# Antibiotics resistance of Stenotrophomonas maltophilia strains isolated from various clinical specimens.

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**Abstract**

**Background:** A limited number of antibiotics are recommended for the therapy of *Stenotrophomonas maltophilia* infections due to therapy difficulties caused by its numerous mechanisms of resistance.

**Objectives:** In this study conducted over a period of approximately 5 years we aimed to determine resistance rates of *S. maltophilia* based on drug classification recommended by Clinical and Laboratory Standards Institute.

**Methods:** A total of 118 *S. maltophilia* strains isolated from various clinical specimens between January 2006 and June 2012 were included in the study. BD Phoenixautomated microbiology system (Becton Dickinson, USA) was utilized for species level identification and antibiotic susceptibility testing.

**Results:** Sixty seven of *S. maltophilia* strains were isolated from tracheal aspirate isolates, 17 from blood, 10 from sputum, 10 from wound and 14 from other clinical specimens. Levofloxacin was found to be the most effective antibiotic against *S. maltophilia* strains with resistance rate of 7.6%. The resistance rates to other antibiotics were as follows: chloramphenicol 18.2%, trimethoprim-sulfamethoxazole 20.3% and ceftazidime 72%.

**Conclusion:** The study revealed that *S. maltophilia* is resistant to many antibiotics. The treatment of infections caused by *S. maltophilia* should be preferred primarily as levofloxacin, chloramphenicol, and TMP-SXT, respectively.

**Keywords:** *Stenotrophomonas maltophilia,* antibiotic, resistance.

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## Introduction

*Stenotrophomonas maltophilia* is a resistant pathogen that can cause bacteremia, endocarditis, respiratory system, central nervous system and urinary tract infections in patients with risk factors like malignancy or neutropenia, use of broad-spectrum antibiotics like carbapenem or long-term hospitalization[1,2].

Outside of hospital, *S. maltophilia* can be found in water resources like rivers, lakes and wells, as well as in soil and various plants. In hospital, these bacteria can be isolated from central venous/arterial monitors, dialysis machines, disinfectant solutions, deionized water, nebulizers, ventilation systems and hands of health care personnel. Although *S. maltophilia* can be isolated from wet environments, its long term survival in a dry environment is not very common[3,4]. *S. maltophilia* possesses virulence factors including DNase, RNase, fibrinolysin, lipases, hyaluronidase, protease, and elastase. These bacteria have the ability to survive in medical soutions and adhere to the prosthetic material[5].

*S. maltophilia* can manifest resistance to many commonly used antibiotics, including carbapenems, which makes infections caused by this bacterium difficult to treat[6]. Inappropriate use of broad-spectrum antibiotics like imipenem presents risk factor for *S. maltophilia* infections. The most important reason for this is the ability of *S. maltophilia* to hydrolyse imipenem[7].

*S. maltophilia* strains are intrinsically resistant to multiple antibiotics due to aminoglycoside acetyl-transferase and enzymes that inactivate erythromycin and genes encoding efflux pumps[8]. Besides the *S. maltophilia* strains being resistant to one antibiotic, these strains can develop resistance to multiple antibiotics (multidrug resistance).

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Due to frequent and irrational use of the broad-spectrum antibiotics, pan resistant strains have been occasionally reported in the hospitals[9]. The aim of this study was to determine resistance rates of *S. maltophilia* strains to the antibiotics specified by CLSI in the context of therapy difficulties caused by its numerous mechanisms of resistance.

## Methods

### Study site

The present study was performed in the microbiology laboratory of Yuzuncu Yil University School of Medicine, Van, Turkey. Our hospital is a 550-bed facility that provides health care to the city of Van and neighboring provinces and thus serves as regional medical center. All together, it provides health care services to the approximately 2.5 million people.

### Collection of strains, bacterial identification and antibiotic susceptibility testing

A total of 118 *S. maltophilia* strains isolated from various clinical specimens between January 2006 and June 2012 were included in the study. In the study, the resistance rates of *Stenotrophomonas* strains were screened retrospectively. Received samples were inoculated onto 5% sheep blood agar and EMB agar and incubated for 24h at 37°C. Blood culture samples were analyzed using fully automated blood culture system BacT/Alert 3D (bioMerieux, France). A quantitative sputum culture was performed and specimens yielding $10^5$ CFU per ml and more were evaluated. BD Phoenix automated microbiology system (Becton Dickinson, USA) was utilized for species level identification and antibiotic susceptibility testing of EMB agar lactose and cytochrome oxidase negative, non-fermentative bacteria. The antibiotic classes for *S. maltophilia* strains recommended by CLSI were included in the study[10]. According to the CLSI, MIC interpretive criteria of antibiotic resistance for ceftazidime, trimethoprim-sulfametoxasole, chloramphenicol, and Levofloxacin were accepted as ≥32, ≥4 PubMed /76, ≥32, and ≥8 (μg/mL), respectively.

### Study design and statistical analysis

This study was conducted as a retrospective clinical study. Z test was used for evaluate the difference between antibiotic resistance rate. Level of statistical significance was considered to be 5% and MINITAB (ver: 14) statistical package program was used for analysis.

## Results

The distribution of 118 *S. maltophilia* strains according to clinics was as follows: 51% Pediatrics, 17% Chest Diseases, 12% Anesthesia -Intensive Care Unit (ICU), 3% Otorhinolaryngology, 3% Internal Medicine, 3% Neurosurgery and 11% other clinics. Sixty seven of *S. maltophilia* strains were isolated from tracheal aspirate isolates, 17 from blood, 10 from sputum, 10 from wound, 3 from ear, 2 from CSF, 2 from paracentesis, 2 from pleural fluid, 2 from urine, 2 from puncture fluid and 1 from catheter. The most effective antibiotic against *S. maltophilia* strains was levofloxacin. The resistance rates of isolated *S. maltophilia* strains to antibiotics recommended by CLSI are shown in Table. Although the difference between trimethoprim-sulfametnoxazole and chloramphenicol has not been found statistically significant, the differences between other antibiotics have been found to be statistically significant ($p<0.05$).

