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Effects of COVID-19 pandemic on healthcare-associated infections, antibiotic resistance and consumption rates in intensive care units

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SUMMARY

Purpose: This paper aimed to evaluate the effects of the COVID-19 pandemic on healthcare-associated infections (HAIs), antibiotic resistance and consumption rates in intensive care units (ICUs) of a tertiary care university hospital.
Patients and Methods: Between 1 January 2018 and 31 December 2021, adult patients diagnosed with HAIs in ICUs were investigated retrospectively. Patients were divided into pre-pandemic (2018-2019) and pandemic periods (2020–2021). Antibiotic consumption index was calculated via using the formula of (total dose (grams)/defined daily dose (DDD) x total patient days) x1000. A p value below 0.05 was accepted as statistically significant.
Results: The incidence of HAIs (per 1000 patient days) in the ICU of COVID-19 patients was 16.59, while it was 13.42 in the other ICUs during the pandemic period (p=0.107). The bloodstream infection (BSI) incidence was 3.32 in the pre-pandemic period and 5.41 in the pandemic period in ICUs other than the ICU of COVID-19 patients (p<0.001). In the pandemic period, the BSI incidence rate was significantly higher in the ICU of COVID-19 patients than in the other ICUs (14.26 vs 5.41, p<0.001). Central venous catheter bloodstream infections incidence rate was 4.72 in the pre-pandemic and 7.52 in the pandemic period in ICUs other than the ICU of COVID-19 patients (p=0.0019). During the pandemic period, the bacteraemia episode rates of *Acinetobacter baumannii* (5.375 vs 0.984, p<0.001), *Enterococcus spp.* (1.635 vs 0.268, p<0.001) and *Stenotrophomonas maltophilia* (3.038 vs 1.297, p=0.0086) in the ICU of COVID-19 patients were significantly found higher than others. The extended-spectrum beta-lactamase (ESBL) positivity rates for *Klebsiella pneumoniae* and *Escherichia coli* were 61% and 42% in the pre-pandemic period; 73% and 69% in the pandemic period in ICUs other than the ICU of COVID-19 patients (p>0.05). In the pandemic period, the ESBL positivity rates for *K. pneumoniae* and *E. coli* were 83% and 100% in the ICU of COVID-19 patients, respectively. Meropenem (p<0.001), teicoplanin (p<0.001) and ceftriaxone (p<0.001) consumptions were increased while ciprofloxacin (p=0.003) consumption was decreased in all ICUs after the pre-pandemic period.
Conclusions: BSI and CVCBSI incidence rates were significantly increased in all ICUs after the COVID-19 pandemic in our hospital. Bacteraemia episode rates of *A. baumannii*, Enterococcus spp. and *S. maltophilia* in ICU of COVID-19 patients were significantly found higher than others. In addition, meropenem, teicoplanin and ceftriaxone consumptions were increased in all ICUs after the COVID-19 pandemic.

Keywords: COVID-19, hospital-acquired infections, bloodstream infections, antimicrobial resistance, antibiotic consumption.

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INTRODUCTION

Healthcare-associated infections (HAIs) are a growing global threat to patient safety worldwide, with more than 2.5 million cases annually in the European Union and European Economic Area [1]. HAIs, which are mostly associated with intensive care unit (ICU) hospitalization, consist of several types of infections related to the administration of medical devices, such as ventilator-associated pneumonia (VAP), central venous catheter bloodstream infections (CVCBSIs) and catheter-associated urinary tract infections (CAUTIs) [2].

Coronavirus disease 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) on 11 March 2020, and a higher incidence of HAIs has been linked with COVID-19 when compared with the pre- and mid-pandemic periods [3]. Due to the increased requirement for ventilation for COVID-19 patients, most ICUs were reorganized, resulting in reduced staff-to-patient ratios, the upscaling of ICU capacity and shortages in personal protective equipment, which is crucial for infection control [4]. Moreover, the pandemic also led to disruptions of antimicrobial stewardship programs and exacerbation of antimicrobial resistance due to the inappropriate use of antibiotics [5]. Surveillance of hospital-acquired infections has helped to rapidly identify changes in different health-care settings. Read et al. estimated that approximately 11.3% of patients with COVID-19 became infected after hospital admission [6]. It is also necessary to take precautions against healthcare-associated infections caused by SARS-CoV-2 to avoid further increasing the number of COVID-19 patients [7-9]. Although SARS-CoV-2 HAIs are also included in HAIs, we focused on bacterial HAIs in this study.

