3-2022

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Publication Info

Published in *Journal of Global Antimicrobial Resistance*, Volume 28, 2022, pages 282-287.

Journal of Global Antimicrobial Resistance 28 (2022) 282–287

Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

journal homepage: www.elsevier.com/locate/jgar

Real-world, multicentre evaluation of the incidence and risk factors for non-susceptible *Stenotrophomonas maltophilia* isolates

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ARTICLE INFO

Article history:
Received 20 January 2021
Revised 15 June 2021
Accepted 3 February 2022
Available online 9 February 2022

Edited by: Dr Fabio Arena

Keywords:
Stenotrophomonas maltophilia
Resistance
Non-susceptible
Trimethoprim-sulfamethoxazole
Levofloxacin

ABSTRACT

Background: *Stenotrophomonas maltophilia* is a cause of infection most commonly in the opportunistic host. Trimethoprim-sulfamethoxazole and levofloxacin are considered first-line treatment agents. With reports of increasing resistance to these first-line agents, it is important to determine risk factors associated with a non-susceptible isolate.

Methods: This was a real-world, multicentre, retrospective case-control study from five centres in the southeast United States evaluating *S. maltophilia*. The primary outcome was risk factors associated with non-susceptibility of *S. maltophilia* isolates to ≥1 antimicrobial agents. Secondary outcomes include incidence of *S. maltophilia* non-susceptibility, all-cause mortality, and 30-day readmission rates.

Results: There were 325 patients included in the study. For the primary outcome, the only factor associated with non-susceptibility per univariate analysis was isolation from urine culture (13.3% vs. 5.4%; $P = 0.014$), whereas the presence of mechanical ventilation (37.7% vs. 21.5%) and intensive care unit admission (35.3% vs. 18.4%) were associated with susceptibility ($P < 0.001$). For the secondary outcomes, non-susceptibility was present in 49% of isolates with 43 of 325 (13.2%), 53 of 324 (16.4%), and 105 of 172 (61%) to TMP-SMX, levofloxacin, and ceftazidime, respectively. Resistance to chloramphenicol and tigecycline was observed among 5/26 and 11/16 of tested isolates, respectively. Sixty-six patients (20%) experienced all-cause, inpatient mortality (18% susceptible vs. 23% non-susceptible; $P = 0.280$) and 44 patients (17%) were readmitted within 30 days of discharge (16% susceptible vs. 18% non-susceptible; $P = 0.673$).

Conclusion: *S. maltophilia* non-susceptibility had a prevalence of ~50% to at least one first-line or commonly used agent. More research is needed to delineate risk factors for non-susceptible isolates.

1. Introduction

Multidrug-resistant organisms (MDROs), including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and certain Gram-negative bacilli, are emerging worldwide health concerns and associated with increased mortality as well as cost to health systems. The CDC estimates that nearly 3 million people in the United States acquire an infection from bacteria that have resistance to at least one guideline-recommended antibiotic. These infections in turn extend hospital stays, require more costly care, and increase morbidity and mortality [1].

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https://doi.org/10.1016/j.jgar.2022.02.001

Stenotrophomonas maltophilia is an aerobic, nonfermenting, Gram-negative bacillus, generally isolated from environmental sources, mainly soil and water [2]. Infections are most commonly opportunistic and associated with the respiratory tract; however, *S. maltophilia* is responsible for various other infections. Risk factors for infection due to *S. maltophilia* include underlying malignancy, presence of indwelling devices, chronic respiratory disease, immunocompromised host, prior use of antibiotics, and long-term hospitalization or intensive care unit (ICU) stay [3].

