

Stenotrophomonas maltophilia Infections in Adults: Primary Bacteremia and Pneumonia

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Background: *Stenotrophomonas maltophilia* is the third most frequent non-fermentative Gram-negative bacilli in nosocomial infections, and usually causes severe infections such as primary bacteremia and pneumonia.

Objectives: The current study aimed to compare the demographic and clinical characteristics, microbiological findings and final outcomes of the patients with primary bacteremia and nosocomial pneumonia caused by *S. maltophilia*.

Patients and Methods: The current study retrospectively evaluated patients aged 18 years and above with primary bacteremia and nosocomial pneumonia caused by *S. maltophilia* from January 2006 to December 2013. Medical records of patients, including reports of clinical microbiology and hospital infection control committee, were evaluated.

Results: A total of 71 patients with *S. maltophilia* nosocomial infections, 35 (49.3%) primary bacteremia and 36 (50.7%) pneumonia, were diagnosed. There were no significant differences in gender, age, and co-morbid diseases, except chronic obstructive pulmonary disease; this infection was significantly higher in patients with pneumonia. A slightly higher 14-day mortality was found in patients with pneumonia, but the difference was not statistically significant. Inappropriate antibiotic use and presence of multiple organ dysfunction syndrome were found as independent risk factors for 14-day mortality in multivariate analysis.

Conclusions: A slightly higher mortality in patients with pneumonia, caused by *S. maltophilia*, was strived to explain by advanced age, higher acute physiology and chronic health evaluation (APACHE II) and sepsis related organ failure assessment (SOFA) score, and also higher inappropriate antibiotic use.

Keywords: Infection; Pneumonia; Mortality; *Stenotrophomonas maltophilia*; Nosocomial Infections; Primary Bacteremia

1. Background

The emergence of nosocomial infections due to multi-drug resistant (MDR) non-fermentative Gram-negative strains is one of the most important problems in the recent years (1). *Stenotrophomonas maltophilia* was reported as the third most frequent non-fermentative Gram-negative bacteria in the SENTRY Antimicrobial Surveillance Program from 1997 to 2001 (2). It causes severe nosocomial infections such as bloodstream infection and pneumonia (2, 3). These are the most frequently reported *S. maltophilia* infection type in nosocomial setting, especially in immunocompromised and debilitated patients (3-6).

In recent years, the increasing rates of MDR strains in Gram-negative bacilli reduce the probability of administering an appropriate empirical antibiotic (7). *Stenotrophomonas maltophilia* is inherently resistant to many of the broad spectrum antibiotics, including broad spectrum beta lactams, aminoglycosides and carbapenems (5, 8). In uncontrolled clinical trials, crude mortality rates associated with *S. maltophilia* infections ranged 21% - 69% (2, 8). *Stenotrophomonas maltophilia* is commonly isolated in the hospital environment (9). Colonization of respiratory

tract and in-dwelling intravascular devices may occur and often precede infection, especially in patients receiving long term broad spectrum antibiotics (2, 10).

2. Objectives

The current study aimed to compare the demographic and clinical characteristics, microbiological findings and the final outcomes of patients with nosocomial pneumonia and primary bacteremia caused by *S. maltophilia*. In addition, considering the fact that pneumonia and bacteremia are the two most common *S. maltophilia* infection types in nosocomial setting, the study evaluated the risk factors associated with mortality.

3. Patients and Methods

The current retrospective study was conducted at the Cumhuriyet University Education and Research Hospital, located in the northeastern of Turkey and serving as a tertiary care referral hospital, from January 2006 to December 2013. All hospitalized patients aged 18 years or

above, with nosocomial pneumonia and primary bacteremia caused by *S. maltophilia*, were included in the study. In patients with multiple episodes of pneumonia or bacteremia caused by *S. maltophilia*, only the first episode of *S. maltophilia* infection was used for the analysis. Medical records of patients, including reports of clinical microbiology and Hospital Infection Control Committee, were evaluated, and the demographic features, clinical conditions, laboratory data, antimicrobial susceptibility, and outcomes were analyzed. The study was approved by the medical ethics committee of Cumhuriyet university (2014-09/27; 29-09-2014).

