

ORIGINAL RESEARCH

https://doi.org/10.54034/mic.e1893

0 3

Unraveling the Prevalence of Antibiotic Resistance in *Stenotrophomonas maltophilia*: Insights into an Emerging Nosocomial Pathogen

Authors: Henry J. Parra-Vera^{ab}, Dayci C. Buele-Chica^{ab}, Galo G. Farfán-Cano^{bade}, Andrea M. Zúñiga-Vinueza^f

Abstract

Introduction. Stenotrophomonas maltophilia is a clinically relevant opportunistic and nosocomial pathogen with increasing concerns regarding antibiotic resistance. Accurate diagnosis and identification are crucial for effective treatment, and misidentification can occur, thereby emphasizing the need for appropriate laboratory testing and surveillance. This review aimed to evaluate the epidemiology, pathogenesis, diagnosis, treatment, and antimicrobial resistance of Stenotrophomonas spp. Materials and Methods. A systematic literature review was conducted using the PubMed Central Database. Inclusion criteria included studies published in open-access scientific journals within the last five years, reporting information on Stenotrophomonas spp. epidemiology, pathogenesis, diagnosis, treatment, and/or antimicrobial resistance. The synthesis of the results involved a narrative synthesis of the findings from the included studies. Results. A total of 25 articles met the inclusion criteria and provided valuable insights into Stenotrophomonas spp. infections. The distribution of reported cases by country, sample type, and antimicrobial resistance patterns was summarized. The prevalence of resistance to various antibiotics was also assessed, highlighting the need for continuous surveillance. Conclusion. This analysis revealed the presence of antimicrobial resistance in Stenotrophomonas spp., particularly in S. maltophilia. The high prevalence of antibiotic resistance underscores the importance of ongoing surveillance and control measures to combat antibiotic resistance. The diverse distribution of S. maltophilia across different sample types emphasizes the need for accurate diagnosis and identification. Addressing antimicrobial resistance in Stenotrophomonas spp. is essential for global public health.

Key word: Stenotrophomonas, Stenotrophomonas maltophilia, epidemiology, pathogenesis, diagnosis, treatment, antimicrobial resistance.

[®]Microbiological Research Centre (CIM), Guayaquil, Ecuador. [®]University of Guayaquil, Guayaquil, Ecuador. [©]Rey Juan Carlos University, Mostoles, Spain. [®]Society of Infectious diseases of Guayas, Guayaquil, Ecuador. [©]Northern Guayaquil General Hospital "Los Ceibos", Guayaquil, Ecuador. [©]Catholic University of Santiago de Guayaquil, Ecuador.

Corresponding author:

Galo Guillermo Farfán Cano Address: MUniversity of Guayaquil, Guayaquil, Ecuador. E-mail: dr.galo.farfan.cano@gmail.com ORCID: 0001-8447-5764 Copyright © 2023 the Author(s)

> Submitted: may 21, 2023 Reviewed : june 18, 2023 Approved: july 26, 2023

How to cite: Parra-Vera HJ, Buele-Chica DC, Farfán-Cano, GG, Zúñiga-Vinueza AM. Unraveling the Prevalence of Antibiotic Resistance in Stenotrophomonas maltophilia: Insights into an Emerging Nosocomial Pathogen. Microbes Infect Chemother. 2023; 3: e1893

Introduction

The Stenotrophomonas genus, belonging to the Xanthomonadaceae family within the order Xanthomonadales of the class Gammaproteobacteria, encompasses a group of aerobic plant growth-promoting bacteria consisting of 18 well-characterized species. The type species, S. maltophilia, was initially isolated from human pleural fluid and is referred to as Bacteriaum bookeri. Subsequently, it has been validated as Pseudomonas maltophilia (1–6). The renaming was based on quinine type, fatty acid composition, enzymatic characteristics, and DNA-rRNA hybridization, which led to its classification as Xanthomonas maltophilia (7). However, numerical taxonomic studies and protein gel electrophoresis patterns indicated that S. maltophilia and Pseudomonas hibiscicola formed a distinct cluster that was not closely related to the genus Xanthomonas. While initially recognized

as opportunistic pathogens with pathogenic properties, subsequent reports have identified numerous plantassociated species (2,3,7–11,4,12)

Formerly known as Xanthomonas maltophilia, S. maltophilia is a gram-negative, non-fermentative, aerobic bacillus (4,7,13–16). It is widely distributed in various natural environments, including water, soil, and plants, where it was originally identified as a plant pathogen. S. maltophilia can also be found in medical settings, colonizing hospital equipment such as blood pressure monitors, ventilators, disinfectants, and dialysis devices (1,17–20). It possesses the potential for transmission from patients to healthy individuals (1,21). Although considered a commensal organism, S. maltophilia has emerged as an important opportunistic and nosocomial pathogen causing diverse infections, particularly in immunocompromised individuals. Infections caused by S.

maltophilia include pneumonia, bloodstream infections, urinary tract infections, and skin and soft tissue infections (22).

Treatment of S. maltophilia infections is often challenging because of intrinsic resistance to multiple antibiotics and the ability to develop resistance through various mechanisms. The justification for this review stems from the growing concern regarding antibiotic resistance in S. maltophilia, a clinically relevant opportunistic and nosocomial pathogen. Understanding the prevalence of antibiotic resistance in S. maltophilia and establishing effective treatment strategies and control measures are imperative. The findings presented in this review offer a comprehensive overview of the prevalence of antibiotic resistance in S. maltophilia and provide valuable insights for selecting appropriate treatments and designing effective control strategies. Identifying common resistance patterns and emerging trends in antibiotic resistance will aid healthcare professionals in making informed decisions regarding managing S. maltophilia infection.