This paper aimed to evaluate the effects of the COVID-19 pandemic on HAIs, pathogens incidence, antibiotic resistance and consumption rates in the ICUs of a 900-bed tertiary care university hospital.

PATIENTS AND METHODS

Adult patients (≥18 years old) diagnosed with HAIs in ICUs (anesthesiology and reanimation, general surgery, cardiovascular surgery, neurosurgery and ICU of COVID-19 patients) between 1 January 2018 and 31 December 2021, were investigated retrospectively in a 900-bed tertiary care university hospital in Turkey. The ICU of COVID-19 patients, was the unit reserved for patients with a diagnosis of COVID-19 only. The data on HAIs in ICUs were collected by the infection control nurses through active surveillance. HAIs were defined as infections that first appeared 48 hours or more after hospitalization with no evidence that the infection was present or incubating at the time of admission to the acute care setting [6]. Patients were divided into two groups in order to compare the differences between the pre-pandemic (2018-2019) and pandemic periods (2020-2021). In addition, ICUs were also investigated separately as ICU of COVID-19 patients versus others for the years 2020 and 2021. HAI/BSI/HAP/UTI incidence rates were calculated using the following formula: the number of events/total patient days x 1000. HAIs consisted of bloodstream infections (BSIs), central venous catheter-related BSIs (CVCBSIs), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), urinary tract infections (UTIs) and catheter-associated UTIs (CAUTIs).

Bloodstream infection (BSI) is defined by positive blood cultures in a patient with systemic signs of infection and can be either primary (a laboratory confirmed BSI (LCBI) that is not secondary to an infection at another body site) or secondary to a documented source [10, 11]. CVCBSI is defined as a laboratory confirmed BSI occurring in the presence of a central venous catheter (CVC) or within 48 hours of CVC removal [10, 11]. According to CDC/NHSN and National Healthcare Associated Infections Surveillance guidelines, urinary tract infections were classified as symptomatic UTI or other infections of the urinary tract with exclusion of asymptomatic bacteriuria. In addition, UTI that occurs in a patient who had an indwelling urethral urinary catheter in place within the 48-hour period before the onset, is defined as CAUTI [10, 11].

HAP diagnoses were made using the criteria for pneumonia, with the infection occurring within 48 hours after hospital admission, new onset or progressing infiltrations in chest radiography and the presence of at least two of the following:

1) fever >38°C,
2) white blood cell (WBC) >10000/mm^3 or <4000/mm^3,

3) purulent bronchial secretion (leukocyte >25 and ≤10 epithelial cells in the gram-staining of deep endotracheal aspirate (x10)) and
4) decrease of oxygenation [12].

Pneumonia that developed more than 48 hours after intubation and mechanical ventilation support was considered to be VAP [12].

Inclusion criteria

Patients ≥18 years of age in ICUs.

Meeting the diagnostic criteria for HAI, BSI, CVCBSI, HAP, VAP, UTI or CAUTI.

Exclusion criteria

Discharged from the ICU within 48 hours of admission.

Infections associated with complications or extensions of infections already present on admission, unless a change in pathogen or symptoms strongly suggested the acquisition of a new infection or reactivation of a latent infection.

Colonization that was not causing clinical signs or symptoms and/or inflammation resulting from tissue response to injury or stimulation by noninfectious agents.

