RBFHSS
Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde

Original Paper

Open Access

Microbiological characteristics and clinical profile of *Stenotrophomonas maltophilia* infections in a teaching hospital in northeastern Brazil

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Submitted: 01-02-2024 Resubmitted: 02-09-2024 Accepted: 05-09-2024

Double blind peer review

Abstract

Objective: This study aimed to elucidate the microbiological and clinical characteristics of patients affected by infection caused by *S.maltophilia* in a tertiary hospital in the north-east of Brazil. **Methodology:** The study consisted of a retrospective analysis of microbiological samples from January 2022 to September 2023 from the microbiology department of the Walter Cantídio University Hospital, Fortaleza, Ceará. The prevalence of these infections was determined, along with the epidemiology and antimicrobial sensitivity profile to sulphamethoxazole/trimethoprim (SMX-TMP) and levofloxacin. Clinical characteristics of the affected patients were identified, such as the use of mechanical ventilation (MV), hemodialysis (HD), previous use of antimicrobials and the outcome of these patients. **Results:** The prevalence of *S.maltophilia* infections was 1.79% in the period (35 positive samples and 26 affected patients). Of the positive clinical isolates, there was a predominance from the respiratory tract, with 23 samples (61.43%) from tracheal aspirates and 5 samples from bronchoalveolar lavage (14.57%). The highest number of positive samples was identified in the clinical ICU (23 isolates). About SMX-TMP, 65.71% of the strains were sensitive to increased exposure, 5.71% were fully sensitive and 28.57% were resistant. A profile of strains predominantly sensitive to levofloxacin was observed (91.49%), with 5.71% of the isolates proving sensitive by increasing exposure and 2.85% proving resistant. Women were more affected (57.69%). The average age was 54.33 years. Patients undergoing HD during the infection accounted for 53.84% of the profile obtained, while the use of MV occurred in around 69.23% of those infected. All patients had previously used antimicrobials. 19 patients (69.23%) died and only 7 were discharged from hospital (30.76%). **Conclusion:** With the findings, it was possible to determine a predominant profile of critically ill patients, with greater involvement of the respiratory tract. We also identified considerable rates of resistance to SMX-TMP, as well as an association between S. maltophilia infection and death.

Key-words: *Stenotrophomonas maltophilia*; Infeccion; Sulfamethoxazole/trimethoprim; Levofloxacin; Intensive care unit

Características microbiológicas e perfil clínico de infecções por *Stenotrophomonas maltophilia* em um hospital de ensino do nordeste brasileiro

Resumo

Objetivo: elucidar características microbiológicas e clínicas de pacientes acometidos por infecção causada por *S. maltophilia* em um hospital terciário do Nordeste brasileiro. **Metodologia:** O trabalho consistiu em um estudo retrospectivo, que analisou as amostras microbiológicas de janeiro de 2022 a setembro de 2023 do setor de microbiologia do Hospital Universitário Walter Cantídio, Fortaleza, Ceará. Foram determinados a prevalência de infecções causadas por *S. maltophilia*, juntamente com a epidemiologia e o perfil de sensibilidade antimicrobiana ao Sulfametoxazol/trimetoprima (SMX-TMP) e levofloxacino. Foram identificadas características clínicas dos pacientes acometidos, como o uso de ventilação mecânica (VM), realização de hemodiálise (HD), uso prévio de antimicrobianos e o desfecho desses pacientes. **Resultados:** A prevalência de infecções por *S. maltophilia* foi de 1,79% no período (35 amostras positivas e 26 pacientes acometidos). Dos isolados clínicos positivos, obteve-se predominância do trato respiratório, com 23 amostras (61,43%) de aspirado traqueal e 5 amostras referentes a lavado broncoalveolar (14,57%). O maior número de amostras positivas foi identificado na UTI clínica (23 isolados). Em relação ao SMX-TMP, 65,71% das cepas apresentaram-se sensíveis aumentando exposição, 5,71% mostraram-se plenamente sensíveis, e 28,57% dos isolados mostraram-se resistentes. Observou-se um perfil de cepas predominantemente sensíveis ao levofloxacino (91,49%), com 5,71% dos isolados mostrando-se sensíveis aumentando exposição e 2,85% apresentaram-se resistentes. Mulheres foram mais afetadas (57,69%). A média de idade foi 54,33 anos. Pacientes realizando HD durante a infecção, representaram 53,84% do perfil obtido, já o uso de VM ocorreu em cerca 69,23% dos infectados. Todos os pacientes usaram previamente antimicrobianos. Foi constado evolução para óbito em 19 pacientes (69,23%) e apenas 7 indivíduos receberam alta hospitalar (30,76%). **Conclusão:** Com os achados, foi possível determinar um perfil predominante de pacientes críticos, com maior acometimento do trato respiratório. Identificou-se, ainda, taxas consideráveis de resistência ao SMX-TMP, bem como uma associação de infecção por *S. maltophilia* com óbito.

