Pediatrics & Neonatology 65 (2024) 183–187

Contents lists available at ScienceDirect

Pediatrics & Neonatology

journal homepage: www.pediatr-neonatol.com

Original Article

Emerging importance of multidrug-resistant *Stenotrophomonas maltophilia* infections in neonatal intensive care unit in a tertiary center in Turkey

Asuman Demirbuğa [a,*], Deniz Bahar Akgün Karapınar [b], Beril Yaşa [c], Asuman Çoban [c], Betigül Öngen [b], Elif Dede [a], Neslihan Mete Atasever [a], Ayper Somer [a], Selda Hançerli Törün [a]

[a] *Istanbul University, Istanbul Faculty of Medicine, Departmenf of Pediatrics, Division of Pediatric Infectious Diseases, Istanbul, Turkey*
[b] *Istanbul University, Istanbul Faculty of Medicine, Departmant of Medical Microbiology, Istanbul, Turkey*
[c] *Istanbul University, Istanbul Faculty of Medicine, Department of Neonatology, Istanbul, Turkey*

ARTICLE INFO

Keywords:
drug-resistance
intensive care unit
newborn
Stenotrophomonas maltophilia
trimethoprim-sulfamethoxazole

Objective: *Stenotrophomonas maltophilia* is an emerging multi-drug resistant, opportunistic pathogen in the neonatal intensive care unit (NICU). In this study, we aimed to assess the incidence, clinical features, antibiotic susceptibility, and treatment options of *S. maltophilia* infection among the healthcare-associated infections (HAIs) in the neonatal unit.

Methods: In this study, the patients who were hospitalized in the NICU between January 2020 and December 2021 with *S. maltophilia* isolated from clinical samples were included. Demographic, clinic features, and microbiological findings of the patients were retrospectively evaluated by using the medical records. The samples (lower respiratory tract, urine, peritoneal fluid) were first examined microscopically by gram preparation and cultured. Antibiotic susceptibility tests were performed according to the recommendations of The European Committee on Antimicrobial Susceptibility Testing (EUCAST) for TMP-SMX.

Results: *S. maltophilia* was isolated in 38 clinical samples of the 20 patients who were hospitalized at the NICU between January 2020 and December 2021. A total of 40 % (n = 8) of samples from different patients were accepted as colonization. Ventilator-associated pneumonia was determined in 55 % (n = 11), and urinary tract infection in 5 % (n = 1). *S. maltophilia*-associated bacteremia was not detected in any of the cases. The TMP-SMX susceptibilities of the strains were as it follows: 3 (15 %) were resistant (R), 7 (28 %) were susceptible (S), and 10 (47 %) were susceptible-increased exposure (I). Three of these patients were given dual antibiotics therapy (levofloxacin plus TMP-SMX) and nine of them were given only TMP-SMX. The most common hospital-acquired infectious agents are Gram negative microorganisms (51 %), followed by coagulase negative staphylococci (CNS), *Staphylococcus aureus* (24 %) and *S. maltophilia* (24 %).

Conclusion: Increasing TMP-SMX resistance and specific drug and dosage-related problems in the neonatal unit are important problems in treatment management.

1. Introduction

Stenotrophomonas maltophilia is a multidrug-resistant, non-fermenting, aerobic, gram-negative bacillus that is generally regarded as an opportunistic pathogen, which causes hospital-acquired infections, such as pneumonia, bacteremia, endocarditis, central nervous system, skin, soft tissue, and gastrointestinal infections, and it is associated with septic shock in critically ill and immunosuppressed patients.[1,2]