Materials and methods

A systematic literature review evaluated the effectiveness and safety of different treatment strategies for *Stenotrophomonas* spp. infections. The search was performed in the PubMed Central database using relevant search terms in English. Studies published up to April 30, 2023, evaluated *Stenotrophomonas* spp. infections were included based on predefined inclusion and exclusion criteria.

Research question. What is the available scientific evidence regarding the epidemiology, pathogenesis, diagnosis, treatment, and antimicrobial resistance of *Stenotrophomonas* spp.?

Justification. Stenotrophomonas spp. is an emerging pathogen associated with serious hospital-acquired infections, particularly in immunocompromised patients. Given its increasing prevalence and the need for up-to-date information, a comprehensive literature review was essential to assess the quality and consistency of existing studies.

Inclusion criteria. Studies published in open-access scientific journals, including information on the epidemiology, pathogenesis, diagnosis, treatment, and/or antimicrobial resistance of *Stenotrophomonas* spp. Studies utilizing human and animal models published in English or Spanish within the last five years were considered.

Search strategy. A systematic search was conducted using PubMed Central, an open-access database. The search terms used included "*Stenotrophomonas*," "*Stenotrophomonas* maltophilia," "epidemiology," "pathogenesis," "diagnosis," "treatment," and "antimicrobial resistance." Studies published between 2013 and the search date (April 30, 2023) were included. The search was limited to studies published in English or Spanish.

Synthesis of Results. The main findings and key conclusions

from the selected studies were summarized to provide a comprehensive overview. A narrative synthesis approach was employed, which involved identifying common themes, patterns, and trends across the literature while also addressing any inconsistencies or divergent findings. The synthesis aimed to integrate and present collective evidence cohesively, highlighting the implications and significance of the findings about the research question and objectives. Through this process, a comprehensive understanding of the current state of knowledge on *Stenotrophomonas* spp. was achieved, enabling the formulation of meaningful conclusions and recommendations.

Study limitations. Only open-access studies were included to ensure unrestricted access to information. Although efforts were made to assess the quality of included studies using a standardized tool, it is important to note that quality assessment does not guarantee the validity of the results. Additionally, the search was limited to studies published in English or Spanish, which may have introduced a language bias and potentially excluded relevant studies published in other languages. Furthermore, it should be noted that this study was conducted without external funding, relying solely on the available resources and expertise of the authors. However, despite these limitations, the research adhered to rigorous ethical standards and fulfilled all ethical requirements throughout the study.

Ethical aspects. The present study was conducted as a literature review, relying on data from published articles and publications. Ethical considerations were diligently addressed throughout the research process to ensure compliance with ethical standards. Firstly, copyright and intellectual property rights were given utmost respect by appropriately citing and referencing all sources used, thereby avoiding plagiarism. The integrity and accuracy of the collected data were rigorously maintained, with a commitment to refraining from manipulating or distorting information to serve personal interests. Furthermore, strict confidentiality and privacy measures were implemented to safeguard the identities and personal information of authors and participants referenced in the included studies, adhering to ethical guidelines and regulations. Lastly, the selection of publications was conducted in an impartial and unbiased manner, with no favoritism or bias toward specific studies. In summary, this study was carried out with a strong commitment to ethical principles, ensuring that all ethical requirements and considerations were met, thus promoting integrity, transparency, and adherence to ethical standards in handling the obtained data from the literature review.

Methods

A total of 27 articles were obtained during the search, in accordance with the information collection strategy detailed before, to which the inclusion and exclusion criteria were applied (those that reported any species of the genus *Stenotrophomonas*), one did not describe the total number of patients with isolated cases of *Stenotrophomonas*, and another did not meet the criteria. Twenty-five articles were selected (Table 1).

Table 1 provides a comprehensive summary of findings related to *Stenotrophomonas* spp. from various studies. The table includes information regarding the origin of the study by country, number of detected cases, type of sample analyzed, and frequency of antimicrobial-resistant isolates. It also contains the detected species of Stenotrophomonas. Additionally, the table includes details of the reporting of antimicrobial resistance, expressed as a percentage, and the type of article. This table is a valuable reference for understanding the distribution of *Stenotrophomonas* spp. across different countries, the sample types utilized, the prevalence of antimicrobial resistance, and the specific species detected.

Table 1

Summary of Stenotrophomonas spp. findings in studies by study origin, cases detected, sample type, and frequency of antimicrobialresistant isolates.

| Origin of Study per country | Detected cases | Type of sample | Detected species | Antimicrobial resistance reported | Percentage | Article type | |
|-----------------------------------|-------------------|--|------------------|-----------------------------------|--|---------------------------|--|
| Palestine | 5 | Blood culture | S. maltophilia | Ceftazidime | 75% | Research article (23) | |
| United States | 7 | Endotracheal suctioning, Bronchoalveolar lavage | Stenotrophomonas | TMP/SMX Not described | 20% Not described | Scientific report (24) | |
| | 45 | Blood culture | S. maltophilia | Ticarcillin- clavulanic acid | 31% | | |
| France | | | | Piperacillin- tazobactam | 62% | Original article (25) | |
| | | | | Ciprofloxacin TMP/SMX | 27% 4% | | |
| United States | 11 | Sputum, Endotracheal aspirate, Bronchioalvelar lavage | S. maltophilia | Not described | Not described | Systematic Review (26) | |
| Vietnam | 71 | Blood culture | S. maltophilia | Not described | Not described | Research article (23) | |
| China | 104 | Sputum, Bronchioalveolar lavage, Endotracheal aspirate, CSF., Drainage fluid, Secretions, Gauze, Shunt tube | S. maltophilia | Not described | Not described | Original research (13) | |
| China | 93 | Sputum, Drains, Pleural Fluid Ascites, Urine and Blood Culture | S. maltophilia | TMP/SMX Levofloxacin | 9.70% 4.30% | Research article (28) | |
| United Kingdom | 45 | Sputum, Urine, Rectal swab, Wound swabs, Blood cultures | S. maltophilia | Carbapenems | 27% | Original article (29) | |
| Japan | 54 | Blood cultures | S. maltophilia | TMP/SMX | Not described | Original article (30) | |
| China | Not described | 300 isolates from Sputum, Secretion, Urine, Blood cultures, Drains, CSF | S. maltophilia | TMP/SMX | 29.7% (2005- 2009) 47.1% (2010- 2014) | Research Article (31) | |
| Taiwan | 25 | Blood culture, Respiratory secretion, Urine, Intra-abdominal infection, Catheter-related infection | S. maltophilia | Not described | Not described | Original article (32) | |
| Türkiye | 61 | Blood cultures, Urine, Skin and subcutaneous tissue, Surgical site infections | S. maltophilia | Not described | Not described | Original article (33) | |

