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Clinical isolation and resistance patterns of *Stenotrophomonas maltophilia* in Ilam, Iran

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A B S T R A C T

Introduction: *Stenotrophomonas maltophilia* (SMA) is a commensal and an emerging nosocomial pathogen responsible for serious infections, especially in immunocompromised hosts. Its intrinsically multidrug-resistant bacteria to multiple antibiotics. Current study aimed to determine the antibiotic susceptibility patterns of SMA isolates from hospitalized patients in Ilam, Iran.

Materials & Methods: This cross-sectional study conducted between September 2022 and February 2023 in Ilam, Iran. Clinical specimens from 85 patients were cultured, and SMA isolates were identified through biochemical testing. Antimicrobial susceptibility testing performed using the disk diffusion method based on CLSI guidelines.

Results: Out of 85 samples, 10 (11.76%) isolates were identified as SMA. All isolates were susceptible to Co-trimoxazole (100%), and most were sensitive to Levofloxacin (90%). High resistance rates were observed toward Meropenem, Piperacillin/Tazobactam, Ceftriaxone (100% each), Cefepime (90%), Gentamicin (80%), Ceftazidime (90%), and Amikacin (60%). Our findings indicated the significant multidrug resistance profile of SMA in Ilam.

Conclusion: Continuous surveillance, strict infection control, better antimicrobial stewardship, enhanced research to develop, effective treatment and prevention strategies should be adopted to management the changing resistance profile of SMA.

Keywords: *Stenotrophomonas maltophilia*, Antibiotic susceptibility patterns, Multidrug-resistant bacteria

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Introduction

Stenotrophomonas maltophilia (SMA) is a non-fermentative gram-negative bacillus that exists widely in the environment(1, 2). SMA has emerged as an important nosocomial pathogen capable of causing serious human infections, especially in severely debilitated patients (patients with cancer and low immune system function). Bloodstream infections (BSI), Ventilator associated pneumonia (VAP), bone and joint infections, urinary tract infections (UTI), endocarditis, and meningitis are among the infections caused by SMA (2). Many medical devices in hospitals may be considered as major reservoirs of infection with SMA (2, 3). The ability to form biofilms and the presence of bacteria on various surfaces in the hospital have made this bacterium an important cause of nosocomial infection (3, 4). The main risk factors for infection with SMA include: prolonged hospital stay, intensive care unit admission, organ transplantation, prolonged use of catheters, prolonged mechanical ventilation, prolonged antibiotic or immunosuppressive therapy, malignancies, chronic lung diseases including cystic fibrosis, tuberculosis and COPD (5). Infections caused by SMA are clinically important due to its inherent resistance to a wide range of antibiotics(1, 6). Therefore, assessing the resistance status of this bacterium and selecting the most appropriate antibiotic for the treatment of SMA infection is of great importance in order to reduce the mortality rate in the hospital. However, there is no study on the incidence and antibiotic resistance patterns of SMA in this region. Therefore, this study aimed to determine the incidence of SMA and its resistance in teaching hospitals in Ilam city, western Iran.

Materials and methods

Study population and bacterial isolates

This cross-sectional study received ethical approval from the local ethics committee of Ilam University of Medical Sciences, Ilam, Iran (IR.MEDILAM.REC.1402.191). Each patient or their legal representatives gave informed written consent and this study was in accordance with the Declaration of Helsinki (from September 2022 to February 2023). All samples were collected from various samples at Razi hospital (this hospital is well known medical facility and also involved in medical education and research in Ilam), Iran. All samples were culture on blood agar, MacConkey agar and EMB agar medium (Merck). SMA isolates were detected by different tests such as gram-negative bacilli and biochemical tests including Catalase, Indole, lactose, Motility, Methyl red, Oxidase, Citrate, Urease, Voges proskauer, Hydrogen sulfide, Lysine decarboxylase, DNase, Bile esculine, and Fermentation of sugars in TSI agar were carried out.