S. maltophilia is intrinsically resistant to many antibiotics. This resistance is hypothesised to be due to low membrane permeability and the presence of multidrug-resistance efflux pumps that are characteristic for this organism [3,4]. Beta-lactams, including carbapenems, as well as beta-lactamase inhibitors are rendered resistant due to the low membrane permeability. Due to a historically high susceptibility rate, trimethoprim-sulfamethoxazole (TMP-SMX) is the treatment of choice for *S. maltophilia* [3]. However, other antimicrobials with in vitro activity against *S. maltophilia* including tigecycline, ceftazidime, levofloxacin, polymyxin B, and ticarcillin-clavulanate have been explored for resistant isolates [4,5]. We have previously reported on increasing resistance rates to *S. maltophilia* at one of our institutions where susceptibility to TMP-SMX and levofloxacin, first-line treatment options, were 78% and 80%, respectively. One-third of respiratory isolates from this group showed non-susceptibility to 1 or more first-line agents [6].

There is an abundance of evidence on risk factors for acquiring MDROs, such as MRSA and *Pseudomonas aeruginosa*; however, there are few, if any, studies that have investigated factors associated with non-susceptible (resistant to TMP-SMX, levofloxacin, or both) isolates of *S. maltophilia.* Montero et al. found that the presence of chronic obstructive pulmonary disease (COPD), mechanical ventilation, haemodialysis, and a history of recent antibiotic use were statically significant independent risk factors for MDR *P. aeruginosa* [7]. The 2016 Infectious Diseases Society of America guidelines for hospital-acquired and ventilator-associated pneumonia cite antibiotic use within 90 days, renal replacement therapy, extended hospital stay, and septic shock as risk factors associated with MDR pathogens [8]. Identification of potential risk factors for non-susceptible *S. maltophilia* could lead to improved empiric antibiotic selection and decreased morbidity and mortality. The primary objective of this study was to identify risk factors associated with *Stenotrophomonas maltophilia* non-susceptibility to one or more antimicrobial agents tested. The secondary objectives were to evaluate the incidence of non-susceptible *Stenotrophomonas maltophilia* isolates, as well as all-cause mortality and 30-day hospital readmission rates associated with *Stenotrophomonas maltophilia* infection.

2. Material and methods

2.1. Data source

This multicentre, retrospective case-control study included patients who had positive cultures for *S. maltophilia* from 1 October 2015 through 30 September 2018. Only the first positive culture per patient within 12 months during the study timeframe was included. Patients who had positive cultures with *S. maltophilia* without laboratory susceptibility reports or positive *S. maltophilia* cultures obtained at an outside facility or outpatient setting, including the emergency department, were excluded. Patients were divided into two groups: non-susceptible *S. maltophilia* and susceptible *S. maltophilia*. Non-susceptible *S. maltophilia* was defined as presence of any resistance (intermediate or resistant susceptibility) for any antibiotic tested by the Clinical and Laboratory Standards Institute (CLSI) on the susceptibility panel for the year the isolate was collected [9]. Isolate susceptibility was tested using VITEK2, Microscan, Etest, or disk diffusion based on microbiology testing protocols and available antimicrobials on the automated testing panels.

2.2. Measures

Baseline demographics, antibiotic allergies (with reactions), and comorbid conditions were collected on each patient. Additional data assessed up to 12 months before index culture included prior positive *S. maltophilia* culture and susceptibility, receipt of antibiotics, ICU or long-term care admission within 90 days of index culture, current or previous mechanical ventilation (within 90 days of index culture), or receipt of immunosuppressive therapy. Microbiology data were collected for each isolate, including culture source, detailed susceptibility, and method for determining susceptibility. Overall treatment characteristics, including medication for acute treatment, presence of ICU stay, hospital length of stay, discharge disposition, and readmission within 30 days were also assessed. Specific risk factors that have been previously identified for isolation of *S. maltophilia* were also collected, including underlying malignancy, presence of indwelling devices, chronic respiratory disease, immunocompromised host, prior use of antibiotics, and long-term hospitalization or ICU stay [3].

2.3. Outcomes

The primary outcome was evaluation of risk factors associated with non-susceptibility of *S. maltophilia* isolates to one or more antimicrobial agents. Secondary outcomes include incidence of *S. maltophilia* non-susceptibility, all-cause, inpatient mortality associated with any *S. maltophilia* infection, and 30-day hospital readmission rates associated with any *S. maltophilia* infection.