**Table. The resistance rates of *S.maltophilia* strains to selected antibiotics (%)**

| Antibiotic | Class* | n | R | Resistance rate (%) |
|---|---|---|---|---|
| Ceftazidime | B | 118 | 85 | 72 |
| TMP-SXT | A | 118 | 24 | 20,3 |
| Chloramphenicol | B | 88 | 16 | 18,2 |
| Levofloxacin | B | 115 | 9 | 7,6 |

***: Drug classes specified in CLSI 2010 guidelines** (A: routinely reported drugs, B: important drugs and drugs that should be tested with priority)
**n:** Number of tested strains, R: Number of resistant strains,
**TMP-SXT:** Trimethoprim-sulfametoxasole

## Discussion

In recent years non fermentative Gram negative bacteria *(Pseudomonas aeruginosa, Acinetobacter baumannii, Stenotrophomonas maltophilia ve Burkholderia cepacia)* have been increasingly recognized as an important cause of nosocomial infections. Many difficulties are encountered in the treatment of these infections due to multiple antibiotic resistance of these bacteria[10,11]. *S. maltophilia* related nosocomial infections occur more frequently in immunocompromised patients and patients on mechanic ventilation in ICU and these infections are usually associated with high morbidity and mortality rates[12]. Natural resistance of *S. maltophilia* to multiple antibiotics used against Gram-negative bacteria increases mortality rates in all *S. maltophilia* infections, especially in bacteremia. Araoka et al[13] reported mortality rate higher than 50% in the patients with *S. maltophilia* related bacteremia.

In the previous studies *S. maltophilia* has been isolated mainly from respiratory (49%) and blood samples (41%). In our country, similarly, the most common clinical material for isolation of *S. maltophilia* consists of respiratory and blood samples. Celebi et al[14] reported that this bacterium was mainly isolated from respiratory (67%) and blood (16%) samples. In accordance with literature, respiratory (65%) and blood (14%) samples were the most common clinical material for the isolation of *S. maltophilia* in the present study as well.
*S. maltophilia* strains isolated from the sample according to the diagnostic criteria were admitted to the respiratory pathogen.

Limited therapy options are available for the treatment of infections associated with *S. maltophilia* strains due to their natural resistance to many antibiotics like beta-lactam antibiotics or aminoglycosides[15]. According to in vitro studies, the most effective antibiotics for *S. maltophilia* strains are levofloxacin and TMP-SXT. In a study of Hankiewicz et al[16] conducted with 80 clinical isolates of *S. maltophilia* strains of which 60% were multiple resistant, resistance rates for levofloxacin and TMP-SXT were found to be 4% and 29%, respectively . Sader et al[17] reported resistance to levofloxacin as 7% and resistance to SXT as 5%. In our country, Turk Dagi et al[18] worked with *S. maltophilia* strains isolated from blood culture and determined resistance rates of levofloxacin and TMP-SXT as 20% and 10%, respectively. On the other hand, Dizbay et al[19] reported resistance to TMP-SXT as 22% in a sample of 89 nosocomial *S.maltophilia* strains. In the present study resistance rate to levofloxacin and TMP-SXT were 7.6% and 20.3% respectively, which is in accordance with previous studies. Some researchers have argued that despite low resistance rate of TMP-SXT it should be used in combination with some other antimicrobial agent due to its low efficacy when used alone[16].

Chloramphenicol has been reported by several studies as a highly efficient antibiotic against *S. maltophilia* strains. In a study of Niks et al[20], chloramphenicol resistance was 23% in multiresistant hospital bacterial pathogens. Nicodemo et al[21] compared three different methods and reported chloramphenicol resistance between 19 and 23%. Although data on chloramphenicol resistance in our country was insufficient, in the present study resistance rate to chloramphenicol was found to be 18%. Despite its low resistance rate chloramphenicol is not widely used in clinical practice due to its potential side effects like bone marrow suppression or plastic anemia[22].

Resistance of *S. maltophilia* strains to ceftazidime vary. In a study from Europe of Masgala et al[23] ceftazidime resistance was reported as 24%. On the other hand, resistance rates to ceftazidime reported in our country are considerable higher. In the studies conducted in Turkey, Dizbay et al[19] found ceftazidime resistance rate to be 45%, TurkDagi et al[18] 78% and Zer et a[l6] 88%. Results regarding ceftazidime resistance rate obtained in this study (72%) are in accordance with national data.

Carbapenems are widely used antibiotics for empirical treatment of infections with Gram negative bacteria in hospital and especially in intensive care units. This causes treatment delay and leads to the rise of infections related to opportunistic pathogens like *S. maltophilia* which is naturally resistant to carbapenems. For this reason, pathogens resistant to multiple commonly used antibiotics, with high transmissibility in ICU and with problematic diagnosis and treatment like *S. maltophilia* should be considered as cause of infection in long-stay patients, patients with malignancy or neutropenia and patients using broad-spectrum antibiotics like carbapenem.

## Limitation

Firstly, the study was conducted retrospectively. Secondly, study was carried out in one center only. Multicenter study should be done with more strains.

## Conclusion

The study revealed that *S. maltophilia* is resistant to many antibiotics. The treatment of infections caused by *S. maltophilia* should be preferred primarily as levofloxacin,chloramphenicol,and TMP-SXT, respectively. Additionally, treatment planning in accordance with in vitro susceptibility test results are required for efficient treatment of *S.maltophilia* infections.

## Conflict of interest

None

## References


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