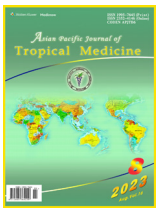

Original Article
Asian Pacific Journal of Tropical Medicine
apjtm.org
doi: 10.4103/1995-7645.380721
Impact Factor: 3.1

Healthcare-associated *Staphylococcus aureus* infections in children in Turkey: A six-year retrospective, single-center study

Nurhayat Yakut[1]✉, Zeynep Ergenc[1], Sevgi Aslan Tuncay[1], Sezin Bayraktar[2], Elvan Sayin[3], Arzu Ilki[3], Eda Kepenekli[1]

[1]*Division of Pediatric Infectious Diseases, Department of Pediatrics, Marmara University School of Medicine, Istanbul, Turkey*
[2]*Department of Pediatrics, Marmara University School of Medicine, Istanbul, Turkey*
[3]*Department of Medical Microbiology, Marmara University School of Medicine, Istanbul, Turkey*

ABSTRACT

Objective: To describe clinical and epidemiological characteristics, antimicrobial susceptibility and mortality-associated factors of healthcare-associated infections (HCAIs) caused by *Staphylococcus* (*S.*) *aureus* in children.

Methods: We conducted a retrospective, single-centre study of pediatric HCAIs caused by *S. aureus* from a tertiary care hospital in Turkey between February 2014 and December 2019. The clinical and epidemiological characteristics and antimicrobial susceptibility of the methicillin-susceptible and methicillin-resistant *S. aureus* (MSSA and MRSA) isolates was evaluated.

Results: A total of 310 pediatric patients were examined. Overall, 225 (72.6%) isolates were MSSA and 85 (27.4%) were MRSA. All *S. aureus* isolates were susceptible to teicoplanin, vancomycin, linezolid, tigecycline, mupirocin, and daptomycin. Penicillin resistance rates were high (89.0%), while fosfomycin, gentamicin, and clindamycin resistance rates were low (1.3%, 1.0%, and 2.3%, respectively). Except susceptibility to fosfomycin, which was significantly lower in 2014 compared to 2018 and 2019, no significant difference was found in the antimicrobial susceptibility of *S. aureus* isolates between the years. Baseline characteristics and mortality rate were similar comparing MRSA and MSSA causing HCAIs. The mortality rate of HCAIs caused by *S. aureus* was 6.5% (20 patients). Malignancy was an independent risk factor associated with mortality in the multivariate analysis (*OR* 5.446, 95% *CI* 1.573-18.849).

Conclusions: Our findings demonstrate that MSSA remained the most causative agent of HCAIs caused by *S. aureus*. The mortality rate was 6.5%, the antibiotic resistance rate was quite high for penicillin and diagnosis of malignancy was the main risk factor for increasing mortality in children. These findings could help improve the management of HCAIs caused by *S. aureus* in children.

KEYWORDS: Healthcare-associated infections; *Staphylococcus aureus*; Children; Antimicrobial susceptibility; Mortality

1. Introduction

Staphylococcus (S.) aureus us is a significant human pathogen that causes healthcare-associated infections in humans, including infections of the skin and soft tissues, bones, joints, pulmonary, blood, and medical devices in children. These infections can result in life-threatening conditions with major morbidity and mortality rate worldwide[1-3]. High antibiotic resistance, high disease burden

Significance

Knowledge of the local antimicrobial susceptibility and characterization of health care-associated infections caused by *Staphylococcus aureus* is essential for successful management of these challenging infections. This study determining species distribution, antimicrobial susceptibility profile, and predictors of mortality highlight the current clinical management and future surveillance studies of healthcare-associated *Staphylococcus aureus* infections.

✉To whom correspondence may be addressed. E-mail: nurhayatyakut@gmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

©2023 *Asian Pacific Journal of Tropical Medicine* Produced by Wolters Kluwer-Medknow.

How to cite this article: Yakut N, Ergenc Z, Tuncay SA, Bayraktar S, Sayin E, Ilki A, et al. Healthcare-associated *Staphylococcus aureus* infections in children in Turkey: A six-year retrospective, single-center study. Asian Pac J Trop Med 2023; 16(8): 354-362.

Article history: Received 4 February 2023 Revision 8 August 2023
Accepted 14 August 2023 Available online 28 August 2023

and high treatment costs are public health concerns. The prevalence of healthcare-associated methicillin-resistant *S. aureus* (MRSA) and antimicrobial susceptibility varies according to geographical location, health and population. Although current studies have largely focused on MRSA, it seems that methicillin-susceptible *S. aureus* (MSSA) remains a public health threat[4–8]. Paediatric data on risk factors for mortality of invasive *S. aureus* infections are limited[9–11]. Determining the regional epidemiologic features, antimicrobial susceptibility, and risk factors associated with mortality is essential for optimizing the appropriate empirical antimicrobial therapy and managing these challenging infections. This study aimed to describe the antimicrobial susceptibility patterns of *S. aureus* isolates, the clinical and epidemiological characteristics of HCAIs caused by *S. aureus*, and to identify the risk factors for mortality in pediatric patients in Turkey.

2. Subjects and methods

2.1. Study design, data collection, and definitions

This retrospective single-center descriptive study examined 310 pediatric patients with HCAIs caused by *S. aureus* from a tertiary care hospital in Istanbul, Turkey. The medical records were obtained from hospitalized children (<18 years old) with HCAIs at the Marmara University Pendik Training and Research Hospital between February 2014 and December 2019. Patients with cystic fibrosis were excluded because of the challenges in determining colonization or infection. The study protocol was approved by the Institutional Ethics Committee of the study hospital (Date: 24 July 2020 and Decision No.: 09.2020.749). The following demographic, clinical and microbiological data were collected retrospectively: age, gender, admitting ward, underlying medical conditions, duration of hospital stay, type and site of infection, *S. aureus* species, mortality, results of antimicrobial susceptibility testing, white blood cell count, C-reactive protein (CRP) values and antibiotic regimen.

Isolation of *S. aureus* from a sterile body site obtained beyond 48 hours of hospitalization was defined as a healthcare-associated infection caused by *S. aureus*. The clinical spectrum was classified as respiratory tract, bloodstream, skin and soft tissue, bone and joint, central nervous system, surgical site and mixed infections according to the isolation site of *S. aureus*.

