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Original Article

Risk Factors Associated with Mortality in Nosocomial Stenotrophomonas maltophilia Pneumonia: A Single-Center Retrospective Study

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Abstract. ***Background*: *Stenotrophomonas maltophilia* (*S. maltophilia*) is a multidrug-resistant pathogen frequently isolated in hospital-acquired pneumonia and represents a significant clinical challenge. This study aimed to investigate the risk factors associated with 30-day mortality in patients diagnosed with *S. maltophilia* pneumonia.**
***Methods*: This retrospective, single-center study included patients aged 18 years and older who were hospitalized between January 2018 and December 2021, had *S. maltophilia* isolated from respiratory samples, and demonstrated clinical and radiological evidence of pneumonia. Patients were grouped by 30-day survival status, and comparisons were made for demographic characteristics, risk factors, and antibiotic regimens.**
***Results*: Among the 200 evaluated patients, colonization was detected in 48%. A total of 104 patients met the inclusion criteria, of whom 75% required ICU admission. The 30-day mortality rate was 55.7%. Malignancies were present in 62.5%. Polymicrobial infections and coinfections were observed in 39.4% and 82.4%, respectively. Multivariate analysis identified SOFA (Sequential Organ Failure Assessment) score (OR = 1.293, 95% CI [1.113-1.501], p = 0.001), mechanical ventilation (OR = 5.005, 95% CI [1.379-18.157], p = 0.014), and a high Charlson Comorbidity Index (OR = 1.353, 95% CI [1.103-1.650], p = 0.004) as independent predictors of mortality. Combination antibiotic therapy had no significant effect on mortality. No resistance to trimethoprim-sulfamethoxazole was detected.**
***Conclusion*: *S. maltophilia* pneumonia is a serious nosocomial infection with high mortality, particularly in ICU patients with malignancies. SOFA score, mechanical ventilation, and a high Charlson Comorbidity Index were independently associated with increased mortality.**

Keywords: *Stenotrophomonas maltophilia*; Nosocomial pneumonia; Mortality; Charlson comorbidity index; SOFA score; Mechanical ventilation.

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Introduction. *Stenotrophomonas maltophilia* (*S. maltophilia*), a prominent pathogen among non-fermenting aerobic Gram-negative bacteria, can cause a wide array of infections, including lower respiratory tract infections and bacteremia, as well as sepsis, meningitis, soft tissue infections, and endocarditis.[1,2] Through its biofilm-forming capability, *S. maltophilia* can colonize various medical devices, including intravascular catheters, implantable devices, and mechanical ventilation circuits. As an opportunistic pathogen, it frequently causes infections in hospitalized patients, particularly those requiring intensive care and those using invasive devices.[3,4] It may present with severe clinical manifestations in immunocompromised patients — such as those with human immunodeficiency virus (HIV), malignancies, or transplantation — as well as in individuals with chronic pulmonary conditions like cystic fibrosis.[5] One of the major challenges in treatment is the intrinsic resistance of *S. maltophilia* to a broad range of antimicrobials, conferred by multiple mechanisms, including β-lactamase production, aminoglycoside-modifying enzyme synthesis, and the expression of multidrug efflux pumps.

S. maltophilia pneumonia ranks among the top ten causative agents of nosocomial pneumonia in intensive care units and accounts for approximately 0.4% to 8.7% of all nosocomial pneumonia cases.[6] It is particularly associated with high mortality rates in patients monitored in intensive care settings.[7] Advanced age, elevated organ failure scores (SOFA (Sequential Organ Failure Assessment), APACHE II), corticosteroid use, neutropenia, prior carbapenem exposure, and concurrent infections are among the most frequently reported risk factors associated with mortality.[3,7]

In this study, we aimed to describe the clinical characteristics of patients presenting with *S. maltophilia* pneumonia and to identify the risk factors independently associated with 30-day mortality among hospitalized patients diagnosed with this infection.

Materials and Methods.

