in our study. However, breakthrough bacteremia during carbapenem therapy showed a higher odds ratio (OR) than previous carbapenem use within 30 days in our study (breakthrough vs previous use, [OR] 10.36 vs 9.56). One prior study reported that *S. maltophilia* was the most common pathogen of breakthrough bacteremia during carbapenem therapy, followed by *Acinetobacter* and *Pseudomonas* [18]. This finding may explain why the previous use of carbapenem was not

Table 1 Clinical characteristics of *Stenotrophomonas maltophilia* bacteremia in patients with hematologic malignancy compared to gram-negative bacteremia other than *Stenotrophomonas maltophilia*

	SM (118)[a]	Controls (118)	*P* value
Age (age ± SD)	55.68 ± 13.12	55.14 ± 14.71	0.163
Sex (male)	69 (58.5)	65 (55.1)	0.599
Length of hospital stay ≥ 30 days	52 (44.1)	31 (26.3)	0.004
Polymicrobial infection	40 (33.9)	13 (11.0)	< 0.001
Previous *S. maltophilia* isolation	43 (36.4)	3 (2.5)	< 0.001
Previous identical causative pathogen isolation	43 (36.4)	21 (17.8)	0.001
Breakthrough bacteremia during carbapenem therapy	75 (63.6)	17 (14.4)	< 0.001
Catheter-related infection	51 (43.2)	62 (52.5)	0.152
Urinary tract infection	0 (0)	13 (11.0)	< 0.001
Pneumonia	55 (46.6)	23 (19.5)	< 0.001
Skin and soft tissue infection	4 (3.4)	6 (5.1)	0.518
Intra-abdominal infection	6 (5.1)	9 (7.6)	0.423
Leukemia	81 (68.6)	61 (51.7)	0.008
Lymphoma	25 (21.2)	36 (30.5)	0.102
Multiple myeloma	3 (2.5)	10 (8.5)	0.083
Allogenic HPSCT	21 (17.8)	10 (8.5)	0.034
Graft versus host disease	8 (6.8)	4 (3.4)	0.236
Malignancy recurrence	62 (52.5)	51 (43.2)	0.152
CCI (IQR)	2 (2–3)	2 (2–3)	0.587
Neutropenia	105 (89.0)	99 (83.9)	0.254
Chemotherapy	111 (94.1)	104 (88.1)	0.110
Central venous catheter	112 (94.9)	108 (91.5)	0.438
Mechanical ventilation	15 (12.7)	29 (24.6)	0.019
Renal replacement therapy	17 (14.4)	18 (15.3)	0.855
Major operation	4 (3.4)	2 (1.7)	0.683
SOFA score (IQR)	8 (5–14)	6 (4–10)	0.061
SOFA ≥ 7	71 (60.2)	56 (47.5)	0.050
Platelet ≤ 10,000/mm^3	52 (44.1)	33 (28.0)	0.010
Previous antibiotic use	114 (97.0)	80 (67.8)	< 0.001
Previous antibiotic use ≥ 3	91 (77.1)	39 (33.1)	< 0.001
Piperacillin/tazobactam	52 (44.1)	31 (26.3)	0.004
Cefepime	66 (55.9)	47 (39.8)	0.013
Fluoroquinolone	20 (16.9)	14 (11.9)	0.266
Aminoglycoside	8 (6.8)	5 (4.2)	0.392
Carbapenem	98 (83.1)	40 (33.9)	< 0.001
Glycopeptide	91 (77.1)	45 (38.1)	< 0.001
Linezolid	18 (15.3)	3 (2.5)	0.001
TMP/SMX (prophylactic)	15 (12.7)	28 (23.7)	0.028
TMP/SMX (therapeutic)	4 (3.4)	12 (10.2)	0.038
TMP/SMX (all)	19 (16.1)	38 (32.2)	0.004
Metronidazole	26 (22.0)	9 (7.6)	0.002

Data are number (%) of patients

SD standard deviation, *HPSCT* hematopoietic stem cell transplantation, *CCI* Charlson comorbidity index, *IQR* interquartile range, *SOFA* Sequential Organ Failure Assessment , *TMP/SMX* trimethoprim/sulfamethoxazole

[a] 2 *Acinetobacter*, 2 *Pseudomonas*, 1 *Enterobacter*, and 1 *Klebsiella* were contained in polymicrobial infection

associated with *S. maltophilia* bacteremia when compared to non-fermenters, given the high rate of carbapenem resistance of non-fermenters in general and in our study [22].