Antimicrobial susceptibility tests

Antibiotic susceptibility test for the isolates was performed by disk-agar diffusion method according to Clinical Laboratory Standard Institute (CLSI) (7). Disk diffusion was carried out using paper disks (Bio-Rad Laboratories, Hercules, CA, USA) on Mueller–Hinton agar (Bio-Rad Laboratories, Hercules, CA, USA). The resistance pattern was determined using Amikacin (AMK, 30 µg), Ceftazidime (CZA, 30 µg), Cefepime (FEP, 5 µg), Cefotaxime (CTX, 10 µg), Meropenem (MER, 10 µg), Levofloxacin (LEV, 5 µg), Co-trimoxazole (TMP-SMX, 5 µg), Gentamicin (GEN, 10 µg), Ceftriaxone (CTX, 10 µg), Piperacillin/ Tazobactam (TZP, 10 µg). Reference strains SMA ATCC 13637 was used as quality controls. Results were read after overnight incubation at 35°C by using specific breakpoints.

Findings

In the present study, from 85 individuals 10 (11/76%) isolates were identified as SMA by different tests. The SMA positive patients were between 25 and 74 years old, comprising 8 males and 2 females. A majority of isolates (40%) were recovered from cases in the Intensive Care Unit (ICU). The rate of SMA isolation from various hospital departments and patients' medical history are shown in Table 1.

Antimicrobial susceptibility tests

In current study, the positive isolates showed a significant susceptibility to Co-trimoxazole 10 (100%) and Levofloxacin 9 (90%), with the lowest susceptibility to Piperacillin/ Tazobactam 10 (100%), Meropenem (100%), and Ceftriaxone 10 (100%). Amongst isolates 9 (90%) were resistance to Ceftazidime and Cefepime. In addition, the rate of Amikacin resistance 6 (60%) was lower compare to Gentamicin 8 (80%) resistance (Table 1).

Table 1. The rate of SMA isolation from various hospital departments and patients' medical history

ID	Resistance	Sensitive	Gender	Age	ward	Patient history
ID 1	Amikacin, Ceftazidime, Cefepime, Gentamicin, Meropenem, Piperacillin/ Tazobactam, Ceftriaxone, Levofloxacin	Co-trimoxazole	Male	40	Internal	Femur fractures and use of platinum
ID 2	Amikacin, Ceftazidime, Cefepime, Gentamicin, Meropenem, Piperacillin/ Tazobactam, Ceftriaxone	Levofloxacin Co-trimoxazole-	Male	74	Nephrology	Prostate cancer
ID 3	Amikacin, Ceftazidime, Cefepime, Gentamicin, Meropenem, Piperacillin/ Tazobactam, Ceftriaxone	Co-trimoxazole-Levofloxacin	Male	68	Internal	rheumatism
ID 4	Amikacin, Ceftazidime, Cefepime, Gentamicin, Meropenem, Piperacillin/ Tazobactam, Ceftriaxone	Co-trimoxazole-Levofloxacin	Male	54	Internal	Diabetes Cellulitis
ID 5	Ceftazidime, Cefepime, Meropenem, Piperacillin/ Tazobactam, Ceftriaxone	Amikacin, Co-trimoxazole-Gentamicin-Levofloxacin	Male	74	Intensive care unit	Bloody Diarrhea, Epigastric pain, HTN, COPD, Heart disease
ID 6	Ceftazidime, Cefepime, Gentamicin, Meropenem, Piperacillin/ Tazobactam, Ceftriaxone	Amikacin, Co-trimoxazole-Levofloxacin	Female	30	Intensive care unit	Thalassemia Major, heartburn, Kidney Pain
ID 7	Ceftazidime, Gentamicin, Meropenem, Piperacillin/ Tazobactam, Ceftriaxone	Amikacin, Co-trimoxazole-Levofloxacin, Cefepime,	Male	52	Nephrology	ESRD, Heart disease
ID 8	Ceftazidime, Cefepime, Meropenem, Piperacillin/ Tazobactam, Ceftriaxone	Amikacin, Co-trimoxazole-Levofloxacin Gentamicin	Female	65	cardiac care unit	Diabetes, Colon cancer, Heart disease

