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Evaluation of Species Distribution and Antibiotic Susceptibility of Blood Culture Isolates of Patients Followed in the Intensive Care Unit Before and During the COVID-19 Pandemic: Retrospective, Single-Center Analysis

COVID-19 Pandemisi Öncesi ve Döneminde Yoğun Bakım Ünitesinde Takip Edilen Hastaların Kan Kültürü İzolatlarının Tür Dağılımı ve Antibiyotik Duyarlılıklarının Değerlendirilmesi: Retrospektif, Tek Merkez Analizi

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ABSTRACT

Objective: *This study aims to identify the microorganism species isolated from blood cultures of patients hospitalized in the ICU of a tertiary center before and during the COVID-19 pandemic and to investigate their antibiotic susceptibility.*

Material and Method: *Patients hospitalized in the ICU two years before and after the COVID-19 pandemic between March 15, 2019, and March 15, 2021, were divided into two groups, and their blood cultures were evaluated retrospectively. Isolated microorganisms and their antibiotic susceptibility were analyzed.*

Results: *A total of 1282 patients' blood cultures were analyzed, and demographic data were similar between groups. Blood culture growth was detected in 39.6% (n=202) of the patients in the pre-pandemic period and 41% (n=317) in the pandemic period. Gram-positive bacteria were isolated in 71.3%, gram-negative bacteria in 21.6%, and Candida spp. in 7.1% of the population. Klebsiella spp. was significantly higher, and Enterococcus spp. was significantly lower in blood cultures during the pandemic. In the COVID-19 period, although not significant, a decrease in antibiotic susceptibility was detected for Staphylococcus aureus, Klebsiella spp., E.coli, Enterobacter spp., and Pseudomonas spp. There was a statistically significant decrease in susceptibility to teicoplanin and linezolid in coagulase-negative staphylococci (CNS). During the pandemic, 57.6% (n=172) of the patients were positive for COVID-19. In COVID-19-positive patients, while Candida spp. was significantly higher, no decrease in antifungal susceptibility was detected.*

Conclusion: *The severe COVID-19 infection in immunocompromised patients may have led to a significant increase in secondary infections, contributing to the increase in Klebsiella strains isolated from patients in the pandemic period and the reduction in antimicrobial susceptibility. The decrease in cross-contamination in these patients, who were followed up in isolated rooms in our ICU, was influential in the significantly lower detection of Enterococcus strains. High-dose steroids in the treatment effectively increased the number of isolated Candida strains.*

Keywords:
Antibiotic sensitivity
COVID-19
Blood culture
Intensive care unit

ÖZET

Amaç: *Bu çalışmanın amacı, COVID-19 pandemisi öncesi ve döneminde tersiyer bir merkezin Yoğun bakım ünitesinde (YBÜ) yatan hastaların kan kültürlerinden izole edilen mikroorganizma türlerinin tanımlanması ve antibiyotik duyarlılıklarının araştırılmasıdır.*

Gereç ve Yöntem: *15 Mart 2019 ile 15 Mart 2021 arasındaki COVID-19 pandemisi öncesi ve sonrası 2 yıllık süreçte YBÜ'de yatan hastalar iki gruba ayrılarak kan kültürleri retrospektif olarak değerlendirildi. İzole edilen mikroorganizmalar ve antibiyotik duyarlılıkları analiz edildi.*

Bulgular: *Toplamda 1282 hastanın kan kültürü analiz edildi, demografik veriler gruplar arasında benzerdi. Pre-pandemik dönemdeki hastaların %39.6'sında (n=202) ve pandemik dönemdekilerin %41'inde (n=317) üreme saptandı. Tüm popülasyonun %71.3'ünde gram pozitif bakteriler, %21.6'sında gram negatif bakteriler ve %7.1'inde Candida spp. izole edildi. Pandemi dönemindeki kan kültürlerinde Klebsiella spp. anlamlı olarak yüksek, Enterococcus spp. ise anlamlı olarak düşüktü. COVID-19 döneminde Staphylococcus aureus, Klebsiella spp., E.coli, Enterobacter spp. ve Pseudomonas spp. için antibiyotik duyarlılıklarında anlamlı olmasa da azalma tespit edildi. Koagülaz negatif stafilokoklarda (KNS) ise teikoplanin ve linezolid duyarlılığında istatistiksel olarak anlamlı azalma mevcuttu. Pandemi dönemindeki hastaların %57.6'sı (n=172) COVID-19 pozitifti. COVID-19 pozitif hastalarda ise Candida spp. oranları anlamlı olarak yüksek iken antifungal duyarlılıkta azalma saptanmadı.*