Blood cultures were performed via BACTEC System. Phoenix System (in 2018) and "matrix-assisted laser desorption ionization time-of-flight mass spectrometry" (MALDI-TOF MS) (in 2019-2021) were used in order to identificate isolates. Antibiotic susceptibility testing was performed with Phoenix System according to recommendations of European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria [13]. The incidence rates of device-associated HAIs were calculated using the following formula: the number of events/total device-day x1000. Defined daily doses (DDDs) and the Anatomical Therapeutic Chemical Classification System (ATC/DDD, 2016) developed by the WHO Collaborating Centre for Drug Statistics Methodology were used to evaluate antibiotic consumption. The antibiotic consumption index was calculated using the following formula: (total dose of antibiotic (grams)/DDD x total patient days) x1000. Statistical analysis was performed using MedCalc® Statistical Software version 20.218 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2023) and IBM SPSS ver.28.0 (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp.). Categorical variables were compared using Pearson chi-square and Fisher's exact tests between groups. A p-value below 0.05 was considered to be statistically significant.

No ethics committee approval was sought due to the retrospective and epidemiological design of the study. Our study was performed in accordance with the ethical standards of the Helsinki Declaration, which was accepted by the World Health Community in 1975 (revised in 2013).

RESULTS

In total, 8157 patients were included in this study. The total patient day number was 55794, and 724 episodes of HAI were recorded. During the four-year period, there were 279 bloodstream infections, 228 CVCBSIs, 197 HAPs, 133 VAPs, 90 UTIs and 86 CAUTIs. HAIs with device utilization rates for each year are provided in Table 1.

The incidence rate of HAIs (per 1000 patient days) in the ICU of COVID-19 patients was 16.59, whereas it was 13.42 in other ICUs during the pandemic period (2020-2021) (p=0.107). The BSI incidence rate was 3.32 in the pre-pandemic period (2018-2019) and 5.41 in the pandemic period in ICUs other than the ICU of COVID-19 patients (p<0.001). In the pandemic period, the BSI incidence rate was significantly higher in the ICU of COVID-19 patients than in other ICUs (14.26 vs 5.41, p<0.001). Similar to BSIs, the CVCBSI incidence rate was 4.72 in the pre-pandemic period (2018-2019) and 7.52 in the pandemic period in ICUs other than the ICU of COVID-19 patients (p=0.0019). In 2021, the CVCBSI incidence rate was significantly higher in the ICU of COVID-19 patients than in the other ICUs (20.21 vs 7.52, p<0.001). The incidence rates of HAIs are provided in Table 2.

The most common pathogen among HAIs was *A. baumannii*. The extended-spectrum beta-lactamase (ESBL) positivity rates for *K. pneumoniae* and *E. coli* were 61% and 42% in the pre-pandemic period (2018–2019) and 73% and 69% in the pandemic period in ICUs other than the ICU of COVID-19 patients (p>0.05). In the pandemic period, the ESBL positivity rates for *K. pneumoniae* and *E. coli* were 83% and 100% in the ICU of COVID-19 patients, respectively. The distribution of HAI pathogens and antibiotic resistance rates are presented in Table 3.

Regarding BSIs during the pandemic period, the bacteraemia episode rates of *A. baumannii* (5.375

vs 0.984, p<0.001), *Enterococcus* spp. (1.635 vs 0.967, p<0.001) and *S. maltophilia* (3.038 vs 1.297, p=0.0086) in the ICU of COVID-19 patients were found to be significantly higher than in the other ICUs. In addition, after the COVID-19 pandemic, coagulase-negative Staphylococci (0.939 vs 0.480, p=0.047) and *S. maltophilia* (1.297 vs 0.205, p<0.001) bacteraemia episode rates were also significantly higher in the ICUs other than the ICU of COVID-19 patients (Table 4).

Meropenem (ACI: 2114 vs 1869, p<0.001), teicoplanin (ACI: 692 vs 540, p<0.001) and ceftriaxone (ACI: 514 vs 306, p<0.001) consumptions were increased while ciprofloxacin (ACI: 283 vs 353,

Table 1 - Healthcare Associated Infections and Device Utilization Ratios.