2.4. Statistical analysis

Statistical analysis was performed using SPSS software version 25.0 (IBM). Categorical data were analysed using χ^2 or Fisher's exact test, and continuous data were analysed using Student's *t* test or Mann-Whitney U test, as appropriate. An alpha of 0.05 was deemed statistically significant. Variables that had a *P*-value <0.2 on univariate analysis or deemed clinically relevant by the investigators were evaluated for inclusion in a multivariable logistic regression model to determine risk factors for non-susceptible isolates of *S. maltophilia*. Variables were formally included into the model at an n:k ratio of 10:1, and the model was evaluated for accuracy of predictive capability.

3. Results

3.1. Baseline characteristics

Five institutions geographically spread through the southeast United States contributed a total of 325 patients to this study. Baseline demographics were similar between groups (Table 1). Most patients were male (59%) and were a median age of 62 (IQR 52–72) years. Just over half of the patients were Caucasian (54%), followed by African American (37%). There were 82 (25%) patients who had an allergy to an antibiotic documented in the medical record, including 16 (10%) to fluoroquinolones and 31 (19%) to sulfonamides. There were no statistically significant differences in baseline comorbid conditions, but, notably, more than 50% of patients were currently mechanically ventilated at the time of positive *S. maltophilia* culture. Additionally, 114 (35%) patients had underlying COPD or other structural lung disease at the time of positive culture.

Table 1
Baseline demographics and comorbid conditions in patients culture-positive for *S. maltophilia*

Variable No. (%) or median [IQR]	Total (N = 325)	Susceptible *S. maltophilia* (n = 167)	Non-susceptible *S. maltophilia* (n = 158)	P-value
Practice site				
Site 1	38 (11.7)	15 (9)	23 (14.6)	0.118
Site 2	107 (32.9)	74 (44.3)	33 (20.9)	<0.001
Site 3	56 (17.2)	43 (25.7)	13 (8.2)	<0.001
Site 4	4 (1.2)	1 (0.6)	3 (1.9)	0.359
Site 5	120 (36.9)	34 (20.4)	86 (54.4)	<0.001
Age, years	62 [52–72]	63 [50–72]	61 [52.75–72]	0.518
Sex, male	193 (59.4)	101 (60.5)	92 (58.2)	0.680
Race				
Caucasian	176 (54.2)	90 (53.9)	86 (54.4)	0.922
African American	119 (36.6)	61 (36.5)	58 (36.7)	0.973
Asian	4 (1.2)	3 (1.8)	1 (0.6)	0.623
Hispanic	13 (4)	5 (3)	8 (5.1)	0.341
Other	12 (3.7)	7 (4.2)	5 (3.2)	0.624
eGFR, mL/min				
≥60 mL/min	181 (56.7)	84 (51.5)	97 (62.2)	0.055
<60 mL/min (n = 138)	29 [18–41.25]	28 [19–43]	32 [18–41]	0.724
Antibiotic allergy				
No allergy	243 (74.8)	126 (75.4)	117 (74.1)	0.772
Sulpha allergy	31 (19.3)	15 (16)	16 (23.9)	0.209
Rash/hives	12 (38.7)	7 (46.7)	5 (31.3)	0.379
Other sulpha reactions	19 (61.3)	8 (53.3)	11 (68.8)	0.379
Comorbidities				
COPD or structural lung disease	114 (35.1)	59 (35.3)	55 (34.8)	0.922
Chronic systemic corticosteroid use (>2 weeks)	53 (16.3)	25 (15)	28 (17.7)	0.502
Receiving immunomodulators	17 (5.2)	8 (4.8)	9 (5.7)	0.714
Cystic fibrosis	2 (0.6)	0 (0)	2 (1.3)	0.236
ESRD	36 (11.1)	15 (9)	21 (13.3)	0.216
Documented liver disease	22 (6.8)	11 (6.6)	11 (7)	0.893
Active cancer	45 (13.8)	22 (13.2)	23 (14.6)	0.718
HIV/AIDS	7 (2.2)	2 (1.2)	5 (3.2)	0.272
Antibiotic exposure	208 (64)	109 (65.3)	99 (62.7)	0.624
ICU admission	88 (27.1)	59 (35.3)	29 (18.4)	0.001
Transfer to LTAC	57 (17.5)	27 (16.2)	30 (19)	0.504
Current mechanical ventilation	166 (51.1)	91 (54.5)	75 (47.5)	0.206
History of mechanical ventilation	97 (29.8)	63 (37.7)	34 (21.5)	0.001

