

Original Article

Seven-year evaluation of *Stenotrophomonas maltophilia* bacteremia in a university-affiliated hospitalAysegul I Sezen¹, Yusuf E Ozdemir¹, Zuhail Yeşilbaş¹, Deniz Borcak¹, Esra Canbolat Ünlü¹, Fatma Bayrak Erdem¹, Zeynep Çizmeci², Enes Topcu¹, Kadriye Kart Yasar¹¹ Infectious Diseases and Clinical Microbiology Department, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey² Microbiology Department, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey**Abstract**

Introduction: *Stenotrophomonas maltophilia* is the only opportunistic human pathogen in the genus *Stenotrophomonas*. These bacteria can be isolated from healthcare settings, possibly resulting in bacterial colonization of medical devices, which cause nosocomial infections. *S. maltophilia* bacteremia results in high mortality and morbidity. This study aimed to determine the outcomes of *S. maltophilia* bacteremia and its associated mortality risk factors.

Methodology: This was a retrospective study conducted at the University of Medical Sciences, Bakirkoy Dr. Sadi Konuk Training and Research Hospital (Istanbul, Turkey) from December 2015 to December 2022. Medical records, demographic information, clinical conditions, laboratory data, antimicrobial susceptibility, and clinical outcomes were retrospectively analyzed for the period between December 2015 and December 2022.

Results: Data from 87 patients (median age 61 years) with bacteremia were included in this study. The most common underlying conditions were diabetes mellitus (DM; 32.2%), hypertension (29.9%), and malignancies (19.5%). The most common sources of bacteremia were central venous catheters (CVCs; 44%), primary blood infection (32%), respiratory tract infection (20.7%), and wound site/abscess infection (2.3%). Seventy-eight percent of the patients were admitted to the intensive care unit (ICU) when bacteremia was detected. The 28-day mortality rate was 55%. The mortality rate was significantly higher in the ICU ($p < 0.001$). Elevated values of procalcitonin and C-reactive protein, and the presence of CVC were significant risk factors for mortality in those with *S. maltophilia* bacteremia.

Conclusions: *S. maltophilia* bacteremia should be carefully monitored in patients with CVCs. Timely removal of CVCs can result in decreased mortality.

Key words: *Stenotrophomonas maltophilia*; bacteremia; mortality; risk factors.

J Infect Dev Ctries 2025; 19(4):498-503. doi:10.3855/jidc.20243

(Received 17 April 2024 – Accepted 25 October 2024)

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Introduction

Stenotrophomonas maltophilia is a non-fermenting, motile, oxidase-negative, catalase-positive, sporeless, aerobic Gram-negative bacillus, widely found in nature and is the only human opportunistic pathogen of the *Stenotrophomonas* genus.

These bacteria are found in various human habitats, including soil and natural water sources. Due to their positively charged cell wall surfaces and fimbriae, they can easily contaminate irrigation fluids and tap water, and can easily attach to various surfaces in the environment in healthcare settings. The bacterium can also cause bacterial colonization of various medical devices, leading to serious nosocomial infections. Community-acquired infections in immunocompetent patients caused by this pathogen are rare [1].

S. maltophilia is a pathogen associated with nosocomial infections, immunosuppressed patients,

and, rarely, community-acquired infections. The most common manifestations of *S. maltophilia* infections are tracheobronchitis, pneumonia, and bacteremia [2]. The source of bacteria in *S. maltophilia* bacteremia, is usually the colonized/infected lungs, colonized central venous catheters (CVCs), or the gastrointestinal tract [3]. Risk factors include prolonged hospitalization, mechanical ventilation, admission to the intensive care unit (ICU), treatment with broad-spectrum antibiotics, and *S. maltophilia* colonization [4]. *S. maltophilia* is a significant factor in morbidity and mortality; and the associated mortality rate of bacteremia has been reported to be between 20% and 70% [5].