Nosocomial pneumonia and primary bacteremia were diagnosed according to the center for disease control (CDC) and Prevention recommendations (11). Primary bacteremia included primary bloodstream infection and pneumonia included pneumonia with specific laboratory findings and Probable ventilator-associated pneumonia according to new center for disease control and prevention/national healthcare safety network) CDC/NHSN surveillance definitions for specific types of infections (http://www.cdc.gov/nhsn/pdfs/pscmanual/17pscnosinfdef_current.pdf). Definition of pneumonia met all of the following criteria: a) clinical symptoms of cough, sputum production, fever, and/or auscultatory findings such as rales; b) a new shadow appeared on chest x-ray. Pneumonia was attributed to *S. maltophilia* if Gram-negative bacilli were detected on Gram staining, and *S. maltophilia* was isolated from a lower respiratory tract sample. Bacteremia was defined as the presence of *S. maltophilia* in at least one blood culture associated with clinical findings of infection such as fever, chills and hypotension.

Catheter-related bloodstream infections were defined as a peripheral blood culture and a blood culture through a catheter that were both positive for the same organism in the absence of apparent source of infection. Primary, non-catheter related bacteremia was defined as no apparent source for bacteremia except the blood. A polymicrobial infection was defined as the presence of an organism other than *S. maltophilia* in the same first lower respiratory tract sample and the same first blood culture. Pneumonia was considered nosocomial if occurred 48 hours or more after hospital admission, or if the patient was readmitted within one week after the discharge from hospital. Bacteremia was defined as nosocomial if occurred 48 hours or more after admission. Appropriate antibiotic therapy was defined as administration of an in vitro susceptible agent within 72 hours after the infection occurrence.

Quantitative deep tracheal aspirates, bronchoscopic and bronchoalveolar lavage, or sputum samples were performed to obtain lower airway secretions for bacterial cultures. Blood agar and Eosin-Methylene Blue agar were used to grow the microorganism in lower airway secretion. Blood culture systems were processed using the BACTEC 9120 (Becton Dickinson, Md, USA) automated system. All positive cultures were Gram stained and sub-

cultured in Blood agar and Eosin-Methylene Blue agar. An automatic identification system for Gram-negative bacilli (Phoenix 100®, NMIC ID/82 Becton Dickinson, Md, USA) was used to identify *S. maltophilia*. The susceptibility of *S. maltophilia* isolates to antimicrobial agents were determined using an automatic system (Phoenix 100®, NMIC ID/82 Becton Dickinson, Md, USA) as recommended by the national committee for clinical laboratory standards (12). Indeterminate susceptibility was considered as drug resistance. *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Klebsiella pneumoniae* ATCC 700603 were used as quality control strains.

Statistical analysis was performed using commercially available software package (SPSS, version 14.0, Inc., Chicago, Illinois, USA). Descriptive statistics were presented as frequency and percent or mean \pm standard deviation. Numerical data were first tested for normality and then analyzed using Student's t-test for parametric data; the Mann-Whitney U-test was used for variables of non-parametric data for group comparisons. Chi-square and Fisher's exact test were used to compare categorical variables. Tests were two-tailed, and a P value < 0.05 was considered statistically significant. Logistic regression was performed to compute the risk odds ratio (OR) for fatality in comparison with survivors at corresponding 95% confidence intervals (CIs). Parameters which showed a P value less than 0.10 in the univariate analysis (Chi-square and Fisher's exact-test) were included in the multivariate model.

4. Results

From January 2006 to December 2013, a total of 71 patients with *S. maltophilia* nosocomial infections, 35 (49.3%) primary bacteremia and 36 (50.7%) pneumonia, were identified. The mean age of the total study group was 65.3 ± 15.2 years (median 68, range 20 - 87), 66.2% were male, and the 14-day mortality was 31.0% (22 of 71). One of primary bacteremia and seven of pneumonia were polymicrobial and the additional isolates included three Enterobacteriaceae, three *Staphylococcus aureus*, one *P. aeruginosa*, and one *Acinetobacter baumannii*.

