Namaji et al | Article 8842
J Pure Appl Microbiol. 2023;17(4):2256-2262. doi: 10.22207/JPAM.17.4.23
Received: 11 July 2023 | Accepted: 18 September 2023
Published Online: 10 November 2023

P-ISSN: 0973-7510; E-ISSN: 2581-690X

RESEARCH ARTICLE OPEN ACCESS

Antibacterial Susceptibility Pattern of *S. maltophilia* Isolates at A Tertiary Care Hospital, India

Mohammed Ashraf Ali Namaji[1], Muzafar Ahmad Bhat[1], Manas Dixit[1], Sanjay Pratap Singh[1] and Raghavendra Huchchannavar[2]*

[1]Department of Microbiology, Armed Forces Medical College, Pune, Maharashtra, India.
[2]Department of Community Medicine, KS Hegde Medical Academy (Nitte University) Mangalore, Karnataka, India.

Abstract

A sudden emergence of *Stenotrophomonas maltophilia*as a primary pathogen both in immunocompromised and immunocompetent individuals has raised a serious concern, as it is associated with significant case fatality ratio. We intended to study the clinico-microbiological profile of *S. maltophilia* isolates from various samples and outcome of the infections in a tertiary healthcare center, Pune, India. This is an observational cross-sectional study was conducted from January 2021 to June 2022 at Department of Microbiology of a tertiary care Centre in Pune, India. Of the 12049 samples received for culture, *S. maltophilia* was isolated in 57 samples. Only 42 samples with pure growth of *S. maltophilia* were included in the study with 15 excluded due to mixed growth. All isolates were confirmed by VITEK-MS (bioMerieux, SA, France) which uses Matrix Assisted Laser Desorption Ionization Time-of-Flight (MALDI-TOF) technology. Of the 42 isolates, majority were isolated from pus(28.6%) and most of patients (61.9%) were from acute health care settings. The isolates had high susceptibility to Cotrimoxazole (85.7%) and Minocycline (85.7%) and low susceptibility to Ceftazidime (45.2%). A case fatality rate of 7.1% (3/42 cases) was noted and 39 cases were discharged after complete treatment. All the three fatal cases were susceptible to levofloxacin, ciprofloxacin, cotrimoxazole and minocycline and all three fatal cases were resistant to ceftazidime. *S. maltophilia* has recently shown an increase in nosocomial infections especially in acute healthcare settings like ICU and other critical care wards. The isolates of the present study had high susceptibility to trimethoprim-sulfamethoxazole (TMP-SXT) and Minocycline and low susceptible to Ceftazidime.

Keywords: *S. maltophilia,* Susceptibility, Cotrimoxazole, Ceftazidime

***Correspondence:** drraghu49@gmail.com

Citation: Namaji MAA, Bhat MA, Dixit M, Singh SP, Huchchannavar R. Antibacterial Susceptibility Pattern of *S. maltophilia* Isolates at A Tertiary Care Hospital, India. *J Pure Appl Microbiol.* 2023;17(4):2256-2262. doi: 10.22207/JPAM.17.4.23

INTRODUCTION

*S. maltophilia*is an aerobic, gram-negative bacterium, traditionally considered as an environmental contaminant (increasingly isolated in hospital settings from different sources like haemodialysis water and dialysate samples,contact lens solutions, sink drains, faucets,hand-washing soap , contaminated chlorhexidine-cetrimide topical antiseptic and tap water) and is also known to produce biofilms.[1,2] *S.maltophilia* is a nosocomial pathogen especially in immunocompromised but community acquired *S. maltophilia* infections in comorbid patients is also reported worldwide.[3] A sudden emergence of *S. maltophilia* as a primary pathogen both in immunocompromised and immunocompetent individuals has raised a serious concern, as it is associated with significant case fatality ratio.[4]

S. maltophilia is commonly associated with bacteraemia, endocarditis, respiratory tract infections like pneumonia, mastoiditis, peritonitis and exit sign infections in patients undergoing peritoneal dialysis, soft tissue and skin infections, joint infections and Central Nervous System (CNS) infections.[5,6] At risk population are patients with immunocompromised states like diabetes mellitus, cancer patients on treatment, patients with indwelling devices. *S. maltophilia*is an emerging pathogen in patients with cystic fibrosis which unlike *Pseudomonas, Burkholderia* spp is multidrug resistant.[7]