According to TOTEM (TOp TEn resistant Microorganisms) study, extended-spectrum beta-lactamase *Serratia marcescens*, vancomycin-resistant Enterococci, and TMP-SMX-resistant *S. maltophilia* were identified as medium priority at intensive care.[3] In the previous studies, the incidence of *S. maltophilia* infections ranged from 7.1 to 37.7 cases per 10,000. Although attention was drawn to infections and risk factors in adult patients in most studies, serious infections associated with *S. maltophilia* were also described in children and in the neonatal unit.[4–7] The prevalence of *S. maltophilia* infection in the general population was about 1.3–1.68 %[8] while the incidence of *S. maltophilia* infection in children in the Intensive Care Unit (ICU) was 0.8–20.3 %.[9,10] In Turkey, critical *S. maltophilia*-related infections with mortality rates of 17 % and 36 % have been reported in neonatal intensive care units (NICU).[5,11]

S. maltophilia infections are an important cause of life-threatening

* Corresponding author.
E-mail address: asumandemirbuga@hotmail.com (A. Demirbuğa).

https://doi.org/10.1016/j.pedneo.2023.04.019
Received 31 October 2022; Received in revised form 10 April 2023; Accepted 21 April 2023
Available online 20 October 2023
1875-9572/Copyright © 2024, Taiwan Pediatric Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

nosocomial infections in children.[4] Previous studies have shown various risk factors for infection or colonization by *S. maltophilia*, including prior use of broad-spectrum antimicrobial agents, or other drugs, immunosuppressive therapy, and parenteral nutrition.[2,12] Also prolonged hospital stays, invasive procedures, lower gestational age and low birth weight, neutropenia, underlying diseases such as chronic pulmonary and cardiovascular diseases, intravenous drug use, and human immunodeficiency virus infection, malignancy, and exposure to patients with *S. maltophilia* wound infection were significantly associated with *S. maltophilia* infections.[5,13] Trimethoprim/sulfamethoxazole (TMP/SMX) has been considered the treatment of first choice for infections caused by *S. maltophilia* although the sensitivity varies between 79 and 96 %.[14] However, the Infectious Diseases Society of America (IDSA) drew attention to the increasing resistance rates, and it was recommended to consider different treatment options in moderate-to-severe disease.[15] This result was consistent with the study by Zhao et al., who found that TMP/SMX resistance was a signal of multi-drug resistance (MDR).[16]

In this study, we aimed to assess the epidemiological and clinical features, TMP-SMX resistance rates and treatment approach of newborns with *S. maltophilia* infection in the NICU.

2. Material and methods

2.1. Participants

In this study, 20 cases who were hospitalized in the NICU of Istanbul University Istanbul Faculty of Medicine in Turkey, between January 2020 and December 2021 with *S. maltophilia* isolated from clinical samples were included. It is a tertiary center and there were 274 (in 2020) and 384 (in 2021) total patient admissions during this period. Demographic and clinical features, and microbiological findings of the cases were retrospectively evaluated using medical records of the patients.

2.2. Study design and definitions

2.2.1. Colonization

Among the cases in which the causative agent was isolated, those cases without clinical signs of infection (increased respiratory support parameters in intubated patients, increased amount of secretion, hypotonicity, circulatory failure, fever/hypothermia, increase in acute phase reactants) were defined as colonization.

2.2.2. Ventilator-associated pneumonia (VAP)

VAP is defined by the Center for Disease Control and Prevention (CDC) and National Healthcare Safety Network as new and persistent radiographic infiltrates and worsening gas exchange in infants who are ventilated for at least 48 h and who exhibit least 3 of the following criteria: temperature instability with no other recognized cause, leukopenia/leukocytosis, change in the characteristic of respiratory secretions, respiratory distress and bradycardia or tachycardia.[17]