Study design and Patient groups. This study was designed as a retrospective, single-center cohort study. Patients over the age of 18 who were hospitalized between January 2018 and December 2021, with *S. maltophilia* isolated from respiratory secretions (sputum, endotracheal aspirate, or bronchoalveolar lavage) and clinical and/or radiological findings consistent with pneumonia, were enrolled in the study. Only the first episode of pneumonia for each patient was included in the study, and any subsequent recurrent pneumonia episodes in the same patient were excluded from the analysis. Data on patient demographics, comorbid conditions, and laboratory findings were obtained from the hospital's electronic medical record system. Patients who met the inclusion criteria were categorized into two groups based on 30-day mortality status. The Ethics Committee approved the study with decision number 13 on September 7, 2021. Due to the retrospective design, informed consent was waived. Patient identifiers were removed before analysis.

Definitions. The diagnosis of *S. maltophilia* pneumonia was established based on the presence of new or progressive pulmonary infiltrates (on chest radiography and/or pulmonary CT), a positive microbiological culture, and at least one of the following clinical symptoms: fever (≥ 38 °C), newly developed cough, chest pain, dyspnea, or worsening oxygenation. *S. maltophilia* colonization was defined as a positive microbiological culture for *S. maltophilia* in the absence of the previously described clinical signs of infection. In lower respiratory tract samples, growth of at least 10^4 CFU/mL for bronchoalveolar lavage and at least 10^5 CFU/mL for endotracheal aspirate was considered significant. Inflammatory biomarkers were not used in the standard case definition; procalcitonin values above 0.5 ng/mL were considered supportive when consistent with clinical and radiological findings. Patients who did not meet the clinical-radiological criteria for pneumonia despite significant growth in respiratory tract samples and who received an alternative non-infectious diagnosis during file review were classified as colonized and excluded from the study. Hospital-acquired pneumonia is defined as pneumonia that occurs ≥48 hours after hospital admission and was not incubating at the time of admission.[8] Polymicrobial infection was defined as the presence of any organism other than *S. maltophilia* in the same index sample. Coinfection was defined as the isolation of an additional bacterial pathogen from any clinical culture, except the index respiratory specimen, within 72 hours of initial sample collection. Appropriate therapy was defined as the initiation of treatment following the identification of Stenotrophomonas maltophilia in respiratory cultures, using at least one antimicrobial agent with proven clinical efficacy against this pathogen. The choice of antimicrobial and intravenous dosing was guided by the Sanford Guide, with dose adjustments made based on estimated creatinine clearance when clinically necessary.

Microbiological Identification. MALDI-TOF MS (VITEK MS, bioMérieux, France) was used for the identification of the isolates, and VITEK 2 (bioMérieux, Marcy l'Étoile, France) was used for phenotypic AST. Susceptibility results were interpreted according to EUCAST clinical breakpoint versions implemented during the study period (2018–2021, depending on the year of isolation).

Statistical Analysis. The groups were compared statistically with respect to demographic characteristics,

underlying comorbidities, mortality-associated risk factors, and administered antimicrobial therapies. Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM Corp., Armonk, NY, USA). The normality of data distribution was evaluated through histograms, Q-Q plots, and the Shapiro-Wilk test. Categorical variables are expressed as frequencies and percentages, and comparisons were made using the chi-square test. Continuous variables are presented as mean ± standard deviation (SD) or as median values with interquartile ranges (IQR, 25th–75th percentiles). For comparing continuous variables, the independent-samples t-test was used for normally distributed data, and the Mann-Whitney U test was used for non-normally distributed data. To identify risk factors influencing 30-day mortality, variables with a p-value <0.20 in univariate analysis-including age, hematologic malignancy, SOFA score at diagnosis, chronic kidney disease, Charlson Comorbidity Index, presence of a central venous catheter, mechanical ventilation, chemotherapy, history of surgery within 30 days, prior use of carbapenems, tigecycline, quinolones, or polymyxins within 30 days, as well as treatment regimens involving quinolones and polymyxins-were entered into a multivariate logistic regression model using the backward likelihood ratio (LR) method, after confirming that the variables were not correlated with each other. A p-value of <0.05 was considered statistically significant.

Results. A total of 200 hospitalized patients with S. maltophilia isolated from respiratory secretions were screened. Ninety-six patients (48%) who met the criteria for colonization were excluded, and the data of a final 104 patients were analysed (**Figure 1**).