Variables	*Reanimation, General Surgery, Cardiovascular Surgery and Neurosurgery Intensive Care Units (ICUs)*				*ICU of COVID-19 patients*	
	2018	*2019*	*2020*	*2021*	*2020*	*2021*
Total number of Healthcare Associated Infection (HAI) episodes	195	158	140	160	24	47
Total number of Bloodstream Infections (BSI)	58	39	42	79	20	41
Total number of Central Venous Catheter BSIs (CVCBSI)	48	31	36	64	17	32
Total number of Hospital- Acquired Pneumonia (HAP)	66	50	44	34	–	3
Total number of Ventilator-Associated Pneumonia (VAP)	46	38	26	20	–	3
Total number of Urinary Tract Infections (UTIs)	20	29	17	21	–	3
Total Number of Urinary Catheter- Associated UTIs (CAUTI)	18	28	17	20	–	3
Central venous catheter day	8426	8283	6292	7006	–	1583
Ventilator day	9320	8508	6528	6272	–	1842
Urinary catheter day	13693	13229	10710	10686	–	2136
Total patient number	1966	2145	1727	1886	218	215
Total patient day	14571	14587	11121	11236	2136	2143
Utilization ratio of central venous catheter	0.57	0.56	0.56	0.62	–	0.73
Utilization ratio of ventilator	0.63	0.58	0.58	0.55	–	0.85
Utilization ratio of urinary catheter	0.93	0.90	0.96	0.95	–	0.99

Table 2 - Incidence rates of Healthcare Associated Infections.

Incidence rates (/1000 patient day)	*Reanimation, General Surgery, Cardiovascular Surgery and Neurosurgery Intensive Care Units (ICUs)*			*ICU of COVID-19 patients*	*P_2 value*
	2018-2019 (Total patient days = 29158)	*2020-2021 (Total patient days = 22357)*	*P_1 value*	*2020-2021 (Total patient days = 4279)*	
HAI	12.11	13.42	0.189	16.59	0.107
BSI	3.32	5.41	**0.0003***	14.26	**<0.0001***
CVCBSI	4.72	7.52	**0.0019***	20.21	**0.0002*$^{\Delta}$**
HAP	3.97	3.48	0.369	1.4	0.189$^{\Delta}$
VAP	4.71	3.59	0.138	1.62	0.268$^{\Delta}$
UTI	1.68	1.74	0.861	1.4	0.638$^{\Delta}$
CAUTI	1.70	1.72	0.956	1.4	0.641$^{\Delta}$

*: p<0.05, Δ: Only the 2021 incidence rates of ICU of COVID-19 patients versus other ICUs were compared, p_1: 2018-2019 versus 2020-2021 in other ICUs, p_2: ICU of COVID-19 patients versus other ICUs in 2020-2021.

Table 3 - Pathogens of HAIs and Antibiotic Resistance Rates.

Pathogens of HAIs	*Antibiotic*	*Other ICUs Resistance Rates (n, %)*			*ICU of COVID-19 patients Resistance Rates (n,%)*	*P_2 value*
		2018-2019	*2020-2021*	*P_1 value*	*2020-2021*	
Acinetobacter baumannii	Colistin	3/30, 10%	11/81, 14%	0.755	2/49, 4 %	0.129
	Meropenem	30/30, 100%	77/81, 95%	0.573	49/49, 100%	0.297
	Imipenem	30/30, 100%	79/81, 98%	0.907	49/49, 100%	0.527
	Amikacin	30/30, 100%	80/81, 99%	0.953	49/49, 100%	1.000
	Gentamicin	29/30, 97%	80/81, 99%	0.921	49/49, 100%	1.000
Pseudomonas aeruginosa	Amikacin	1/8, 13%	0/9, 0%	0.471	–	–
	Gentamycin	2/8, 25%	6/9, 67%	0.153	–	–
	Cefepime	4/8, 50%	7/9, 78%	0.335	–	–
	Ceftazidime	3/8, 38%	7/9, 78%	0.153	–	–
	Meropenem	3/8, 38%	3/9, 33%	1.000	–	–
	Imipenem	3/8, 38%	6/9, 67%	0.347	–	–
Klebsiella pneumoniae	Colistin	7/18, 39%	14/30, 47%	0.599	4/6, 67%	0.658
	Meropenem	8/18, 44%	20/30, 67%	0.131	5/6, 83%	0.643
	Imipenem	8/18, 44%	21/30, 70%	0.080	5/6, 83%	0.655
	Ertapenem	9/18, 50%	22/30, 73%	0.102	5/6, 83%	1.000
	ESBL (+)	11/18, 61%	22/30, 73%	0.376	5/6, 83%	1.000
Escherichia coli	Colistin	2/12, 17%	0/13, 0%	0.220	0/2, 0%	–
	Meropenem	1/12, 8%	5/13, 38%	0.160	0/2, 0%	0.524
	Imipenem	1/12, 8%	3/13, 23%	0.593	0/2, 0%	1.000
	Ertapenem	1/12, 8%	6/13, 46%	0.073	0/2, 0%	0.486
	ESBL (+)	5/12, 42%	9/13, 69%	0.165	2/2, 100%	1.000
Staphylococcus aureus	MRSA	3/6, 50%	4/5, 80%	0.545	2/3, 67%	1.000
Coagulase - negative staphylococci	MRCNS	15/15, 100%	12/13, 92%	0.464	6/8, 75%	0.531
Enterococcus spp.	VRE	1/8, 13%	1/6, 17%	1.000	0/7, 0%	1.000