Palavras-chave: *Stenotrophomonas maltophilia*; Infecção; Sulfametoxazol/trimetoprima; Levofloxacino; Unidade de terapia intensiva.

Introduction

Healthcare-associated infections (HAIs) are the most common adverse events in healthcare delivery, directly affecting patient safety and significantly contributing to morbidity, mortality, and financial costs[1,2].

In this context, gram-negative bacteria are considered a global health problem due to the selection of multi- and pan-resistant strains, substantially impacting the morbidity and mortality of hospitalized patients, especially those admitted to intensive care units (ICUs), where they are the leading cause of ventilator-associated pneumonia and bloodstream infections[3-5].

Two major groups of gram-negative microorganisms stand out: Enterobacterales and non-fermenting bacteria (NFB). Despite the lower incidence of NFB in clinical isolates compared to Enterobacterales, these agents are responsible for causing severe infections and possess intrinsic resistance to a wide range of antimicrobials[6,7]. In this context, the species Stenotrophomonas maltophilia, an aerobic NFB, deserves special attention due to its multidrug-resistant profile and opportunistic nature[8,9].

The increasing incidence of nosocomial and community-acquired infections caused by S. maltophilia in recent years has led the World Health Organization to recognize it as an underestimated multidrug-resistant microorganism in hospital settings[10,11]. As an organism that can easily be isolated from the environment, it is commonly found in healthcare facilities (e.g., faucets, dialysis machines, nebulizers, respiratory circuits), presenting a major challenge for immunocompromised patients (such as those with neutropenia or who have undergone transplantation), patients on hemodialysis, as well as individuals with prolonged ICU stays, mechanical ventilation, and broad-spectrum antibiotic use[12,13].

Intrinsically resistant to several antimicrobials, this phenomenon is based on various resistance mechanisms, such as the production of penicillinase and cephalosporinase, production of aminoglycoside-modifying enzymes[14], and an efflux pump system[15]. The continuous emergence of multidrug-resistant S. maltophilia isolates has presented significant challenges.

The main treatment regimens consist of sulfamethoxazole-trimethoprim (SMX-TMP), a drug with a convincing historical evidence base. When toxicity or allergies prevent its use, levofloxacin (750 mg/day) emerges as a therapeutic option. Minocycline, tigecycline, cefiderocol, and combination therapies with ceftazidime/avibactam and aztreonam are alternative regimens[11]. With limited treatment options and high rates of intrinsic resistance, studies aiming to understand the epidemiological profile of infections caused by this pathogen are increasingly necessary[16].

In Brazil, there are still few studies outlining the microbiological and clinical characteristics of S. maltophilia infections. Rodrigues and colleagues[17] highlighted high sensitivity rates to SMX-TMP in samples from patients at a teaching hospital in southeastern Brazil, though resistant strains had already been identified. In the South, a study conducted with clinical isolates from a pediatric hospital showed a resistance profile of approximately 20% to SMX-TMP[18]. From the perspective of northeastern Brazil, a retrospective study emphasized the sensitivity of all clinical samples (94 isolates) to SMX-TMP[19]. However, as a limitation, this study analyzed data from 2008 to 2012, not reflecting the current microbiological profile.