The 30-day mortality rate among the patients included in the study was 55.7%. Seven patients had concomitant *S. maltophilia* bacteremia. Solid organ malignancies were present in 37.5%, and hematological malignancies in 25%. Polymicrobial infections and coinfections were observed in 39.4% and 82.4%, respectively. Patient characteristics according to 30-day mortality status are presented in **Table 1**. In univariate analysis, hematologic malignancy (32.8% (n=19) vs. 15.2% (n=7), p=0.040), SOFA score (9 (5-13) vs. 5 (3-7), p<0.001),chronic kidney disease (20.7% (n=12) vs. 6.5% (n=3), p=0.041), Charlson Comorbidity Index (6 (5–8) vs. 5 (3–6), p=0.002), presence of a central venous catheter (87.9% (n=51)vs. 67.4% (n=31), p=0.011), mechanical ventilation (87.9% (n=51) vs. 54.3% (n=25), p <0.001), and the use of carbapenems (91.4% (n=53) vs. 78.3% (n=36), p=0.059), tigecycline (58.6% (n=34) vs. 39.1% (n=18), p =0.048) within the past 30 days were all significantly associated with increased 30-day mortality. Prior quinolone exposure within 30 days was significantly associated with reduced 30-day mortality

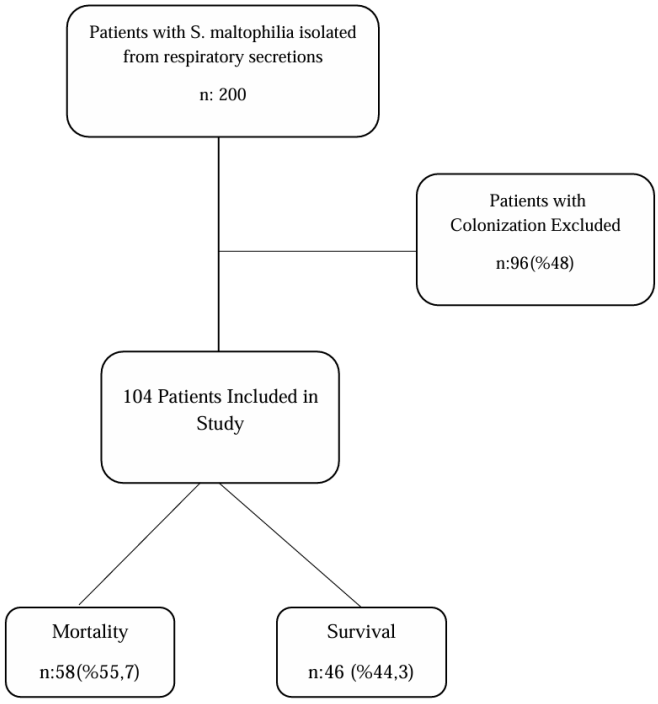

Figure 1. Flowchart of the study.

(31.0% vs. 58.7%, p=0.005). No resistance to TMP-SXT was detected in any of the isolates.

Preferred antimicrobial regimens for the treatment of *S. maltophilia pneumonia* are presented in **Table 2**. The analysis was based on 87 observations due to missing data. A total of 45 patients (51.7%) received monotherapy, whereas 42 patients (48.3%) were administered combination therapy. The most frequently preferred treatment was TMP-SXT (28.7%).

In the multivariate analysis SOFA score (OR = 1.293, 95% CI [1.113-1.501], p = 0.001), mechanical ventilation (OR = 5.005, 95% CI [1.379-18.157], p = 0.014), and a high Charlson Comorbidity Index (OR = 1.353, 95% CI [1.103-1.650], p = 0.004) were identified as independent risk factors significantly associated with mortality (**Table 3**).

