

# Antimicrobial Susceptibility of *Stenotrophomonas maltophilia* Clinical Isolates from Blood Samples in Iran

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**Introduction:** *Stenotrophomonas maltophilia* is a nosocomial multi drug resistant opportunistic pathogen which causes infections in vulnerable patients with cancer, cystic fibrosis and indwelling catheters. **Methods:** 45 clinical *S. maltophilia* isolates were collected from blood samples and identified by biochemical tests. Susceptibility to different antibiotics including co-trimoxazole, levofloxacin, minocycline, ticarcillin/clavulanic acid, chloramphenicol and ceftazidime were determined by disk diffusion and E-test methods. **Results:** All isolates were resistant to ceftazidime and susceptible to co-trimoxazole and 11.1% were resistant to ticarcillin/clavulanic acid. **Conclusion:** Ceftazidime as one of the extended spectrum  $\beta$ -lactams was the least effective antibiotic. Ticarcillin/clavulanic acid is one of the chosen antibiotics for *S. maltophilia* infections treatment. Here, we report ticarcillin/clavulanic acid resistance in *S. maltophilia* isolates for the first time in Iran. *J Med Microbiol Infect Dis*, 2015, 3 (1-2): 35-37.

**Keywords:** *Stenotrophomonas maltophilia*, Antimicrobial susceptibility, Iran.

## INTRODUCTION

*Stenotrophomonas maltophilia* is a gram negative rod shaped bacteria which causes serious nosocomial infections in immuno-deficient populations such as HIV infected ones, patients with cancer, neutropenia and specially cystic fibrosis and stem cell transplantation recipients. This microorganism has a high mortality rate and is one of the most important agents of blood and respiratory tract infections in patients with cancer and venous catheter [1-4]. This bacterium has been recovered from soil, plants, animals, water resources and various wet surfaces in hospitals [5]. *S. maltophilia* infections can occur in children and adults and community-acquired infections include bacteremia, wound/soft tissue infections and urinary tract infections has been reported [6]. Some inherited molecular mechanisms such as outer membrane decreased permeability, efflux pumps,  $\beta$ -lactamases, integrons and biofilm formation have made this bacterium resistant to a large number of antimicrobials such as  $\beta$ -lactams, quinolones, co-trimoxazole, carbapenems, tetracyclines, chloramphenicol, and disinfectants [1, 5, 7, 8]. Antibiotics that commonly are used for *S. maltophilia* infections include co-trimoxazole, levofloxacin, ticarcillin/clavulanic acid and minocycline. Co-trimoxazole is the first choice treatment but increasing resistance to that has been reported [9, 10]. Ticarcillin/clavulanic acid has been suggested as an alternative for co-trimoxazole resistant isolates while emerging resistance to this agent also has been reported [10]. Combination of antibiotics is a new strategy and synergistic effect for *S. maltophilia* infections between co-trimoxazole and ticarcillin/clavulanic acid or ceftazidim was observed [11]. Increasing rate of immunocompromised patients, prolonged consumption of antibiotics in hospitalized patients and some genetic disorders like cystic

fibrosis make it essential to monitor *S. maltophilia* drug resistance status. In this study, our objective was determining the antimicrobial susceptibility of *S. maltophilia* clinical isolates to different antibiotics.

## MATERIAL AND METHODS

**Isolation and identification.** Isolates were collected from blood samples of hospitalized patients that have symptoms including fever, nausea, general body ache and tachycardia in Imam Khomeini hospital laboratory. They were identified by conventional biochemical tests such as cytochrome oxidase activity, motility, TSI medium growth pattern, lysin decarboxylase activity and extracellular DNase production (Difco, Detroit, MI, USA) [12].

**Antimicrobial susceptibility test.** Susceptibility to co-trimoxazole, levofloxacin, minocycline, ticarcillin/clavulanic acid, chloramphenicol and ceftazidime were determined by disk diffusion (Mast Ltd, UK) and Minimum Inhibitory Concentration (MIC) of ticarcillin/clavulanic acid tested by E-test (Lioflichem, Teramo, Italy) according to Clinical and Laboratory Standards Institute (CLSI). All antibiotic disks and strips have been quality controlled by *Escherichia coli* ATCC 25922 [13].

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Pure stored isolates were subcultured for recovery then microbial suspensions with turbidity equivalent to 0.5 McFarland were cultured on mueller hinton agar plates (Difco, Detroit, MI, USA); disks and strips were put on plates and results were checked after 18 to 24 h incubation at 37°C.