Due to the lack of recent studies that, in addition to sensitivity profiles, also identify clinical characteristics of patients affected by S. maltophilia infections, the present work aimed to establish the clinical and microbiological profile of infections caused by S. maltophilia in a tertiary hospital in northeastern Brazil.

Methods

Study Type

This is a descriptive study based on retrospective data collected from January 2022 to September 2023.

Research Location

The study was conducted at Walter Cantídio University Hospital, located in Fortaleza, Ceará, comprising Clinical and Post-Surgical Intensive Care Units (ICU), medical wards 2A and 2B, surgical wards 1 and 2, transplant units (kidney and liver), oncohematology unit (medical clinic 1), Bone Marrow Transplant Unit (BMT), and a pediatric ward.

Study Population

The inclusion criteria for analyzing the epidemiological profile and microbiological characteristics were positive samples for S. maltophilia growth from adult patients (over 18 years) hospitalized at Walter Cantídio University Hospital between January 2022 and September 2023, as confirmed by the hospital's Microbiology Laboratory.

Bacterial Isolation and Antimicrobial Susceptibility Testing

The patients' biological materials were analyzed at the institution's Microbiology Laboratory, where microorganism identification was carried out using the automated VITEK® 2 system (BioMérieux®, Marcy-l'Etoile, France), which uses the OBSERVA system for data archiving. The Antimicrobial Susceptibility Testing (AST) was performed according to the BrCAST (2023) breakpoints for SMX-TMP and CLSI (Clinical and Laboratory Standard Institute, 2023) breakpoints for levofloxacin, using the disk diffusion method. SMX-TMP is the only therapeutic option available for susceptibility testing according to BrCAST (2023)[20]. For other antimicrobials used in treatment, breakpoints were based on CLSI (2023)[21]. (See Table 1 in the supplementary material). Control strains E. coli ATCC® 25922 and P. aeruginosa ATCC® 27853 were used as method controls.

Epidemiological and Clinical Variables of the Study

The variables analyzed included the institutional prevalence of S. maltophilia infections in the hospital's clinical units, the infection sites, demographic profile (gender and age), presence of invasive mechanical ventilation, hemodialysis during S. maltophilia isolation, prior use of antimicrobials (up to 30 days before the isolation of S. maltophilia strains), the selected treatment (SMX-TMP or levofloxacin), and individual outcomes (death, discharge, hospital transfer).

Statistical Analysis

Data collection and analysis were performed using Microsoft Excel® 2023, maintaining a confidential database. Descriptive statistical analysis (mean, standard deviation) was conducted based on relative frequency. Fisher's exact test was used to compare categorical variables, with statistical significance considered when $p \leq 0.05$.

Ethical Aspects

The study was conducted in accordance with the guidelines and regulations for research involving human subjects (Resolution 466/12, National Health Council) and was approved by the hospital's Research Ethics Committee (Approval number: 5409579).

Results

Institutional Microbiological and Epidemiological Profile of *S. maltophilia Infections*

Between January 2022 and September 2023, a total of 9,051 clinical isolates were analyzed in the hospital's microbiology department, of which 1,928 (21.60%) tested positive for microorganism growth. Among these, 35 samples (1.79%) were positive for S. maltophilia growth. Regarding the number of affected patients, 7 patients had more than one positive sample (totaling 16 isolates; two patients tested positive for S. maltophilia three times, while the others had two positive isolates). Therefore, the final number of individuals included in the analysis was 26 patients.

Of the clinical isolates evaluated, 23 samples (61.43%) were isolated from tracheal aspirates (TA) of infected patients. To a lesser extent, 5 samples were from blood cultures (14.57%) and 5 from bronchoalveolar lavage (BAL) (14.57%). Additionally, 2 positive isolates were identified from urine cultures, representing 9.74% of the positive samples (Table 1).