Discussion. *S. maltophilia* pneumonia predominantly occurs in critically ill patients in intensive care units, particularly those requiring mechanical ventilation support. In our study, similar to the literature, approximately three-quarters of the patients had ICU admission with ventilator support.[9] Moreover, well-known risk factors for *S. maltophilia* infection – such as solid organ malignancies and hematologic malignancies – were present in 37.5% and 25% of our patients, respectively, consistent with prior reports.[10] Antibiotic exposure (notably prior carbapenem use) is also a recognized risk factor associated with *S. maltophilia* infections.[11] Polymicrobial infections and co-infections were frequently observed (39.4% and 82.4% of cases, respectively). About half of the patients (48.3%) received combination antimicrobial therapy; however, we did not find any significant impact of combination

Table 1. Analysis of Risk Factors for 30-Day Mortality.

Variables	Total n=104 (%)	Mortality n=58 (%)	Survival n=46 (%)	P value
Age, median (IQR)	69 (60.2–76.0)	69.5 (63.0–76.2)	65.5 (55.7–74.5)	0.123
Male, gender	76(73.1)	39 (67.2)	37 (80.4)	0.132
ICU admission	78 (75.0)	48 (82.8)	30 (65.2)	0.040
SOFA score, median (IQR)	7 (4-10)	9 (5-13)	5 (3-6)	<0.001
Polymicrobial infection	41 (39.4)	23 (39.7)	18 (39.1)	0.957
Coinfection	84 (82.4)	45 (78.9)	39 (86.7)	0.310
Comorbidity	98 (94.2)	56 (96.6)	42 (91.3)	0.402
Hypertension	41 (39.8)	24 (41.4)	17 (37.8)	0.711
Solid organ malignancy	39 (37.5)	23 (39.7)	16 (34.8)	0.610
Chronic pulmonary disease	35 (34.0)	19 (32.8)	16 (35.6)	0.766
Hematologic malignancy	26 (25.0)	19 (32.8)	7 (15.2)	0.040
Chronic heart disease	25 (24.3)	16 (27.6)	9 (20.0)	0.373
Diabetes mellitus	19 (18.4)	12 (20.7)	7 (15.6)	0.505
Chronic neurological disease	17 (16.5)	8 (13.8)	9 (20.0)	0.400
Chronic kidney disease	15 (14.4)	12 (20.7)	3 (6.5)	0.041
Solid organ transplantation	11 (10.6)	7 (12.1)	4 (8.7)	0.751
Charlson Comorbidity Index, median (IQR)	5 (4–7)	6 (5–8)	5 (3–6)	0.002
Central venous catheter	82 (78.8)	51 (87.9)	31 (67.4)	0.011
Mechanical ventilation	76 (73.1)	51 (87.9)	25 (54.3)	<0.001
Steroid use (within 90 days)	69 (68.3)	37 (64.9)	32 (72.9)	0.403
Total parenteral nutrition	55 (53.9)	34 (58.6)	21 (47.7)	0.274
Other immunosuppressive therapies	45 (46.9)	26 (47.3)	19 (46.3)	0.928
Chemotherapy	34 (32.6)	23 (41.1)	11 (26.2)	0.126
Neutropenia	19 (18.4)	13 (22.4)	6 (13.3)	0.239
Surgery within 30 days	15 (14.4)	6 (10.3)	9 (19.6)	0.184
Broad-spectrum antibiotics (last 30 days)	103 (99.0)	58 (100)	45 (97.8)	0.442
Carbapenem	89 (85.6)	53 (91.4)	36 (78.3)	0.059
Trimethoprim-sulfamethoxazole	63 (60.6)	38 (65.5)	25 (54.3)	0.247
Tigecycline	52 (50.0)	34 (58.6)	18 (39.1)	0.048
Quinolone	45 (43.3)	18 (31.0)	27 (58.7)	0.005
Polymyxin	44 (42.3)	29 (50.0)	15 (32.6)	0.075
Cephalosporins(3rd/4th gen.)	32 (30.8)	20 (34.5)	12 (26.1)	0.357
Aminoglycoside	6 (5.8)	3 (5.2)	3 (6.5)	0.769
Treatment				
Monotherapy Combination	45 (51.7) 42 (48.3)	23 (46.0) 27 (54.0)	22 (59.5) 15 (40.5)	0.214
Time to appropriate therapy (n=87)	2 (0-4)	1 (0-3)	3 (0-5)	0.067

Abbreviations: ICU: Intensive Care Unit, SOFA: Sequential Organ Failure Assessment.

therapy on 30-day mortality (p = 0.214).

