ORIGINAL ARTICLE

Eastern Journal of Medicine
East J Med 30(3): 354-360, 2025
DOI: 10.5505/ejm.2025.40111

Distribution and Antibiotic Susceptibilities of *Stenotrophomonas Maltophilia* Isolates Detected In Ümraniye Training and Research Hospital

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ABSTRACT

Stenotrophomonas maltophilia is becoming increasingly important due to its increasing incidence, natural resistance to many antibiotics and increasing resistance rates to trimethoprim-sulfamethoxazole. This study was conducted in the Microbiology Laboratory of Ümraniye Training and Research Hospital of Health Sciences University between 2021 and 2023. A total of 410 samples from 295 patients isolated from different samples from various clinics were included in the study. Bacterial identifications were performed by VITEK®MS device (Bio-Mérieux v.3.2, France) and susceptibility tests were performed according to EUCAST and CLSI recommendations. In this study, *S.maltophilia* was detected in 149 patients in 2021, 66 patients in 2022 and 80 patients in 2023. In the study, isolates of the agents were detected in patients hospitalized in the Anesthesiology and Reanimation, Pediatric, Neonatal, Pediatric Cardiovascular Surgery and Internal Medicine intensive care units at rates of 30%, 16.3%, 15.4%, 13.2% and 4.6%, respectively. In tracheal aspirate, blood, catheter, peritoneal, biliary, wound and sputum samples of the patients, isolates of this agent were found in 48.8%, 23.7%, 8%, 2.7%, 2.7%, 2.7%, 2.7%, 2.4%, respectively. This agent was resistant to TMP-SXT, levofloxacin and ceftazidime at rates of 15.4%, 10.2% and 32.8%, respectively. In this study, it was determined that the number of *S.maltophilia* samples and the resistance rates of *S.maltophilia* to TMP-SXT, ceftazidime and levofloxacin increased gradually over the years. As a result, the importance of this bacterium is increasing due to the increase in the prevalence rates of *S.maltophilia* and TMP-SXT resistance rates against this agent.

Keywords: *Stenotrophomonas maltophilia*, distribution rates, resistance

Introduction

Stenotrophomonas maltophilia, defined by the World Health Organization (WHO) as a pathogenic, multidrug-resistant and important nosocomial infection agent, is a pathogen that can colonize and cause infections in immunocompromised patients. Infection rates caused by *S.maltophilia* have increased from 2.7% to 4.4% over the years (1,2). This agent has been encountered in soil, plant rhizosphere, animal organisms, water, washed food, household environment, moist surfaces, various environments and solutions used in hospitals. Although *S.maltophilia* is a pathogen with low virulence, it has recently been recognised as an important infection agent due to the increase in infection rates in hospitals (3). *S.maltophilia* causes infections in the bloodstream, heart, respiratory tract, eye, central nervous system, gastrointestinal system, liver, urinary tract, soft tissues, bone and medical implants (4). This agent has a natural resistance to β-lactam drugs, aminoglycosides, quinolones, macrolides, cephalosporins, carbapenems, tetracyclines, chloramphenicol, polymyxins and biocides. The emergence of new resistance mechanisms and resistance profiles of *S.maltophilia* against antimicrobial drugs requires monitoring and reporting of antimicrobial susceptibility tests (5). However, since the methods used in vitro

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Received: 04.01.2025, **Accepted:** 10.05.2025

antimicrobial susceptibility tests (such as E-tests, disc diffusion and agar dilution) of the isolates of this agent are difficult to compare, there are still difficulties in interpretation. According to the recommendations of the Clinical and Laboratory Standards Institute (CLSI), minimum inhibitory concentration (MIC) limit values are available for trimethropim-sulfmethoxazole (TMP-SXT), levofloxacin and ceftazidime. However, there are no tested limit values for all antibiotics used against this organism (6). In recent years, TMP-SXT has been preferred in the treatment of *S.maltophilia* infections and an increase in the resistance of this organism against this antimicrobial combination has been detected (7). In addition to the increase in the incidence of *S.maltophilia*, the increase in the resistance of this agent against TMP-SXT, levofloxacin and ceftazidime is also worrying (7-9).