Types of infections were categorized as bloodstream, skin and soft tissue/bone and joint, pneumonia, central nervous system, surgical site, mixed, and other.

2.2. S. aureus identification and antimicrobial susceptibility testing

A total of 310 non-repetitive *S. aureus* isolates were evaluated retrospectively. All isolates were identified by MALDI-TOF MS (VITEK MS. BioMérieux. France). Methicillin susceptibility was determined using cefoxitin disc tests. Antimicrobial susceptibility testing was carried out using the VITEK®2 system (BioMérieux, France) for penicillin, gentamicin, ciprofloxacin, levofloxacin, moxifloxacin, erythromycin, clindamycin, linezolid, teicoplanin, vancomycin, daptomycin, tetracycline. The data collected during the study period were analyzed by the European Committee on Antimicrobial Susceptibility Testing criteria for current clinical breakpoints (Version 11.0)[12].

2.3. Statistical analysis

Data were entered into Microsoft Office Excel 2010 (Microsoft. Redmond. WA. USA). The statistical analysis was performed using SPSS version 22.0 (IBM, SPSS). Continuous variables in abnormal distribution were expressed as median (IQR). Frequencies and percentages were used to summarize categorical data. The significance of the nonparametric data was assessed using the Mann–Whitney *U* test. The statistical significance of dichotomous outcomes was determined using the *Chi*-square test, Fisher's exact test, Fisher Freeman Halton test, and Yates's continuity correction as appropriate. A multivariate logistic regression analysis was performed. A P value of < 0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

Three hundred and ten pediatric patients with HCAIs caused by *S. aureus* were included during the six-year study period. Of these, 162 were male (52.3%), and 148 were female (47.7%). The median (IQR) age was 8 (2-51) months. Pneumonia (37.1%) was the most common type of infection, followed by bloodstream infections (34.2%). Two hundred nineteen patients (70.6%) had underlying medical conditions. The most common medical conditions were neuromuscular diseases/epilepsy in 71 patients and malignancy in 37 patients. A total of 225 (225/310, 72.6%) isolates were MSSA. At the time of diagnosis, 146 (47.1%) patients were in the pediatric wards, 64 (20.6%) were in the pediatric intensive care unit (PICU). The median (IQR) duration of hospital stay was 15 days (10-31). The most commonly used antimicrobial agents were vancomycin in 124 (40.0%) patients and ampicillin-sulbactam in 74 (23.9%) patients.

Comparison of the clinical and epidemiological characteristics and treatment modalities between MSSA and MRSA infections revealed no significant difference. Descriptive data and comparison of other variables were shown in Table 1.

Table 1. Clinical and epidemiological characteristics and treatment modalities of patients with *Staphylococcus aureus* infections [*n* (%)].

Variables		*Staphylococcus aureus* strain		Total	*P*
		MSSA	MRSA		
Age, months*		9 (2.0-53)	5 (2.0-43.5)	8 (2.0-51.0)	0.340[1]
Sex	Female	113 (50.2)	35 (41.2)	148 (47.7)	0.155[2]
	Male	112 (49.8)	50 (58.8)	162 (52.3)	
Hospital stay, day*		14 (10-31)	15 (10-32)	15 (10-31)	0.304[1]
Duration of antibiotic therapy, day*		12 (8-14)	10 (8.5-14)	12 (8-14)	0.620[1]
White blood cells, mm^{3*}		11 600 (7 100-16 850)	129 00 (8 700-18 700)	11 900 (7 575-17 175)	0.188[1]
Granulocytes, mm^{3*}		6 800 (3300-11500)	8 400 (3 400-12 550)	7 100 (3 300-11 900)	0.217[1]
Underlying condition (*n*=219)	Malignancy	30 (19.4)	7 (10.9)	37 (16.9)	0.189[3]
	Neuromuscular diseases/Epilepsy	47 (30.3)	24 (37.5)	71 (32.4)	0.302[2]
	Chronic kidney disease	9 (5.8)	4 (6.3)	13 (5.9)	0.559[4]
	Intracranial/ head and neck pathology	23 (14.8)	5 (7.8)	28 (12.8)	0.233[3]
	Type 1 diabetes mellitus	0 (0.0)	2 (3.1)	2 (0.9)	-
	Prematurity	8 (5.2)	1 (1.6)	9 (4.1)	-
	Chronic skin disease	3 (1.9)	2 (3.1)	5 (2.3)	0.457[4]
	Chronic lung disease/Asthma	18 (11.6)	5 (7.8)	23 (10.5)	0.554[3]
	Others	7 (4.5)	8 (12.5)	15 (6.8)	0.342
	Congenital heart disease	5 (3.2)	5 (7.8)	10 (4.6)	0.132[4]
	Immune deficiency	5 (3.2)	1 (1.6)	6 (2.7)	-
Risk factors	No	109 (48.4)	38 (44.7)	147 (47.4)	0.990[5]
	Central venous catheter	34 (15.1)	16 (18.8)	50 (16.1)	
	Mechanical ventilation	29 (12.9)	12 (14.1)	41 (13.2)	
	Prior surgical intervention	32 (14.2)	12 (14.1)	44 (14.2)	
	Ventriculoperitoneal shunt	9 (4.0)	3 (3.5)	12 (3.9)	
	Others	12 (5.3)	4 (4.8)	16 (5.2)	
Hospitalization unit	Pediatrics	105 (46.7)	41 (48.2)	146 (47.1)	0.805[2]
	Emergency	19 (8.4)	6 (7.1)	25 (8.1)	0.868[3]
	Pediatric surgery ICU	6 (2.7)	1 (1.2)	7 (2.3)	-
	Neurosurgery	17 (7.6)	6 (7.1)	23 (7.4)	>0.999[3]
	PICU	44 (19.6)	20 (23.5)	64 (20.6)	0.441[2]
	Others	12 (5.3)	4 (4.7)	16 (5.2)	0.382[4]
	NICU	13 (5.8)	3 (3.5)	16 (5.2)	0.316[4]
	Orthopedic unit	9 (4.0)	4 (4.7)	13 (4.2)	0.498[4]
Types of infection	Bloodstream	77 (34.2)	29 (34.1)	106 (34.2)	0.986[2]
	Skin and soft tissue/ bone and joint	28 (12.4)	5 (5.9)	33 (10.6)	0.143[3]
	Pneumonia	81 (36.0)	34 (40.0)	115 (37.1)	0.515[2]
	Central nervous system	19 (8.5)	9 (10.6)	28 (9.1)	0.620[3]
	Surgical site	7 (3.1)	3 (3.5)	10 (3.2)	0.548[4]
	Mixt/ Others	13 (5.8)	5 (5.9)	18 (5.8)	0.579[4]
Isolation site	Blood	79 (35.1)	32 (37.6)	111 (35.8)	0.668[3]
	Abscess	26 (11.6)	6 (7.1)	32 (10.3)	
	Tissue	16 (7.1)	5 (5.9)	21 (6.8)	
	Endotracheal aspirate	68 (30.2)	29 (34.1)	97 (31.3)	
	Cerebrospinal fluid	18 (8.0)	7 (8.2)	25 (8.1)	
	Mixed/Others	18 (8.0)	6 (7.1)	24 (7.8)	