Sonuç: *COVID-19 enfeksiyonunun bağışıklık sistemi zayıflamış hastalarda ağır seyretmesi, sekonder enfeksiyonlarda anlamlı artışa yol açarak pandemi dönemindeki hastalardan izole edilen Klebsiella suşlarında artışta ve antimikrobiyal duyarlılıktaki azalmalarda etkili olmuş olabilir. YBÜ'mizde izole odalarda takip edilen bu hastalardaki çapraz bulaşın azalmasının Enterococcus suşlarının anlamlı olarak düşük saptanmasında, tedavide yüksek doz steroidlerin kullanılmasının ise izole edilen Candida suşlarının artmasında etkili olduğunu düşünüyoruz.*

Anahtar Kelimeler:
Antibiyotik duyarlılığı
COVID-19
Kan kültürü
Yoğun bakım ünitesi

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INTRODUCTION

Intensive Care Units (ICUs) are the hospital departments where nosocomial infections, antibiotic use, and resistant microorganisms are frequently seen due to invasive procedures and lengthy hospital stays. Over the years, the types of microorganisms that cause bacteremia and their antibiotic susceptibility may change. Intermittent determination of the distribution of causative organisms and their antibiotic susceptibility is essential, as it guides empirical treatment (1).

Despite optimization of the conditions of ICUs and advances in antimicrobial therapy, bloodstream infections are still a cause of high mortality and morbidity (2). Blood cultures are an essential diagnostic test frequently used in ICUs. Demonstrating microorganisms in the patient's bloodstream is vital for diagnosing and diagnosing sepsis (3). Extended length of stay in ICUs due to the COVID-19 pandemic and the use of various drugs in the treatment may change the distribution of microorganisms that may cause secondary infections and their antibiotic susceptibility.

This study aims to identify the microorganism species isolated from blood cultures of patients hospitalized in the ICU of a tertiary center before and during the COVID-19 pandemic and to investigate their antibiotic susceptibility.

MATERIAL AND METHOD

For this retrospective cross-sectional study, approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, Istanbul, Turkey (date:22.06.2022 number:152). The principles of the Declaration of Helsinki complied with the investigation.

Microorganisms and antibiotic susceptibilities grew in the blood cultures of patients hospitalized at the University of Health Sciences Istanbul Kanuni Sultan Süleyman Training and Research Hospital ICU between March 15, 2019, and March 15, 2020, before the COVID-19 pandemic and between March 15, 2020, and March 15, 2021, were compared. All patients aged 18 years and older who stayed in the ICU for more than 24 hours without missing clinical and laboratory results were included in the study. This retrospective cross-sectional study did not determine the sample size; all patients between the relevant dates were included.

It was accepted as causative when the same microorganism was produced simultaneously in at least two blood cultures taken from the patients. If only one of the blood cultures showed growth, if the patient's clinic was compatible, or if the same microorganism was isolated in a different infection site, it was considered a factor. When *Bacillus* spp., *Corynebacterium* spp., *coagulase-negative staphylococcus* (CNS), *Micrococcus* spp., and *Propionibacterium acnes*, which belong to the skin flora, grew in only one of the blood cultures taken at the same time, it was considered as contamination (4). Repeated blood cultures from patients were not included in the study.

Blood cultures in BACTEC Plus aerobic media bottles sent to the laboratory were incubated in the BACTEC-FX automated blood culture (Becton Dickinson, USA) device. All plates were incubated for 18–24 hours at 37 °C. All strains were identified at the species level using the VITEK 2 (bioMerieux, France) method. Antimicrobial susceptibility tests of the identified strains were performed in Phoenix 100 (Becton Dickinson Co., Sparks, Maryland, USA) device according to the manufacturer's operating procedures, according to the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

Statistical analysis

SPSS 29.0 (SPSS Inc., Chicago, USA) program was used to analyze the data. Descriptive data are expressed as the number of patients, percentage, mean, and standard deviation. The conformity of the variables to the normal distribution was evaluated analytically (Shapiro-Wilks test) and visually (histogram). The Mann-Whitney U test was used to analyze the quantitative variables that were not normally distributed among the groups. Chi-square tests were applied to examine whether the isolated microorganisms and their antibiotic susceptibility significantly changed in the pre-pandemic and pandemic periods. The statistical significance limit was accepted as $p<0.05$.