This organism has ability to form biofilms on moist surfaces such as respiratory tubing,hospital water plumbing systems, dental suction tubing, Intra Venous (I.V) lines, dialysis equipment,catheters,domestic sink drains,clinical sink drains, and faucets.[8] The transmission of *S. maltophilia* to susceptible individuals may occur through direct contact with the source.[9] *S. maltophilia* can be identified by automated methods like VITEK. Lack of automated systems hampers the early diagnosis leading to prolongation of illness and Intensive Care Unit(ICU) stay.[10]

Studies from India have shown that 90.9% *S. maltophilia* were susceptible to colistin and 27.3% susceptible to ceftazidime and minocycline.[11]

S. maltophilia is primarily isolated in patients in the intensive care unit and need for vasopressors, autoimmune disease, lower P/F ratios and thrombocytopenia were associated with higher mortality.[12]

We intended to study theclinic-microbiological profile of *S. maltophilia* isolates from various samples and outcome of the infections in our tertiary healthcare center.

METHODOLOGY

This is an observational and cross-sectional study which was carried out at Department of Microbiology of a tertiary care centre in Pune, India between 01 Jan 2021 till 30 Jun 2022. Ethical committee approval was obtained from the institution. All cases found positive for *S. maltophilia* were included in the study and samples with mixed type of growth were excluded. Sample collection was done as per standard protocol and was transported immediately to the laboratory. Sample collection was done only once per patient.

All samples (except blood and urine) were inoculated on Blood agar and MacConkey agar where as urine samples were inoculated on Cysteine Lactose Electrolyte Deficient agar and blood was inoculated in BACT/Alert blood culture bottles and all the samples were incubated at 35-37°C. Isolates were identified using Matrix assisted Laser Desorption/ionization- time of fight(MALDI-TOF), Mass spectrometry (MS) or VITEK 2 Compact. Antimicrobial susceptibility testing was performed as per Clinical Laboratory Standards Institute (CLSI) guidelines M100 31st and 32nd edition.

MALDI-TOF MS identification

Strains were identified by MALDI-TOF MS principle using the VITEK MS (bioMꞌrieux SA, France). Isolates were smeared onto the sample spots on the target slide and 1µL VITEK MS-CHCA matrix was applied over the sample and air dried till both the matrix and sample co-crystallized. The target slide was loaded into the VITEK MS system to acquire the mass spectra and data was compared with known mass spectra contained in the database.

Staphylococcus aureus ATCC 25923 and *Escherichia coli* ATCC 25922 were used as the quality control strain.

VITEK 2 susceptibility testing

The isolates were subjected to Antimicrobial susceptibility testing using VITEK 2 (bioMerieux SA, France). The cards used were GN AST 280 and 281. *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were used as the quality control strain. Quality controls of all the bacteriological AST procedures are carried out on a weekly cycle.

Statistical analysis

Data was tabulated and analyzed using software Open Epi version 3.01 and Statistical Package for Social Sciences (SPSS) version 22. Categorical data have been presented as numbers and percentages (%) and quantitative data in terms of mean and standard deviation. Categorical variables have been analysed using Pearson's chi-square test and Fisher exact tests (when the expected count of 20% of cells is less than 5). A p value of <0.05 has been considered as statistically significant.

RESULTS

Forty-two culture positive cases were identified and included in the study. Table 1 shows the list of various clinical specimens from where *S. maltophilia* was isolated.

The mean age of study subjects was 48.6 ± 12.1 years with a third of patients in the age group of 41 to 50 years (14 cases, 33.3%), followed by 31 to 40 years (12 cases, 28.6%). There was a male predominance with a ratio of 6:1(36 men and 06 women).

Majority of isolates (61.9%) were from patients admitted in Acute healthcare settings including Intensive Care Units (ICU), High Dependency Units (HDU)and acute wards. Amongst the non-ICU patients *S. maltophilia* was isolated from surgical wards and Cancer wards. Sixteen cases (38.1%) had an immunocompromised state, while remaining (61.9%) were non-immunocompromised.

The isolates had high susceptibility to trimethoprim-sulfamethoxazole (TMP-SXT) (85.7%) and Minocycline (85.7%) and least susceptible to Ceftazidime (45.2%). The isolates found to be susceptible to all drugs were 33.33% while 16.7% of isolates were resistant to Ciprofloxacin, Minocycline and Ceftazidime. The drug susceptibility among fluoroquinolones was comparable with levofloxacin having slightly higher (76.9%) sensitivity than ciprofloxacin (71.4%). Amongst isolates 19.04% were resistant to both Fluoroquinolones (Levofloxacin, ciprofloxacin) tested. Antibiogram of isolates is depicted in Table 2.