Among the variables associated with *S. maltophilia* bacteremia, previous *S. maltophilia* isolation within 30 days showed the highest association with *S. maltophilia* bacteremia (OR,

Table 2 Factors associated with *Stenotrophomonas maltophilia* bacteremia among the gram-negative bacteremia: multivariate analysis

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Length of hospital stay ≥ 30 days	2.21 (1.28–3.82)	0.002		
Polymicrobial infection	4.14 (2.08–8.27)	< 0.001	4.79 (1.81–12.70)	0.002
Previous *S. maltophilia* isolation	21.97 (6.58–73.41)	< 0.001	26.43 (6.67–104.83)	< 0.001
Breakthrough infection during carbapenem therapy	10.36 (5.49–19.58)	< 0.001	9.28 (4.15–20.75)	< 0.001
Pneumonia	3.61 (2.02–6.45)	< 0.001		
Leukemia	2.05 (1.20–3.48)	0.008		
Multiple myeloma	0.28 (0.08–1.05)	0.083		
Allogenic HPSCT	2.34 (1.05–5.21)	0.034		
Mechanical ventilation	0.52 (0.29–0.91)	0.019		
SOFA ≥ 7	1.67 (1.00–2.80)	0.050		
Platelet ≤ 10,000/mm^3	2.03 (1.18–3.49)	0.010		
No. of previous antibiotic use ≥ 3	6.83 (3.84–12.14)	< 0.001	3.38 (1.57–7.29)	0.002
Piperacillin/tazobactam	2.21 (1.28–3.82)	0.004		
Cefepime	1.92 (1.14–3.22)	0.013		
Glycopeptide	5.47 (3.10–9.65)	< 0.001		
Linezolid	6.9 (1.97–24.11)	0.001		
Previous TMP/SMX use	0.40 (0.22–0.76)	0.004	0.23 (0.09–0.59)	0.002
Metronidazole	3.42 (1.53–7.67)	0.002		

OR odds ratio, *CI* confidential index, *HPSCT* hematopoietic stem cell transplantation, *SOFA* sepsis-related organ failure assessment, *TMP/SMX* trimethoprim/sulfamethoxazole

26.25; 95% CI, 6.67–104.83). The previous study by Go Hotta et al. reported that previous *S. maltophilia* isolation was related to *S. maltophilia* bacteremia when compared to a group with *Pseudomonas* bacteremia or a group with *Acinetobacter* bacteremia [12]. Interestingly, in a subgroup analysis comparing previous isolation of identical causative pathogens, both patients with *S. maltophilia* and the non-fermenter group showed frequent isolation of the same pathogen preceding bacteremia. This finding is consistent with studies on the association between previous colonization with a non-fermenter or a MDR gram-negative bacillus and bloodstream infection [18, 23, 24].