| China | Not described | 426 isolates from Sputum, pharyngeal swab, Drainage, Blood cultures, CSF | S. maltophilia | Minocycline TMP/SMX Levofloxacin | 0.5-0.7% 53-86.6% 4-4.1% | Original article (34) |
|------------------|------------------|--|----------------|--|---|--------------------------------|
| China | 16 | Urine, Respiratory secretions, Gastrointestinal secretions, Blood cultures | S. maltophilia | Not individually described per species | Not described per species | Research article (35) |
| Hungary | 77 | Blood cultures, Respiratory secretions | S. maltophilia | TMP/SMX Ciprofloxacin Levofloxacin Moxifloxacin Doxycycline Tigecycline Colistin | 1% 54% 7% 7% Insufficient evidence 50% 91% | Research article (18) |
| South Korea | 126 | Blood cultures, Intra-abdominal secretion, respiratory secretions | S. maltophilia | Not described | Not described | Research article (36) |
| Taiwan | 34 | Blood cultures | S. maltophilia | Not described | Not described | Original Article (37) |
| Brazil | 106 | Blood cultures, Respiratory secretions Urine | S. maltophilia | TMP/SMX Levofloxacin Ciprofloxacin Ceftazidime Tigecycline Chloramphenicol Ticarcillin/Clavulan ate | Not described | Original Article (38) |
| United States | 27 | Not described | S. maltophilia | Not described | Not described | Short communication (39) |
| United States | 130 | Cystic fibrosis Blood cultures Stool Other sites of infection | S. maltophilia | Not described | Not described | Original article (40) |
| Iran | 16 | Hemocultivos | S. maltophilia | Ceftazidime | Not described | Original article (41) |
| Oman | 41 | Blood cultures, Respiratory secretions Urine | S. maltophilia | TMP/SMX Ceftazidime Levofloxacin Minocycline | 7% 50% 8% 3% | Original article (22) |
| Germany | 20 | Hisopados rectales, faríngeos y nasales | S. maltophilia | TMP/SMX Ciprofloxacina y levofloxacina Ceftazidima | 15% 10% 55% | Research article (42) |
| China | 1058 | Sputum, endotracheal aspirates, oral swabs, urine, blood, catheter, and drainage samples | S. maltophilia | Not described | Not described | Research article (14) |
| Taiwan | 184 | Blood cultures | S. maltophilia | TMP/SMX Ciprofloxacin Ceftazidime | 30.43% 92.90% 2.17% | Research article (43) |

 ${\sf CSF}, cerebrospinal fluid. {\sf TMP/SMX}: trime tho prim-sulfame tho xazole.$

Review

S. maltophilia is a gram-negative bacterium that can grow in a wide range of temperatures (20-30°C); most isolates are able to survive at 4°c for a long time, tolerate a wide range of pH but is sensitive to saline concentrations; they can grow various culture media, B (Luria or Lennox) or nutrient agar, blood (are not hemolytic), and MacConkey agar (appear colorless). It is a versatile microorganism that can utilize different carbon and nitrogen sources and is often found in soil and aquatic environments. In healthcare settings, S. maltophilia is an emerging opportunistic pathogen that can cause infections in immunocompromised patients, particularly those with cystic fibrosis or malignancies. Resistance to multiple antibiotics such as β -lactams, aminoglycosides, and fluoroquinolones poses a challenge for effective treatment. Therefore, accurate identification and characterization of S. maltophilia strains and surveillance of their antibiotic susceptibility patterns are essential for preventing and controlling infections caused by this bacterium (1,12,44).

Misidentification of *S. maltophilia* is common. Burgge et al. reported that their study misidentified 9% of 32 clinical isolates as *Pseudomonas cepacia*. This error was due to a delay in oxidase test reading and failure to maintain DNase production tests for 72 h prior to observation. Misinterpretation of these tests is clinically significant, as *P. cepacia* is a significant pathogen in patients with CF (44–46).

The use of culture media to differentiate *S. maltophilia* growth from *P. aeruginosa* in mixed culture samples, such as the production of acid from maltose instead of glucose by *S. maltophilia*, is observed as yellow and blue color changes in media containing BTB containing both maltose and glucose; Their culture colonies are typically yellow-green on nutrient agar, non-hemolytic with a slight lavender hue and ammonia odor on blood agar, and colorless on MacConkey plates as it does not ferment lactose (21,44,47).

In vitro, laboratory identification of *S. maltophilia* indicates that it is an obligate aerobe that is generally negative for the oxidase test. However, it has been shown to exhibit positive oxidase activity for up to 20% of the time. Additionally, the strain was positive for catalase and DNase, positive for lysine decarboxylase, negative for indole and H2S, and negative for urease. This bacterium is known to produce acid from maltose, hence the name maltophilia, although it does not always produce acid from glucose (1,5,6,44,46).