2.2.3. Microbiological assessment

The cultures of the lower respiratory tract samples taken from the patients were evaluated in the Istanbul University Istanbul Faculty of Medicine Medical Microbiology Laboratory. The samples (lower respiratory tract, urine, peritoneal fluid) were first examined microscopically by Gram preparation and cultured. Inoculated blood agar and chocolate agar media were incubated in 5 % CO_2 and MacConkey agar and for urine culture BBL CHROMagar Orientation (BD, Germany) was incubated in normal atmosphere at 37 °C for 24–48 h. The microorganisms were identified by conventional methods and automated identification system (VITEK 2, bioMérieux, France). Antibiotic susceptibility tests were performed according to the recommendations of The European Committee on Antimicrobial Susceptibility Testing (EUCAST) and the results were evaluated according to the same guideline. There are only TMP-SMX clinical breakpoints at EUCAST. For levofloxacin, the breakpoints recommended by The Clinical and Laboratory Standards Institute (CLSI) for *S. maltophilia* were used in the study. The first clinical isolate of the patients was evaluated, and the results of the recurrent isolates were not included in the study.

2.2.4. Statistical analysis

Statistical data were analyzed with SPSS v.21 (SPSS Inc., Chicago, IL, USA). Values for numerical variables were given as mean ± standard deviation, depending on the normality distribution. Categorical variables were presented as numbers and percentages.

2.2.5. Ethics committee approval

The study was approved by the Istanbul University Clinical Research Ethics Committee (2022/637, 25.04.2022–862269). The informed consent form was not recommended by the ethics committee.

3. Results

3.1. Demographic and clinical characteristics

S. maltophilia was isolated in 38 clinical samples of the 20 patients who were hospitalized at the NICU between January 2020 and December 2021. *S. maltophilia* was detected in 8 (2.9 %) of 274 patients hospitalized in the NICU in 2020 and in 12 (3.1 %) of 384 patients hospitalized in 2021. Of the 20 patients, 30 % (n = 6) were female and 70 % (n = 14) were male, 95 % (n = 19) were preterm birth and 5 % (n = 1) was term. According to birth weight of gestational age, 30 % (n = 6) were small for gestational age (SGA), and 70 % (n = 14) were appropriate for gestational age (AGA). The demographic characteristics of the patients with *S. maltophilia* infection are shown in Table 1.

S. maltophilia was detected on the mean postnatal 27,9 ± 32,9 (0–120) day of the patients and it was detected in 40 % (n = 8) of patients in the first 7 postnatal days. In all cases, at least one risk factor was such as central catheter use, total parenteral nutrition, or broad-spectrum antibiotic use.

A total of 40 % (n = 8) of samples from different patients were accepted as colonization because these patients had no infection criteria. Ventilator-associated pneumonia in 55 % (n = 11) and urinary tract infection in 5 % (n = 1) were determined. *S. maltophilia*-associated bacteremia was not detected in any of the cases.

Three cases among the patients (14 %) died. However, there were additional accompanying anomalies (osteogenesis imperfecta, ileal atresia, severe respiratory distress syndrome). *S. maltophilia*-related septicemia was not considered as the cause of death.

3.2. Microbiological assessment

S. maltophilia was detected on the mean postnatal 27,9 ± 32,9 (0–120) day of the patients and it was detected in 40 % (n = 8) of patients in the first 7 postnatal days. It was isolated from tracheal aspiration in 19 samples, urine in one sample, and peritoneal fluid in one

Table 1
The demographic characteristics of the patients with *S. maltophilia* infection.

Characteristics of cases % (n)		
Gestational age (w)	Term (>37)	5 (1)
	Preterm (≤36 6/7)	95 (19)
Sex	Female	30 (6)
	Male	70 (14)
Birth weight for gestational age	AGA	70 (14)
	SGA	30 (6)
Postnatal day (mean ± SD)	27,9 ± 32,9 (0–120)	

AGA: appropriate for gestational age, SGA: small for gestational age, w:week, SD: standard deviation.

Table 2
Distribution of pathogens in healthcare-associated infections.