*: Data expressed as median (IQR); -: Data not suitable for statistical comparison. [1]Mann Whitney *U* test; [2]*Chi*-square test; [3]Yates's continuity correction; [4]Fisher's exact test; [5]Fisher freeman Halton test. MSSA: methicillin-susceptible *S. aureus*; MRSA: methicillin-resistant *S. aureus*; ICU: Intensive care unit; PICU: Pediatric intensive care unit; NICU: Neonatal intensive care unit. For each column the total number can be different because of missing data.

Table 2. The antimicrobial susceptibility pattern of *Staphylococcus aureus* isolates [*n* (%)].

MSSA/MRSA		2014	2015	2016	2017	2018	2019	Total	*P*
Penicillin	S	4 (12.1)	5 (13.2)	5 (8.9)	4 (9.8)	9 (12.2)	7 (10.3)	34 (11.0)	0.982[1]
	R	29 (87.9)	33 (86.8)	51 (91.1)	37 (90.2)	65 (87.8)	61 (89.7)	276 (89.0)	
Gentamycin	S	33 (100.0)	38 (100.0)	55 (98.2)	41 (100.0)	74 (100.0)	66 (97.1)	307 (99.0)	0.570[1]
	R	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	2 (2.9)	3 (1.0)	
Ciprofloxacin	R	0 (0.0)	1 (2.6)	5 (8.9)	2 (4.9)	3 (4.1)	3 (4.4)	14 (4.5)	0.584[1]
	I	33 (100.0)	37 (97.4)	51 (91.1)	39 (95.1)	71 (95.9)	65 (95.6)	296 (95.5)	
Moxifloxacin	S	33 (100.0)	19 (100.0)	-	-	-	-	52 (100.0)	0.409[1]
Levofloxacin	R	-	0 (0.0)	4 (7.1)	0 (0.0)	2 (2.7)	3 (4.4)	9 (3.5)	
	I	-	19 (100.0)	52 (92.9)	41 (100.0)	72 (97.3)	65 (95.6)	249 (96.5)	
Erytromycin	S	29 (87.9)	34 (89.5)	49 (87.5)	38 (92.7)	58 (78.4)	54 (79.4)	262 (84.5)	0.224[2]
	R	4 (12.1)	4 (10.5)	7 (12.5)	3 (7.3)	16 (21.6)	14 (20.6)	48 (15.5)	
Clindamycin	S	33 (100.0)	38 (100.0)	53 (94.6)	41 (100.0)	72 (97.3)	66 (97.1)	303 (97.7)	0.546[1]
	R	0 (0.0)	0 (0.0)	3 (5.4)	0 (0.0)	2 (2.7)	2 (2.9)	7 (2.3)	
Linezolid	S	33 (100)	38 (100.0)	56 (100.0)	41 (100.0)	74 (100.0)	68 (100.0)	310 (100.0)	-
Daptomycin	S	-	19 (100.0)	56 (100.0)	41 (100.0)	74 (100.0.0)	68 (100.0)	258 (100.0)	-
Teicoplanin	S	33 (100)	38 (100.0)	56 (100.0)	41 (100.0)	74 (100.0)	68 (100.0)	310 (100.0)	-
Vancomycin	S	33 (100)	38 (100.0)	56 (100.0)	41 (100.0)	74 (100.0)	68 (100.0)	310 (100.0)	-
Tetracycline	S	31 (93.9)	31 (81.6)	50 (89.3)	35 (85.4)	60 (81.1)	58 (85.3)	265 (85.5)	0.524[2]
	R	2 (6.1)	7 (18.4)	6 (10.7)	6 (14.6)	14 (18.9)	10 (14.7)	45 (14.5)	
Tigecycline	S	33 (100.0)	38 (100.0)	56 (100.0)	41 (100.0)	74 (100.0)	68 (100.0)	310 (100.0)	-
Fosfomycin	S	30 (90.9)	38 (100.0)	55 (98.2)	41 (100.0)	74 (100.0)	68 (100.0)	306 (98.7)	0.003[1*]
	R	3 (9.1)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.3)	
Fusidic acid	S	31 (93.9)	37 (97.4)	55 (98.2)	41 (100.0)	73 (98.6)	61 (89.7)	298 (96.1)	0.055[1]
	R	2 (6.1)	1 (2.6)	1 (1.8)	0 (0.0)	1 (1.4)	7 (10.3)	12 (3.9)	
TMP/SMX	S	30 (90.9)	38 (100.0)	51 (91.1)	40 (97.6)	71 (95.9)	62 (91.2)	292 (94.2)	0.079[2]
	R	3 (9.1)	0 (0.0)	2 (3.6)	0 (0.0)	2 (2.7)	6 (8.8)	13 (4.2)	
	I	0 (0.0)	0 (0.0)	3 (5.4)	1 (2.4)	1 (1.4)	0 (0.0)	5 (1.6)	
Mupirocin	S	-	19 (100.0)	56 (100.0)	41 (100.0)	74 (100.0)	68 (100.0)	258 (100.0)	-

[1]Fisher Freeman Halton test; [2]*Chi*-square test; S: Susceptible; R: Resistant; I: Indeterminate; -: None or data not suitable for statistical comparison.