A case fatality rate of 7.1% (3/42 cases) was noted in the present study among patients

Table 1. Demographic details and sample report of patients

No.	Parameter	Percentage (n=42)
1	**Gender of patients**	
	Male	85.7(36) *
	Female	14.2 (06)
2	**Age of patients**	
	31 to 40 years	28.5(12)
	41 to 50 years	33.3(14)
	51 to 60 years	21.4 (09)
	> 60 years	16.6 (07)
3	**Mean age of the patients**	48.6 ± 12.1 years
4	**Sample wise distribution of *S. maltophilia***	
	Pus swab	28.5(12) *
	Blood	26.1(11)
	Sputum	16.6(07)
	Tracheal aspirate	9.5(04)
	Urine	7.1 (03)
	Tissue	4.7 (02)
	Corneal swab	2.3 (01)
	Bile	2.3 (01)
	Pleural fluid	2.3 (01)

*Statistically significant

Table 2. Antibiogram of *S. maltophilia*

Drugs	Susceptible Percentage (n=42)	Resistant Percentage (n=42)
Levofloxacin	78.5 (33)	21.4(9)
Trimethoprim-sulfamethoxazole (TMP-SXT)	88 (37)	11.9 (5)
Minocycline	85.7 (36)	14.2 (6)
Ceftazidime	45.2(19)	54.7 (23)

Table 3. Comparison of outcome among study subjects

Parameter	Outcome		Total N (%)	p-value
	Death N (%)	Discharged N (%)		
Age group				
31 to 40 years	0(0.0)	12 (100)	12 (100)	
41 to 50 years	2 (14.3)	12 (85.7)	14 (100)	0.513
51 to 60 years	1 (11.1)	8 (88.9)	9 (100)	
> 60 years	0(0.0)	7 (100)	7 (100)	
Sex				
Male	3 (8.3)	33 (91.7)	36 (100)	1.000
Female	0(0.0)	6 (100)	6 (100)	
Comorbidity				
Absent	1 (2.8)	35 (97.2)	36 (100)	0.049*
Present	2 (33.3)	4 (66.7)	06 (100)	
System involved				
Single	0(0.0)	30 (100)	30 (100)	
Multi-organ	3 (25.0)	9 (75)	12 (100)	0.019*
Total	3 (7.1)	39 (92.9)	42 (100)	--

*Statistically significant

with *S. maltophilia* and the remaining 39 cases were discharged after complete treatment. We further tried to explore the association of factors that may be responsible for mortality among the cases. Case fatality in the age group of 41 to 50 years and 51 to 60 years was observed to be 14.3% and 11.1%, respectively, with no deaths in the age group of 31 to 40 years and more than 60 years. All three deaths that occurred were among men. In the present study, the case fatality rate (CFR) was significantly higher among cases with one or more comorbidities (33.3%), while the CFR among patients without co-morbidity was 2.8%. Similarly, CFR among patients with multi-system involvement was 25% and all cases with single organ involvement were discharged after complete treatment (Table 3).

On comparison of final outcome (death or discharge) with drug susceptibility, it was noted that among the three cases with ill-fated outcome all were sensitive to levofloxacin, ciprofloxacin, cotrimoxazole and minocycline. Drug resistance among survival cases varied from 15.4% to 30.8% for these drugs with least drug resistance being in cotrimoxazole, minocycline (15.4%) and ciprofloxacin having a drug resistance of 30.8%. On the contrary to the above findings, all three fatal cases were resistant to ceftazidime (100%), and among discharged cases, 51.3% of cases were resistant to the drug (Table 4).

One interesting finding in our study was isolation of *S. maltophilia* from bile in a 72 year old male patient of cholelithiasis, patient had no comorbidities. The isolate was sensitive to all the drugs tested. Patient was treated with Co-trimoxazole (TMP-SMX), later operated, and discharged.

DISCUSSION

The important finding of the study was that *S. maltophilia* is also emerging as a primary pathogen in the immunocompetent individuals, as evident by our results where 61.9% of patients had no immunocompromised state. As *S. maltophilia*is an established nosocomial pathogen and also there are numerous case reports on community acquired *S. maltophilia* infections.[13] The present study findings will further open up research questions to understand pathogenicity and virulence factors responsible for the *S. maltophilia* infections.

The other important finding in our study is relation of outcome with ceftazidime resistance.