# RESULTS

Totally 45 clinical isolates collected from blood samples of hospitalized patients during 2013 to 2014. The identity of the isolates was confirmed as *S. maltophilia* by various

biochemical tests. Then they were stored at -80°C in nutrient broth (Difco, Detroit, MI, USA) containing 15% glycerol. Detailed data is shown in table 1.

**Antimicrobial susceptibility testing.** All isolates (100%) were resistant to ceftazidime and were susceptible to co-trimoxazole, levofloxacin and minocycline. 11.1% of isolates were resistant to ticarcillin/clavulanic acid by disk diffusion and MIC of ticarcillin/clavulanic acid for these isolates were ranged from 128 to 256 µg/ml and all of them were resistant (Table 2).

**Table 1.** Data of patients and their related collected isolates

Variable	Number of Patients (%)	Ward	Number of Samples (%)
<b>Gender</b>			
Female	25 (55.6%)	Emergency 1	19 (42.2%)
Male	20 (44.4%)	Emergency 2	11 (24.4%)
		Heart surgery	1 (2.2%)
<b>Age</b>		Infectious diseases	5 (11.1%)
≤1	3 (6.6%)	Neurology	1 (2.2%)
≥20-40	9 (20%)	General	3 (6.6%)
>40-60	22 (48.8%)	NICU	3 (6.6%)
>60	11 (24.4%)	Nephrology	2 (4.4%)
		<b>TOTAL</b>	<b>45</b>

**Table 2.** Antimicrobial susceptibility test

Antibiotic	Sensitive (%)	Disk diffusion	
			Resistant (%)
Co-trimoxazole	45 (100%)		0 (0.0%)
Levofloxacin	45 (100%)		0 (0.0%)
Minocycline	45 (100%)		0 (0.0%)
Ticarcillin/clavulanic acid	40 (88.8%)		5 (11.1%)
Chloramphenicol	38 (84.4%)		7 (15.5%)
Ceftazidime	0 (0.0%)		45 (100%)

# DISCUSSION

Choosing the appropriate antibiotic for *S. maltophilia* infections treatment is difficult due to lack of adequate and precise information about its susceptibility to antimicrobial agents. In this study we determined *S. maltophilia* antimicrobial susceptibility to recommend efficient antibiotics. The highest resistance rate was detected against ceftazidime (100%), chloramphenicol (15.5%) and ticarcillin/clavulanic acid (11.1%). The ceftazidime resistance was higher than those of two other studies in Imam Khomeini hospital in Iran [14, 15]. Most of isolates were collected from Emergency 1 and 2 in Imam Khomeini hospital and all of them were recovered from blood samples, which is in agreement with another study (41.5%, emergency 1 and 23.6%, emergency 2) [14]. It is the first report on resistance of *S. maltophilia* isolates to ticarcillin/clavulanic acid in Iran. Another study reported more ticarcillin/clavulanic acid resistance rate (59.3%) compared to 11.1% in our study and the least effective antibiotic was ceftazidime which is in concordant with our results [16]. Co-trimoxazole, quinolones like levofloxacin and ticarcillin/clavulanic acid are the most effective antibiotics which are used for *S. maltophilia* infections

worldwide [2, 10]. Different reports in resistance rates may be originated from geographic conditions and less studies on *S. maltophilia* drug resistance in Iran. *S. maltophilia* is an emerging microorganism and its antimicrobial resistance in Iran is not as high as other countries but there is a few studies about its drug resistance in Iran. Reports in South Korea, Japan and Germany mentioned different resistance rate to ticarcillin/clavulanic acid (59.3%, South Korea) [16], co-trimoxazole (17.7%, Japan) [17], levofloxacin (28.8%, Germany) and ceftazidime (54.4%, Germany) [18]. We tested MIC only for ticarcillin/clavulanic acid because it was the only choice antibiotic that some isolates were resistant by disk diffusion method. E-test results for ticarcillin/clavulanic acid confirmed disk diffusion results. Regarding the prevalence of *S. maltophilia* associated infections in hospitalized patients, and its increasing antibiotic resistance, correct investigation of resistance profile can help us to adopt appropriate prevention and control measures for associated infections and to avoid increase in drug resistance. We recommend that antibiotic resistance associated genes to be investigated for better and comprehensive report of *S. maltophilia* antimicrobial resistance status.