Our results highlight the frequent occurrence of *S. maltophilia* colonization in the respiratory tract (48%). Recent multicenter studies have reported colonization rates ranging from 56% to 79% in hospitalized patients.[12,13] These findings support the notion that a

Table 2. Preferred antimicrobial regimens for the treatment of *S. maltophilia* pneumonia.

Preferred Antimicrobial Regimens	Frequency, n=87 (%)*
Monotherapy	**45(51.7)**
Trimethoprim-sulfamethoxazole	25 (28.7)
Fluoroquinolone	11 (12.6)
Polymyxin	5 (5.7)
Tigecycline	3 (3.4)
Ceftazidime	1 (1.1)
Combination Therapy	**42 (48.3)**
Tigecycline + Polymyxin	10 (11.5)
Trimethoprim-sulfamethoxazole + Fluoroquinolone	7 (8.0)
Trimethoprim-sulfamethoxazole + Polymyxin	5 (5.7)
Trimethoprim-sulfamethoxazole + Tigecycline	4 (4.6)
Ceftazidime + Polymyxin	1 (1.1)
Fluoroquinolone + Ceftazidime	2 (2.3)
Fluoroquinolone + Polymyxin	2 (2.3)
Trimethoprim-sulfamethoxazole + Ceftazidime	3 (3.4)
Triple Combination Therapy	**8 (9.2)**

*Analysis based on 87 observations due to missing data

significant proportion of *S. maltophilia* isolations are attributable to colonization rather than infection.

In our study, the mortality rate was 55%, and the SOFA score, the need for mechanical ventilation, and a high Charlson Comorbidity Index are significant risk factors for 30-day mortality in patients with *S. maltophilia* pneumonia. *S. maltophilia* infections are particularly associated with high mortality rates among intensive care patients and immunosuppressed individuals. Although mortality data often derive from single-center studies, overall mortality rates have been reported to range from 18% to 69%, with attributable mortality rates ranging from 24% to 58%.[1] Pneumonia is the infection type with the highest mortality rate.[14] In the ICU, mortality rates as high as 82.1% have been documented.[9] A study from Turkey investigating all *S. maltophilia* infections reported a mortality rate of 53% among patients with pneumonia.[15] Consistent with these findings, our study also revealed a high mortality rate of 55.7%, further supporting the data reported in the literature.

In our study, the SOFA score was significantly higher in the mortality group and was identified as an independent predictor of mortality (OR = 1.293, 95% CI [1.113–1.504], p = 0.001). This finding suggests that

Table 3. Analysis of Independent Risk Factors for 30-Day Mortality*.

	P value	aOdds Ratio	95% Confidence Interval
Hematologic malignancy	0.052	3.685	0.990 – 13.720
Charlson Comorbidity Index	0.004	1.353	1.103 - 1.650
Mechanical ventilation	0.014	5.005	1.379 – 18.157
Recent fluoroquinolone use	0.134	0.455	0.163 – 1.274
SOFA score	0.001	1.293	1.113 – 1.501

Abbreviations: SOFA: Sequential Organ Failure Assessment. *n=104; 5 variables; EPV=11.6. Multicollinearity not detected. Hosmer–Lemeshow p=0.458, Nagelkerke R^2=0.504.

to the pathogen's resistance profile or the treatment used, but also closely linked to the patient's level of organ dysfunction and physiological reserve at the time of infection. Our results align with previous studies showing a link between higher SOFA scores and increased mortality.[9,13] Similarly, in the study by Hasbek et al., the SOFA score was identified as an independent risk factor for 28-day mortality in patients with S. maltophilia infections, supporting its value as a prognostic tool in this patient group.[15] Therefore, early and systematic evaluation of the SOFA score in patients with S. maltophilia infections appears clinically important for quickly identifying high-risk individuals and more accurately predicting mortality risk.