AIDS, acquired immunodeficiency syndrome; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HIV, human immunodeficiency virus; ICU, intensive care unit; IQR, interquartile range; LTAC, long-term acute care facility.

3.2. Primary and secondary outcomes

There were 167 (51%) unique patients who had a susceptible isolate of *S. maltophilia*, whereas 158 (49%) patients possessed a non-susceptible *S. maltophilia* isolate. Two of five sites had significantly more susceptible *S. maltophilia* isolates than non-susceptible isolates, but one site had significantly more non-susceptible *S. maltophilia* isolates than susceptible. For the primary outcome, prior ICU admission 90 days from index culture (35% susceptible [59/167] vs. 18% non-susceptible [29/158]; $P = 0.001$) and prior mechanical ventilation 90 days from index culture (38% susceptible [63/167] vs. 22% non-susceptible [34/158]; $P = 0.001$) were statistically significant for culturing susceptible isolates of *S. maltophilia*. There were 53 (16%) patients with no comorbid conditions, and 68 patients (21%) with no known risk factors for culturing a non-susceptible *S. maltophilia* isolate based on risk factors identified in prior literature for culturing drug-resistant organisms [3]. Statistically significantly more patients with susceptible *S. maltophilia* were located in the ICU at the time of culture than patients with non-susceptible *S. maltophilia* (74% [123/167] vs. 57% [90–158]; $P = 0.002$). Although not significant, patients with susceptible *S. maltophilia* spent more time within the ICU than those with non-susceptible isolates (14 days vs. 11.5 days; $P = 0.069$).

A majority of *S. maltophilia* cultures were respiratory or sputum cultures (76%); however, the organism was also cultured from urine (9%), wounds (9%), blood (4%), and other sites (2%) (Table 2). Statistically significantly more susceptible *S. maltophilia* were isolated from the respiratory tract than non-susceptible (82% [137/167] vs. 70% [111/158]; $P = 0.013$), whereas more non-susceptible isolates were cultured from the urine (13% [21/158] vs. 5% [9/167]; $P = 0.014$). Additionally, there was no difference in the proportion of polymicrobial cultures between groups (56% susceptible [94/167] vs. 60% non-susceptible [94/158]; $P = 0.559$). To determine susceptibility of available agents against *S. maltophilia*, VITEK2 was used most commonly (61%–94%), followed by Microscan (7%–38%). Disk diffusion and gradient strip testing were also used to determine susceptibility manually to available antibiotics. VITEK2 was used by sites 3, 4, and 5; Microscan was used by sites 1 and 2; gradient strip testing was used by site 4 for specific antibiotics; and disk diffusion was used by sites 3 and 4 for specific antibiotics. Isolates were tested against TMP-SMX, levofloxacin, ceftazidime, polymyxin B, chloramphenicol, and tigecycline. The percentage of isolates that tested susceptible varied with 87% susceptible (282/325) to TMP-SMX, 84% susceptible (271/324) to levofloxacin, and 39% susceptible (67/172) to ceftazidime. For polymyxin B, 6/6 isolates tested susceptible, and for chloramphenicol and tigecycline 21/26 and 5/16 tested susceptible, respectively. There were 158/325 (48.6%) isolates that were intermediate or resistant to more than one antimicrobial, and 22/325 (6.8%) isolates resistant to both TMP-SMX and levofloxacin. Most patients were treated with levofloxacin (52%, 170/325) or TMP-SMX (32%, 105/325). Statistically significantly more patients with isolates susceptible to both levofloxacin and TMP-SMX received levofloxacin compared to non-susceptible (59% [98/167] vs. 46% [72/158]; $P = 0.018$).