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## CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

## REFERENCES

- Looney WJ, Narita M, Mühlemann K. *Stenotrophomonas maltophilia*: an emerging opportunist human pathogen. *Lancet Infect Dis*. 2009; 9 (5): 312-23.
- Ryan RP, Monchy S, Cardinale M, Taghavi S, Crossman L, Avison MB, Berg G, van der Lelie D, Dow JM. The versatility and adaptation of bacteria from the genus *Stenotrophomonas*. *Nat Rev Microbiol*. 2009; 7 (7): 514-25.
- Sakhnini E, Weissmann A, Oren I. Fulminant *Stenotrophomonas maltophilia* Soft Tissue Infection in Immunocompromised Patients: An Outbreak Transmitted via Tap Water. *Am J Med Sci*. 2002; 323 (5): 269-72.
- Yeshurun M, Gaftor-Gvili A, Thaler M, Keller N, Nagler A, Shimoni A. Clinical characteristics of *Stenotrophomonas maltophilia* infection in hematopoietic stem cell transplantation recipients: a single center experience. *Infection*. 2010; 38 (3): 211-5.
- Brooke JS. *Stenotrophomonas maltophilia*: an emerging global opportunistic pathogen. *Clin Microbiol Rev*. 2012; 25 (1): 2-41.
- Falagas ME, Kastoris AC, Vouloumanou EK, Dimopoulos G. Community-acquired *Stenotrophomonas maltophilia* infections: a systematic review. *Eur J Clin Microbiol Infect Dis*. 2009; 28 (7): 719-30.
- Sanchez MB, Hernandez A, Martinez JL. *Stenotrophomonas maltophilia* drug resistance. *Future Microbiol*. 2009; 4 (6): 655-60.
- Abbott IJ, Slavin MA, Turnidge JD, Thursky KA, Worth LJ. *Stenotrophomonas maltophilia*: emerging disease patterns and challenges for treatment. *Expert Rev Anti Infect Ther*. 2011; 9 (4): 471-88.
- Toleman MA, Bennett PM, Bennett DM, Jones RN, Walsh TR. Global emergence of trimethoprim/sulfamethoxazole resistance in *Stenotrophomonas maltophilia* mediated by acquisition of sul genes. *Emerg Infect Dis*. 2007; 13 (4): 559-65.
- Wu H, Wang J-T, Shiau Y-R, Wang H-Y, Lauderdale T-LY, Chang S-C. A multicenter surveillance of antimicrobial resistance on *Stenotrophomonas maltophilia* in Taiwan. *J Microbiol Immunol Infect*. 2012; 45 (2): 120-6.
- Gülmez D, Çakar A, Şener B, Karakaya J, Haşcelik G. Comparison of different antimicrobial susceptibility testing methods for *Stenotrophomonas maltophilia* and results of synergy testing. *J Infect Chemother*. 2010; 16 (5): 322-8.
- Connie R. Mahon DCL, George Manuselis. *Textbook of Diagnostic Microbiology*. 5 ed. Maryland Heights, Missouri 63043: Saunders Elsevier; 2015; 479.
- Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fifth Informational Supplement*. CLSI document M100-S25. Wayne, PA: 19087 USA; 2015; 35 (3).
- Jamali F, Boroumand MA, Yazdani F, Anvari MS, Pourgholi L, Mahfouzi S, Khak M. Minimal inhibitory concentration of ceftazidime and Co-trimoxazole for *Stenotrophomonas maltophilia* using E-test. *J Glob Infect Dis*. 2011; 3 (3): 254-8.
- Moradi Tabriz H, Abdollahi A, Mahfoozi S. Frequency of pathogens and antimicrobial susceptibility of bacteria isolated from bloodstream infections. *Iran J Pathol*. 2010; 5 (3): 143-9.
- Cho SY, Lee DG, Choi SM, Park C, Chun HS, Park YJ, Choi JK, Lee HJ, Park SH, Choi JH, Yoo JH. *Stenotrophomonas maltophilia* bloodstream infection in patients with hematologic malignancies: a retrospective study and in vitro activities of antimicrobial combinations. *BMC Infect Dis*. 2015; 15 (1): 69.
- Kanamori H, Yano H, Tanouchi A, Kakuta R, Endo S, Ichimura S, Ogawa M, Shimojima M, Inomata S, Ozawa D, Aoyagi T, Weber DJ, et al. Prevalence of Smqnr and plasmid-mediated quinolone resistance determinants in clinical isolates of *Stenotrophomonas maltophilia* from Japan: novel variants of Smqnr. *New Microbes New Infect*. 2015; 7: 8-14.
- Vidigal PG, Dittmer S, Steinmann E, Buer J, Rath P-M, Steinmann J. Adaptation of *Stenotrophomonas maltophilia* in cystic fibrosis: molecular diversity, mutation frequency and antibiotic resistance. *Int J Med Microbiol*. 2014; 304 (5): 613-9.