RESULTS

One thousand two hundred eighty-two patients' blood culture samples were analyzed in the ICU two years before and after the COVID-19 pandemic between March 15, 2019, and March 15, 2021. No significant difference was observed in demographic data before and during COVID-19. Of the blood culture samples included in the study, 39.7% (n=510) were sent during the pre-pandemic

Table 1: Demographic data of patients and classification of microorganisms isolated from blood cultures

Variable	Total (n=519)	Pre-pandemic period (n=202)	Pandemic period (n=317)	P-value
Age (years)	62.4 (19.3)	60.4 (20.4)	63.6 (18.4)	0.087*
Gender, n (%)				0.071**
Female	239 (46.1)	103 (51)	136 (42.9)	
Male	280 (53.9)	99 (49)	181 (57.1)	
Microorganism classification, n (%)				
Gram positive	370 (71.3)	147 (72.8)	223 (70.3)	0.552**
Gram negative	112 (21.6)	42 (20.8)	70 (22.1)	0.728**
Candida spp.	37 (7.1)	13 (6.4)	24 (7.6)	0.624**

Values are the number of patients (n), percentage, mean, and standard deviation.
**Mann-Whitney U test, **Pearson Chi-square test*

period and 60.3% (n=772) during the pandemic period. Growth was detected in the patient's blood cultures of 39.6% (n=202) in the pre-pandemic period and 41% (n=317) in the pandemic period. Contamination was detected in 11.9% (n=61) of blood cultures in the pre-pandemic period and 12.4% (n=96) of blood cultures in the pandemic period. In the whole population, gram-positive bacteria were isolated in 71.3% (n=370), gram-negative bacteria in 21.6% (n=112), and *Candida* spp. in 7.1% (n=37) of blood cultures (Table 1).

CNS was isolated from 62.4% (n=126) of the blood cultures in the pre-pandemic period, *Acinetobacter* spp. from 8.4% (n=17), and *Enterococcus* spp. from 8.4% (n=17). During the pandemic, CNS was isolated in 60.6% (n=192) of blood cultures, *Klebsiella* spp. in 10.8% (n=34), and *Candida* spp. in 7.9%. In blood cultures during the pandemic, *Klebsiella* spp. was significantly higher (p=0.006), and *Enterococcus* spp. was significantly lower (p=0.04). However, an insignificant increase in *Candida* spp. (6.4% vs. 7.6%) was observed during the pandemic period (p=0.536) (Table 2).

In the pandemic period, antibiotic susceptibility decreased in *E.coli*, *Enterobacter* spp, and *Pseudomonas* spp, although it was not significant (p>0.05) (Table 3).

During the pandemic, a decrease in the sensitivity of almost all antibiotics was observed in CNS and *Staphylococcus aureus*, although it was not significant. A significant decrease in sensitivity to erythromycin, clindamycin, levofloxacin, linezolid, and teicoplanin was observed in CNS during the pandemic period (p<0.05). There was no significant difference in antibiotic susceptibility in *Staphylococcus aureus* before and after the pandemic. However, *Staphylococcus aureus* was found to be methicillin-resistant at a rate of 26.3% (n=5). A significant decrease in ampicillin susceptibility was detected for *Enterococcus* spp. (p<0.05) (Table 4).

During the pandemic period, 57.6% of the patients followed in the ICU were positive for COVID-19 (n=172). Compared to COVID-19-positive patients with COVID-19-negative patients during and before the pandemic, isolated *Candida* spp. were significantly higher (p=0.022). There was no significant difference in

Table 2: Distribution of microorganisms isolated from blood cultures in the pre-pandemic and pandemic period

	Pre-pandemic period (n=202)	Pandemic period (n=317)	P-value
CNS	126 (62.4)	192 (60.6)	0.935*
Enterococcus spp.	17 (8.4)	13 (4.1)	0.04*
Staphylococcus aureus	4 (2)	15 (4.7)	0.104*
Klebsiella spp.	8 (4)	34 (10.7)	0.006*
Escherichia coli	11 (5.4)	15 (4.7)	0.716*
Acinetobacter spp.	17 (8.4)	14 (4.4)	0.061*
Pseudomonas spp.	2 (1)	5 (1.6)	-
Enterobacter spp.	3 (1.5)	2 (0.6)	-
Candida spp.	13 (6.4)	25 (7.9)	0.536*

Values are the number of patients (n) and percentage.
CNS: Coagulase-negative staphylococcus
**Pearson Chi-square test*