HAIs	% (n)
Gram-negative microorganisms	50 (25)
K. pneumoniae	28 (14)
P. aeruginosa	10 (5)
Acinetobacter spp.	6 (3)
Serratia spp.	6 (3)
Coagulase negative staphylococci	26 (13)
S. maltophilia	24 (12)
Total	100 (50)

HAIs; Healthcare-Associated Infections, *Spp*; species.

sample (also in tracheal fluid). There were polymicrobial infections in 40 % (n = 8) of patients [*Klebsiella pneumoniae* (n = 2), *Acinetobacter baumannii* (n = 2), *Pseudomonas aeruginosa* (n = 3), *Candida albicans* (n = 1)]. The frequency of hospital-acquired infectious agents in our unit is shown in Table 2.

3.2.1. *Antibiotics susceptibility, treatment and characteristics of resistant cases*

The TMP-SMX susceptibilities of the strains were as it follows: three (15 %) were resistant (R), seven (28 %) were susceptible (S), and 10 (50 %) were susceptible-increased exposure (I). During the follow-up time, it was observed that TMP-SMX resistance developed in the control culture samples of two patients who were sensitive to TMP-SMX. Three of these patients were given dual antibiotics therapy (levofloxacin plus TMP-SMX) and 9 of them were given only TMP-SMX. The clinical samples of three patients who received dual therapy were susceptible to increased exposure to TMP-SMX. All of them were SGA babies, and one had coinfection with *P. aeruginosa.* Three of the TMP-SMX resistant cases were considered as colonized. Two were twins born at the 28th week of gestation, the agent was isolated on the postnatal day 0, and no treatment was given considering colonization. All isolates were susceptible to levofloxacin according to CLSI, except for one patient who was colonized. The data on resistance and treatment of the patients are given in Table 3.

4. Discussion

In this study, we found that *S. maltophilia* was an important pathogen among healthcare-associated infections (HAIs) in NICU, and sometimes choose combined treatments were necessary. According to the CDC definition of HAIs and hospital surveillance data, the most common hospital-acquired infectious agents are gram-negative microorganisms (51 %) such as *K. pneumoniae, P. aeruginosa*, A*cinetobacter* spp.*,* and *Serratia* spp.*,* followed by coagulase negative staphylococci (CNS), *S. aureus* (25 %) and *S. maltophilia* (24 %) in the NICU in 2020 and 2021.[17] All of our patients were infants who needed intensive care and had at least one of the risk factors that were mentioned in previous studies.

Respiratory tract is the most common site of *S. maltophilia* infections, which has biofilm-forming capacity.[12,18] Moreover, medical equipment and a contaminated water system may be sources of nosocomial infections due to *S. maltophilia*. Studies have shown that the main source of infections is respiratory tract, central and urinary catheters.[19] However, it is difficult to distinguish between colonization and infection. In previous studies, it was reported that 46 % and 49 % of tracheal aspiration samples identified from the patients were accepted as respiratory tract infection.[5,12] In one study of newborns with *S. maltophilia* infection, ventilator-associated pneumonia and sepsis were determined in 82 % and in 9 % of neonates, respectively.[5] In addition, bacteremia due to *S. maltophilia* has been described in infants hospitalized in the NICU.[7,11] In our study, a total of 40 % (n = 8) of samples from different patients were accepted as colonization, and 50 % (n = 10) of the patients who had *S. maltophilia* in clinical samples were accepted as VAP, in line with other studies.

S. maltophilia often forms a part of polymicrobial infections; the rate of isolation of this pathogen as a component of a mixed infection ranges from 33 % to 70 %.[20,21] The most common additional pathogens are *P. aeruginosa*, Klebsiella spp.*, and Enterobacter cloacae*, Enterococcus sp., and coagulase negative staphylococci. *In these situations, the pathogenic role of S. maltophilia is difficult to assess exactly.*[22] *In one study,* a higher mortality rate was reported for pneumonia patients coinfected with *P. aeruginosa* and *S. maltophilia*.[23] Polymicrobial infection occurred in 40 % (n = 8) of our patients.

According to previous reports, the mortality rates vary from 14 % to

Table 3
Gestational age, birth weight, diagnosis, site of positive cultures, antimicrobial susceptibility and treatment, patient outcomes.