3.2. Antimicrobial susceptibility pattern

Antimicrobial susceptibility testing of 17 antimicrobial agents was performed in MSSA and MRSA isolates for the obtained normally sterile body site cultures. This analysis revealed that all *S. aureus* isolates were susceptible to teicoplanin, vancomycin, linezolid, tigecycline, mupirocin, and daptomycin. The highest resistance (89.0%) was detected against penicillin. Resistance to fosfomycin, gentamicin, and clindamycin was rare (1.3%, 1.0%, and 2.3%, respectively) among the *S. aureus* isolates. The prevalence of resistance to fusidic acid and TMP/SMX was 3.9% and 4.2%, respectively. *S. aureus* susceptibility to fosfomycin was significantly lower in 2014 compared to 2018 and 2019 (P_1=0.027; P_1=0.033). No statistically significant differences in the other antibiotic susceptibility were observed between the years. The antimicrobial susceptibility pattern according to the years of all *S. aureus* isolates is shown in Table 2.

No significant differences in the susceptibility of MSSA isolates were observed between the years. Antimicrobial susceptibility comparisons for the MSSA isolates between the years are shown in Table 3.

Methicillin-resistant *S. aureus* susceptibility to fosfomycin was significantly lower in 2014 compared to 2019 (*P*=0.022). No significant difference was observed in susceptibility to other antimicrobials between the years. Antimicrobial susceptibility comparisons for the MRSA isolates between years are shown in Table 4.

3.3. Risk factors associated with mortality

Twenty patients with HCAIs caused by *S. aureus* died during the study period, with a mortality rate of 6.5% (20/310). According to the univariate analysis, diagnosis of malignancy, pediatric and neonatal intensive care unit admission were significantly associated with mortality (*P*=0.005, *P*=0.002 and *P*=0.014, respectively) (Table 5).

Diagnosis of malignancy was significantly associated with mortality in the multivariate analysis (*P*=0.07, *OR* 5.446, 95% *CI* 1.573-18.849) (Table 6).

Table 3. Antimicrobial susceptibility comparison in methicillin-susceptible *Staphylococcus aureus* isolates between years [*n* (%)].

MSSA		2014	2015	2016	2017	2018	2019	Total	*P*
Penicillin	S	4 (16.0)	5 (15.2)	5 (11.4)	4 (14.3)	9 (17.0)	7 (16.7)	34 (15.1)	0.980[1]
	R	21 (84.0)	28 (84.8)	39 (88.6)	24 (85.7)	44 (83.0)	35 (83.3)	191 (84.9)	
Gentamycin	S	25 (100.0)	33 (100.0)	44 (100)	28 (100.0)	53 (100.0)	42 (100.0)	225 (100.0)	-
Ciprofloxacin	R	0 (0.0)	1 (3.0)	3 (6.8)	0 (0.0)	1 (1.9)	2 (4.8)	7 (3.1)	0.656[1]
	I	25 (100.0)	32 (97.0)	41 (93.2)	28 (100.0)	52 (98.1)	40 (95.2)	218 (96.9)	
Moxifloxacin	S	25 (100.0)	17 (100.0)	-	-	-	-	42 (100.0)	-
Levofloxacin	R	-	0 (0.0)	2 (4.5)	0 (0.0)	1 (1.9)	2 (4.8)	5 (2.7)	0.765[1]
	I	-	16 (100.0)	42 (95.5)	28 (100.0)	52 (98.1)	40 (95.2)	178 (97.3)	
Erytromycin	S	24 (96.0)	31 (93.9)	39 (88.6)	28 (100.0)	47 (88.7)	37 (88.1)	206 (91.6)	0.390[1]
	R	1 (4.0)	2 (6.1)	5 (11.4)	0 (0.0)	6 (11.3)	5 (11.9)	19 (8.4)	
Clindamycin	S	25 (100.0)	33 (100.0)	41 (93.2)	28 (100.0)	52 (98.1)	42 (100).0	221 (98.2)	0.247[1]
	R	0 (0.0)	0 (0.0)	3 (6.8)	0 (0.0)	1 (1.9)	0 (0.0)	4 (1.8)	
Linezolid	S	25 (100.0)	33 (100.0)	44 (100.0)	28 (100.0)	53 (100.0)	42 (100.0)	225 (100.0)	-
Daptomycin	S	-	16 (100.0)	44 (100.0)	28 (100.0)	53 (100.0)	42 (100.0)	183 (100.0)	-
Teicoplanin	S	25 (100.0)	33 (100.0)	44 (100.0)	28 (100.0)	53 (100.0)	42 (100.0)	225 (100.0)	-
Vancomycin	S	25 (100.0)	33 (100.0)	44 (100.0)	28 (100.0)	53 (100.0)	42 (100.0)	225 (100.0)	-
Tetracycline	S	23 (92.0)	28 (84.8)	41 (93.2)	25 (89.3)	48 (90.6)	39 (92.9)	204 (90.7)	0.863[1]
	R	2 (8.0)	5 (15.2)	3 (6.8)	3 (10.7)	5 (9.4)	3 (7.1)	21 (9.3)	
Tigecycline	S	25 (100.0)	33 (100.0)	44 (100.0)	28 (100.0)	53 (100.0)	42 (100.0)	225 (100.0)	-
Fosfomycin	S	24 (96.0)	33 (100.0)	44 (100.0)	28 (100.0)	53 (100.0)	42 (100.0)	224 (99.6)	0.111[1]
	R	1 (4.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	
Fusidic acid	S	25 (100.0)	33 (100.0)	44 (100.0)	28 (100.0)	52 (98.1)	40 (95.2)	222 (98.7)	0.537[1]
	R	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.9)	2 (4.8)	3 (1.3)	
TMP/SMX	S	25 (100.0)	33 (100.0)	41 (93.2)	28 (100.0)	53 (100.0)	39 (92.9)	219 (97.3)	0.058[2]
	R	0 (0.0)	0 (0.0)	1 (2.3)	0 (0.0)	0 (0.0)	3 (7.1)	4 (1.8)	
	I	0 (0.0)	0 (0.0)	2 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	
Mupirocin	S	-	16 (100.0)	44 (100.0)	28 (100.0)	53 (100.0)	42 (100.0)	183 (100.0)	-

[1]Fisher Freeman Halton test; [2]*Chi*-square test; S: Susceptible; R: Resistant; I: Indeterminate; -: None, or data not suitable for statistical comparison.