Table 4. Comparison of drug susceptibility with final outcome among study subjects

Parameter	Outcome		Total N (%)	p-value
	Death N (%)	Discharged N (%)		
Levofloxacin				
Resistant	0 (0.0)	9 (23)	9 (23.1)	1.000
Sensitive	3 (100)	30 (77)	33 (76.9)	
Ciprofloxacin				
Resistant	0(0.0)	12 (30.8)	12 (28.6)	0.545
Sensitive	3 (100)	27 (69.2)	30 (71.4)	
Cotrimoxazole				
Resistant	0(0.0)	6 (15.4)	6 (14.3)	1.000
Sensitive	3 (100)	33 (84.6)	36 (85.7)	
Ceftazidime				
Resistant	3 (100)	20 (51.3)	23 (54.8)	0.239
Sensitive	0(0.0)	19 (48.7)	19 (45.2)	
Minocycline				
Resistant	0(0.0)	6 (15.4)	6 (14.3)	1.000
Sensitive	3 (100)	33 (84.6)	36 (85.7)	
Total	3 (100)	39 (100)	42 (100)	--

Resistance to the drug ceftazidime was seen in all the three cases succumbing to death. Though the cause of death was multifactorial, and all three patients had comorbidities, the slightest delay in the initiation of appropriate antibiotic was the major contributor to the ill-fated outcome.

The resistance patterns of *S. maltophilia* was comparable with studies done by Hafiz TA *et al.,* where 95.9% of samples were susceptible to Trimethoprim-Sulfamethoxazole, followed by 68.9% of samples to levofloxacin. The least susceptibility was seen with ceftazidime (33.1%).[14]

New treatment guidelines recommend combination of antibiotics to obtain synergic effect.[15] Few studies have shown the synergic effect with Trimethoprim-Sulfamethoxazole and Tigecycline, and between Amikacin and Tigecycline.[16] It is also observed that when TMP-SMX is combined with either ceftazidime, ciprofloxacin or tobramycin, it produces higher bactericidal efficacy against *S. maltophilia* clinical isolates.[17] Moxifloxacin has shown some promising effects for the treatment of multi drug resistant *S. maltophilia* infections in some of the studies.[18]

In one of the recent studies, *S. maltophilia* isolates were resistant to at least six of the antibiotics tested, including *Trimethoprim/Sulfamethoxazole* (*SXT*).[19] However, Tigecycline which has good *in vitro* activity against trimethoprim/sulfamethoxazole resistant strains, is a promising alternative for treating *S. maltophilia* infections.[20]

Limitations of the study

The present study is single centric study with smaller sample size of only 42 isolates. Moreover, only 3 isolates were ceftazidime resistant, and disease outcome prediction cannot be concluded on such a small sample size. None of the samples were clones, as all three samples were from different patients and from different wards. However, the study provides an opportunity for further investigation on the role of ceftazidime resistance and mortality.

CONCLUSION

The mean age of present study subjects was 48.6 ± 12.1 years, with a third of patients in the age group of 41 to 50 years and male predominance with a ratio of 6:1 was observed. Majority of isolates were from patients admitted in Acute healthcare settings like Intensive Care Units (ICU), High Dependency Units (HDU) and

acute wards. The isolates of present study had high susceptibility to trimethoprim-sulfamethoxazole (TMP-SXT) and Minocycline and low susceptibility to Ceftazidime.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

FUNDING

None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

This study was approved by the Institutional Ethics Committee, Armed Forces Medical College, Pune, India.

INFORMED CONSENT

Written informed consent was obtained from the participants before enrolling in the study.