Overall, 127 patients (39%) were discharged home, and 81 (25%) were transferred to another institution. Sixty-six patients (20%) experienced all-cause, inpatient mortality (30/167 [18%] susceptible

Table 2
Location of cultured *S. maltophilia* isolates

Variable presented as no. (%)	Total (N = 325)	Susceptible *S. maltophilia* (n = 167)	Non-susceptible *S. maltophilia* (n = 158)	P-value
Culture type*				
Blood	12 (3.7)	7 (4.2)	5 (3.2)	0.624
Respiratory or sputum	248 (76.3)	137 (82)	111 (70.3)	0.013
Wound	28 (8.6)	11 (6.6)	17 (10.8)	0.180
Urine	30 (9.2)	9 (5.4)	21 (13.3)	0.014
Other	7 (2.2)	3 (1.8)	4 (2.5)	0.717
Sterile site	12 (3.7)	7 (4.2)	5 (3.2)	0.624
Polymicrobial culture	188 (57.8)	94 (56.3)	94 (59.5)	0.559

* *S. maltophilia* was not isolated in more than one location. Polymicrobial cultures were defined as *S. maltophilia* and a different organism cultured from the same location.

Table 3
Variables significant on univariate analysis with predictive value for determining non-susceptible *S. maltophilia* isolates

Variable (n = 319)	Unadjusted				Adjusted				
	Exp(B)	Lower 95% CI	Upper 95% CI	P-value	B	Exp(B)	Lower 95% CI	Upper 95% CI	P-value
Practice site	0.655	0.524	0.820	<0.001	-0.332	0.718	0.551	0.935	0.014
eGFR ≥60 mL/min	1.546	0.990	2.416	0.056	0.485	1.624	1.015	2.601	0.043
Previous ICU admission	0.412	0.246	0.687	0.001	-0.323	0.724	0.341	1.535	0.399
Previous mechanical ventilation	0.453	0.277	0.740	0.002	-0.352	0.704	0.347	1.429	0.331
Respiratory culture	0.517	0.307	0.872	0.013	-0.663	0.515	0.181	1.462	0.213
Wound culture	1.710	0.775	3.775	0.184	-0.267	0.765	0.204	2.867	0.691
Urine culture	2.691	1.193	6.072	0.017	0.184	1.203	0.324	4.459	0.783

CI, confidence interval; ICU, intensive care unit.

vs. 36/158 [23%] non-susceptible; $P = 0.280$). The median length of total hospital stay was 19 (IQR 11–38) days, with a longer stay experienced by patients with non-susceptible *S. maltophilia* isolates (20.5 days vs. 18 days; $P = 0.528$). Forty-four patients (17%) were readmitted within 30 days of discharge (16% susceptible [22/167] vs. 18% non-susceptible [22/158]; $P = 0.673$).

3.3. Logistic regression analysis

The following variables were entered into the logistic regression analysis: Estimated Glomerular Filtration Rate (eGFR) ≥60 mL/min, previous ICU admission, previous mechanical ventilation, respiratory culture, wound culture, and urinary tract culture; 319 patients were included with a 60% accuracy in predicting a susceptible *S. maltophilia* isolate and 67% accuracy in predicting a non-susceptible isolate (Table 3). In this second model, practice site and eGFR ≥60 mL/min remained statistically significant; practice site location was associated with susceptible isolates, and eGFR was associated with higher odds of non-susceptible isolates.