We also demonstrated two unique factors associated with *S. maltophilia* bacteremia in patients with hematologic malignancy. One was polymicrobial infection which showed a positive association with *S. maltophilia* bacteremia, and the other was the previous use of TMP/SMX which showed a negative association with *S. maltophilia* bacteremia. High rates of polymicrobial bacteremia, ranging from 19.8 to 37.7%, have been reported in patients with *S. maltophilia* bacteremia [5, 7, 12, 13, 25]. However, previous studies excluded cases of polymicrobial infection or excluded the variable "polymicrobial infection" when they analyzed the predictive factors of *S. maltophilia* bacteremia. Given that polymicrobial

Table 3 Factors associated with *Stenotrophomonas maltophilia* bacteremia compared with gram-negative bacteremia divided by fermenter and non-fermenter group

	SM (118)[a]	Fermenter (86)	*P* value	Non-fermenter[b] (32)	*P* value
Polymicrobial infection	40 (33.9)	9 (10.5)	< 0.001	4 (12.5)	0.018
Previous *S. maltophilia* isolation	43 (36.4)	0 (0.0)	< 0.001	3 (9.4)	0.003
Breakthrough bacteremia during carbapenem therapy	75 (63.6)	0 (0.0)	< 0.001	17 (53.1)	0.244
No. of previous antibiotic use ≥ 3	91 (77.1)	22 (25.6)	< 0.001	17 (53.1)	0.007
Previous TMP/SMX use	19 (16.1)	29 (33.7)	0.003	9 (28.1)	0.122

TMP/SMX trimethoprim/sulfamethoxazole

[a] 2 *Acinetobacter*, 2 *Pseudomonas*, 1 *Enterobacter*, and 1 *Klebsiella* were contained in polymicrobial infection

[b] 1 *Enterobacter*, 1 *Klebsiella*, and 1 *Escherichia coli* were contained in polymicrobial infection

Table 4 Summary of prior studies comparing cases of SM bacteremia with other controls

Study and study design (no. of patients in cases)	Study population (rate of hematologic malignancy patient in cases)	Comparative pathogen of control group (no. of patients in controls)	Risk factor
Sumida K et al. 2015. Japan, matched case-control study (30 cases) [13]	All patients (53%)	*Pseudomonas aeruginosa* (30)	In univariate analysis: Artificial products other than CVC Use of Anti-MRSAs agent
Hotta G et al. 2014. Japan, case-control study (54 cases) [12]	All patients (13%)	*Pseudomonas aeruginosa* (167) *Acinetobacter* (69)	In multivariate analysis: Use of carbapenem Use of anti-pseudomonal antibiotics Previous *S. maltophilia* isolation within 30 days
Meta G et al. 2006. Turkey, matched case-control study (37 cases) [11]	All patients (30%)	*Escherichia coli* (37) Non-bacteremic patients (74)	In univariate analysis compared with *E.coli*: Use of CVC Use of carbapenem
Apisarnthanarak A et al. 2003. USA, case-control study (13 cases) [10]	Hemato-oncology patients (85%)	Non-bacteremic patients (39)	In univariate analysis: Severe mucositis Diarrhea Use of metronidazole
Micozzi A. et al. 2001. Rome, case-control study (37 cases) [8]	Hematologic malignancy (100%)	*Pseudomonas aeruginosa* (37)	In univariate analysis: Cellulitis Breakthrough bacteremia during antibiotic therapy
Victor MA et al. 1994. Denmark, case-control study (12 cases) [9]	Hematologic malignancy (100%)	*Escherichia coli* (25)	In univariate analysis: Use of broad-spectrum antibiotics Use of CVC Previous use of corticosteroids

CVC central venous catheter, *MRSA* methicillin-resistant *Staphylococcus aureus*

infection might be a unique feature of *S. maltophilia* bacteremia, especially in patients with hematologic malignancy, we classified polymicrobial infection with both *S. maltophilia* bacteremia and other GNB as the case group. As *S. maltophilia* bacteremia accounts for only a small portion of GNB compared to other gram-negative bacilli [15], the inclusion of polymicrobial infection with *S. maltophilia* bacteremia would not distort the real clinical situation.