Table 1 shows the results of a univariate analysis comparing the primary bacteremia and pneumonia groups. There were no significant differences in gender, age, and co-morbid diseases, except Chronic Obstructive Pulmonary Disease; which was significantly higher in patients with pneumonia, between the patients with primary bacteremia and pneumonia. While the central venous catheter (CVC) use was significantly higher among patients with bacteremia, polymicrobial infection was higher among patients with pneumonia. A total of 38 (53.5%) patients (21 bacteremia and 17 pneumonia) were in the intensive care unit, and acute physiology and chronic health evaluation II (APACHE II) and sepsis related organ failure assessment (SOFA) scores were significantly higher in the intensive care units (ICU) patients with pneumonia. There was no statistically significant difference in the rates of appropriate antibiotic use, and also 14-day mortality in the two groups.

Table 1. Comparison of Demographic, Clinical Characteristics and Mortality of Patients with Nosocomial Primary Bacteremia (Group 1) and Nosocomial Pneumonia (Group 2) Caused by *Stenotrophomonas maltophilia* (N = 71) ^{a,b,c}

Demographic Characteristics	Group 1 (Primary Bacteremia, n = 35)	Group 2 (Pneumonia, n = 36)	P Value ^d
Age, y	61.9 ± 18.0	68.4 ± 11.3	0.071
Male gender	22 (62.9)	25 (69.4)	0.557
Admission diagnosis			
Respiratory failure	12 (34.3)	13 (36.1)	0.872
Trauma	6 (17.1)	7 (19.4)	0.802
Infection ^e	6 (17.1)	9 (25.0)	0.417
Others ^f	11 (31.4)	7 (19.4)	0.246
Co-morbid diseases			
Hypertension	18 (51.4)	16 (44.4)	0.556
Congestive heart failure	6 (17.1)	3 (8.3)	0.265
Cerebral vascular disease	10 (28.6)	4 (11.1)	0.079
COPD	13 (37.1)	23 (63.9)	0.024
Chronic renal failure	4 (11.4)	2 (5.6)	0.374
Diabetes mellitus	11 (31.4)	10 (27.8)	0.736
Malignancy			
Hematologic malignancy	3 (8.6)	2 (5.6)	0.674
Solid organ	7 (20)	7 (19.4)	0.953
Immunosuppression			
Cytotoxic chemotherapy	4 (11.4)	2 (5.6)	0.374
Corticosteroids	3 (8.6)	2 (5.6)	0.674
Recent surgery	7 (20.0)	3 (8.3)	0.189
Devices, used			
Central venous catheter	33 (94.3)	20 (55.6)	0.001
Foley catheter	30 (85.7)	23 (63.9)	0.055
Nasogastric tube	19 (54.3)	19 (52.8)	0.899
Mechanical ventilation	19 (54.3)	17 (47.2)	0.552
Clinical conditions			
Prior antibiotic use ^g	8 (22.9)	11 (30.6)	0.464
Prior hospitalization ^h	11 (31.4)	18 (50.0)	0.111
Time of acquiring infection after hospitalization, d	14 (4 - 90)	16.5 (5 - 94)	0.222
Stay in ICU	21 (60.0)	17 (55.6)	0.705
LOS in ICU, d	45.6 ± 37.4	45.3 ± 35.5	0.98
LOS in hospital, d	39.4 ± 34.4	38.2 ± 29.2	0.874
Severe sepsis	4 (11.4)	7 (19.4)	0.351
Septic shock	3 (8.6)	9 (25.0)	0.111
MODS	2 (5.7)	6 (16.7)	0.145
Polymicrobial infection	1 (2.9)	7 (19.4)	0.027
Laboratory findings			
Anemia	29 (82.9)	26 (72.2)	0.284
Leukocytosis	14 (40.0)	22 (61.1)	0.075
Thrombocytopenia	13 (37.1)	14 (38.9)	0.88
Elevated C-reactive protein	34 (97.1)	36 (100)	0.493
Raised erythrocyte sedimentation rate	30 (85.7)	35 (97.2)	0.107
Increased blood urine nitrogen	17 (48.6)	22 (61.1)	0.288
Hypercreatininemia	13 (37.1)	10 (27.8)	0.399
Severity score [±]			
APACHE II	23.7 ± 5.9	28.8 ± 3.4	0.002
SOFA	6.7 ± 2.4	8.5 ± 3.1	0.048
CCI	2.7 ± 1.9	2.3 ± 1.7	0.519
Appropriate antibiotic use	31 (88.6)	26 (72.2)	0.083
14-day mortality	8 (22.9)	14 (38.9)	0.144