S. maltophilia is intrinsically resistant to several antibiotics that are commonly used to treat multidrug-resistant Gram-negative bacilli, including penicillins, cephalosporins, and carbapenems. Therefore, trimethoprim-sulfamethoxazole (TMP-SMX),

levofloxacin, and minocycline are preferred. There are concerns about the increased acquired resistance to these antibiotics; and resistance, hypersensitivity, and expected severe side effects related to TMP-SMX present serious challenges to clinicians [6]. Some authors have recorded high resistance to TMP-SMX (36.84%), levofloxacin (19.29%), and minocycline (1.75%), which can be a problem in choosing the drug of choice for infections caused by this pathogen [7].

Geographical location and type of healthcare facility can significantly affect the epidemiology of bacterial infections. Therefore, analysis of local data for “spot trends” over time is critical. This study aimed to determine the outcomes of *S. maltophilia* bacteremia and its associated mortality risk factors.

Methodology

This retrospective study was conducted at the University of Medical Sciences, Bakirkoy Dr. Sadi Konuk Training and Research Hospital (Istanbul, Turkey), a tertiary care referral hospital. Data from all hospitalized patients, ≥ 18 years of age, and diagnosed with healthcare-associated *S. maltophilia* bacteremia between December 2015 and December 2022, were included in the study; while those living with human immunodeficiency virus (HIV) were excluded. A total of 87 bacteremic patients were included in this study. Only the initial episodes of bacteremia in individual patients were evaluated. Patients with polymicrobial infections were excluded. Medical records, demographic features, clinical conditions, laboratory data, antimicrobial susceptibility, and clinical outcomes were retrospectively analysed.

The hospital’s Ethics Committee approved this study (approval no. 2023/178).

Laboratory methods

The samples were cultured on standard nutrient and selective media, and identification was performed using conventional methods and automated systems. The automated systems included the Phoenix BD (Becton Dickinson, Franklin Lakes, NJ, USA) until 2020, and the VITEK 2 Compact (bioMérieux, Marcy-l’Étoile, France) after 2020.

Antimicrobial susceptibility testing for TMP-SMX was performed and evaluated in parallel according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) using the VITEK 2 compact system (bioMérieux, Marcy-l’Étoile, France) and the Kirby Bauer method. Levofloxacin susceptibility was tested using an antibiotic gradient test (E-test, bioMérieux, Marcy-l’Étoile, France) and

evaluated in accordance with Clinical Laboratory Standards Institute (CLSI) standards.

Definitions

S. maltophilia bacteremia was defined as the presence of ≥ 1 positive blood culture(s) and systemic inflammatory response syndrome symptoms. Hospital-associated bacteremia was defined as bacteremia that occurred at least 48 h after admission to the hospital. Healthcare-associated episodes of bacteremia were defined as patients undergoing hemodialysis, hospitalized within one month of onset, treated with intravenous antibiotics, or admitted to a nursing home [8]. Bacteremia that developed in patients within 48 hours after arrival and with no recent contact with a healthcare facility was referred to as community-acquired bacteremia [8].

The source of bacteremia was defined as an active site of infection, where *S. maltophilia* was detected immediately before or on the same day as the onset of bacteremia. Immunosuppressive treatment was defined as treatment with monoclonal antibodies, T-cell inhibitors, antimetabolite drugs, or steroids at a dose equivalent to at least 10 mg of prednisolone daily within 30 days of bacteremia onset.

Empirical antibacterial therapy was defined as treatment that began no later than 24 hours after blood cultures were obtained. Mortality was defined as death within 28 days of hospitalization.

The prognostic nutritional index (PNI) was used to evaluate patient nutritional status. The PNI was calculated using the following equation: $PNI = 10 \times \text{serum albumin (g/dL)} + 0.005 \times \text{total lymphocyte count}$.

The severity of diabetes mellitus (DM) was defined according to criteria from the American Diabetes Association [9]. The inflammation-related Glasgow prognostic score (GPS) was calculated using C-reactive protein (CRP) and albumin concentrations. Socioeconomic status was evaluated according to income, job, and education.