The highest number of positive isolates was identified in the clinical ICU, with 23 samples (65.71%). Following that, the CMI units, surgical ICU, and CM2A unit each had 3 positive samples, representing 8.57% of infections in each unit. Lastly, with only 1 positive sample (2.9%) each, were the hemodialysis service, the surgical transplant ward, and the Bone Marrow Transplant Unit (BMT).

Table 1: Topography of Infections Caused by *Stenotrophomonas maltophilia*

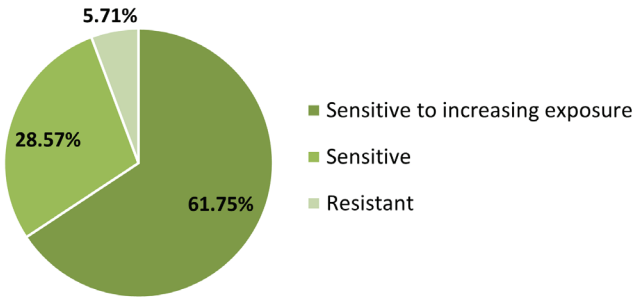
Infection Topography	
Tracheal Aspirate (n) (%)	23 (61.43%)
Blood (n) (%)	5 (14.57%)
Bronchoalveolar Lavage (n) (%)	5 (14.57%)
Urine (n) (%)	2 (9.74%)
Total Number of Isolates (n) (%)	**35 (100%)**
Institutional Epidemiological Profile	
Clinical Intensive Care Unit (n) (%)	23 (65.71%)
Surgical Intensive Care Unit (n) (%)	3 (8.57%)
Internal Medicine Clinic 1	3 (8.57%)
Internal Medicine Clinic 2A	3 (8.57%)
Surgical Clinic 1	1 (2.9%)
Transplant	1 (2.9%)
Hemodialysis Service	1 (2.9%)
Bone Marrow Transplant	1 (2.9%)

Self-authored;

Sensitivity Profile of S. maltophilia Strains

The sensitivity profile of the S. maltophilia strains can be observed in Figures 1 and 2. Regarding sulfamethoxazole-trimethoprim (SMX-TMP), approximately 65.71% of the strains (23 samples) exhibited intermediate susceptibility (I), 5.71% (2 samples) were fully sensitive, and 28.57% of the isolates (10 samples) were resistant.

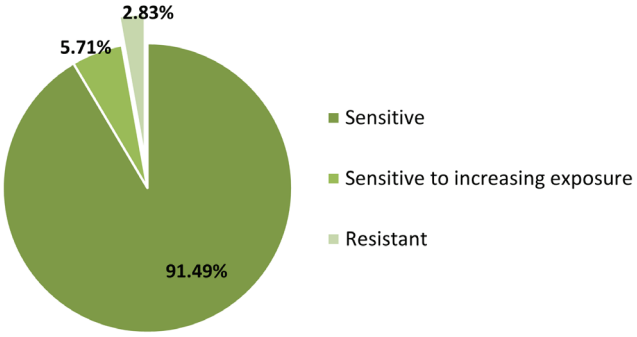
Figure 1: Sensitivity Profile of *S. maltophilia* Strains to SMP/TMX



BRCast 2023 breakpoints; SMP-TMX – Sulfamethoxazole-Trimethoprim; Self-authored.

In contrast, a predominantly sensitive profile to levofloxacin was observed, with approximately 91.49% of the isolates (32 samples) being fully sensitive. Only 5.71% (2 samples) showed intermediate susceptibility, and just 2.85% (1 sample) was resistant. The graphical representation of this data can be seen in Figure 2.