^a Estimated only in ICU patients.^b Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; CCI, Charlson Co-morbidity Index; COPD, Chronic Obstructive Pulmonary Disease; ESR, Erythrocyte Sedimentation Rate; SD, standard deviation; ICU, Intensive Care Unit; LOS, Length of Stay; MODS, Multiple Organ Dysfunction Syndrome; SOFA, Sepsis Related Organ Failure Assessment.^c Data are presented as No. (%) except age, LOS in ICU and LOS in hospital that are presented as mean ± SD, and time of acquiring infection after hospitalization which is presented as median (min-max values).^d Univariate analysis.^e Six pneumonia, three intra-abdominal, three soft tissue, two urinary tract, one meningitis.^f Six immunosuppressive treatment, four surgical therapy, four bleeding, three acute renal failure, one diabetic ketoacidosis.^g Administration of antibiotics for more than 24 hours within 30 days.^h Hospitalization for more than 48 hours within three months.

The univariate analyses of the factors associated with the 14-day mortality are presented in Table 2. Advanced age (65 years and older), staying in ICU, septic shock, severe sepsis, invasive mechanical ventilation, Foley catheter and nasogastric catheter usage, thrombocytopenia, increased blood urea nitrogen, and inappropriate use of antibiotics were significantly associated with the 14-day mortality. Inappropriate antibiotic use and presence of multi organ dysfunction syndrome were found as independent risk factors for the 14-day mortality in multivariate analysis (Table 3).

All the 71 isolates were tested for antimicrobial resistance, and the most susceptible antibiotics were levofloxacin and trimethoprim-sulfamethoxazole (93% and 91.5% were susceptible, respectively). While the resistance of trimethoprim-sulfamethoxazole was statistically higher in primary bacteremia group, ceftazidim resistance was higher in pneumonia group. There were no statistically significant differences, but a slight increase in resistance to levofloxacin and piperacillin-tazobactam in pneumonia group (Table 4).

Table 2. Comparison of Risk Factors for Fatal and Non-Fatal Patients With Primary Bacteremia and Pneumonia Caused by *Stenotrophomonas maltophilia* (Univariate Analysis)^a