TMP/SMX is a drug of choice for serious *S. maltophilia* infection. Both prophylactic and therapeutic doses of TMP/SMX administration within 30 days showed negative association with *S. maltophilia* bacteremia, especially when compared with the fermenter group. Colonization might be an important step to develop *S. maltophilia* bacteremia in patients with hematologic malignancy and TMP/SMX may suppress both *S. maltophilia* and fermenters. However, fermenters might be able to develop bacteremia easily, because of their characteristics that need not be colonized before developing bacteremia. Compared with non-fermenters, there was no statistical significance even though *S. maltophilia* showed negative association to TMP/SMX.

The risk factors presented in this study differed from the traditional risk factors identified in previous studies. Although neutropenia and mechanical ventilation have been suggested in previous studies, one study reported that infection with *S. maltophilia* also occurs in cancer patients without those traditional risk factors [26].

There are several limitations in our study. First, this study was conducted in a single medical institute and collected data retrospectively. Some of the medical records in charts may have not been complete, even though we tried to enroll patients who had more concrete information. This study was performed in a tertiary-care hospital, wherein conditions, patient populations, and outcomes may differ from those in non-tertiary-care centers. Second, the association of carbapenem and TMP/SMX with *S. maltophilia* bacteremia can be changed by local resistance rate of these agents. If carbapenem resistance rate of GNB is high, positive association between *S. maltophilia* bacteremia and use of carbapenem might be decreased. Similarly, if TMP/SMX resistance rate of SM isolates is high, negative association between *S. maltophilia* and TMP/SMX might be decreased. Finally, the unique epidemiological composition of microorganisms in specific local area might also affect predictive factor of *S. maltophilia* bacteremia. Hence, our results may not apply directly in other institutions or countries. Despite these limitations, the findings of this investigation may improve the ability of clinicians to identify hematologic patients who are at high risk for *S. maltophilia* bacteremia.

In conclusion, our data suggest that *S. maltophilia* bacteremia in adult patients with hematologic malignancy has become a severe and urgent problem. Its mortality is still high and early administration of appropriate antimicrobial agents is still challenging. Several clinical factors associated with *S. maltophilia* bacteremia identified in our study might be useful to predict cases of *S. maltophilia* bacteremia among suspected GNB in patients with hematologic malignancy. Further study may be warranted for external validation of these clinical factors.