Case No	GA (w)	BW-GA	HAIs	Diag.	Culture Site	Susceptibility TMP-SMX/Lev		Treatment	Outcome
1	26	SGA	VAP	RDS	TAF	I	S	TMP-SMX + LEV	Discharged
2	28	AGA	C	Twin, RDS	TAF	R	S	–	Discharged
3	28	AGA	C	Twin, Ileum Perforation	TAF	R	S	–	Discharged
4	24	AGA	C	RDS	TAF	R	R	–	Discharged
5	33	SGA	VAP	Osteogenezis Imperfecta	TAF	R	S	TMP-SMX + LEV	Exitus
6	28	AGA	C	RDS	TAF	I	S	–	Discharged
7	30	SGA	VAP	RDS, NEC	TAF	I	S	TMP-SMX	Discharged
8	25	SGA	VAP	NEC	TAF	I	S	TMP-SMX + LEV	Discharged
9	27	SGA	VAP	İleal Atresia	TAF	I	S	TMP-SMX	Exitus
10	29	AGA	UTI	Twin, IUGR	URINE	I	S	TMP-SMX	Discharged
11	29	AGA	VAP	Twin, IUGR, Intestinal perforation	TAF	I	S	TMP-SMX	Discharged
12	35	AGA	C	TTN	TAF	S	S	–	Discharged
13	25	AGA	VAP	Twin, Chorioamnionitis	TAF	S	S	TMP-SMX	Discharged
14	30	SGA	C	RDS, Suspected Genetic Disorders	TAF	S	S	–	Exitus
15	24	SGA	C	–	TAF	S	S	–	Discharged
16	30	SGA	VAP	NEC	TAF, Periton	S	S	TMP-SMX	Discharged
17	38	AGA	C	CHD	TAF	S	S	–	Discharged
18	25	AGA	VAP	–	TAF	S	S	TMP-SMX	Discharged
19	31	AGA	VAP	NIH	TAF	S	S	TMP-SMX	Discharged
20	24	AGA	VAP	NIH/Intrauterine Bowel Perforation	TAF	S	S	TMP-SMX	Discharged

HAIs: Healthcare-Associated Infections, GA: gestational age, w: week, BW-GA: Birthweight for gestational age, AGA: appropriate for gestational age, SGA: small for gestational age, VAP: ventilator-associated pneumonia, C: colonization, TAF: tracheal aspirate fluid, TMP-SMX: trimetoprim-sulfamethoxazole, Lev: levofloxacin, CHD: congenital heart disease, S: susceptible, I: susceptible-increased exposure R: resistant, NEC: necrotizing enterocolitis, RDS; respiratory distress syndrome; NIH; non-immune hydrops, Diag.:diagnosis.

62 % and from 24 % to 58 % for attributable mortality in another studies.[24–26] Three cases (15 %) died among our patients. These patients had comorbid diseases including osteogenesis imperfecta, severe RDS. and two out of the three patients had co-infection (*P. aeruginosa* and *Klebsiella* spp.*)*. Therefore, mortality was not associated with *S. maltophilia*.