MRSA: Methicillin-resistant *Staphylococcus aureus*. MRCNS: Methicillin-resistant coagulase-negative Staphylococci. VRE: Vancomycin-resistant Enterococci. ESBL: Extended spectrum beta-lactamase. p_1: 2018-2019 versus 2020-2021 in other ICUs. p_2: ICU of COVID-19 patients versus other ICUs in 2020-2021.

Table 4 - Bacteraemia episode rates of BSIs.

Pathogens of BSIs (Bacteraemia episode/1000 patient day)	*Reanimation, General Surgery, Cardiovascular Surgery and Neurosurgery Intensive Care Units (ICUs)*			*ICU of COVID-19 patients*	*P_2 value*
	2018-2019 (n=number)	*2020-2021 (n=number)*	*P_1 value*	*2020-2021 (n=number)*	
Total patient days	29158	22357		4279	
Acinetobacter baumannii	0.685 (n=20)	0.984 (n=22)	0.240	5.375 (n=23)	*<0.0001**
Pseudomonas aeruginosa	0.308 (n=9)	0.268 (n=6)	0.790	–	–
Klebsiella pneumoniae	0.720 (n=21)	1.073 (n=24)	0.178	0.934 (n=4)	0.797

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Pathogens of BSIs (Bacteraemia episode/1000 patient day)	*Reanimation, General Surgery, Cardiovascular Surgery and Neurosurgery Intensive Care Units (ICUs)*			*ICU of COVID-19 patients*	*P_2 value*
	2018-2019 (n=number)	*2020-2021 (n=number)*	*P_1 value*	*2020-2021 (n=number)*	
Escherichia coli	–	0.044 (n=1)	–	0.233 (n=1)	0.191
Staphylococcus aureus	0.068 (n=2)	0.089 (n=2)	0.790	–	–
Coagulase-negative Staphylococci	0.480 (n=14)	0.939 (n=21)	*0.047**	1.635 (n=7)	0.197
Enterococcus spp.	0.274 (n=8)	0.268 (n=6)	0.967	1.635 (n=7)	*0.0002**
Stenotrophomonas maltophilia	0.205 (n=6)	1.297 (n=29)	*<0.0001**	3.038 (n=13)	*0.0086**
Candida spp.	0.548 (n=16)	0.581 (n=13)	0.876	0.934 (n=4)	0.401

*: p<0.05, p_1: 2018-2019 versus 2020-2021 in other ICUs, p_2: ICU of COVID-19 patients versus other ICUs in 2020-2021.

Table 5 - Antibiotic Consumption Index (ACI) in Intensive Care Units (ICUs).

ACI (Total dose of antibiotic (grams) / DDD x total patient days) x1000)	*ICUs*		
	2018-2019	*2020-2021*	*P value*
Total patient days	29158	26636	
Meropenem	1869	2114	*<0.001**
Imipenem	43	39	0.614
Vancomycin	384	340	0.068
Teicoplanin	540	692	*<0.001**
Amikacin	182	184	0.978
Piperacillin-tazobactam	350	325	0.253
Ceftriaxone	306	514	*<0.001**
Ciprofloxacin	353	283	*0.003**

*p<0.05.

p=0.003) consumption was decreased in all ICUs after the pre-pandemic period (Table 5).