Variable	Non-Survivors (N = 22)	Survivors (N = 49)	P Value ^b	Odds Ratio (95% CI)
Age ≥ 65, y	18 (81.8)	27 (55.1)	0.036	3.67 (1.08 - 12.43)
Male gender	15 (68.2)	32 (65.3)	1	1.14 (0.39 - 3.33)
Co-morbid diseases				
Hypertension	12 (54.5)	22 (44.9)	0.608	1.47 (0.54 - 4.05)
Congestive heart failure	5 (22.7)	4 (8.2)	0.124	3.31 (0.79 - 13.81)
Cerebral vascular disease	5 (22.7)	9 (18.4)	0.75	1.31 (0.38 - 4.48)
COPD	12 (54.5)	24 (49.0)	0.799	1.25 (0.46 - 3.43)
Chronic renal failure	0 (0)	6 (12.2)	0.167	0.15 (0.01 - 2.76)
Diabetes mellitus	6 (27.3)	15 (30.6)	1	0.85 (0.28 - 2.60)
Malignancy	5 (22.7)	14 (28.6)	0.774	0.74 (0.23 - 2.38)
Immunosuppression	2 (9.1)	7 (14.3)	0.711	0.60 (0.11 - 3.15)
Stay in ICU	17 (77.3)	20 (40.8)	0.005	4.93 (1.56 - 15.55)
Prior hospitalization ^c	7 (31.8)	22 (44.9)	0.434	0.57 (0.19 - 1.65)
Prior antibiotic use ^d	4 (18.2)	15 (30.6)	0.387	0.50 (0.15 - 1.74)
Presence of severe sepsis	8 (36.4)	3 (6.1)	0.003	8.76 (2.04 - 37.57)
Presence of septic shock	9 (40.9)	3 (6.1)	0.008	10.62 (2.50 - 45.02)
Presence of MODS	5 (22.7)	3 (6.1)	0.097	4.51 (0.97 - 20.95)
Polymicrobial infection	2 (9.1)	6 (12.2)	1	1.39 (0.36 - 4.45)
Devices, used				
Invasive mechanical ventilation	17 (77.3)	19 (38.8)	0.004	5.37 (1.69 - 16.97)
Central venous catheter	19 (86.4)	34 (69.4)	0.153	2.79 (0.72 - 10.90)
Urinary catheter	20 (90.9)	33 (67.3)	0.042	4.85 (1.0 - 23.35)
Nasogastric catheter	16 (72.7)	22 (44.9)	0.04	3.27 (1.09 - 9.78)
Laboratory data				
Anemia	19 (86.4)	36 (73.5)	0.358	2.29 (0.58 - 9.03)
Leukocytosis	14 (63.6)	22 (44.9)	0.2	2.15 (0.76 - 6.05)
Thrombocytopenia	14 (63.6)	13 (26.5)	0.004	4.85 (1.65 - 14.21)
Elevated C-reactive protein	22 (100)	48 (98.0)	1	1.39 (0.05 - 35.54)
Raised erythrocyte sedimentation rate	21 (95.5)	44 (89.8)	0.658	2.38 (0.26 - 21.74)
Increased blood urine nitrogen	18 (81.8)	21 (42.9)	0.005	6.0 (1.77 - 20.38)
Hypercreatininemia	11 (50.0)	12 (24.5)	0.054	3.08 (1.07 - 8.89)
Treatment data				
Inappropriate antibiotic use	14 (63.6)	0 (0.0)	< 0.0001	168.9 (9.18 - 3107)

^a Abbreviations: CI, Confidence Interval; COPD, Chronic Obstructive Pulmonary Disease; ICU, Intensive Care Unit; MODS, Multiple Organ Dysfunction Syndrome.

^b Univariate analysis.

^c Hospitalization for more than 48 hours within three months.

^d Administration of antibiotics for more than 24 hours within 30 days.

Table 3. Independent Risk Factors for Death in Patients With Bacteremia and Pneumonia Caused by *Stenotrophomonas maltophilia* (Multivariate Logistic Regression Analysis)^a

Variable	Coefficient	Standard Error	P Value ^b	Odds Ratio (95%CI)
Inappropriate antibiotic use	0.860	0.065	< 0.001	1.000 (0.869 - 1.131)
Presence of MODS	0.256	0.113	0.001	0.375 (0.131 - 0.619)

^a CI, Confidence Interval; MODS, Multiple Organ Dysfunction Syndrome.

^b Multivariate analysis.

Table 4. Comparison Between Antimicrobial Resistance of *Stenotrophomonas maltophilia* Strains Isolated From Patients With Primary Bacteremia and Pneumonia