There are limited antimicrobial options for infection due to *S. maltophilia* because of its extensive resistance to most antibiotics, including β-lactam antibiotics, cephalosporins, macrolides, aminoglycosides, and carbapenems.[8] Interpretive breakpoints for susceptibility are available only for ticarcillin/clavulanate, ceftazidime, minocycline, levofloxacin, TMP-SMX, and recently cefiderecol breakpoint was acknowledged in CLSI.[27] In contrast, EUCAST only defines MIC and zone diameter breakpoints for TMP-SMX.[26] The optimal treatment for *S. maltophilia* infections is not well-established and despite the lack of randomized controlled trials comparing TMP-SMX with any other available treatment of *S. maltophilia* infections, TMP-SMX is considered the 'drug of choice' for treating susceptible *S. maltophilia* infections.[15] IDSA also makes the following recommendations for moderate and severe infections: the use of combination therapy with a second agent added to TMP-SMX (e.g., minocycline, tigecycline, levofloxacin, cefiderocol) at least until clinical improvement is observed; or, in less severe infections, a sequential approach of initiating TMP-SMX and adding a second agent if an appropriate clinical response is not observed. Fluoroquinolones are commonly used as an alternative for patients infected with TMP-SMX-resistant-*S. maltophilia* or in those with intolerance due to adverse side effects.[28] However, increased levofloxacin resistance rates are of particular concern when it is used alone; up to 40 % resistance was reported in a pediatric study.[26,29] Although the rates of resistance to TMP-SMX have been reported in various studies, Chang et al. reported that TMP-SMX susceptibility is still high worldwide.[8] Although antibiotic susceptibility varies from country to country, the increasing rate of resistance for the TMP-SMX, which is the first choice in treatment, is a concern all over the world. Studies showed that resistance rates in Turkey were also rising (4.08 %, 7.7 %, 8.6 % and 9.4 %).[6,30–32] In our study, TMP-SMX resistance was 15 % during the study duration but in some countries it was as high as 41.7 %.[33] In addition to resistance and drug selection difficulties, drug dosage and side effects are the main problems in the neonatal unit. TMP-SMX competes with bilirubin for binding to albumin, and it can increase the level of indirect bilirubin. Thyagarajan et al. prescribed TMP-SMX for treatment of sepsis and pneumonia in newborns and noted no adverse effects, including signs of central nervous system toxicity. Thyagarajan et al.[34] suggested that TMP-SMX in oral doses administered to neonates for 7–10 days was unlikely to cause kernicterus but also recommended further studies using animal models and clinical studies in humans to address TMP-SMX toxicity.[7] The other problem is that there are no dosing recommendations for TMP-SMX in neonates.[35]

Considering the high morbidity and mortality with this pathogen and drug side effects, there are approaches recommending the use of levofloxacin over TMP-SMX or its use in combination.[36,37] In our study, no drug-related side effects were observed when used alone or in combination with other drugs.

Our study has some limitations. It was performed in a single center. Multicenter studies are needed to understand the prevalence and resistance rates of *S. maltophilia* in our country. In addition, the study includes data from during the COVID 19 pandemic. During this time, various factors such as the total number of inpatients, differences in infection control measures, and more limited working areas and personnel may have affected the results of the study.

In conclusion, *S. maltophilia* infections are also an important cause of morbidity and mortality in the neonatal unit. Increasing TMP-SMX resistance and specific drug- and dosage-related problems in the neonatal unit are important problems in treatment management. The VAP is the most common form of infection with *S. maltophilia* in this study. It can be expected that *S. maltophilia*-related morbidity and mortality will also decrease with the prevention bundle (personnel training, hand hygiene, management of equipment, etc.) against VAP development.

Funding

There was no funding for this study.

Declaration of competing interest

The authors have no conflicts of interest to declare.