Compliance with ethical standards This study was approved by the institutional review board at our institution (number: 2017-08-016-001). All procedures were performed in accordance with the principles of the Declaration of Helsinki.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Looney WJ, Narita M, Muhlemann K (2009) Stenotrophomonas maltophilia: an emerging opportunist human pathogen. Lancet Infect Dis 9(5):312–323. https://doi.org/10.1016/S1473-3099(09)70083-0
2. Brooke JS (2012) Stenotrophomonas maltophilia: an emerging global opportunistic pathogen. Clin Microbiol Rev 25(1):2–41. https://doi.org/10.1128/CMR.00019-11
3. Safdar A, Rolston KV (2007) Stenotrophomonas maltophilia: changing spectrum of a serious bacterial pathogen in patients with cancer. Clin Infect Dis 45(12):1602–1609. https://doi.org/10.1086/522998
4. Crossman LC, Gould VC, Dow JM, Vernikos GS, Okazaki A, Sebaihia M, Saunders D, Arrowsmith C, Carver T, Peters N, Adlem E, Kerhornou A, Lord A, Murphy L, Seeger K, Squares R, Rutter S, Quail MA, Rajandream MA, Harris D, Churcher C, Bentley SD, Parkhill J, Thomson NR, Avison MB (2008) The complete genome, comparative and functional analysis of Stenotrophomonas maltophilia reveals an organism heavily shielded by drug resistance determinants. Genome Biol 9(4):R74. https://doi.org/10.1186/gb-2008-9-4-r74
5. Cho SY, Kang CI, Kim J, Ha YE, Chung DR, Lee NY, Peck KR, Song JH (2014) Can levofloxacin be a useful alternative to trimethoprim-sulfamethoxazole for treating Stenotrophomonas maltophilia bacteremia? Antimicrob Agents Chemother 58(1):581–583. https://doi.org/10.1128/AAC.01682-13
6. Wang YL, Scipione MR, Dubrovskaya Y, Papadopoulos J (2014) Monotherapy with fluoroquinolone or trimethoprim-sulfamethoxazole for treatment of Stenotrophomonas maltophilia infections. Antimicrob Agents Chemother 58(1):176–182. https://doi.org/10.1128/AAC.01324-13
7. Cho SY, Lee DG, Choi SM, Park C, Chun HS, Park YJ, Choi JK, Lee HJ, Park SH, Choi JH, Yoo JH (2015) Stenotrophomonas maltophilia bloodstream infection in patients with hematologic malignancies: a retrospective study and in vitro activities of antimicrobial combinations. BMC Infect Dis 15(1):69. https://doi.org/10.1186/s12879-015-0801-7
8. Micozzi A, Venditti M, Monaco M, Friedrich A, Taglietti F, Santilli S, Martino P (2000) Bacteremia due to Stenotrophomonas maltophilia in patients with hematologic malignancies. Clin Infect Dis 31(3):705–711. https://doi.org/10.1086/314043
9. Victor MA, Arpi M, Bruun B, Jonsson V, Hansen MM (1994) Xanthomonas maltophilia bacteremia in immunocompromised hematological patients. Scand J Infect Dis 26(2):163–170. https://doi.org/10.3109/00365549409011780
10. Apisarnthanarak A, Mayfield JL, Garison T, McLendon PM, DiPersio JF, Fraser VJ, Polish LB (2003) Risk factors for Stenotrophomonas maltophilia bacteremia in oncology patients: a case-control study. Infect Control Hosp Epidemiol 24(4):269–274. https://doi.org/10.1086/502197
11. Metan G, Hayran M, Hascelik G, Uzun O (2006) Which patient is a candidate for empirical therapy against Stenotrophomonas maltophilia bacteraemia? An analysis of associated risk factors in a tertiary care hospital. Scand J Infect Dis 38(6–7):527–531. https://doi.org/10.1080/00365540500452481
12. Hotta G, Matsumura Y, Kato K, Nakano S, Yunoki T, Yamamoto M, Nagao M, Ito Y, Takakura S, Ichiyama S (2014) Risk factors and outcomes of Stenotrophomonas maltophilia bacteraemia: a comparison with bacteraemia caused by Pseudomonas aeruginosa and Acinetobacter species. PLoS One 9(11):e112208. https://doi.org/10.1371/journal.pone.0112208
13. Sumida K, Chong Y, Miyake N, Akahoshi T, Yasuda M, Shimono N, Shimoda S, Maehara Y, Akashi K (2015) Risk factors associated with Stenotrophomonas maltophilia bacteremia: a matched case-control study. PLoS One 10(7):e0133731. https://doi.org/10.1371/journal.pone.0133731
14. Seifert H (2009) The clinical importance of microbiological findings in the diagnosis and management of bloodstream infections. Clin Infect Dis 48(Suppl 4):S238–S245. https://doi.org/10.1086/598188
15. Huh K, Kim J, Cho SY, Ha YE, Joo EJ, Kang CI, Chung DR, Lee NY, Song JH, Peck KR, Korean Network for Study on Infectious Diseases (2013) Continuous increase of the antimicrobial resistance among gram-negative pathogens causing bacteremia: a nationwide surveillance study by the Korean Network for Study on Infectious Diseases (KONSID). Diagn Microbiol Infect Dis 76(4):477–482. https://doi.org/10.1016/j.diagmicrobio.2013.04.014
16. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40(5):373–383. https://doi.org/10.1016/0021-9681(87)90171-8
17. Ferreira FL, Bota DP, Bross A, Melot C, Vincent JL (2001) Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA 286(14):1754–1758. https://doi.org/10.1001/jama.286.14.1754
18. Lee JY, Kang CI, Ko JH, Lee WJ, Seok HR, Park GE, Cho SY, Ha YE, Chung DR, Lee NY, Peck KR, Song JH (2016) Clinical features and risk factors for development of breakthrough gram-negative bacteremia during carbapenem therapy. Antimicrob Agents Chemother 60(11):6673–6678. https://doi.org/10.1128/AAC.00984-16
19. Metan G, Uzun O (2005) Impact of initial antimicrobial therapy in patients with bloodstream infections caused by Stenotrophomonas maltophilia. Antimicrob Agents Chemother 49(9):3980–3981. https://doi.org/10.1128/AAC.49.9.3980-3981.2005
20. Kang CI, Song JH, Chung DR, Peck KR, Ko KS, Yeom JS, Ki HK, Son JS, Lee SS, Kim YS, Jung SI, Kim SW, Chang HH, Ryu SY, Kwon KT, Lee H, Moon C, Korean Network for Study of Infectious Diseases (2011) Risk factors and pathogenic significance of severe sepsis and septic shock in 2286 patients with gram-negative bacteremia. J Inf Secur 62(1):26–33. https://doi.org/10.1016/j.jinf.2010.10.010
21. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, Kumar A, Sevransky JE, Sprung CL, Nunnally ME, Rochwerg B, Rubenfeld GD, Angus DC, Annane D, Beale RJ, Bellinghan GJ,