The introduction of blood agar containing imipenem for routine sputum culture at a CF center in the UK increased the prevalence of S. *maltophilia* from 8% to 16% compared to the previous year. However, this study did not directly compare the sensitivity of a selective medium with that of a non-selective medium. Therefore, we conducted a study to evaluate the sensitivity of a selective medium (VIA medium) that incorporated vancomycin, imipenem, and amphotericin B as selective agents (48). *S. maltophilia* is a versatile gram-negative bacterium that can survive in various conditions and is commonly found in aquatic and soil environments.

In healthcare settings, it is an emerging opportunistic pathogen that can cause infections in immunocompromised patients, and its resistance to multiple antibiotics makes its treatment challenging. It is important to accurately identify *S*. *maltophilia* strains and monitor their antibiotic susceptibility patterns to prevent and control infections caused by this bacterium.

Additionally, misidentification of S. maltophilia can occur, highlighting the need for appropriate laboratory testing and careful surveillance to avoid identification errors. Overall, continued research on the identification and treatment of S. maltophilia is essential to address the clinical challenges posed by this bacterium.

Like other Gram-negative bacteria, *S. maltophilia* has low membrane permeability because it has two cell membranes and a peptidoglycan wall. The outer membrane acts as an effective barrier. Mutants with modified outer membrane permeability or different lipopolysaccharide structures have an altered antibiotic susceptibility. The efflux pumps SmeABC, SmeDEF, and SmeVWX, members of the RND family, are encoded by the same operon with a typical genomic arrangement. These efflux pumps' functions in intrinsic and acquired resistance have been wellcharacterized.(49).

From the above analysis, it can be concluded that the accurate diagnosis and identification of S. maltophilia are crucial for effectively treating infections caused by this bacterium. As S. maltophilia is resistant to multiple antibiotics, it is important to conduct susceptibility testing to determine the best possible treatments. Furthermore, due to the possibility of misidentification, it is important to perform appropriate laboratory tests and maintain careful surveillance to avoid identification errors. Ongoing research on the identification and treatment of S. maltophilia is essential for addressing the clinical challenges posed by this bacterium. Characterization of the resistance mechanisms in S. maltophilia, such as the presence of efflux pumps, can provide valuable information for developing new therapies and designing strategies to combat antibiotic resistance in this bacterium. Additionally, it is worth noting that despite the low global prevalence of S. maltophilia (0.03), the high frequency of antibiotic-resistant strains reported in several studies, particularly ceftazidime, ticarcillin/clavulanate, piperacillintazobactam, and in some populations of TMP/SMX, highlights the importance of well-equipped laboratories for the identification of these microorganisms.

Data results

Figures 1 and 2 visually represent relevant information related to S. *maltophilia*. Figure 1 presents a color-coded map highlighting countries with articles reporting S. *maltophilia*, providing an overview of the geographical

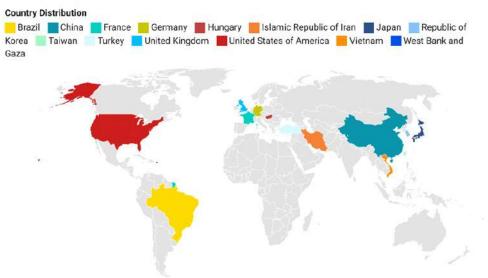
distribution of research on this bacterium. The map was based on the articles retrieved during the search process, and the details are presented in Table 1.

Figure 1

Color-coded map of countries with articles reporting S. maltophilia. The graph is based on the articles retrieved in the search and is detailed in Table 1

Distribution of reported S. maltophilia isolates by cases detected worldwide.

The map displays the countries with reports of S. maltophilia detected in the search.



Map: Galo Farfan Cano • Created with Datawrapper

On the other hand, Figure 2 presents a bar chart that depicts the total number of cases categorized by country of origin. This chart provides insights into the distribution and magnitude of S. *maltophilia* infections across different countries. Together, these figures aim to enhance the understanding and provide visual representations of key aspects of S. *maltophilia*.

Figure 2

Bar chart detailing the total number of cases by country of origin

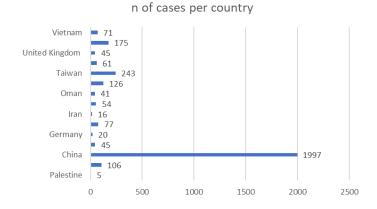
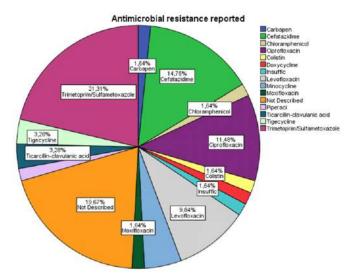


Figure 3

The percentage of resistance to their respective antibiotics was observed



The different antibiotics and their percentages of resistance obtained from the literature search are detailed. It is worth mentioning that among the articles reviewed, 19.67% reported no resistance to S. maltophilia.

The data provided in Table 2 represent the distribution of the types of samples in which *S. maltophilia* was detected in the studies analyzed. Table 2 provides information on the frequency, percentage, valid percentage, cumulative percentage, and actual prevalence of resistance (with a 95% confidence interval) for different antibiotics.