ID 9	Amikacin, Cefepime, Gentamicin, Meropenem, Piperacillin/ Tazobactam, Ceftriaxone	Co-trimoxazole-Levofloxacin , Ceftazidime	Male	25	Intensive care unit	Lung cancer, Multiple oral ulcers
ID 10	Amikacin, Cefepime, Gentamicin, Meropenem, Piperacillin/ Tazobactam, Ceftriaxone	Co-trimoxazole-Levofloxacin , Ceftazidime	Male	55	Intensive care unit	Kidney Pain

Discussion

Choosing the right antibiotic for treating SMA infections is challenging due to its intrinsic and acquired resistance mechanisms. In This study the highest resistance rate was detected against Meropenem (100%), Piperacillin/ Tazobactam (100%), Ceftriaxone (100%) Cefepime (90%), Gentamicin (80%), Ceftazidime (80%) and Amikacin (60%). These findings indicate that SMA exhibits natural resistance to many β-lactams and aminoglycosides, largely because of the presence of multidrug efflux pumps and β-lactamases. Co-trimoxazole, quinolones such as levofloxacin, are the most effective antibiotics utilized for SMA infections globally (8-10). Nonetheless, resistance rates to these agents are also increasing in different regions. For example, our study found a comparatively lower resistance to these drugs, but the global trend indicates rising resistance, which poses a serious challenge to effective treatment(6, 11). For example, susceptibility to Co-trimoxazole and Levofloxacin have been reported at 100% and 65.2%% in Japan(12). Variations in resistance patterns might be influenced by geographic differences, hospital infection control methods, and the rate of antibiotic use. In Iran, research on the resistance of SMA is scarce, and enhanced monitoring is required. Our results indicate that the antimicrobial resistance of SMA in Iran is lower than many other countries, however this may be due to the small amount of data rather than an actual difference. Reports from South Korea, Japan, Germany, Pakistan and Hungary, have indicated varying resistance rates to Ticarcillin/Clavulanic acid (59.3%, South Korea)(13), Co-trimoxazole (17.7%, Japan)(14), Levofloxacin (28.8%, Germany), Ceftazidime (54.4%, Germany)(15), and Ciprofloxacin (9.6%, Pakistan, 54%, Hungary) (16, 17). These findings highlight the differences across regions. In our study, 10 isolates were identified as SMA. Juhász et al., reported that 70% of the SMA were obtained from ICU while in our study 40% were from ICU (17). Our results, similar to majority of the studies, showed that most SMA isolates were collected from ICU (18-20). This supports the idea that the ICU is a major reservoir for SMA. The higher prevalence of SMA isolates during the COVID-19 pandemic may be due to factors such as prolonged hospital stays and broad-spectrum antibiotic use. Due to the increasing incidence and drug resistance, it is crucial to implement strict infection control protocols, proper use of antibiotics, and ongoing monitoring. Moreover, clinical laboratories must implement reliable and standardized methods for susceptibility testing of SMA. New treatment approaches, including combination therapy and novel antimicrobials, are presently being studied and may provide alternatives in the near future (20-22). This study has limitations, including, small samples (n=10 SMA isolates), and molecular methods were not used to confirm species identification.

Conclusion

The increasing incidence of SMA-associated infections, especially in hospitalized patients, is a significant concern. Its changing resistance profile demands continuous monitoring, better antimicrobial stewardship, enhanced research to develop effective treatment, and prevention strategies.

Ethics approval

This research is approved in Ethical Committee of Ilam University of Medical Sciences (Register Code: IR.MEDILAM.REC.1402.191).

Financial support

No financial support was provided for conducting this study.

Conflict of interest

The authors report no conflict of interest in this study.

Authors' contributions

M.Y.M and A.H contributed to the study conception and design. Data collection and analysis were performed by S.Kh, I.A, M.K and L.Gh. The first draft of the manuscript was written by N.M and M.Y.M and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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