Another independent risk factor identified in our study was the Charlson Comorbidity Index (CCI) (OR = 1.353, 95% CI [1.103-1.650], p = 0.004). In a national cohort study in the United Kingdom that included all *S. maltophilia* infections, researchers demonstrated that a CCI score of 4 or higher was associated with a 36% increase in mortality.[19] In a recent study from Turkey by Hasbek et al., which included cases of primary bacteremia and pneumonia, a high CCI score (≥5) was significantly associated with increased mortality, particularly in the pneumonia subgroup.[15] Our findings support previous data indicating that mortality is significantly higher in patients with *S. maltophilia* infections who have underlying comorbidities.

Approximately 76–80% of *S. maltophilia* pneumonia cases have been reported to manifest as ventilator-associated pneumonia (VAP).[9,20] In our study, the rate of patients requiring mechanical ventilation was similarly high, at 73.1%. Moreover, mechanical ventilation was identified as an independent risk factor for 30-day mortality, increasing the risk of death by fivefold (OR = 5.005, 95% CI [1.379-18.157], p = 0.014). In a large

multicenter cohort, the rate of invasive mechanical ventilation was significantly higher among patients who died within 30 days compared to those who survived.[18] Other studies have likewise shown that mechanical ventilation raises mortality risk by 4.4 to 5.7 times.[21,22] These findings suggest that the need for mechanical ventilation is a critical factor that directly increases mortality risk.

The optimal treatment strategy for *S. maltophilia* infections has not been definitively established, although TMP-SXT remains the most commonly used agent for susceptible strains. Fluoroquinolones, another frequently employed therapeutic option, are widely used in patients who are either resistant to or intolerant of TMP-SXT. While increasing resistance to TMP-SXT has been reported in the literature, no resistance to TMP-SXT was detected in our study. Among the 10 levofloxacin-tested isolates, resistance was identified in 2. A meta-analysis evaluating resistance rates of *S. maltophilia* worldwide, including data from Turkey, reported a global levofloxacin resistance rate of 14.4% and a TMP-SMX resistance rate of 9.2%, with an upward trend in resistance to both agents over time.[23] Another Turkish study found resistance rates of 5.6% for tigecycline, 7% for levofloxacin, and 8.5% for TMP-SXT.[24] Although TMP-SXT and levofloxacin remain among the most frequently preferred agents in treatment, the increasing resistance observed in various bacterial pathogens underscores the importance of monitoring antimicrobial susceptibility patterns.

In our study, the most frequently preferred therapeutic agents were TMP-SXT and fluoroquinolones. Notably, the proportion of patients receiving combination regimens was relatively high. This finding may be attributable to the high prevalence of polymicrobial infections and coinfections among our cohort. However, combination therapy did not confer an additional survival benefit. Guerci P et al. reported that appropriate antibiotic use, timing of initiation, combination therapy, and treatment duration have not generally had a significant impact on mortality in *S. maltophilia* pneumonia.[20] Combination therapy also did not affect 30-day mortality. Liang et al. reported no mortality benefit from combination therapy in the general cohort, though a potential benefit was observed in immunocompromised patients and those with APACHE II scores≥15.[18] Another ICU-based study found no effect of appropriate or combination therapy on mortality.[9] These findings support the idea that mortality is more influenced by host-related risk factors than by therapeutic interventions.

Our study has several limitations. This study was conducted in a single center with a retrospective design and a relatively small sample size, which may limit the generalizability of the findings to other patient populations and healthcare settings. Due to the retrospective design, certain potentially important clinical parameters — such as the exact timing and appropriateness of antimicrobial initiation, dosing adjustments, and detailed severity scores — could not be consistently obtained, which may have affected the interpretation of treatment outcomes. Finally, the comparison between combination therapy and monotherapy is observational and may be biased by confounding by indication and immortal time bias; therefore, differences in outcomes may not solely reflect the effect of the treatment regimen.

Conclusions. *S. maltophilia* pneumonia is a severe nosocomial infection associated with high mortality, particularly among intensive care patients with malignancies. Polymicrobial infections and coinfections are also common. In this study, SOFA score, mechanical ventilation, and a high Charlson Comorbidity Index were identified as independent risk factors for mortality. No significant impact of combination therapy on 30-day mortality was detected. Risk stratification and individualized monitoring may play a critical role in reducing mortality in this vulnerable patient population.

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