Antibiotics	Number of resistant strains,%			P Value
	Group 1 (Primary bacteremia, n = 35)	Group 2 (Pneumonia, n = 36)	Total (N = 71)	
Amikacin	35 (100)	36 (100)	71 (100)	-
Aztreonam	35 (100)	36 (100)	71 (100)	-
Ceftazidime	12 (34.3)	27 (75.0)	39 (54.9)	0.001
Ciprofloxacin	34 (97.1)	35 (97.2)	69 (97.2)	1
Cefepim	35 (100)	36 (100)	71 (100)	-
Imipenem	35 (100)	36 (100)	71 (100)	-
Levofloxacin	1 (2.9)	4 (11.1)	5 (7.0)	0.357
Piperacillin-tazobactam	22 (62.9)	29 (80.6)	51 (71.8)	0.097
Trimethoprim-sulfamethoxazole	6 (17.1)	0 (0)	6 (8.5)	0.009

5. Discussion

The current retrospective study aimed to identify the differences of demographic and clinical characteristics, microbiological findings and the final mortality outcomes of patients with nosocomial primary bacteremia and pneumonia caused by *S. maltophilia*. These infections are the most frequently reported infection types in the nosocomial setting, but no studies compared the clinical characteristics and outcomes of these two infections caused by *S. maltophilia* in the literature. *Stenotrophomonas maltophilia* pneumonia-associated mortality was previously reported as 23% - 44%. (4, 13-15). *Stenotrophomonas maltophilia* bacteremia was reported as 21% - 51% (8, 16-20). Lai et al. (21) found that while *S. maltophilia* bacteremia originating from respiratory tract was associated with higher mortality, CVC-related bacteremia was inversely associated with mortality. Another study found that secondary bacteremia was associated with a worse prognosis than catheter related bacteremia (22).

The current study data exhibited a slight elevation in mortality in patients with *S. maltophilia* pneumonia, but the difference was not statistically significant. Compared with patients with *S. maltophilia* bacteremia, patients with *S. maltophilia* pneumonia were older and used more inappropriate antibiotics. Patients with pneumonia staying in ICU were significantly more likely to have more severe illnesses as determined by APACHE II score and SOFA score. And also the polymicrobial infection rate was significantly higher such patients had. Previous studies

frequently observed polymicrobial infection in nosocomial *S. maltophilia* infection, if polymicrobial infection increases the mortality is controversial (4, 21). The 14-day mortality rate was not statistically different due to the small number of cases in the two groups. However, the above mentioned findings may explain that the slight increase on mortality in patients with pneumonia was thought.

Stenotrophomonas maltophilia is an environmental microorganism, is isolated from various sources in a hospital setting (15, 23, 24). *Stenotrophomonas maltophilia* is naturally resistant to many antibiotics, including broad spectrum antimicrobials such as carbapenems, third and fourth generations of cephalosporins. These drugs are used extensively in healthcare setting to treat nosocomial infections and that leads to colonization of in-dwelling devices with resistant and environmental microorganism like *S. maltophilia*. Colonization of in-dwelling devices is a key requirement for developing infection (25, 26). Primary bacteremia due to *S. maltophilia* usually occurs after the CVC colonization; similarly, pneumonia occurs after the colonization of respiratory tract (22, 26). CVC usage was more common in bacteremia group and almost all of the primary bacteremia was associated with CVC use in the study.

Most of the subjects had at least one co-morbid disease, however, chronic obstructive pulmonary disease was more common in pneumonia group and that could ex-

plain why the rate of polymicrobial infection was higher in pneumonia group. Patients with such infections are often forced to use antibiotics repetitively, which causes more than one multi drug resistant bacteria colonization of respiratory tract. Prior hospitalization and prior antibiotic use were slightly more common in pneumonia group, but the differences were not significant, that also supported the higher polymicrobial infection in this group. In addition, it was found that *S. maltophilia* strains, isolated from patients with pneumonia, were more resistant to ceftazidim and slightly more resistant to piperacillin-tazobactam and levofloxacin. The current study expected that these factors may also explain why the *S. maltophilia* strains isolated from patients with pneumonia tended to be more resistant to antibiotics. However, no resistance was determined to trimethoprim-sulfamethoxazole in these strains and that can be explained by repeated antibiotic use in patients with chronic obstructive pulmonary disease that usually includes beta-lactams and quinolones, and not trimethoprim-sulfamethoxazole. These antibiotics lead to the development of resistance to many antibiotics especially in Gram-negative bacilli (27, 28).