Discussion

Table 2

Details of the antimicrobial resistance reported in the different articles, with their percentage and the prevalence of each antimicrobial, were estimated (95% CI)

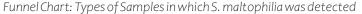
| Antimicrobial resistance reported | | | | | | | |
|-----------------------------------|-----------|------------|---------------------|-----------------------|---|--|--|
| Valid | Frequency | Percentage | Valid percentage | Cumulative percentage | Real prevalence of resistance IC 95% | | |
| Carbapen | 1 | 1,6 | 1,6 | 1,6 | 1,64% (0,00, 4,79% | | |
| Ceftazidime | 9 | 14,8 | 14,8 | 16,4 | 14.75% (5.94%, 23.57%) | | |
| Chloramphenicol | 1 | 1,6 | 1,6 | 18,0 | 1,64% (0,00, 4,79% | | |
| Ciprofloxacin | 7 | 11,5 | 11,5 | 29,5 | 11.48% (3.56%, 19.39%) | | |
| Colistin | 1 | 1,6 | 1,6 | 31,1 | 1,64% (0,00, 4,79% | | |
| Doxycycline | 1 | 1,6 | 1,6 | 32,8 | 1,64% (0,00, 4,79% | | |
| Insuffic | 1 | 1,6 | 1,6 | 34,4 | 1,64% (0,00, 4,79% | | |
| Levofloxacin | 6 | 9,8 | 9,8 | 44,3 | 9.84% (2.44%, 17.24%) | | |
| Minocycline | 3 | 4,9 | 4,9 | 49,2 | 4.92% (0.00%, 10.29%) | | |
| Moxifloxacin | 1 | 1,6 | 1,6 | 50,8 | 1,64% (0,00, 4,79% | | |
| Not Described | 12 | 19,7 | 19,7 | 70,5 | 19.67% (9.80%, 29.55%) | | |
| Piperaci | 1 | 1,6 | 1,6 | 72,1 | 1,64% (0,00, 4,79% | | |
| Ticarcillin-clavulanic acid | 2 | 3,3 | 3,3 | 75,4 | 3.28% (0.00%, 7.70%) | | |
| Tigecycline | 2 | 3,3 | 3,3 | 78,7 | 3.28% (0.00%, 7.70%) | | |
| Trimetoprim/Sulfametoxazole | 13 | 21,3 | 21,3 | 100,0 | 21.31% (11.14%, 31.49%) | | |
| Total | 61 | 100,0 | 100,0 | | | | |

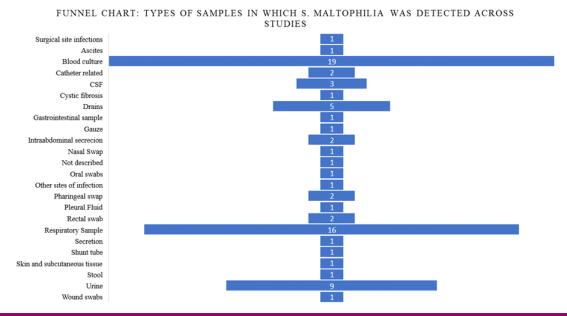
Based on a global population of approximately 8 billion people, with several reports of Stenotrophomonas spp. (n=3082) and an estimated sample size of 100,000 cases, the estimated prevalence of Stenotrophomonas spp. detection ranges between 2.97% and 3.19% (3.08%), whereas for S. *maltophilia* (n=2242), the prevalence in the population ranges between 2.15% and 2.33% (2.24%).

The data provided represent the distribution of the types of samples in which *S. maltophilia* was detected in the studies analyzed. The funnel chart (Figure 4) visually displays this distribution, with the samples with the highest number of reported detections at the top of the chart and those with the

lowest number of detections at the bottom. The chart shows that Blood cultures had the highest number of *S. maltophilia* detections, with 19 reported cases. This was followed by respiratory samples from 16 reported cases and urine samples from 9 reported cases. The number of detections in the remaining sample types was relatively low, with most sample types having only one or two reported cases. These included samples from surgical site infections, cystic fibrosis, gastrointestinal samples, and nasal swabs. Overall, the funnel chart allowed for a clear visualization of the distribution of *S. maltophilia* across different types of samples, with the chart tapering down from the highest number of detections to the lowest.

Figure 4





Antibiotic prevalence values were based on a sample of 61 cases (composed of reports of antimicrobial resistance and undescribed or insufficient data from the analyzed articles) for a population of 3082 reports of *Stenotrophomonas* spp. Overall, these results suggest the need for continuous surveillance and control measures to prevent increased antibiotic resistance, particularly in S. maltophilia.

The synthesis-analysis method was used based on the articles selected from the PubMed search to elaborate on the review detailed in the discussion.

Discussion

The provided information discusses antimicrobial resistance (AMR) reported for *Stenotrophomonas* spp., specifically focusing on *S. maltophilia*. The data included the frequency and percentage of resistance observed for various antibiotics and their valid and cumulative percentages. The estimated prevalence of resistance was also provided, along with the corresponding 95% confidence intervals (CI).

The analysis was based on a global population of approximately 8 billion people, with 3,082 reports of *Stenotrophomonas* spp. and an estimated sample size of 100,000 cases. For *S. maltophilia*, the estimated prevalence of detection in the population is expected to range between 2.15% and 2.33% (with a point estimate of 2.24%).

The data further revealed the distribution of samples in which *S. maltophilia* was detected in the analyzed studies. A funnel chart was presented to visually represent this distribution, with samples with the highest number of reported detections at the top and those with the lowest number at the bottom. The chart shows that blood cultures had the highest number of *S. maltophilia* detections (19), followed by respiratory (16) and urine (9) times. Other sample types had relatively fewer reported cases, such as surgical site infections, cystic fibrosis, gastrointestinal samples, and nasal swabs, with most having only one or two times. The funnel chart effectively illustrated the varying distribution of *S. maltophilia* across different sample types employed by the investigators reviewed.

The prevalence of antibiotic resistance was based on a sample of 61 cases, which included reports of antimicrobial resistance and cases with undescribed or insufficient data from the analyzed articles. These prevalence values are crucial for highlighting the need for continuous surveillance and control measures to prevent further increases in antibiotic resistance, especially in S. maltophilia.

To conduct this analysis, the review utilized the synthesis analysis method, which involved selecting articles from the PubMed search. This approach allowed for a comprehensive understanding of the current antimicrobial resistance in Stenotrophomonas spp., specifically focusing on *S. maltophilia*.