Statistical analyses

Continuous variables are expressed as mean \pm standard deviation, while categorical variables are expressed as numbers and percentages. The Chi squared test was used to compare categorical variables. Statistical analyses were performed using SPSS version 26.0 (IBM Corporation, Armonk, NY, USA). Differences with $p < 0.05$ were considered to be statistically significant. The distribution of variables was evaluated using the Shapiro–Wilk and

Kolmogorov–Smirnov tests. Non-parametric tests (Mann–Whitney U test and Chi squared test) were applied to data that were not normally distributed. Multivariate analysis (multivariate regression analysis) was performed for variables that were significant in the univariate analysis.

Results

The patient demographic information is summarized in Table 1. The most common underlying conditions were DM (32.2%), hypertension (29.9%), and malignancy (19.5%). The most common source of bacteremia was bacterial colonization of CVCs (44%), followed by bacteremia of unknown origin (32%), respiratory tract infection (20.7%), and wound site/abscess infection (2.3%). Most patients (78%) were

admitted to the ICU. Eleven patients underwent empirical antibacterial therapy. The 28-day mortality rate was 55%. When mortality risk factors were examined, no statistically significant differences were found in age, gender, or accompanying comorbidities. The presence of CVC was a risk factor for mortality ($p < 0.05$). An analysis of the inflammatory phase parameters revealed that CRP and procalcitonin levels were significantly higher in patients with fatal outcomes ($p < 0.05$). Additionally, albumin level ($p = 0.009$) and PNI ($p = 0.042$) were lower in patients who died (Table 1).

Regarding the relationship between socioeconomic level and mortality, patients with a higher socioeconomic level had a 50% mortality rate, whereas

Table 1. Comparison of outcomes between survivors and non-survivors of *Stenotrophomonas maltophilia* bacteremia.

Variables	Survived	Died	p value
	n (%)	n (%)	
Age (median) years	61	62.5	0.205**
Total number (n)	39 (44.8%)	48 (55.2%)	
Age (n) years			0.583*
< 65	25 (64.1%)	28 (58.3%)	
≥ 65	14 (35.9%)	20 (41.7%)	
Gender (n)			0.927*
Male	24 (61.5%)	30 (62.5%)	
Female	15 (38.5%)	18 (37.5%)	
Accompanying condition (n)			
DM	13 (33.3%)	15 (31.3%)	0.836*
HT	12 (30.8%)	14 (29.2%)	0.871*
CAD	9 (23.1%)	9 (18.8%)	0.620*
CRF	8 (20.5%)	10 (20.8%)	0.971*
COPD	5 (12.8%)	3 (6.3%)	0.292*
BPH	2 (5.1%)	3 (6.3%)	0.823*
Malignancy	7 (17.9%)	10 (20.8%)	0.736*
CVC	10 (25.6%)	29 (60.4%)	< 0.001*
COVID-19 history (between 1–6 months)	2 (5.1%)	4 (8.3%)	0.557*
COVID-19 history (in last 1 month)	11 (28.2%)	21 (43.8%)	0.135*
Immunosuppressive therapy	8 (20.5%)	11 (22.9%)	0.787*
Laboratory			
Leukocyte (cell/ μL) (median)	10,690	13,960	0.131**
Neutrophil (cell/ μL) (median)	9,210	12,060	0.020**
Lymphocyte (cell/ μL) (median)	850	845	0.969**
Platelet (cell/ μL) (median)	208,000	175,000	0.302**
CRP (mg/dL) (median)	48	187	< 0.001**
Procalcitonin (ng/mL) (median)	0.56	0.58	< 0.001**
BUN (mg/dL) (median)	60	74	0.095**
Creatinine (mg/dL) (median)	0.76	1.08	0.481**
ALT (U/L) (median)	27	31.5	0.597**
AST (U/L) (median)	31	43.5	0.059**
Albumin (g/dl) (mean)	27.64 ± 4.39	24.94 ± 5.03	0.009***
Prognostic nutritional index (PNI)	32.6 ± 1.07	29.8 ± 0.85	0.042***
Appropriate empiric treatment (n)	7 (8.3%)	4 (18.4%)	0.164*
Antibiotic resistance (n)			
SXT resistance	1 (1%)	5 (6%)	0.151*
Source of bacteremia			0.846*
Blood-CVC	36 (75%)	31 (79.5%)	
Lung	11 (22.9%)	7 (17.9%)	
Wound Site	1 (2.1%)	1 (2.6%)	