4. Discussion

S. aureus remains a major cause of HCAIs, with important morbidity and mortalit[1–3,13]. This study evaluated the antimicrobial susceptibility pattern, characteristics, mortality rate, and associated factors of 310 pediatric HCAIs caused by *S. aureus* in Turkey. Regional epidemiological studies identifying characteristics and antimicrobial susceptibility patterns of *S. aureus* isolates causing HCAIs are important to determine empirical and therapeutic antibiotic treatment. The major results of our study demonstrated the high prevalence of MSSA, multi-drug susceptibility of HCAIs caused by *S. aureus*, and a similar mortality rate for MRSA compared with MSSA. A few studies have evaluated *S. aureus* infections in hospitalized children in Turkey, but data about the rate of antimicrobial resistance and mortality is still limited[14,15]. Therefore, determining empirical, therapeutic and oral sequential antibiotic treatment choices is challenging for clinicians. We believe these results could provide important information on this challenging issue.

The species distribution of *S. aureus* differs across geographical locations. We found that 27.4% of all HCAIs were MRSA. Similar to our results, the rate of MRSA in hospitalized children was 18.2% according to Arikan *et al.*, 15% according to Gordon *et al.*, and 27% according to Waitayangkoon *et al.*[8,11,14]. The higher rates of MRSA have been reported in several epidemiologic studies with 56.8%, 38.3% 48%, and 42%[16–19]. The species distribution differences may be caused by patient population, study site, and geographical stratification[20]. These studies highlight that each population and geographical region should accurately identify its epidemiological data to manage these challenging infections.

To date, the associations between underlying medical conditions, including pulmonary, cardiovascular, and neurological diseases, and MRSA have been reported by previous studies[8,21]. Waitayangkoon *et al.*[8] reported that chronic lung, cardiovascular, and neurological diseases were associated with MRSA isolation. In accordance with this study, neuromuscular diseases/epilepsy was significantly associated with MRSA in our study. We found that baseline characteristics and outcomes of patients with MRSA and MSSA infections were similar to the study conducted by Gomes *et al.*[22] This study reported that both MSSA and MRSA species resulted in similar features and treatment outcomes[22]. These results can be explained by the fact that most of our patients have an underlying disease (70.6%).

Table 4. Antimicrobial susceptibility comparison in methicillin-resistant *Staphylococcus aureus* isolates between years [*n* (%)].

MRSA		2014	2015	2016	2017	2018	2019	Total	*P*
Penicillin	R	8 (100.0)	5 (100.0)	12 (100.0)	13 (100.0)	21 (100.0)	26 (100.0)	85 (100.0)	-
	S	8 (100.0)	5 (100.0)	11 (91.7)	13 (100.0)	21 (100.0)	24 (92.3)	82 (96.5)	0.609[1]
Gentamycin	R	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	2 (7.7)	3 (3.5)	
Ciprofloxacin	R	0 (0.0)	0 (0.0)	2 (16.7)	2 (15.4)	2 (9.5)	1 (3.8)	7 (8.2)	0.590[1]
	I	8 (100.0)	5 (100.0)	10 (83.3)	11 (84.6)	19 (90.5)	25 (96.2)	78 (91.8)	
Moxifloxacin	S	8 (100.0)	2 (100.0)	-	-	-	-	10 (100.0)	-
Levofloxacin	R	-	0 (0.0)	2 (16.7)	0 (0.0)	1 (4.8)	1 (3.8)	4 (5.3)	0.499[1]
	I	-	3 (100.0)	10 (83.3)	13 (100.0)	20 (95.2)	25 (96.2)	71 (94.7)	
Erytromycin	S	5 (62.5)	3 (60.0)	10 (83.3)	10 (76.9)	11 (52.4)	17 (65.4)	56 (65.9)	0.532[1]
	R	3 (37.5)	2 (40.0)	2 (16.7)	3 (23.1)	10 (47.6)	9 (34.6)	29 (34.1)	
Clindamycin	S	8 (100.0)	5 (100.0)	12 (100.0)	13 (100.0)	20 (95.2)	24 (92.3)	82 (96.5)	0.928[1]
	R	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.8)	2 (7.7)	3 (3.5)	
Linezolid	S	8 (100.0)	5 (100.0)	12 (100.0)	13 (100.0)	21 (100.0)	26 (100.0)	85 (100.0)	-
Daptomycin	S	-	3 (100.0)	12 (100.0)	13 (100.0)	21 (100.0)	26 (100.0)	75 (100.0)	-
Teicoplanin	S	8 (100.0)	5 (100.0)	12 (100.0)	13 (100.0)	21 (100.0)	26 (100.0)	85 (100.0)	-
Vancomycin	S	8 (100.0)	5 (100.0)	12 (100.0)	13 (100.0)	21 (100.0)	26 (100.0)	85 (100.0)	-
Tetracycline	S	8 (100.0)	3 (60.0)	9 (75.0)	10 (76.9)	12 (57.1)	19 (73.1)	61 (71.8)	0.263[1]
	R	0 (0.0)	2 (40.0)	3 (25.0)	3 (23.1)	9 (42.9)	7 (26.9)	24 (28.2)	
Tigecycline	S	8 (100.0)	5 (100.0)	12 (100.0)	13 (100.0)	21 (100.0)	26 (100.0)	85 (100.0)	-
Fosfomycin	S	6 (75.0)	5 (100.0)	11 (91.7)	13 (100.0)	21 (100.0)	26 (100.0)	82 (96.5)	0.022[1]
	R	2 (25.0)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.5)	
Fusidic acid	S	6 (75.0)	4 (80.0)	11 (91.7)	13 (100.0)	21 (100.0)	21 (80.8)	76 (89.4)	0.064[1]
	R	2 (25.0)	1 (20.0)	1 (8.3)	0 (0.0)	0 (0.0)	5 (19.2)	9 (10.6)	
TMP/SMX	S	5 (62.5)	5 (100.0)	10 (83.3)	12 (92.3)	18 (85.7)	23 (88.5)	73 (86.9)	0.351[2]
	R	3 (37.5)	0 (0.0)	1 (8.3)	0 (0.0)	2 (9.5)	3 (11.5)	9 (10.6)	
	I	0 (0.0)	0 (0.0)	1 (8.3)	1 (7.7)	1 (4.8)	0 (0.0)	3 (3.5)	
Mupirocin	S	-	3 (100.0)	12 (100.0)	13 (100.0)	21 (100.0)	26 (100.0)	75 (100.0)	-

[1]Fisher Freeman Halton test; [2]*Chi*-square test; S: Susceptible; R: Resistant; I: Indeterminate; -: None or data not suitable for statistical comparison.