The aim of this study was to determine the distribution of *S.maltophilia* isolates in hospitalized patients according to clinical and sample types and to reveal the antibiotic resistance rates of this organism.

Material and Methods

Before starting the study, study approval (Document number: B.10.1.TKH.4.34.H.GP.0.01/390) was obtained from the Scientific Research Ethics Committee of Ümraniye Training and Research Hospital, the University of Health Sciences. This study was conducted in the Microbiology Laboratory of Ümraniye Training and Research Hospital between 2021-2023. *S.malthophilia* isolates grown in 410 different samples of 295 patients sent to the laboratory from different clinics were included in the study. The same samples of the patients sent on consecutive days were excluded from the study. However, different samples belonging to the same patient were included in the study. Data for this study were obtained from the Laboratory Information Management System (LIMS). Sterile samples such as blood, cerebrospinal fluid (CSF) and peritoneal fluid were incubated in a fully automatic blood culture device (BacTALERT, bio-Mérieux, France). The samples in the blood culture bottles detected positive by the device and also non-sterile samples such as wounds, tissue biopsies, urine, tracheal aspirates, etc. were inoculated onto plates containing chocolate agar (BD), 5-10% sheep blood agar (BD), MacConkey agar (BD) and sabouraud dextrose agar (BD) media. The plates were incubated in an oven at 37°C for 24-96 hours. Gram staining was performed from the colonies of the cultures that grew after incubation. After microscopic examination of the stained preparations, the identification of Gram-negative bacilli, which were negative for oxidase test, was performed on VITEK® 2 COMPACT (VITEK 2 bio-Mérieux, France) and VITEK® MS (bio-Mérieux, France v.3.2) automated systems. Antibiotic susceptibilities of the samples were performed on VITEK® 2 COMPACT device (VITEK 2 bio-Mérieux, France) using VITEK2 AST-GN420 card. Accordingly, TMP-SXT MIC values determined for *S.maltophilia* in the gram negative antibiogram panel performed on the VITEK® 2 COMPACT system were considered as S≤0.001 mg/L, R>4 mg/L. The results were evaluated according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria and reported according to the recommendations of the Turkish Microbiological Society (TMC) (10,11). Antibiotic susceptibility results for levofloxacin and ceftazidime were studied within the framework of antibiotic gradient test (E-test, bio-Mérieux, France) and CLSI standards, MIC values were determined and reported according to TMC recommendations (6,11).

Statistics Analysis: In this study, the data were transferred to the computer and evaluated in IBM SPSS (version 23.0) package program. Chi-square test was used to analyze the data. Significance value was accepted as $p<0.05$ in statistical analysis.

Results

Among the patients included in the study, 168 (56.97%) were male and 127 (43.03%) were female. It was determined that 112 (37.96%) of the patients were under 18 years of age and 183 (62.04%) were over 18 years of age (Figure 1).

In the study, the causative agent was detected in 124 (30.2%), 67 (16.34%), 63 (15.36%) and 54 (13.17%) samples sent from Anesthesiology and Reanimation, Paediatrics, Neonatology and Paediatric Cardiovascular Surgery intensive care units, respectively (Table 1).

In the study, in tracheal aspirate, blood, catheter, urine, peritoneal fluid, wound, bile, sputum, pleural fluid, nasopharyngeal, conjunctiva, broncho-alveolar lavage (BAL), tissue biopsy and CSF samples, 48.78% (200), 23.65% (97), 8.04% (33), 5.12% (21), 2.68% (11), 2.68% (11), 2.68% (11), 2.43% (10), 1.21% (5), 0.97% (4), 0.48% (2),