ALT: alanine aminotransaminase; AST: aspartate aminotransferase; BPH: benign prostatic hypertrophy; BUN: blood urea nitrogen; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; COVID-19: coronavirus disease 2019; CRF: chronic renal failure; CRP: C-reactive protein; CVC: central venous catheter; DM: diabetes mellitus; HT: hypertension; SXT: trimethoprim sulfomethaxazole. *Chi-square test; **Mann-Whitney U test; ***independent sample t test. p values less than 0.05 were considered statistically significant.

Table 2. Comparison of mortality according to the hospitalization department where bacteremia was detected.

Department	Patients survived	Patients died	p value
Ward	20 (51%)	2 (4%)	< 0.001
Intensive care unit	19 (49%)	46 (96%)	

The Chi-square test was used for the analyses, and *p* values < 0.05 were considered statistically significant.

mortality rate was 73.7% among patients belonging to a lower socioeconomic level (*p* = 0.066).

Among the cohort, 5.7% of patients had a GPS of 1, and 94.3% had a GPS of 2. Mortality was observed in 1 patient with a GPS score of 1, and mortality was recorded in 47 patients with a GPS score of 2 (*p* = 0.169). The mortality rate of those who acquired bacteremia in the ICU versus other hospital wards was significantly higher (*p* < 0.001) (Table 2). Multivariate analysis of the factors affecting mortality revealed that PCT level, elevation of CRP level, and the presence of a CVC were significant risk factors for mortality in those with *S. maltophilia* bacteremia (Table 3).

The TMP-SMX and levofloxacin resistance rates were 7% and 14%, respectively.

Although mortality occurred in 56.5% of patients with severe DM and 35.7% of patients with controlled DM, there was no statistically significant difference between the groups (*p* = 0.219). There was no statistically significant association between mortality and socioeconomic level, despite mortality being higher among patients with a lower socioeconomic status compared to those with a higher status (73.7% vs. 50%, *p* = 0.066).

Discussion

In this study, the presence of CVC was a significant risk for the development of *Stenotrophomonas* bacteremia; as such, the timely removal of CVC could result in reduction in the rate of bacteremia caused by *S. maltophilia*. Mortality risk factors for *S. maltophilia* bacteremia have been the subject of various studies and have attracted increasing attention in recent years. It has been associated with a significant mortality rate ranging from 22% to 62% [10]. The mortality rate in our study (55%) was similar to that reported previously.

S. maltophilia bacteremia mainly affects immunocompromised or critically ill patients, and previous research has shown that a high number of

patients with this condition undergo placement of CVCs [11]. *S. maltophilia* is also a biofilm producer that hinders the function of immune cells, inhibits the diffusion of antimicrobial drugs in vivo, and persists in CVCs [12]. CVCs have been linked to an increased incidence of *S. maltophilia* infection [13]. In our study, CVC was also an important risk factor for mortality (*p* < 0.05).

Some studies have suggested that removing CVC(s) from patients with *S. maltophilia* bacteremia is beneficial. However, others have commented that this may imply colonization rather than being a trustworthy source of bacteremia in cases where *S. maltophilia* was isolated from other sources, such as the respiratory tract.

When treating patients with *S. maltophilia* bacteremia, physicians should be highly vigilant for infections from vascular devices. Multiple studies have reported that most cases of bacteremia are associated with devices requiring vascular access [14].

In this study, the common underlying conditions in patients who died of *S. maltophilia* bacteremia were DM (31.3%), hypertension (29.2%), chronic renal disease (20.8%), malignancy (20.8%), and coronary arterial disease (18.8%). These results are consistent with those of other studies and are associated with prolonged hospital stays, underlying chronic diseases, immunocompromised status after chemotherapy, use of medical devices, and exposure to antibiotics. Another important source of bacteremia observed in our study was the respiratory tract (23%), which, along with CVCs, is a well-known cause of *S. maltophilia* infection.