Conclusion

In conclusion, the findings of this analysis highlight the presence of antimicrobial resistance in *Stenotrophomonas* spp., specifically in *S. maltophilia*. There is a significant prevalence of resistance to multiple antibiotics, indicating the need for continuous surveillance and control measures to prevent the escalation of antimicrobial resistance, especially in *S. maltophilia*. Furthermore, diverse distributions of *S. maltophilia* across different sample types were identified, with higher detection rates in blood cultures, followed by respiratory and urine samples. These findings underscore the importance of addressing antimicrobial resistance in *Stenotrophomonas* spp. as a part of global public health efforts.

Author Contribution Statement

The authors confirm their contribution to the paper as follows: study conception and design: G. Farfan-Cano; data collection: A. Zuñiga-Vinueza; analysis and interpretation of results: G. Farfan-Cano, H. Parra-Vera. D. Buele-Chica; draft manuscript preparation: G Farfan-Cano. H. Parra-Vera, D. Buele-Chica, A. Zuñiga-Vinueza: All authors reviewed the results and approved the final version of the manuscript. All authors agree to be responsible for all aspects of the work to ensure the accuracy and integrity of the published manuscript.

Ethics statement

The authors declare that the published work reflects an investigation and analysis carried out truthfully and completely.

Conflict of Interest

The authors declare no conflict of interest.

Funding

None.

Availability of data

The corresponding author will provide the datasets used and/or analyzed during the current work upon reasonable request.

References

- 1. Brooke JS. Stenotrophomonas maltophilia is an emerging opportunistic pathogen globally. Clinical Microbiology Reviews. 2012;25(1): 2–41. https://doi.org/10.1128/CMR.00019-11.
- 2. Ghosh R, Chatterjee S, Mandal NC. Stenotrophomonas. In: Beneficial Microbes in Agro-Ecology. Elsevier; 2020. p. 427–442. https://doi.org/10.1016/B978-0-12-823414-3.00020-4. [Accessed May 6 2023].
- 3. Hugh R, Ryschenkow E. Pseudomonas maltophilia, an Alcaligenes-like Species. Journal of General Microbiology.

1961;26(1): 123–132. https://doi.org/10.1099/00221287-26-1-123.

4. Palleroni NJ, Bradbury JF. Stenotrophomonas, a New Bacterial Genus for Xanthomonas maltophilia (Hugh 1980) Swings et al. 1983. International Journal of Systematic Bacteriology. 1993;43(3): 606–609.

https://doi.org/10.1099/00207713-43-3-606.

- Abbott IJ, Slavin MA, Turnidge JD, Thursky KA, Worth LJ. Stenotrophomonas maltophilia : emerging disease patterns and challenges for treatment. Expert Review of Anti-infective Therapy. 2011;9(4): 471–488. https://doi.org/10.1586/eri.11.24.
- 6. Abbott I, Peleg A. Stenotrophomonas, Achromobacter, and Nonmelioid Burkholderia Species: Antimicrobial Resistance and Therapeutic Strategies. Seminars in Respiratory and Critical Care Medicine. 2015;36(01): 099–110. https://doi.org/10.1055/s-0034-1396929.
- 7. Swings J, De Vos P, Van Den Mooter M, De Ley J. Transfer of Pseudomonas maltophilia Hugh 1981 to the Genus Xanthomonas as Xanthomonas maltophilia (Hugh 1981) comb. nov. International Journal of Systematic Bacteriology.1983;33(2):409–413.

https://doi.org/10.1099/00207713-33-2-409.

- 8. Ouattara AS, Le Mer J, Joseph M, Macarie H. Transfer of Pseudomonas pictorum Gray and Thornton 1928 to genus Stenotrophomonas as Stenotrophomonas pictorum comb. nov., and emended description of the genus Stenotrophomonas. International Journal of Systematic and Evolutionary Microbiology. 2017;67(6): 1894–1900. https://doi.org/10.1099/ijsem.0.001880.
- 9. Notification that New Names and New Combinations Have Appeared in Volume 43, No. 3, of the IJSB. International Journal of Systematic Bacteriology. 1993;43(4): 866–866. https://doi.org/10.1099/00207713-43-4-866.
- 10. Whitman WB, [ed.]. Bergey's Manual of Systematics of Archaea and Bacteria.. 1st ed. Wiley; 2015. https://doi.org/10.1002/9781118960608. [Accessed May 6 2023].
- 11. Van Zyl E, Steyn PL. Differentiation of Phytopathogenic Pseudomonas and Xanthomonas Species and Pathovars by Numerical Taxonomy and Protein Gel Electrophoregrams. Systematic and Applied Microbiology. 1990;13(1): 60-71. https://doi.org/10.1016/S0723-2020(11)80181-5.
- 12. Mahdi O, Eklund B, Fisher N. Laboratory Culture and Maintenance of Stenotrophomonas maltophilia. Current Protocols in Microbiology. 2014;32(1).

https://doi.org/10.1002/9780471729259.mc06f01s32.

- 13. Duan Z, Qin J, Li C, Ying C. Clinical and Molecular Epidemiology of Stenotrophomonas maltophilia in Pediatric Patients From a Chinese Teaching Hospital. Frontiers in cellular and infection microbiology. 2020;10: 411.https://doi.org/10.3389/fcimb.2020.00411.
- 14. Tan R, Liu J, Li M, Huang J, Sun J, Qu H. Epidemiology and antimicrobial resistance among commonly encountered bacteria associated with infections and colonization in intensive care units in a university-affiliated hospital in Shanghai. Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi. 2014;47(2): 87–94. https://doi.org/10.1016/j.jmii.2012.11.006.