DISCUSSION

HAIs are considered to be a predictor of the quality of patient care and are associated with higher mortality among COVID-19 patients [14]. Our results highlight the increase of HAIs especially in the BSI and CVCBSI subgroups. In addition, this is one of the rare studies emphasizing the effects of the COVID-19 pandemic on HAIs, pathogens, antibiotic consumption and resistance rates in critically ill patients.

Musuuza et al. showed a higher prevalence of superinfection (41%) than co-infection, especially among ICU patients with COVID-19, and they also found that super-infected patients had an increased risk of death and a higher prevalence of mechanical ventilation [15]. A retrospective, case-control study including 140 ICU patients with severe COVID-19 revealed that 40.7% of the patients had a bacterial or fungal nosocomial infection during the ICU stay, with the most frequent infection being BSI (primary 31% and catheter-related 25%) [16].

In examining the impact of COVID-19 on the incidence of HAIs in United States, Weiner-Lastinger et al. emphasized the significant increase in the national standardized infection ratios for central-line-associated bloodstream infections (CLABSIs), CAUTIs, ventilator-associated events and MRSA bacteraemia that was observed in 2020 [17]. Izadi et al. also evaluated the national rate of HAIs. They reported that the overall rate of ICU-acquired infections was 16.82 per 1000 patient days while that of ventilator-associated infections was 26.29 per 1000 ventilator days [18]. A retrospective, single-center study on 78 critically ill COVID-19 patients reported that the incidence rate of ICU-acquired BSIs was 47 episodes per 1000 patient days, and the estimated cumulative risk of having at least one BSI episode was found to be 50% after 30 days [19]. Buetti et al. observed a higher ICU-BSI rate in the COVID-19 patients (14.9% vs 3.4%, p≤0.0001) [20]. In addition, a systematic review and meta-analysis on the pooled occurrence of BSIs among hospitalized patients with COVID-19 estimated a BSI occurrence as high as 29.6% in patients admitted to the ICU, and a higher number of BSIs was observed in patients with COVID-19 than in patients without COV-

ID-19 (OR=2.77; 95% CI=1.53-5.02; p<0.001) [21]. Meanwhile, Fakih et al. showed a substantial increase in CLABSI rates of 51.0% during the pandemic period, from 0.56 to 0.85 per 1000 line days (p<0.001), and of 62.9% from 1.00 to 1.64 per 10,000 patient days (p<0.001), but they did not find any significant change in CAUTI rates (0.86 vs 0.77 per 1,000 catheter days, p=0.19) [22]. In our study, although the increase in the HAI incidence rate was not statistically significant, we also found a significant increase in BSIs and CVCBSIs after the COVID-19 pandemic in both the ICU of COVID-19 patients and other ICUs.

Several studies showed differences in HAIs regarding the causative pathogens during the pandemic period. In a study on super-infected COVID-19 patients, *Acinetobacter* spp. (22.3%) was the most frequently identified pathogen [15]. Similarly, Baccolini et al. investigated HAIs in ICU patients and found that the most common pathogen was *A. baumannii* (31.6% in the 2019 cohort and 29% in the 2020 cohort) [4].

Conversely, Giacobbe et al. examined ICU-acquired BSIs in critically ill COVID-19 patients and reported that the most frequent pathogens were coagulase-negative staphylococci (24%), followed by *Enterococcus faecalis* (18%) and *S. aureus* (13%) [19]. Buetti et al. studied the distribution of microorganisms in ICU-BSIs among COVID-19 and non-COVID-19 patients and reported that coagulase-negative staphylococci (35.9%) were the most common pathogens in COVID-19 patients, while other gram-positive agents (33.3%) were more common in non-COVID-19 patients [20]. We also found the most frequent pathogen in HAIs to be *A. baumannii* among the ICU patients in our study. Regarding BSIs during the pandemic period, the bacteraemia episode rates of *A. baumannii*, *Enterococcus* spp. and *S. maltophilia* in the ICU of COVID-19 patients were found to be significantly higher than in the other ICUs. Further, after the COVID-19 pandemic, coagulase-negative staphylococci and *S. maltophilia* bacteraemia episode rates were also significantly higher in the ICUs other than the ICU of COVID-19 patients in our study. We believe that a possible contributor to these results might be the significant increase in the consumption rates of meropenem and ceftriaxone in ICUs during the pandemic period.