REFERENCES

1. Bennett JE, Dolin R, Blaser MJ. Mandell, douglas, and bennett's principles and practice of infectious diseases E-book. Elsevier health sciences. 2019.
2. Brooke JS. Advances in the microbiology of *Stenotrophomonas maltophilia*. *Clin Microbiol Rev.* 2021;34(3):e0003019. doi: 10.1128/CMR.00030-19
3. Carmody LA, Spilker T, LiPuma JJ. Reassessment of *S. maltophilia* phenotype. *J Clin Microbiol.* 2011;49(3):1101-1103. doi: 10.1128/JCM.02204-10
4. Araoka H, Baba M, Yoneyama A. Risk factors for mortality among patients with *S. maltophilia* bacteraemia in Tokyo, Japan, 1996-2009. *Eur J Clin Microbiol Infect Dis.* 2010;29(5):605-608. doi: 10.1007/s10096-010-0882-6
5. Jacob A, Iyadurai R, Punitha JV, et al. Stenotrophomonas isolates in a tertiary care centre in South India. *Indian J Med Microbiol.* 2022;40(1):46-50. doi: 10.1016/j.ijmmb.2021.11.004
6. Soni M, Kapoor G, Perumal N, et al. Emergence of Multidrug-Resistant Non-Fermenting Gram-Negative Bacilli in a Tertiary Care Teaching Hospital of Central India;Is Colistin Resistance Still a Distant Threat?. *Cureus.* 2023;15(5);e39243. doi: 10.7759/cureus.39243
7. Chien YC, Liao CH, Sheng WH, et al. Clinical characteristics of bacteremia caused by Burkholderia cepacia complex species and antimicrobial susceptibility of the isolates in a medical center in Taiwan. *Int J Antimicrob Agents.* 2018; 51 : 357-64.
8. Sethi S, Sharma M, Kumar S, Singhal L, Gautam V, Ray P. Antimicrobial susceptibility pattern of *Burkholderia cepacia* complex & *Stenotrophomonas maltophilia* from North India;Trend over a decade (2007-2016). *Indian J Med Res.* 2020;152(6):656-661. doi: 10.4103/ijmr.IJMR_9_19
9. Mojica MF, Humphries R, Lipuma JJ, et al. Clinical challenges treating *Stenotrophomonas maltophilia* infections;An update. *JAC-Antimicrobial Resistance.* 2022;4(3);dlac040. doi: 10.1093/jacamr/dlac040
10. 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 Microbiol.* 2020;20(1):294. doi: 10.1186/s12866-020-01985-3
11. Alsuhaibani M, Aljarbou A, Althawadi S, Alsweed A, Al-Hajjar S. *Stenotrophomonas maltophilia* bacteremia in children;risk factors and mortality rate. *Antimicrob Resist Infect Control* . 2021;10(1):19. doi: 10.1186/s13756-021-00888-w
12. Said MS, Tirthani E, Lesho E. *Stenotrophomonas Maltophilia.* Treasure Island (FL). StatPearls. 2023. https://www.ncbi.nlm.nih.gov/books/NBK572123
13. Montoya-Hinojosa E, Bocanegra-Ibarias P, Garza-Gonzalez E, et al. Discrimination of biofilm-producing *Stenotrophomonas maltophilia* clinical strains by matrix-assisted laser desorption ionization-time of flight. *PLoS One.* 2020;15(12):e0244751. doi: 10.1371/journal.pone.0244751
14. Hafiz TA, Aldawood E, Albloshi A, et al. *S. maltophilia* Epidemiology, Resistance Characteristics, and Clinical Outcomes; Understanding of the Recent Three Years' Trends. *Microorganisms.* 2022;10(12);2506. doi: 10.3390/microorganisms10122506
15. Biagi M, Tan X, Wu T, et al. Activity of Potential Alternative Treatment Agents for *Stenotrophomonas maltophilia* Isolates Nonsusceptible to Levofloxacin and/or Trimethoprim-Sulfamethoxazole. *J Clin Microbiol.* 2020;58(2). doi: 10.1128/JCM.01603-19
16. Patterson SB, Mende K, Li P, Lu D, et al, *Stenotrophomonas maltophilia* infections;Clinical characteristics in a military trauma population. *Diagn Microbiol Infect Dis.* 2020;96(2):114953. doi: 10.1016/j.diagmicrobio.2019.114953
17. Flores-Trevino S, Bocanegra-Ibarias P, Camacho-Ortiz A, Morfin-Otero R, Salazar-Sesatty HA, Garza-Gonzalez E. *Stenotrophomonas maltophilia* biofilm;its role in infectious diseases. *Expert Rev Anti Infect Ther.* 2019;17(11):877-893. doi:

10.1080/14787210.2019.1685875

18. Blanco P, Corona F, Martinez JL. Mechanisms and phenotypic consequences of acquisition of tigecycline resistance by *Stenotrophomonas maltophilia*. *J AntimicrobChemother.* 2019;74(11):3221-3230. doi: 10.1093/jac/dkz326
19. Elufisan TO, Luna ICR, Oyedara OO, et al. Antimicrobial susceptibility pattern of *Stenotrophomonas* species isolated from Mexico. *Afr Health Sci.* 2020;20(1):168-181. doi: 10.4314/ahs.v20i1.22
20. Gil-Gil T, Martɒnez JL, Blanco P. Mechanisms of antimicrobial resistance in *Stenotrophomonas maltophilia*; a review of current knowledge. *Expert Rev Anti Infect Ther.* 2020;18(4):335-347. doi: 10.1080/14787210.2020.1730178