Prolonged hospitalization, staying in ICU, and mechanical ventilation are reported as precipitating risk factors for *S. maltophilia* infections (22, 26, 29-31). Time of acquiring infection after hospitalization (median; min-max values were presented in Table 1) was not different in the two groups, and more than half of the patients in the groups were in ICU. Also, clinical presentation and laboratory findings were not different.

Stenotrophomonas maltophilia is naturally resistant to many antibiotics such as beta-lactams and aminoglycosides, and these agents are widely used in empirical treatment of nosocomial bacteremia and pneumonia. Very few antibiotics such as trimethoprim-sulfamethoxazole and levofloxacin were effective on *S. maltophilia* and used to treat *S. maltophilia* infections, and the national committee for clinical laboratory standards recommended only antimicrobial susceptibility testing for minocycline, levofloxacin and trimethoprim-sulfamethoxazole (4, 6). However these antibiotics are usually not used for initial empirical treatment of nosocomial infections such as bacteremia and pneumonia (4, 5, 32, 33). Current antimicrobial treatment recommendation for *S. maltophilia* infections are based on case series, case reports and in vitro susceptibility tests, and levofloxacin and trimethoprim-sulfamethoxazole are the most commonly used agents to treat these infections (4).

Antimicrobial susceptibility tests were applied to all the strains in the study, and levofloxacin or trimethoprim-sulfamethoxazole, according to susceptibility tests, was selected. High crude mortality rate was reported for *S. maltophilia* bacteremia and pneumonia (5, 30, 34). In accordance to the literature, total mortality was 31.0% in the study. It seems to be relatively associated with initiation of treatment according to culture result, and also the fact

that these infections occurred in immunocompromised and debilitated patients, and those undergoing invasive procedures. Advanced age, staying in ICU, septic shock, severe sepsis, invasive procedures such as mechanical ventilation, Foley catheter and nasogastric catheter, and also thrombocytopenia and increased blood urine nitrogen were risk factors for the 14-day mortality by univariate analysis and they were consistent with the literature (21). But, it was important that all of the patients who died were in the group that used antibiotics inappropriately (63.6% versus 0%, $P < 0.001$, Table 2). Inappropriate antimicrobial treatment was associated with mortality in a lot of studies (16, 34) and the current study confirmed it too (Table 3).

There were some limitations; although a long period was viewed, there were a relatively small number of cases in each group due to evaluation of a single institution's data. In addition retrospective design hampered to manage some aspects of the study and explained some controversial issues such as selection of antibiotic or combined antimicrobial therapy (2, 10). In the current study, no antibiotic combination was tested on *S. maltophilia* infections, and the potential influences of the selected antibiotics were not evaluated. Also removal of the infected CVC is controversial and the therapeutic benefit of removal of infected CVC additional to antibiotic therapy in CVC related bacteremia was not examined in the current study. Polymicrobial infection was another problematic issue, the patients with polymicrobial growth were not excluded; all bacteria in the study were treated by adequate antibiotic. However, it was the first study comparing two most frequently observed infection types caused by *S. maltophilia* in hospital setting that did not find differences in mortality rate but demonstrated the importance of appropriate antimicrobial therapy.

In conclusion, although there was no significant difference, a slightly higher mortality was observed in patients with pneumonia, which was strived to explain by advanced age, higher APACHE II and SOFA score, and also higher inappropriate use of antibiotics. All patients were analyzed for the 14-day mortality by multivariate analyses and results indicated that the inappropriate use of antibiotics was critically important for mortality. Mortality rates between the two groups were not statistically different. However, as mentioned above, a relatively small number of subjects was an obvious limitation of the study. Therefore, multicenter retrospective or prospective studies including huge number of patients should be designed to confirm the current study findings.

Authors' Contributions

Mustafa Gokhan Gozel: Planning, analysis of medical records, article writing; Cem Celik: Planning, analysis of medical records; Nazif Elaldi: Statistical analysis and article writing.

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