Early initiation of appropriate antimicrobial therapy is essential to treat HCAIs caused by *S. aureus* successfully. Thus, determining antimicrobial susceptibility patterns is important for providing appropriate and effective treatment. Our study determined the antimicrobial susceptibility against 17 different antimicrobial agents and susceptibility patterns according to years. No resistance was detected to vancomycin, teicoplanin, linezolid, tigecycline, mupirocin, and daptomycin among *S. aureus* isolates. Similar to our study, many studies have shown low resistance rates for vancomycin, linezolid and daptomycin in S. aureus isolates[8,23–25]. Waitayangkoon *et al.*[21] reported that one MRSA isolate exhibited resistance to vancomycin and one to linezolid. A recent study by Pignataro *et al.*[25] determined that 2/140 MRSA cases exhibited intermediate resistance to vancomycin. Therefore, glycopeptides as an empirical treatment of HCAIs caused by *S. aureus* appear to be an effective choice until antimicrobial susceptibility results are available.

Studies have shown a high resistance rate of *S. aureus* isolates to fosfomycin, gentamicin, TMP/SMX, and clindamycin[11,19,23]. A recent study by Cay *et al.*[15] conducted on children with community and hospital-acquired *S. aureus* infections in southern Turkey reported that the clindamycin resistance rate was 20% of all *S. aureus* isolates in different clinical specimens. Conversely, in this study, most of the *S. aureus* isolates showed high susceptibility to fosfomycin, gentamicin, TMP/SMX, and clindamycin. Different study designs, populations and types of infections may have been the cause of these results.

No statistical difference in antibiotic resistance was noted for MRSA, and MSSA isolates over the six-year-study period. However, the susceptibility to fosfomycin of MRSA isolates was significantly lower in 2014 than in the other years. This result may be explained by the limited use of gentamicin in children, especially for these infections. Our findings suggest that glycopeptides, mupirocin, TMP/SMX, clindamycin, and fusidic acid remain good treatment options for HCAIs caused by MSSA and MRSA in our region. Clindamycin, TMP/SMX, mupirocin and fusidic acid can be used for oral and local treatment in follow-up due to their high sensitivity, affordability and availability in Turkey.

Invasive *S. aureus* infections are a major cause of mortality and morbidity, notably in hospitalized children. The literature

Table 5. Mortality-associated risk factors of patients with *Staphylococcus aureus* infections [*n* (%)].

Variables		Mortality		Total	*P*
		No	Yes		
Age, months*		8.0 (2.0-51.0)	10.5 (1.0-56.3)	8 (2.0-51.0)	0.994[1]
Sex	Female	136 (46.9)	12 (60.0)	148 (47.7)	0.366[2]
	Male	154 (53.1)	8 (40.0)	162 (52.3)	
Hospital stay, day*		14.5 (10.0-30.0)	17 (10.0-65.0)	15 (10.0-31.0)	0.243[1]
Duration of antibiotic therapy, day*		11.5 (8.0-14.0)	13.5 (10.0-25.3)	12 (8-14)	0.310[1]
White blood cells, mm^{3}*		11 700 (7 775-16 700)	16 000 (3 125-18 975)	11 900 (7 575-17 175)	0.555[1]
Granulocytes, mm^{3}*		7 050 (3 400-11 625)	9 750 (575-15 275)	7 100 (3 300-11 900)	0.995[1]
Staphylococcus aureus strain	MSSA	211 (72.8)	14 (70.0)	225 (72.6)	0.993[2]
	MRSA	79 (27.2)	6 (30.0)	85 (27.4)	
Underlying condition (*n*=219)	Malignancy	30 (14.7)	7 (46.7)	37 (16.9)	0.005[3]
	Neuro-muscular diseases/Epilepsy	67 (32.8)	4 (26.7)	71 (32.4)	0.430[3]
	Chronic kidney disease	13 (6.4)	0 (0.0)	13 (5.9)	-
	Intracranial/head and neck pathology	28 (13.7)	0 (0.0)	28 (12.8)	-
	Type 1 diabetes mellitus	2 (1.0)	0 (0.0)	2 (0.9)	-
	Prematurity	8 (3.9)	1 (6.7)	9 (4.1)	-
	Chronic skin disease	4 (2.0)	1 (6.7)	5 (2.3)	-
	Chronic lung disease/Asthma	23 (11.3)	0 (0.0)	23 (10.5)	-
	Others	15 (7.4)	0 (0.0)	15 (6.8)	-
	Congenital Heart Disease	8 (3.9)	2 (13.3)	10 (4.6)	0.143[3]
	Immune deficiency	6 (2.9)	0 (0.0)	6 (2.7)	-
Risk factors	No	138 (47.6)	9 (45.0)	147 (47.4)	0.078[4]
	Central venous catheter	48 (16.6)	2 (10.0)	50 (16.1)	
	Mechanical ventilation	35 (12.1)	6 (30.0)	41 (13.2)	
	Prior surgical intervention	44 (15.2)	0 (0.0)	44 (14.2)	
	Ventriculoperitoneal shunt	11 (3.8)	1 (5.0)	12 (3.9)	
	Others	14 (4.8)	2 (10.0)	16 (5.2)	
Hospitalization unit	Pediatrics	144 (49.7)	2 (10.0)	146 (47.1)	0.001[2]
	Emergency	25 (8.6)	0 (0.0)	25 (8.1)	-
	Pediatric surgery ICU	6 (2.1)	1 (5.0)	7 (2.3)	-
	Neurosurgery	22 (7.6)	1 (5.0)	23 (7.4)	-
	PICU	54 (18.6)	10 (50.0)	64 (20.6)	0.002[3]
	Other	14 (5.9)	2 (10.0)	16 (5.2)	0.088[3]
	NICU	12 (4.1)	4 (20.0)	16 (5.2)	0.014[3]
	Orthopedic unit	13 (4.5)	0 (0.0)	13 (4.2)	
Types of infection	Bloodstream	95 (32.8)	11 (55.0)	106 (34.2)	0.574[4]
	Skin and soft tissue/ bone and joint	32 (11)	1 (5.0)	33 (10.6)	
	Pneumonia	108 (37.2)	7 (35.0)	115 (37.1)	
	Central nervous system	27 (9.3)	1 (5.0)	28 (9.0)	
	Surgical site	10 (3.4)	0 (0.0)	10 (3.2)	
	Mixt, others	18 (6.2)	0 (0.0)	18 (5.8)	
Isolation site	Blood	101 (34.8)	10 (50.0)	111 (35.8)	0.668[4]
	Abscess	32 (11)	0 (0.0)	32 (10.3)	
	Tissue	19 (6.6)	2 (10.0)	21 (6.8)	
	Endotracheal aspirate	90 (31)	7 (35.0)	97 (31.3)	
	Cerebrospinal fluid	24 (8.3)	1 (5.0)	25 (8.1)	
	Mixed, others	24 (8.2)	0 (0.0)	24 (7.8)	