Figure 2: Sensitivity Profile of *S. maltophilia* Strains to Levofloxacin



Self-authored;

4.4 Clinical Profile of Patients Infected with *S. maltophilia*

The retrospective analysis of the study identified 26 patients affected by S. maltophilia infections during the evaluation period. Women were more affected, comprising 57.70% of the study population (15 patients), while men represented 42.30% (11 patients). Additionally, patient outcomes were analyzed, revealing that 19 patients (73.08%) with S. maltophilia infections progressed to death, while only 7 individuals (26.92%) were discharged from the hospital (Table 2).

The study analyzed the presence of clinical characteristics and their possible relationship with mortality among the selected patients (Table 3). Hemodialysis (HD) was performed in 53.84% of the cases (14 individuals), with 13 of these patients progressing to death. Mechanical ventilation (MV) was used in approximately 69.23% of the infected patients (18 individuals), with 17 resulting

in death. All patients included in the study (26 individuals) had previously used antimicrobials. It is notable that 21 patients were treated with levofloxacin as guided antimicrobial therapy, five patients did not start treatment due to therapeutic limitations, and no patients received SMX-TMP as antimicrobial therapy.

Table 2: Demographic Characteristics of Patients Affected by S. maltophilia Infections

Demographic Characteristics	
Men n (%)	11 (42.30%)
Women n (%)	15 (57.70%)
Age in years ± SD	54.33 ± 14.66
Total number of patients	26 (100%)
Outcome:	
Death n (%)	19 (73.08%)
Discharge	7 (26.92%)

Self-authored; SD – Standard Deviation.

Table 3: Clinical Characteristics Related to Patients Infected with S. maltophilia with Mortality Outcome

Variables	**n (%)**	**Mortality Outcome**		**p Value**
		Yes	**No**	
Patients on HD	14 (53.84%)	13	1	0.02
Patients on MV	18 (69.23%)	17	1	0.004
Previous Use of Antimicrobials	26 (100%)	19	7	0.01
Chosen Antimicrobial Therapy: Levofloxacin	21 (80.76%)	5	16	-

p-value < 0.05 foi considerado significante após teste exato de Fisher.

Discussion

Among non-fermenting gram-negative bacteria (NFGNB), infections caused by S. maltophilia rank third, behind only P. aeruginosa and A. baumannii infections.[22] As an opportunistic pathogen, studies report a prevalence rate that does not exceed 2% in clinical isolates from hospital settings.[19,22,23] The findings of this study align with this literature, as a similar prevalence range was observed.

Several studies have highlighted the higher infection rates of S. maltophilia in respiratory tract samples due to its ability to colonize epithelial cells and cause bacteremia, especially in immunocompromised patients, through contamination of hospital equipment.[24-26] As expected, the present study found a predominance of isolates from the respiratory tract (tracheal aspirates and bronchoalveolar lavage), with a smaller contribution from blood cultures, confirming the microorganism's ability to contaminate nosocomial[8] devices.

The high levels of intrinsic antimicrobial resistance, coupled with limited therapeutic options, make the sensitivity profile of S. maltophilia strains a critical aspect of hospital epidemiological[27] studies. In this study, a significant resistance rate to SMX-TMP, the first-line treatment, was observed. Additionally, intermediate susceptibility (I) was found in more than 50% of the clinical isolates. This concept suggests that higher concentrations of the antimicrobial, either by increasing the dose or prolonging infusion time, are necessary to achieve adequate concentrations and improve clinical outcomes.[20] However, higher doses may be associated with a greater risk of adverse effects, such as Clostridioides difficile infections, hepatotoxicity, and hematological events like agranulocytosis and hemolytic anemia.[28-30]

Fully sensitive strains to SMX-TMP were rare in this study. Silva[31] previously reported the emergence of resistant isolates to this treatment option in a tertiary hospital in Central Brazil, representing 7% (6 isolates) of the positive strains. Grácia and colleagues[32] also observed similar behavior in a southeastern Brazilian hospital (2 resistant isolates, 15% of the samples). In contrast, other studies conducted in Brazil report predominantly sensitive profiles to SMX-TMP[17,33], differing from our main findings. This resistance may be due to the excessive and irrational use of SMX-TMP, as well as mutational changes in resistant strains.