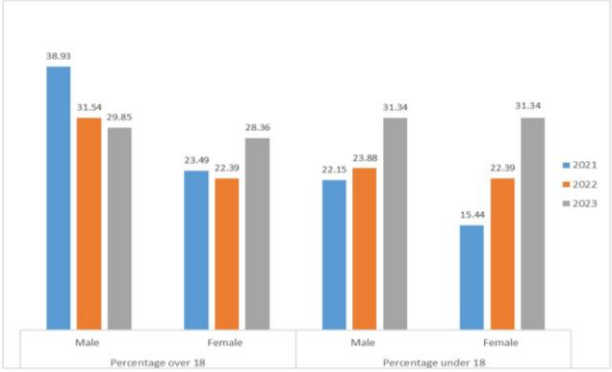

Fig. 1. Distribution of *Stenotrophomonas maltophilia* isolates according to gender, age and years

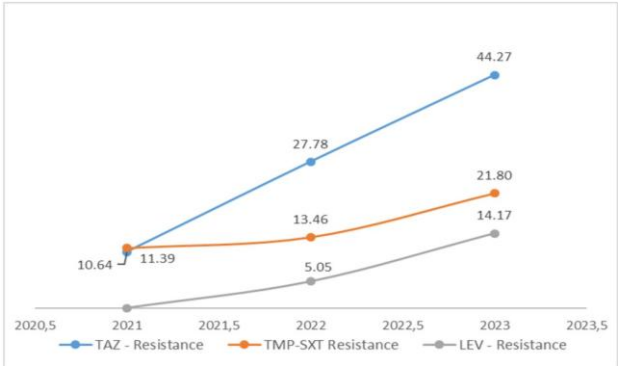

Fig. 2. Distribution of drug resistance of *Stenotrophomonas maltophilia* according to years (%)

0.48% (2), 0.48% (2) and 0.24% (1), respectively (Table 2).

Antibiotic resistance rates of this bacterium were detected to have increased gradually over the years. TMP-SXT resistance rates were 11.39% in 2021, 13.46% in 2022 and 21.80% in 2023 (p=0.039), levofloxacin resistance rates were 5.05% in 2022 and 14.17% in 2023 (p=0.024), and ceftazidime resistance rates were 10.64% in 2021, 27.78% in 2022 and 44.27% in 2023 (p=0.000) (Figure 2).

Discussion

Although TMP-SXT is the antibiotic of first choice in the treatment of *S.maltophilia* infections, it has been reported that the development of resistance to this antibiotic has increased rapidly. Increasing resistance to TMP-SXT reduces the treatment options and serious problems are experienced in treatment. The data of the TMP-SXT-resistant microorganisms (TOTEM) study included TMP-SXT-resistant *S.maltophilia* in the scope of middle priority agents (12). In studies conducted in South Korea (13) and China (14), 16% and 68% of *S.maltophilia* isolates were resistant to TMP-SXT, respectively. In a study conducted by Dadashi et al. in 2023, it was reported that 9.2% of *S.maltophilia* samples were resistant to TMP-SXT worldwide, and this rate increased to 19.2% in Asia. In the mentioned study, it was reported that this agent was resistant to levofloxacin at rates of 44.11%, 27.94%, 26.47% and 1.47% in Asia, America, Europe and Africa, respectively (7). In the SENTRY report, it was reported that the resistance of the agent to TMP-SXT was 2% in Canada and Latin America, 4.7% in the USA, 3.9% in Eastern Europe, 3.2% in Western Europe and 10% in Asia-Pacific countries (15). In a study conducted in Taiwan, resistance to TMP-SXT was found to be 85% (16). In a study conducted in New Delhi (17), it was reported that the rates of resistance to TMP-SXT and levofloxacin were 5.4% and 12%, respectively, and in a study conducted in China (18), the rates of resistance to TMP-SXT and levofloxacin were 5.1% and 8.6%, respectively. In a study conducted by Mendes et al. it was reported that the rates of resistance to TMP-SXT and levofloxacin were 21.6% and 13.3%, respectively (19). In a study conducted by Erinmez et al. in Gaziantep, it was found that the resistance rate of *S.maltophilia* against TMP-SXT was 3% (20). In a study conducted by Çopur et al. it was found that this agent was resistant to TMP-SXT and ceftazidime at rates of 12% and 37.5%, respectively (21). In a study conducted by Arabacı et al. in Istanbul, it was reported that this agent was resistant to TMP-SXT, levofloxacin and ceftazidime at rates of 11.4%, 15% and 70%, respectively (22). In a study conducted by Çaylan et al. in a paediatric age group, it was found that this agent was resistant to TMP-SXT at a rate of 10% (23). In a multicentre study conducted by Gezer et al. it was reported that the agent was resistant to TMP-SMX and levofloxacin at rates of 8.8% and 3.1%, respectively (24). In a study conducted by Kandemir et al. in Diyarbakır, it was reported that the agent was resistant to TMP-SXT, levofloxacin and ceftazidime at rates of 9.5%, 13.7% and 87.4%, respectively (25). In a study conducted by Bilgin et al. in Samsun and divided into two periods, it was determined that the agent was resistant to ceftazidime, levofloxacin and TMP-SXT at rates of 60.5%, 12.9% and 5.6% in the first period, respectively; and to ceftazidime, levofloxacin and TMP-SXT at rates of 12.9%, 5.6% and 8.6% in the second period, respectively (26). In a study conducted by Taşçılar et al. in Istanbul, it was reported that this agent was resistant to TMP-SXT, levofloxacin and