The six pathogens (*E. coli*, *S. aureus*, *K. pneumoniae*, *S. pneumoniae*, *A. baumannii* and *P. aeruginosa*) that contribute most to the burden of antimicrobial resistance were responsible for approximately 929,000 deaths in 2019 [23]. In 2020, third-generation cephalosporin resistance in *Enterobacteriaceae* was widespread in the WHO European Region: 18 (44%) countries reported resistance levels of 50% or higher for *K. pneumoniae*, while resistance levels of 50% or higher were observed in five (13%) countries for *E. coli* [24]. Carbapenem resistance was more frequently reported in *K. pneumoniae* (equal to or greater than 50% in six (15%) countries) than in *E. coli* (equal to or greater than 1% in six (15%) countries) [24]. Several studies showed a possible connection between COVID-19 and antimicrobial resistance. Porretta et al. reported an increased risk of carbapenem-resistant *Enterobacterales* acquisition in COVID-19 patients compared to other patients (75.9 vs 25.3 cases/10,000 patient days) [25]. Pasero et al. reviewed multi-drug resistant (MDR) infections in critically ill patients with COVID-19 and found that the reported incidence of MDR bacterial infections ranged between 32% and 50% among these patients [26]. Cole et al. also investigated the effects of the COVID-19 pandemic on HAIs with MDR organisms, including MRSA, ESBL and VRE, and they found that MDR infection rates decreased from 0.3% to 0.2% per 1000 patient days (p=0.03) due to increased compliance with infection prevention measures by healthcare workers [27]. Although we found an increase of ESBL rates in HAIs for the isolates of *K. pneumoniae* and *E. coli* after the COVID-19 pandemic, it was not statistically significant. After the pandemic period, we also observed an increase in carbapenem and colistin resistance for the isolates of *K. pneumoniae* in HAIs, but the difference was not significant.

In the European Union and European Economic Area countries, the consumption of carbapenems was found to be 0.05 DDD per 1000 inhabitants per day in 2020, with a significant increase in the population-weighted mean consumption of carbapenems during the period of 2011-2020, which was similar to the consumption of polymyxins [28]. Despite the fact that the COVID-19 pandemic had a significant impact on antimicrobial stewardship, the long-term effects of the pandemic on antimicrobial resistance are still not known [29]. In our study, we found a significant increase in meropenem, teicoplanin and ceftriaxone consumption in all ICUs after the COVID-19 pandemic. Al-

though the differences in the ESBL and carbapenem resistance rates were not significant after the COVID-19 pandemic, we believe that increased consumption of meropenem and ceftriaxone might have contributed to this antimicrobial resistance.

Our study has several limitations, including the use of retrospective analysis, lack of a surgical site infection subgroup, lack of polymyxin consumption data and difficulties in diagnosing HAP or VAP in patients with severe COVID-19 pneumonia. In addition, the lack of evaluation in terms of compliance with infection control measures, was another limitation of our study. Due to the design of the study, we mainly focused on epidemiological data rather than on clinical aspects of the patients.

CONCLUSION

The results of the study showed that the incidence rates of BSIs and CVCBSIs were significantly increased in all ICUs after the pre-pandemic period in our hospital. Regarding BSIs during the pandemic period, the bacteraemia episode rates of *A. baumannii*, *Enterococcus* spp. and *S. maltophilia* in the ICU of COVID-19 patients were found to be significantly higher than in the other ICUs. We also found that meropenem, teicoplanin and ceftriaxone consumption increased in all ICUs after the pre-pandemic period.

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Conflict of interest
All authors declare that they have no competing interests.

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None to declare.

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