Bernard GR, Chiche JD, Coopersmith C, De Backer DP, French CJ, Fujishima S, Gerlach H, Hidalgo JL, Hollenberg SM, Jones AE, Karnad DR, Kleinpell RM, Koh Y, Lisboa TC, Machado FR, Marini JJ, Marshall JC, Mazuski JE, McIntyre LA, McLean AS, Mehta S, Moreno RP, Myburgh J, Navalesi P, Nishida O, Osborn TM, Perner A, Plunkett CM, Ranieri M, Schorr CA, Seckel MA, Seymour CW, Shieh L, Shukri KA, Simpson SQ, Singer M, Thompson BT, Townsend SR, Van der Poll T, Vincent JL, Wiersinga WJ, Zimmerman JL, Dellinger RP (2017) Surviving sepsis campaign: international guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med 43(3):304–377. https://doi.org/10.1007/s00134-017-4683-6

22. Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J, Srinivasan A, Kallen A, Limbago B, Fridkin S, National Healthcare Safety Network Team, Participating Nhsn Facilities (2013) Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009-2010. Infect Control Hosp Epidemiol 34(1):1–14. https://doi.org/10.1086/668770
23. Jung JY, Park MS, Kim SE, Park BH, Son JY, Kim EY, Lim JE, Lee SK, Lee SH, Lee KJ, Kang YA, Kim SK, Chang J, Kim YS (2010) Risk factors for multi-drug resistant Acinetobacter baumannii bacteremia in patients with colonization in the intensive care unit. BMC Infect Dis 10(1):228. https://doi.org/10.1186/1471-2334-10-228
24. Cohen R, Babushkin F, Cohen S, Afraimov M, Shapiro M, Uda M, Khabra E, Adler A, Ben Ami R, Paikin S (2017) A prospective survey of Pseudomonas aeruginosa colonization and infection in the intensive care unit. Antimicrob Resist Infect Control 6(1):7. https://doi.org/10.1186/s13756-016-0167-7
25. Araoka H, Baba M, Yoneyama A (2010) Risk factors for mortality among patients with Stenotrophomonas maltophilia bacteremia in Tokyo, Japan, 1996-2009. Eur J Clin Microbiol Infect Dis 29(5):605–608. https://doi.org/10.1007/s10096-010-0882-6
26. Aisenberg G, Rolston KV, Dickey BF, Kontoyiannis DP, Raad II, Safdar A (2007) Stenotrophomonas maltophilia pneumonia in cancer patients without traditional risk factors for infection, 1997-2004. Eur J Clin Microbiol Infect Dis 26(1):13–20. https://doi.org/10.1007/s10096-006-0243-7