- Palleroni NJ, Kunisawa R, Contopoulou R, Doudoroff M. Nucleic Acid Homologies in the Genus Pseudomonas. International Journal of Systematic Bacteriology. 1973;23(4): 333–339. https://doi.org/10.1099/00207713-23-4-333.
- Van Den Mooter M, Swings J. Numerical Analysis of 295 Phenotypic Features of 266 Xanthomonas Strains and Related Strains and an Improved Taxonomy of the Genus. International Journal of Systematic Bacteriology. 1990;40(4): 348–369. https://doi.org/10.1099/00207713-40-4-348.
- 17. Brooke JS. Advances in the Microbiology of Stenotrophomonas maltophilia. Clinical Microbiology Reviews. 2021;34(3): e00030-19. https://doi.org/10.1128/CMR.00030-19.

 18. Juhász E, Krizsán G, Lengyel G, Grósz G, Pongrácz J, Kristóf
K. Infection and colonization by Stenotrophomonas maltophilia: antimicrobial susceptibility and clinical background of strains isolated at a tortiany care, contra in

- background of strains isolated at a tertiary care centre in Hungary. Annals of clinical microbiology and antimicrobials. 2014;13: 333. https://doi.org/10.1186/s12941-014-0058-9.
- 19. Adegoke AA, Stenström TA, Okoh AI. Stenotrophomonas maltophilia as an Emerging Ubiquitous Pathogen: Looking Beyond Contemporary Antibiotic Therapy. Frontiers in Microbiology.2017;8:2276.

https://doi.org/10.3389/fmicb.2017.02276.

20. Sánchez MB. Antibiotic resistance in the opportunistic pathogen Stenotrophomonas maltophilia. Frontiers in Microbiology.2015;6.

https://doi.org/10.3389/fmicb.2015.00658.

21. Said M, Tirthani E, Lesho E. Stenotrophomonas Maltophilia.. 2023rd ed. Treasure Island (FL): StatPearls Publishing; 2023.

https://www.ncbi.nlm.nih.gov/books/NBK572123/

- 22. Sannathimmappa MB, Nambiar V, Aravindakshan R, Al-Kasaby NM. Stenotrophomonas maltophilia: An emerging opportunistic nosocomial pathogen in a tertiary care hospital in Al Batinah North Governorate, Oman. Sultan Qaboos University medical journal. 2021;21(1): e66–e71. https://doi.org/10.18295/squmj.2021.21.01.009.
- 23. AbuTaha SA, Al-Kharraz T, Belkebir S, Abu Taha A, Zyoud SH. Patterns of microbial resistance in bloodstream infections of hemodialysis patients: a cross-sectional study from Palestine. Scientific reports. 2022;12(1): 18003. https://doi.org/10.1038/s41598-022-21979-7.
- 24. Behnia M, Logan SC, Fallen L, Catalano P. Nosocomial and ventilator-associated pneumonia in a community hospital intensive care unit: a retrospective review and analysis. BMC research notes. 2014;7: 232.

https://doi.org/10.1186/1756-0500-7-232.

25. Bousquet A, Malfuson JV, Sanmartin N, Konopacki J, MacNab C, Souleau B, et al. An 8-year survey of strains identified in blood cultures in a clinical haematology unit. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2014;20(1): O7-12. https://doi.org/10.1111/1469-0691.12294.

26. Chong WH, Saha BK, Ramani A, Chopra A. State-of-the-art review of secondary pulmonary infections in patients with COVID-19 pneumonia. Infection. 2021;49(4): 591–605. https://doi.org/10.1007/s15010-021-01602-z.

27. Dat VQ, Vu HN, Nguyen The H, Nguyen HT, Hoang LB, Vu Tien Viet D, et al. Bacterial bloodstream infections in a tertiary infectious diseases hospital in Northern Vietnam: aetiology, drug resistance, and treatment outcome. BMC infectious diseases. 2017;17(1): 493.

https://doi.org/10.1186/s12879-017-2582-7.

28. Duan Z, Qin J, Liu Y, Li C, Ying C. Molecular epidemiology and risk factors of Stenotrophomonas maltophilia infections in a Chinese teaching hospital. BMC microbiology.2020;20(1):294.

https://doi.org/10.1186/s12866-020-01985-3.

- 29. Goldenberg SD, Dodgson AR, Barlow G, Parcell BJ, Jones L, Albur M, et al. Epidemiology, Outcomes and Resource Utilisation in Patients with Carbapenem Non-susceptible Gram-Negative Bacteria in the UK: A Retrospective, Observational Study (CARBAR UK). Advances in therapy. 2022;39(8): 3602–3615. https://doi.org/10.1007/s12325-022-02177-3.
- 30. Hotta G, Matsumura Y, Kato K, Nakano S, Yunoki T, Yamamoto M, et al. Risk factors and outcomes of Stenotrophomonas maltophilia bacteraemia: a comparison with bacteraemia caused by Pseudomonas aeruginosa and Acinetobacter species. PloS one. 2014;9(11):e112208.

https://doi.org/10.1371/journal.pone.0112208.

31. Hu LF, Chen GS, Kong QX, Gao LP, Chen X, Ye Y, et al. Increase in the Prevalence of Resistance Determinants to Trimethoprim/Sulfamethoxazole in Clinical Stenotrophomonas maltophilia Isolates in China. PloS one. 2016;11(6):e0157693.

https://doi.org/10.1371/journal.pone.0157693.