Table 1: Distribution of Numbers and Rates of *Stenotrophomonas Maltophilia* Isolates According to Clinics and Years

Clinics	Years			Total (Number and percent)
	2021 (Number and percent)	2022 (Number and percent)	2023 (Number and percent)	
Anaesthesiology and Reanimation Intensive Care Unit	71 (41.76)	26 (24.30)	27 (20.30)	124 (30.2)
Paediatric Intensive Care Unit	7 (4.12)	21 (19.63)	39 (29.32)	67 (16.34)
Neonatal Intensive Care Unit	26 (15.29)	14 (13.08)	23 (17.29)	63 (15.36)
Paediatric Cardiovascular Surgery Intensive Care Unit	27 (15.88)	14 (13.08)	13 (9.77)	54 (13.17)
General Surgery	7 (4.12)	6 (5.61	10 (7.52)	23 (5.6)
Internal Medicine Intensive Care Unit	8 (4.71)	6 (5.61)	5 (3.76)	19 (4.63)
Internal Medicine	7 (4.12)	2 (1.87)	--	9 (2.19)
Palliative Care Unit	2 (1.18)	3 (2.80)	2 (1.50)	7 (1.70)
Urology	2 (1.18)	2 (1.87)	3 (2.26)	7 (1.70)
Paediatrics	1 (0.59)	2 (1.87)	3 (2.26)	6 (1.46)
Gastroenterology	2 (1.18)	1 (0.93	3 (2.26)	6 (1.46))
Emergency Department	3 (1.76)	1 (0.93)	1 (0.75)	5 (1.22)
Paediatric Haematology and Oncology	--	4 (3.74)	--	4 (0.98))
Nephrology	2 (1.18)	1 (0.93)	--	3 (0.73)
Paediatrics Emergency Service	3 (1.76)	--	--	3 (0.73)
Paediatric Stem Cell Transplantation Center	1 (0.59)	1 (0.93)	1 (0.75)	3 (0.73)
Orthopaedics and Traumatology	--	2 (1.87)	--	2 (0.48)
Paediatric Surgery	--	--	1 (0.75)	1 (0.24)
Infectious Diseases	--	--	1 (0.75)	1 (0.24)
Thoracic Diseases	--	--	1 (0.75)	1 (0.24)
Neurosurgery	--	1 (0.93)	--	1 (0.24)
Otorhinolaryngology (ENT)	1 (0.59)	--	--	1 (0.24)

ceftazidime at rates of 12.6%, 14.5% and 65.9%, respectively (27). In a study conducted by Hazırolan et al. in Ankara, it was reported that the agent was resistant to TMP-SXT and levofloxacin at rates of 4.08% and 11.71%, respectively (28).