4. Discussion

4.1. Main findings of this study

S. maltophilia is an important pathogen in immunocompromised and other high-risk patient populations. Although most commonly associated with respiratory tract infections, other invasive infections such as bloodstream infections are increasing. A recent study found *S. maltophilia* to be the most common cause of carbapenem-resistant Gram-negative bacteremia. Even more surprising was that nearly half of these bacteremias were of community onset, occurring within 3 days of admission [10]. We found that 1 in 5 isolates included in our study had no hypothesised risk factor for nosocomial onset. Although known to have a high level of intrinsic resistance to many antimicrobials, resistance to commonly used first-line agents, such as TMP-SMX, is increasing [11,12]. Our results show that almost 50% of isolates were non-susceptible to one or more antimicrobials tested. More concerning is that the two agents considered first-line for treatment, levofloxacin and TMP-SMX, had susceptibilities of 84% and 87% in this cohort, respectively. Additionally, 6.8% of isolates were either intermediate or resistant to both TMP-SMX and levofloxacin, which is higher than reported in the SENTRY Surveillance Program [12]. As expected, many of these patients had baseline structural lung disease, were located in the ICU, and were mechanically ventilated. Levofloxacin was used for treatment in a majority of cases (52.3%), with TMP-SMX being the second most common (32.3%). The increased use of levofloxacin could be due to its use as common empiric therapy for hospital-acquired pneumonia, while also noting that ~20% of patients had a listed sulpha allergy.

The findings regarding non-susceptibility are concerning for a number of reasons. Due to the prevalence of *S. maltophilia*'s intrinsic resistance, it does not often meet consensus definitions of MDR bacteria. This prevents its inclusion often in national and international antimicrobial resistance surveillance studies, thus limiting trend assessment of resistance within first-line agents [10]. However, recently, the SENTRY Antimicrobial Surveillance Program specifically examined *S. maltophilia* isolates and reported a decrease in susceptibility to TMP-SMX over time with variance by geographic regions [12]. Additionally, of the 6450 isolates tested, resistance to both TMP-SMX and levofloxacin was reported to be 1.7%; however, this combination of resistance is increasing.

4.2. Other potential treatment options

Currently, there are limited Food and Drug Administration (FDA)–approved treatment options for *S. maltophilia*, especially non-susceptible strains. One previous therapeutic option, ticarcillin/clavulanate, is no longer being manufactured in the United States. Sulpha allergy was present in nearly 1 in 5 patients, further limiting first-line options for therapy. A recent article demonstrated that few older antimicrobials retained *in vitro* activity against *S. maltophilia* isolates with non-susceptibility to levofloxacin and/or TMP-SMX. Minocycline possessed the highest susceptibility rate against these isolates at 92.7%, but clinical outcome data remain sparse with this agent [13]. Conversely, a recent evaluation of *S. maltophilia* isolates ($n = 50$) exclusively from cancer patients demonstrated 98% susceptibility vs. TMP-SMX [14].

Therefore, it is possible that certain geographical regions or populations of patients may be associated with higher risk of non-susceptible strains to first-line agents. Data regarding risk factors for predicting non-susceptible *S. maltophilia* isolates are needed to ensure appropriate empiric therapy.

4.2. Recently approved antimicrobials with in vitro activity against S. maltophilia

Although a number of newer antimicrobials have been FDA approved in the last 10 years, primarily for pathogens such as MDR *P. aeruginosa* or carbapenem-resistant *Enterobacterales* (CRE), few have *in vitro* activity against *S. maltophilia*. Most approvals have been for beta-lactams, which are generally inactive against *S. maltophilia*. Two approved agents with in vitro activity against *S. maltophilia* are eravacycline and cefiderocol. Biagi et al. evaluated 14 isolates that were resistant to levofloxacin and/or TMP-SMX. The MIC_{50} and MIC_{90} for eravacycline were 2 mcg/mL and 8 mcg/mL, respectively [13]. Morrissey et al. demonstrated an MIC_{90} of 2 mcg/mL for eravacycline across 1210 respiratory, urinary, and intra-abdominal clinical *S. maltophilia* isolates across 36 countries. Only 41% of isolates would be susceptible at the current Enterobacterales breakpoint of 0.5 mcg/mL [15]. To date, there are few clinical outcome data available regarding eravacycline when treating *S. maltophilia* infections. The lack of outcome data coupled with higher MICs detected in vitro should provide clinicians pause when considering eravacycline.