The levofloxacin sensitivity profile (a therapeutic option based on CLSI guidelines) in this study revealed highly sensitive strains, with over 90% of the clinical isolates being susceptible. Other studies in Brazil also identified a favorable sensitivity profile, supporting the use of levofloxacin for treating S. maltophilia infections. Braga[34] demonstrated a similar profile, with around 95% of clinical isolates being sensitive to levofloxacin. Similarly, Rodrigues and colleagues[17] reported approximately 97% sensitivity in their samples. These findings emphasize the importance of considering levofloxacin as a viable treatment option, especially given the increasing resistance to SMX-TMP.

On a global scale, the literature highlights a predominantly sensitive profile for SMX-TMP and levofloxacin, with resistance rates of approximately 10% for both treatments[35,36]. Regional variations in microbial resistance may account for differences in susceptibility to these antimicrobials.

Infections caused by *S. maltophilia* are frequently associated with critically ill patients, especially in intensive care units (ICUs), where a range of risk factors, such as prolonged hospital stays, advanced age, and life-threatening[37-39] conditions, predispose this population to such infections. In our study, a predominant profile of ICU patients was identified, comprising more than 70% of the individuals. Additionally, the average age of the patients showed a trend towards an elderly profile, with women being more affected, which is consistent with previous[23,31] findings.

The use of mechanical ventilation (MV), hemodialysis (HD), and invasive devices are also linked to increased severity and mortality in patients with *S. maltophilia*[40] infections. The majority of participants in our study were on MV and undergoing HD during the infection period, aligning with findings from Silva[31] in a teaching hospital in Central Brazil. Another critical factor associated with the prevalence of *S. maltophilia* infections and mortality is prior antimicrobial[41,42] use. All selected patients had undergone broad-spectrum antimicrobial treatment within 30 days before the isolation of *S. maltophilia* strains, highlighting the importance of implementing rational antimicrobial use policies in hospital settings.

All antimicrobial therapies targeting *S. maltophilia* infections in this study were carried out with levofloxacin. Institutional difficulties in acquiring intravenous SMX-TMP for treating critically ill patients contributed to the choice of levofloxacin, which was readily available in intravenous form. These findings underscore the importance of this study in identifying a concerning resistance profile to SMX-TMP and highlighting the potential for empirical

institutional coverage using levofloxacin, especially in the context of a more precise antimicrobial therapy approach, facilitated in part by the involvement of clinical pharmacists.

Furthermore, patient outcomes were assessed, and prior studies have already associated factors such as previous antimicrobial[42] use, ICU[43] admission, and MV[40] use with mortality in patients infected with *S. maltophilia*. In our study, more than half of the patients succumbed to the infection. Silva[31] had previously reported a mortality rate of 62.5% in Brazil. Globally, studies cite mortality rates ranging from 44% to 65% in patients infected with *S. maltophilia*[44,45].

Finally, the main limitations of this study include its retrospective nature, the small number of selected patients, and the short analysis period, making it difficult to definitively associate *S. maltophilia* infections with mortality in critically ill patients. Additionally, since this study was conducted in only one institution in northeastern Brazil, further data are needed to better correlate these findings with those from other regions in the country.

Conclusion

This study has provided unprecedented insights into the increasing resistance to SMX-TMP in clinical isolates from this institution. It also identified the clinical characteristics of affected patients, reinforcing the need for additional studies to better understand the impact of these characteristics and others that may be associated with the lethality of *S. maltophilia* infections.

Funding Sources

No funding was received for this study.

Contributors

JA contributed to the project design, development, and review. RM contributed to the writing and review. CC contributed to the writing and review. LF contributed to the development and review. GM contributed to the development and review. MC contributed to the development and review. IF contributed to the development and review. PC contributed to the project design, development, and review. AB contributed to the project design, development, and review.

Conflict of Interest Declaration

The authors declare no conflicts of interest regarding this article.

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