*: Data expressed as median (IQR); -: Data not suitable for statistical comparison. [1]Mann Whitney *U* test; [2]*Chi*-square test; [3]Yates's continuity correction; [4]Fisher's exact test; [5]Fisher freeman Halton test. ICU: Intensive care unit; PICU: Pediatric intensive care unit; NICU:Neonatal intensive care unit. For each column the total number can be different because of missing data.

Table 6. The risk factors associated with mortality by logistic regression analysis.

Variables	*OR*	95% *CI*	*P*
Malignancy	5.446	1.573-18.849	0.007
Pediatrics unit	0.168	0.017-1.713	0.132
Pediatric intensive care unit	2.854	0.684-11.910	0.150
Neonatal intensive care unit	5.414	0.763-38.398	0.091
Constant	0.037	-	-

demonstrates that the mortality rates vary depending on the study population and geographic region, despite the lack of data on mortality rates and risk factors in children. In this study, we described the mortality rate and risk factors of the mortality of HCAIs caused by *S. aureus*. In a retrospective study conducted on children with *S. aureus* bacteremia, Gordon *et al.*[11] reported that in-hospital, 30-day and one-year mortality were 3%, 3.5%, and 12%, respectively. Another prospective study by McMullan *et al.*[9] showed that seven-and 30-day mortality rates were 2.6% and 4.7%, respectively. Cay *et al.*[15] showed that the mortality rate was 10% in patients with HCAIs caused by *S. aureus*. Of all patients in our study, 20 died during the study period, with a mortality rate of 6.5%. Our data demonstrate mortality was not increased for MRSA compared with MSSA infections. Naves *et al.*[16] reported high mortality rates in MRSA infections compared to MSSA (70.8% *vs.* 29.2%)[11,16,22]. However, similar to our results, Gordon *et al.*[11] reported that MRSA was not associated with increased one-year mortality compared to MSSA.

In this study, we found that having malignancy and admission to the pediatric and neonatal intensive care unit were associated with mortality. McMullan *et al.*[9] found that age of younger than one year, ethnicity of Māori or Pacific, and having endocarditis, pneumonia or sepsis were related to mortality in their large cohort study. Naves *et al.*[16] detected that risk factors for mortality were the use of more than two antimicrobial agents and the long duration of hospitalization before bacteremia (>7 days). Gordon *et al.*[11] identified an association between increased one-year mortality and prior morbidity in children with *S. aureus* bacteremia. In a review and meta-analysis of patients with malignancy, Li *et al.*[26] reported that a high mortality rate was associated with MRSA bacteremia in patients with malignancy. This finding might be explained by exposure to chemotherapy, broad-spectrum antibiotics, and invasive procedures leading to immunosuppression and predisposition to MRSA.

This study's major limitations were its relatively small sample size, retrospective, single-center design. Additionally, the isolates in the present study could not be typed. Inconclusion, this study determined that MSSA remained the predominant species responsible for HCAIs caused by *S. aureus* in children. The mortality rate was 6.5%, and diagnosis of malignancy was significantly associated with mortality in children. We found that glycopeptides, mupirocin, TMP/SMX, clindamycin or fusidic acid can be used as effective options in the first-line treatment of *S. aureus* HCAIs. We think our results are beneficial for achieving optimal clinical outcomes of HCAIs caused by *S. aureus* by determining species distribution, antibiotic susceptibility patterns, and predictors of mortality.

Conflict of interest statement

We declare that we have no conflict of interest.

Funding

No funding was utilized for this manuscript.

Authors' contribution

NY: Conception and design of the study, acquisition of data, literature research, writing manuscript, final approval of the version to be submitted; ZE: Conception and design of the study, acquisition of data, analysis and interpretation of data; SAT: Acquisition of data, analysis and interpretation of data; SB: Data collection and processing, conception and design of the study, acquisition of data; ES: Conception and design of the study, acquisition of data, analysis and interpretation of data; AI: Conception and design of the study, acquisition of data, analysis and interpretation of data, critical review; EK: Conception and design of the study, acquisition of data, analysis and interpretation of data, critical review. All authors read and approved the final manuscript. All authors meet the ICMJE authorship criteria.

References

[1] Rasigade JP, Vandenesch F. *Staphylococcus aureus*: A pathogen with still unresolved issues. *Infect Genet Evol* 2014; **21**: 510-514.

[2] Tong SYC, Davis JS, Eichenberger E, Holland TL, Fowler VG. *Staphylococcus aureus* ınfections: Epidemiology, pathophysiology, clinical manifestations, and management. *Clin Microbiol Rev* 2015; **28**(3): 603-661.

[3] Zervou FN, Zacharioudakis IM, Ziakas PD, Mylonakis E. MRSA colonization and risk of ınfection in the neonatal and pediatric ICU: A meta-analysis. *Pediatrics* 2014; **133**(4): e1015-e1023.

[4] Koeck M, Como-Sabetti K, Boxrud D, Dobbins G, Glennen A, Anacker M, et al. Burdens of invasive methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* disease, Minnesota, USA. *Emerg Infect Dis* 2019; **25**(1): 171-174.

[5] Jokinen E, Laine J, Huttunen R, Lyytikäinen O, Vuento R, Vuopio J, et al. Trends in incidence and resistance patterns of *Staphylococcus aureus* bacteremia. *Infect Dis* 2018; **50**(1): 52-58.