References

[1] Viswanathan R, Singh AK, Ghosh C, Basu S. *Stenotrophomonas maltophilia* causing early onset neonatal sepsis. Indian Pediatr 2011;48:397–9.
[2] Denton M, Kerr KG. Microbiological and clinical aspects of infection associated with *Stenotrophomonas maltophilia*. Clin Microbiol Rev 1998;11:57–80.
[3] Rello J, Kalwaje Eshwara V, Lagunes L, Alves J, Wunderink RG, Conway-Morris A, et al. A global priority list of the TOp TEn resistant Microorganisms (TOTEM) study at intensive care: a prioritization exercise based on multi-criteria decision analysis. Eur J Clin Microbiol Infect Dis 2019;38:319–23.
[4] Kagen J, Zaoutis TE, McGowan KL, Luan X, Shah SS. Blood-stream infection caused by *Stenotrophomonas maltophilia* in children. Pediatr Infect Dis J 2007;26:508–12.
[5] Mutlu M, Yılmaz G, Aslan Y, Bayramoğlu G. Risk factors and clinical characteristics of *Stenotrophomonas maltophilia* infections in neonates. J Microbiol Immunol Infect 2011;44:467–72.
[6] Sadıç B, Başaran S, Şimşek-Yavuz S, Çağatay A, Özsüt H, Eraksoy H. Stenotrophomonas maltophilia: results of antimicrobial susceptibility testing and in vitro activity of the combination of ceftazidime and moxifloxacin. Klimik Derg 2019;32:29–34 [Article in Turkish].
[7] Behera B. *Stenotrophomonas maltophilia*, an emerging pathogen in newborns: three case reports and a review of the literature. World J Clin Infect Dis 2021;11:11–8.
[8] Chang YT, Lin CY, Chen YH, Hsueh PR. Update on infections caused by Stenotrophomonas maltophilia with particular attention to resistance mechanisms and therapeutic options. Front Microbiol 2015;6:893.
[9] Arthur C, Tang X, Romero JR, Gossett JG, Harik N, Prodhan P. Stenotrophomonas maltophilia infection among young children in a cardiac intensive care unit: a single institution experience. Pediatr Cardiol 2015;36:509–15.
[10] Ning BT, Zhang CM, Liu T, Ye S, Yang ZH, Chen ZJ. Pathogenic analysis of sputum from ventilator-associated pneumonia in a pediatric intensive care unit. Exp Ther Med 2013;5:367–71.
[11] Çetin BS, Çelebi S, Özkan H, Köksal N, Salı E, Çelik T, et al. *Stenotrophomonas maltophilia* outbreak in neonatal intensive care unit and outbreak management. J Pediatr Inf 2015;9:147–52.
[12] del Toro MD, Rodríguez-Bano J, Herrero M, Rivero A, García-Ordoñez MA, Corzo J, et al. Clinical epidemiology of *Stenotrophomonas maltophilia* colonization and infection: a multicenter study. Medicine (Baltimore) 2002;81:228–39.
[13] Nseir S, Di Pompeo C, Brisson H, Dewavrin F, Tissier S, Diarra M, et al. Intensive care unit-acquired *Stenotrophomonas maltophilia*: incidence, risk factors, and outcome. Crit Care 2006;10:R143.
[14] Gibb J, Wong DW. Antimicrobial treatment strategies fo *Stenotrophomonas maltophilia*: a focus on novel therapies. Antibiotics (Basel) 2021;10:1226.
[15] Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America guidance on the treatment of AmpC β-lactamase-producing enterobacterales, carbapenem-resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* infections. Clin Infect Dis 2022;74:2089–114.
[16] Zhao S, Yang L, Liu H, Gao F. Stenotrophomonas maltophilia in a university hospital of traditional Chinese medicine: molecular epidemiology and antimicrobial resistance. J Hosp Infect 2017;96:286–9.
[17] Center for Disease Control and Prevention (CDC). Pediatric ventilator-associated event (PedVAE). Available at https://www.cdc.gov/nhsn/pdfs/pscmanual/pedvae-current-508.pdf. Accessed May 25, 2022.
[18] Fujita J, Yamadori I, Xu G, Hojo S, Negayama K, Miyawaki H, et al. Clinical features of Stenotrophomonas *maltophilia* pneumonia in immunocompromised patients. Respir Med 1996;90:35–8.
[19] Bilgin K, Çaycı YT, Bıyık İ, Gür-Vural D, Torun EG, Birinci A, et al. Comparing the biofilm formation properties of S. maltophilia isolates obtained from the pulmonary and extrapulmonary samples. Turk Hij Den Biyol Derg 2021;78:147–52.
[20] Hamdi AM, Fida M, Abu Saleh OM, Beam E. Stenotrophomonas bacteremia antibiotic susceptibility and prognostic determinants: Mayo Clinic 10-year experience. Open Forum Infect Dis 2020;7:ofaa008.
[21] Sarzynski SH, Warner S, Sun J, Matsouaka R, Dekker JP, Babiker A, et al. Trimethoprim-sulfamethoxazole versus levofloxacin for Stenotrophomonas maltophilia infections: a retrospective comparative effectiveness study of electronic health records from 154 US hospitals. Open Forum Infect Dis 2022;9:ofab644.
[22] Brooke JS. Advances in the microbiology of Stenotrophomonas maltophilia. Clin Microbiol Rev 2021;34:e0003019.
[23] Yin C, Yang W, Meng J, Lv Y, Wang J, Huang B. Co-infection of *Pseudomonas aeruginosa* and Stenotrophomonas maltophilia in hospitalized pneumonia patients