In the present study, the rates of resistance to TMP-SXT were 11.39%, 13.46% and 21.80% in 2021, 2022 and 2023, respectively; to levofloxacin 5.05% and 14.17% in 2022 and 2023, respectively; to ceftazidime 10.47%, 27.77% and 44.72% in 2021, 2022 and 2023, respectively. These results were compatible with the results of other studies except the study conducted by Bilgin et al. in Samsun, and it was determined that the resistance rates of *S.maltophilia* against all three antibiotics increased rapidly over the years.

In the SENTRY report, it was reported that *S.maltophilia* was the most frequently isolated agent in respiratory tract infections, it was found four times higher in respiratory tract samples than in blood culture samples, and it was rarely isolated in wound and urinary tract infections (15). In a study conducted by Dadashi et al. it was reported to be detected in blood, tear and respiratory tract samples at rates of 36.8%, 19.3% and 15.8%, respectively (7). In a study conducted by Yang et al. this agent was isolated from sputum, tracheal aspirate, bronchoalveolar lavage, blood and wound samples at rates of 70.6%, 6.2%, 4.3%, 4.2% and 3.9%, respectively (18). In a study conducted by Mendes et al. this agent was isolated from blood, catheter tip, tracheal aspirate, pleural fluid, urine samples and bone with rates of 44.3%, 3.8%, 29.2%, 0.9%, 10.3% and 1.8%, respectively (19). In a study conducted by Batra et al. in New Delhi, this agent was found in blood, tracheal

Table 2: Distribution of Numbers and Rates of *Stenotrophomonas maltophilia* Sample Types According to Years

Types of the samples	2021 (Number and percent)	2022 (Number and percent)	2023 (Number and percent)	Total (Number and percent)
Tracheal Aspirate	51 (30.0)	62 (57.94)	87 (65.41)	200 (48.78)
Blood	76 (44.71)	15 (14.02)	6 (4.51)	97 (23.65)
Catheter	19 (11.18)	2 (1.87)	12 (9.02)	33 (8.04)
Urine	6 (3.53)	8 (7.48)	7 (5.26)	21 (5.12)
Peritoneal Fluid	2 (1.18)	4 (3.74)	5 (3.76)	11 (2.68)
Bile Fluid	3 (1.76)	2 (1.87)	6 (4.51)	11 (2.68)
Wound Culture	4 (2.35)	5 (4.67)	2 (1.50	11 (2.68)
Sputum	6 (3.53)	2 (1.87)	2 (1.50)	10 (2.43)
Pleural Fluid	2 (1.18)	1 (0.93)	2 (1.50)	5 (1.21)
Nasopharyngeal	--	2 (1.87)	2 (1.50)	4 (0.97)
BAL	--	1 (0.93)	1 (0.75)	2 (0.48)
Conjunctival	--	1 (0.93)	1 (0.75)	2 (0.48)
Tissue Biopsy	--	2 (1.87)	--	2 (0.48)
CSF	1 (0.59)	--	--	1 (0.24)

aspirate and skin/soft tissue samples with rates of 45.5%, 37.4% and 6.7%, respectively (17).

In a study by Kandemir et al. it was reported that this agent was isolated in blood cultures with a rate of 39.6% (25). In a study by Arabacı et al. this agent was found in 48%, 18%, 16% and 14% of blood, soft tissue, urine and tracheal aspirate samples, respectively (22). In a study conducted by Gezer et al. this agent was found in 33%, 21%, 1.3% and 2.3% of catheter, tracheal aspirate, urine and wound/tissue samples, respectively (24). In a study conducted by Erinmez et al. *S.maltophilia* was found in 70.4% and 22.5% of blood and respiratory tract samples, respectively (20). In a study conducted by Filiz et al. this agent was isolated from respiratory tract, blood, wound and urine samples at rates of 50%, 15.6%, 14.5% and 9.3%, respectively (29). In the study conducted by Taşçılar et al. this agent was found in 39%, 15.2%, 13.3%, 11.4% and 6.7% of tracheal aspirate, blood, sputum, urine and wound samples, respectively (27). In the study conducted Hazırolan et al. this agent was found in urine, tracheal aspirate, wound, sputum, blood and bile/peritoneal/pleural samples at rates of 30%, 30%, 21%, 7%, 6% and 6%, respectively (28). In the present study, *S.maltophilia* was found in 48.8%, 23.7%, 8.0%, 5.2%, 2.7%, 2.7%, 2.7%, 2.7% and 2.43% of tracheal aspirate, blood, catheter, urine, peritoneal fluid, bile fluid, wound, sputum samples, respectively. The rates of *S.maltophilia* according to the samples in this study are compatible with the results of previous studies.