Cefiderocol is a novel siderophore cephalosporin that chelates iron, facilitating its crossing of the outer membrane of a number of Gram-negative bacteria into the periplasmic space through an iron transport system known as the “trojan horse” [16]. It additionally possesses stability against a variety of serine and metalloenzyme beta-lactamases, which confers in vitro activity against a number of MDR Gram-negative bacteria, including *S. maltophilia*. Biagi et al. evaluated 37 *S. maltophilia* isolates not susceptible to levofloxacin and/or TMP-SMX for cefiderocol in vitro activity both alone and in combination with levofloxacin, minocycline, polymyxin B, and TMP-SMX. Cefiderocol was active against all 37 tested isolates (100%) alone and displayed synergy in 44%, 67%, 56%, and 67% of isolates when combined with levofloxacin, minocycline, polymyxin B, and TMP-SMX, respectively [17] Cefiderocol is currently FDA-approved for the treatment of complicated urinary tract infections and hospital-acquired bacterial pneumonia when limited options are available. It has been evaluated in the treatment of critically ill patients with carbapenem-resistant Gram-negative infections, including *S. maltophilia* [18]. Infections included pneumonia, bloodstream, or complicated UTI. The comparator group consisted of best available therapy (BAT) containing up to three antibiotics with activity vs. Gram-negative bacteria. Cefiderocol patients experienced higher numerical 28-day mortality vs. BAT (25% vs. 18%) that persisted until day 49 (34% vs. 18%). Deaths were primarily in patients with infections caused by *Acinetobacter* species, with only five patients infected with *S. maltophilia* evaluated, all in the cefiderocol arm who were being treated for nosocomial pneumonia [18]. All-cause mortality at end of study occurred in 4 of 5 patients (80%) while occurring in 2 of 3 patients (67%) who were not also co-infected with *Acinetobacter* species. Another recently published study evaluated cefiderocol vs. high-dose, extended-infusion meropenem for the treatment of Gram-negative nosocomial pneumonia, demonstrating noninferiority in terms of day 14 all-cause mortality with comparable tolerability (12.4% vs. 11.6%; 95% $P = 0.002$ for noninferiority). Details on outcomes specific to patients infected with *S. maltophilia* were difficult to ascertain, as it was included within ‘other’ baseline Gram-negative pathogens [19]. While data with cefiderocol are promising against *S. maltophilia* in relation to *in vitro* activity, initial findings from outcomes studies are inconclusive due to few patients overall treated with cefiderocol compared to other agents.

4.3. Limitations

Limitations to this study include the retrospective nature of review and limited outcomes data collected. Retrospectively, we were not able to distinguish infection vs. colonisation, as *S. maltophilia* is a known coloniser of the respiratory tract. Due to the inclusion of multiple geographic sites, multiple testing methods were performed based on the automated testing used at an individual site. The study was, however, a real-world collection of isolates geographically located from community and academic medical centres.

5. Conclusion

S. maltophilia non-susceptibility (intermediate or resistance to at least one antimicrobial) had a prevalence of almost 50% to at least one first-line or commonly used agent. Except for isolation from the urine, there were no risk factors associated with resistance to these agents. Further research should evaluate national and international prevalence of as well as risk factors associated with non-susceptibility, as current treatment options as well as data with newer agents are limited.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

Not required.

Declaration of Competing Interest

The following authors report potential conflicts of interest: Jones BM: Speaker’s bureau (Allergan/Abbvie, La Jolla, Paratek), Grant Funding (Merck, ALK Abello), Bookstaver PB: Speaker’s bureau (Biomerieux), Consulting (TRC Healthcare, FreeCE.com), Bland CM: Speaker’s bureau (Merck, La Jolla), Grant Funding (Merck, ALK Abello), Advisory Board (Merck), Consulting (BioMerieux). All other authors report no conflicts of interest. These findings were presented, in part, as an accepted abstract at the European Congress of Clinical Microbiology and Infectious Diseases 2020 in Paris, France (conference cancelled due to COVID-19).

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