has a synergic and significant impact on clinical outcomes. Eur J Clin Microbiol Infect Dis 2017;36:2231–5.
[24] Nayyar C, Thakur P, Tak V, Saigal K. *Stenotrophomonas maltophilia*: an emerging pathogen in paediatric population. J Clin Diagn Res 2017;11. DC8–11.
[25] 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;10:19.
[26] Mojica MF, Humphries R, Lipuma JJ, Mathers AJ, Rao GG, Shelburne SA, et al. Clinical challenges treating *Stenotrophomonas maltophilia* infections: an update. JAC Antimicrob Resist 2022;4:dlac040.
[27] CLSI. Performance standards for antimicrobial susceptibility testing. In: CSLI supplement M100. 30th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2020.
[28] Brooke JS. Stenotrophomonas maltophilia: an emerging global opportunistic pathogen. Clin Microbiol Rev 2012;25:2–41.
[29] Wang L, Zhou W, Cao Y, Yang C, Liu H, Chen T, et al. Characteristics of Stenotrophomonas maltophilia infection in children in Sichuan, China, from 2010 to 2017. Medicine (Baltimore) 2020;99:e19250.
[30] Şen P, Yula E, Er H, Güngör S, Özdemir R, Baran N, et al. Antimicrobial resistance of *Stenotrophomonas maltophilia* isolated from various clinical specimens. Ortadoğu Tıp Derg 2017;9:113–7.
[31] Bilgin M, İsler H, Basbulut E, Yılmaz Mutlu E. Antimicrobial resistance in clinical strains of Stenotrophomonas maltophilia: 10-year surveillance. ANKEM Derg 2022; 36:16–22.
[32] Özkaya E, Aydın F, Bayramoğlu G, Buruk CK, Sandallı C. Investigation of integrons, sul1-2 and dfr genes in trimethoprim-sulfametoxazole-resistant Stenotrophomonas maltophilia strains isolated from clinical samples. Mikrobiyol Bul 2014;48:201–12.
[33] Hu LF, Xu XH, Li HR, Gao LP, Chen X, Sun N, et al. Surveillance of antimicrobial susceptibility patterns among Stenotrophomonas maltophilia isolated in China during the 10-year period of 2005–2014. J Chemother 2018;30:25–30.
[34] Thyagarajan B, Deshpande SS. Cotrimoxazole and neonatal kernicterus: a review. Drug Chem Toxicol 2014;37:121–9.
[35] Ryan KL, Dersch-Mills D, Clark D. Trimethoprim-sulfamethoxazole for treatment of *Stenotrophomonas maltophilia* pneumonia in a neonate. Can J Hosp Pharm 2013;66: 384–7.
[36] Ko JH, Kang CI, Cornejo-Juárez P, Yeh KM, Wang CH, Cho SY, et al. Fluoroquinolones versus trimethoprim-sulfamethoxazole for the treatment of *Stenotrophomonas maltophilia* infections: a systematic review and meta-analysis. Clin Microbiol Infect 2019;25:546–54.
[37] Faghihi T. Facing neonatal *Stenotrophomonas Maltophilia* infection: trimethoprim sulfamethoxazole or levofloxacin? J Pharm Care 2019;7:39–40.