- 32. Huang YC, Wu PF, Lin YT, Wang FD. Comparison of clinical characteristics of bacteremia from Elizabethkingia meningoseptica and other carbapenem-resistant, non-fermenting Gram-negative bacilli at a tertiary medical center. Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi. 2019;52(2): 304–311. https://doi.org/10.1016/j.jmii.2018.06.007.
- Ince N, Yekenkurul D, Danış A, Çalışkan E, Akkaş İ. An evaluation of six-year Stenotrophomonas maltophilia infections in a university hospital. African health sciences. 2020;20(3):1118–1123. https://doi.org/10.4314/ahs.v20i3.13.
- 34. Jia W, Wang J, Xu H, Li G. Resistance of Stenotrophomonas maltophilia to Fluoroquinolones: Prevalence in a University Hospital and Possible Mechanisms. International journal of environmental research and public health. 2015;12(5): 5177–5195. https://doi.org/10.3390/ijerph120505177.
- 35. Jiang AM, Shi X, Liu N, Gao H, Ren MD, Zheng XQ, et al. Nosocomial infections due to multidrug-resistant bacteria in cancer patients: a six-year retrospective study of an oncology Center in Western China. BMC infectious diseases. 2020;20(1): 452. https://doi.org/10.1186/s12879-020-05181-6.
- 36. Kim EJ, Kim YC, Ahn JY, Jeong SJ, Ku NS, Choi JY, et al. Risk factors for mortality in patients with Stenotrophomonas maltophilia bacteremia and clinical impact of quinoloneresistant strains. BMC infectious diseases. 2019;19(1): 754. https://doi.org/10.1186/s12879-019-4394-4.

37. Kuo SH, Lin WR, Lin JY, Huang CH, Jao YT, Yang PW, et al. The epidemiology, antibiograms and predictors of mortality among critically-ill patients with central lineassociated bloodstream infections. Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi. 2018;51(3): 401–410.

https://doi.org/10.1016/j.jmii.2017.08.016.

38. Mendes ET, Paez JIG, Ferraz JR, Marchi AP, Silva ILAFE, Batista MV, et al. Clinical and microbiological characteristics of patients colonized or infected by Stenotrophomonas maltophilia : is resistance to sulfamethoxazole/ trimethoprim a problem? Revista do Instituto de Medicina Tropical de Sao Paulo. 2020;62: e96.

https://doi.org/10.1590/S1678-9946202062096.

39. Mojica MF, Papp-Wallace KM, Taracila MA, Barnes MD, Rutter JD, Jacobs MR, et al. Avibactam Restores the Susceptibility of Clinical Isolates of Stenotrophomonas maltophilia to Aztreonam. Antimicrobial agents and chemotherapy.2017;61(10).

https://doi.org/10.1128/AAC.00777-17.

40. Mojica MF, Rutter JD, Taracila M, Abriata LA, Fouts DE, Papp-Wallace KM, et al. Population Structure, Molecular Epidemiology, and β -Lactamase Diversity among Stenotrophomonas maltophilia Isolates in the United States.mBio.2019;10(4).

https://doi.org/10.1128/mBio.00405-19.

- 41. Motamedifar M, Heidari H, Yasemi M, Sedigh Ebrahim-Saraie H. Molecular epidemiology and characteristics of 16 cases with Stenotrophomonas maltophilia bacteraemia in pediatric Intensive Care Units. Annali di igiene : medicina preventiva e di comunita. 2017;29(4): 264–272. https://doi.org/10.7416/ai.2017.2154.
- 42. Scheich S, Koenig R, Wilke AC, Lindner S, Reinheimer C, Wichelhaus TA, et al. Stenotrophomonas maltophilia colonization during allogeneic hematopoietic stem cell transplantation is associated with impaired survival. PloS one. 2018;13(7): e0201169.

https://doi.org/10.1371/journal.pone.0201169.

- 43. Wang CH, Lin JC, Lin HA, Chang FY, Wang NC, Chiu SK, et al. Comparisons between patients with trimethoprimsulfamethoxazole-susceptible and trimethoprimsulfamethoxazole-resistant Stenotrophomonas maltophilia monomicrobial bacteremia: A 10-year retrospective study. Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi. 2016;49(3): 378–386. https://doi.org/10.1016/j.jmii.2014.06.005.
- 44. Carmody LA, Spilker T, LiPuma JJ. Reassessment of Stenotrophomonas maltophilia Phenotype. Journal of Clinical Microbiology.2011;49(3):1101–1103. https://doi.org/10.1128/JCM.02204-10.
- 45. Burdge DR, Noble MA, Campbell ME, Krell VL, Speert DP. Xanthomonas maltophilia Misidentified as Pseudomonas cepacia in Cultures of Sputum from Patients with Cystic Fibrosis: A Diagnostic Pitfall with Major Clinical Implications. Clinical Infectious Diseases. 1995;20(2): 445–448. https://doi.org/10.1093/clinids/20.2.445.
- 46. Denton M, Kerr KG. Microbiological and Clinical Aspects of Infection Associated with Stenotrophomonas maltophilia. Clinical Microbiology Reviews. 1998;11(1): 57–80. https://doi.org/10.1128/CMR.11.1.57.

- 47. Kataoka D, Fujiwara H, Kawakami T, Tanaka Y, Tanimoto A, Ikawa S, et al. The indirect pathogenicity of Stenotrophomonas maltophilia. International Journal of Antimicrobial Agents. 2003;22(6):601–606. https://doi.org/10.1016/S0924-8579(03)00244-9.
- 48. Denton M, Hall MJ, Todd NJ, Kerr KG, Littlewood JM. Improved isolation of Stenotrophomonas maltophilia from the sputa of patients with cystic fibrosis using a selective medium. Clinical Microbiology and Infection. 2000;6(7): 395–396.

https://doi.org/10.1046/j.1469-0691.2000.00098.x.

49. Hafiz TA, Aldawood E, Albloshi A, Alghamdi SS, Mubaraki MA, Alyami AS, et al. Stenotrophomonas maltophilia Epidemiology, Resistance Characteristics, and Clinical Outcomes: Understanding of the Recent Three Years' Trends. Microorganisms. 2022;10(12): 2506.

https://doi.org/10.3390/microorganisms10122506.