[6] Jokinen E, Laine J, Huttunen R, Rahikka P, Huhtala H, Vuento R, et al. Comparison of outcome and clinical characteristics of bacteremia caused by methicillin-resistant, penicillin-resistant and penicillin-susceptible *Staphylococcus aureus* strains. *Infect Dis* 2017; **49**(7): 493-500.

[7] Lyles RD, Trick WE, Hayden MK, Lolans K, Fogg L, Logan LK, et al. Regional epidemiology of methicillin-resistant *Staphylococcus aureus* among critically ill children in a state with mandated active surveillance. *J Pediatr Infect Dis Soc* 2016; **5**(4): 409-416.

[8] Waitayangkoon P, Thongkam A, Benjamungkalarak T, Rachayon M, Thongthaisin A, Chatsuwan T, et al. Hospital epidemiology and antimicrobial susceptibility of isolated methicillin-resistant *Staphylococcus*

aureus: A one-year retrospective study at a tertiary care center in Thailand. *Pathog Glob Health* 2020; **114**(4): 212-217.

[9] McMullan BJ, Bowen A, Blyth CC, Van Hal S, Korman TM, Buttery J, et al. Epidemiology and mortality of *Staphylococcus aureus* bacteremia in Australian and New Zealand children. *JAMA Pediatr* 2016; **170**(10): 979-986.

[10]Campbell AJ, Al Yazidi LS, Phuong LK, Leung C, Best EJ, Webb RH, et al. Pediatric *Staphylococcus aureus* bacteremia: Clinical spectrum and predictors of poor outcome. *Clin Infect Dis* 2022; **74**(4): 604-613.

[11]Gordon O, Cohen MJ, Gross I, Amit S, Averbuch D, Engelhard D, et al. *Staphylococcus aureus* bacteremia in children: Antibiotic resistance and mortality. *Pediatr Infect Dis J* 2019; **38**(5): 459-463.

[12]The European Committee on Antimicrobial Susceptibility Testing. *Breakpoint tables for interpretation of MICs and zone diameters. Version 11.0. 2021*. [Online]. Available from: http://www.eucast.org. [Accessed on 21 May 2023].

[13]Roediger JC, Outhred AC, Shadbolt B, Britton PN. Paediatric *Staphylococcus aureus* bacteraemia: A single-centre retrospective cohort. *Paediatr Child Health* 2017; **53**(2): 180-186.

[14]Arikan K, Karadag-Oncel E, Aycan AE, Yuksekkaya S, Sancak B, Ceyhan M. Epidemiologic and molecular characteristics of *Staphylococcus aureus* strains isolated from hospitalized pediatric patients. *Pediatr Infect Dis J* 2020; **39**(11): 1002-1006.

[15]Cay U, Celik U, Barutcu A, Ozdemir U, Unal N. Clinical characteristics and resistance patterns of *Staphylococcus aureus* infections in children at a tertiary care hospital in southern Turkey. *Cukurova Med J* 2022; **47**(2): 580-588.

[16]Naves KS, Vaz da Trindade N, Gontijo Filho PP. Methicillin-resistant *Staphylococcus aureus* bloodstream infection: Risk factors and clinical outcome in non-intensive-care units. *Rev Soc Bras Med Trop* 2012; **45**(2): 189-193.

[17]J Davis WT, Gilbert SR. Comparison of methicillin-resistant versus susceptible *Staphylococcus aureus* pediatric osteomyelitis. *J Pediatr Orthop* 2018; **38**(5): e285-e291.

[18]Baranovich T, Zaraket H, Shabana II, Nevzorova V, Turcutyuicov V, Suzuki H. Molecular characterization and susceptibility of methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* isolates from hospitals and the community in Vladivostok, Russia. *Clin Microbiol Infect* 2010; **16**(6): 575-582.

[19]Sutter DE, Milburn E, Chukwuma U, Dzialowy N, Maranich AM, Hospenthal DR. Changing susceptibility of *Staphylococcus aureus* in a US pediatric population. *Pediatrics* 2016; **137**(4): e20153099.

[20]Junaidi NSSA, Shakrin NNSM, Huri MFD, Kamarudin AZ, Desa MNM, Yunus WMZW. Antibiotic resistance and molecular typing of clinical *Staphylococcus aureus* isolates from Malaysian military hospital. *Asian Pac J Trop Med* 2023; **16**(5): 220-231.

[21]Ramarathnam V, De Marco B, Ortegon A, Kemp D, Luby J, Sreeramoju P. Risk factors for development of methicillin-resistant *Staphylococcus aureus* infection among colonized patients. *Am J Infect Control* 2013; **41**(7): 625–628.

[22]Gomes RT, Lyra TG, Alves NN, Caldas RM, Barberino MG, Nascimento-Carvalho CM. Methicillin-resistant and methicillin-susceptible community-acquired *Staphylococcus aureus* infection among children. *Braz J Infect Dis* 2013; **17**(5): 573-578.

[23]La Vecchia A, Ippolito G, Taccani V, Gatti E, Bono P, Bettocchi S, et al. Epidemiology and antimicrobial susceptibility of *Staphylococcus aureus* in children in a tertiary care pediatric hospital in Milan, Italy, 2017-2021. *Ital J Pediatr* 2022; **48**(1): 67.

[24]Naimi HM, Rasekh H, Noori AZ, Bahaduri MA. Determination of antimicrobial susceptibility patterns in *Staphylococcus aureus* strains recovered from patients at two main health facilities in Kabul, Afghanistan. *BMC Infect Dis* 2017; **17**(1): 737.

[25]Pignataro D, Foglia F, Della Rocca MT, Melardo C, Santella B, Folliero V, et al. Methicillin-resistant *Staphylococcus aureus*: Epidemiology and antimicrobial susceptibility experiences from the University Hospital 'Luigi Vanvitelli' of Naples. *Pathog Glob Health* 2020; **114**(8): 451-456.

[26]Li Z, Zhuang H, Wang G, Wang H, Dong Y. Prevalence, predictors, and mortality of bloodstream infections due to methicillin-resistant *Staphylococcus aureus* in patients with malignancy: Sreview and meta-analysis. *BMC Infect Dis* 2021; **21**(1): 74.

Publisher's note

The Publisher of the *Journal* remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.