Wild-type *S. maltophilia* does not present with resistance to TMP-SXT and levofloxacin. A recent study investigating military trauma patients infected with *S. maltophilia* reported that *S. maltophilia* isolates were mainly susceptible to TMP-SMX (99%), minocycline (100%), and moxifloxacin (97%) [15].

Table 3. Multivariate analysis of factors affecting mortality.

Variables	HR	95% confidence interval		p value
		Lower	Upper	
Neutrophil (cell/ μL)	1	1	1	0.818
Procalcitonin (ng/mL)	3.57	1.02	12.45	0.046
CRP (mg/dL)	1.02	1.0	1.03	0.004
PNI	0.93	0.81	1.06	0.309
CVC	6.76	1.84	42.19	0.041

CRP: *C-reactive protein*; CVC: central venous catheter; HR: hazard ratio; PNI: prognostic nutritional index. Multivariate regression test was used. *p* values < 0.05 were considered statistically significant.

Other studies showed slightly lower values of sensitivity to TMP-SMX (81%), while sensitivity to minocycline (100%) was the same [15]. There are concerns regarding increased antimicrobial resistance to TMP-SMX among *S. maltophilia* strains [6]. The TMP-SMX resistance rate has been reported to vary between 7.8% and 21.6% [16–18]. In our study, the TMP-SMX and levofloxacin resistance rates were 7% and 14%, respectively.

PNI reflects the relationship between the nutritional status and the immune system [19]. It is also used for risk assessment of cancer, infections, and surgery-related diseases [20,21]. Studies have shown that low PNI values are associated with poor prognosis [20,21]. PNI can also be related to socioeconomic status [22]. We found a correlation between PNI and socioeconomic level ($r = 0.256, p = 0.017$).

In our study, univariate analysis of PNI values compared between deceased and surviving patients revealed a significant difference ($p = 0.042$). Further analysis using multivariate regression testing yielded a p value of 0.952, which may be explained by the low number of patients included in our study.

Although a significant relationship between socioeconomic level and mortality was reported in a previous study, no such significant results were obtained in our study ($p = 0.066$), likely due to the small sample size [23]. As such, further studies with a larger number of patients are recommended.

In our study PCT and CRP values were significantly higher in the mortality group than in the control group. Previous studies have shown that PCT has high sensitivity and specificity for predicting patient mortality [24]. Other studies have also shown that PCT and CRP levels have moderate value in diagnosing sepsis in adult patients. The diagnostic accuracy and specificity of PCT are presumed to be higher than those of CRP [25]. Similar studies have provided data regarding the utility of plasma PCT levels on admission as a risk-indicating biomarker for predicting mortality in patients with bloodstream infections [24].

Our study had several limitations. First, it was a single-centre design, which may make it challenging to generalize our findings to other medical facilities in other regions. Second, this was a retrospective study; as such, information and selection bias may have been introduced. Third, it was difficult to distinguish between colonization and infection, which made it difficult to determine the actual cause of the bacteremia. This may be related to the possibility of identifying an incorrect source of infection.

Conclusions

The results of the present study suggest that patients with CVCs may need careful monitoring for infection with *S. maltophilia* in order to potentially reduce mortality from bacteremia caused by this pathogen. In addition, a well-designed study with a larger number of patients is required to evaluate other factors affecting mortality.

Ethical approval and informed consent

Informed consent was obtained from all individual participants. The hospital's Ethics Committee provided approval for our study (approval no. 2023/178).

Authors' contributions

Concept: AIS, YEO; design: ECU, DB; data collection and/or processing: FBE, ZC, ET; analysis and interpretation: ZY; literature search: AIS; manuscript writing: AIS; approval: KKY. All the authors reviewed the results and approved the final version of the manuscript.

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Conflict of interests

No conflict of interests is declared.

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