In some studies, *S.maltophilia* was found at higher rates in intensive care unit patients. In the study conducted by Yang et al. 37.1%, 10.7%, 7.3% and 6.7% rates of this agent were found in patients hospitalized intensive care units, neurosurgery service, integrative medicine service and general surgery service, respectively (18). In the study conducted by Kandemir et al. *S.maltophilia* was found at the highest rate in patients hospitalized the intensive care unit (70%) (25). In the study conducted by Erinmez et al, this agent was found inpatients hospitalized 65% of intensive care units and 35% of other wards. In the aforementioned study, this agent was isolated with a rate of 17%, 15%, 14%, 10% and 8% in patients hospitalized Anesthesiology and Rehabilitation, Neurology, Internal Medicine, Surgery and Paediatric intensive care units, respectively (20). In the study conducted by Arabacı et al. this agent was found in 50% of the patients hospitalised in the intensive care unit (22). In a study by Solmaz et al. this agent was found in 79% of hospitalised patients and 50% of the agents were isolated from patients hospitalised in the intensive care unit (30). In a study by Bilgin et al. this agent was found in 38.8%, 19.2%, 17% and 13% of patients in intensive care unit, internal medicine, chest diseases and infection clinics, respectively (26). In a study conducted by Filiz et al. *S.maltophilia* was found in 28.1%, 23.9% and 7.2% of patients hospitalised in anaesthesiology and reanimation,

neonatal and chest diseases intensive care units, respectively (29). In a study conducted by Yeşil et al. this agent was found in 9.6% and 14.9% of patients hospitalised in paediatric and neonatal intensive care units, respectively (31).

In this study, *S.maltophilia* was found in 30%, 16.3%, 15.4%, 13.2%, 5.6% and 4.63% of the patients hospitalised in the intensive care units of Anaesthesiology and Reanimation, Paediatrics, Neonatology, Paediatric Cardiovascular, General Surgery and Internal Medicine, respectively. These findings are consistent with the results of previous studies.

Mendes et al. reported that 58% of the patients with *S.maltophilia* were male and the mean age of the patients was 57 years (19). Bilgin et al. found that 64.5% of the patients with *S.maltophilia* were male and the mean age of the patients was 60 years in males and 66 years in females. In the aforementioned study, it was reported that 3.3% of the patients were in the 0-18 age group, 41.3% in the 19-64 age group and 55.4% in the 65 and over age group (26). Çopur et al. reported that 53.3% of the patients were male and the mean age was 64 years (21). Gezer et al. found that 62.3% of the patients were male and the mean age was 64.6 years (21,24). Arabacı et al. reported that 64% of the patients were male and the mean age was 48 years in males and 60 years in females (22). Filiz et al. reported that 65.6% of the patients were male and the mean age of males and females was 47.66 years (29). In the present study, 57% of the patients with *S.maltophilia* were male, 38% of the patients were under 18 years of age and 62% of the patients were over 18 years of age. These results are compatible with the results of studies conducted by other investigators.

In conclusion, in this study, it was determined that the resistance rate of *S.maltophilia* to TMP-SXT, levofloxacin and ceftazidime has been increasing gradually over the years. In addition, the incidence of *S.maltophilia* is increasing and treatment options are becoming more limited due to increasing resistance rates to TMP-SXT, levofloxacin and ceftazidime. Therefore, new effective drugs should be investigated, and new treatment protocols should be determined.

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