Table 3: Antibiotic susceptibility of gram-negative microorganisms isolated from blood cultures in the pre-pandemic and pandemic period

	***Klebsiella* spp.**		***E.coli***		***Acinetobacter* spp.**		***Pseudomonas* spp.**		***Enterobacter* spp.**	
	BP n=8	AP n=34	BP n=11	AP n=15	BP n=17	AP n=14	BP n=2	AP n=5	BP n=3	AP n=2
Amikacin	50	32.4	81.8	73.3	29.4	14.3	50	60	100	50
Gentamicin	50	52.9	81.8	66.7	23.5	14.3	100	60	66.7	50
İmipenem	25	20.6	90.9	60	11.8	7.1	100	20	100	50
Meropenem	25	20.6	72.7	46.7	11.8	14.3	100	40	100	50
Ciprofloxacin	12.5	17.6	54.5	46.7	17.6	14.3	100	60	66.7	50
PIP-TAZO	100	100	100	100	0	100	100	100	100	0
Cefepime	0	100	100	100	100	100	100	100	100	100
TMP-SMX	37.5	41.2	81.8	46.7	17.6	21.4	0	0	100	50
Ampicilin	12.5	8.8	36.4	33.3	0	0	0	0	0	0
Colistin	100	100	100	100	100	100	100	100	100	100

Values are given as a percentage.
BP: Before the pandemic, AP: After the pandemic
PIP-TAZO: Piperacilin-tazobactam, TMP-SMX: Trimethoprim-sulfamethoxazole

Table 4: Antibiotic susceptibility of gram-positive microorganisms isolated from blood cultures in the pre-pandemic and pandemic period.

	CNS		*Staphylococcus aureus*		*Enterococcus* spp.	
	BP n=25	AP n=40	BP n=4	AP n=15	BP n=17	AP n=13
Penicillin	0	5	0	0	-	-
Erythromycin	32*	7.5	75	53.3	-	-
Clindamycin	48**	17.5	100	60	-	-
Levofloxacin	32*	2.5	100	33.3	-	-
Linezolid	96*	75	100	53.3	76.5	84.6
Teicoplanin	92**	62.5	100	73.3	82.4	76.9
Vancomycin	88	87.5	100	86.7	88.2	76.9
Ampicillin	-	-	-	-	76.5**	38.5
Gentamicin	48	27.5	100	93.3	47.1	15.4
TMP-SMX	68	70	100	93.3	5.9	30.8

Values are given as a percentage.
BP: Before the pandemic, AP: After the pandemic, CNS: Coagulase-negative staphylococcus,
TMP-SMX: Trimethoprim-sulfamethoxazole
**There is a significant difference p<0.05, Fisher's Exact test*
***There is a significant difference p<0.05, Pearson Chi-square test*

Table 5: Antifungal susceptibilities for Candida spp isolated from pre-pandemic and pandemic blood cultures

	Candida spp.	
	BP n=13	AP n=24
Amphotericin B	84.6	92
Fluconazole	61.5	60.0
Caspofungin	69.2	88
Voriconazole	76.9	72
Micafungin	69.2	88.0
Flucytosine	69.2	68

Values are given as a percentage.
BP: Before the pandemic, AP: After the pandemic

antifungal susceptibility for *Candida* spp. according to the periods (p>0.05) (Table 5).

DISCUSSION

Sepsis is an important problem with high morbidity and mortality. The treatment must determine antibiotic susceptibility by isolating the microorganism causing sepsis in the blood culture (5). It has been reported that 14% of COVID-19-positive patients have a severe clinical course, and 5% need ICU (6). Zhou et al. reported secondary bacterial infection in 50% of patients infected with SARS-CoV-2 and died (4).

Microorganisms grown in blood cultures vary over time and between hospitals and countries. An international cohort study reported that gram-negative bacteria were isolated more frequently (58.3%) in ICUs (7). In a multicenter study from Canada, the rates of gram-positive and negative bacteria isolated from patients in the ICU were reported as 58.6% and 21.2%, respectively (8). In studies from Turkey, the most commonly reproduced microorganisms in ICUs are *gram-positive cocci,* especially c*oagulase-negative staphylococci* (1,3,9). Sirin et al. (1) reported the rates of gram-positive and negative bacteria isolated as 44.9% and 40.3%, respectively, and Küçükateş et al. (9) reported 58.5% and 35.7%. Aytac et al. reported 60.7% gram-positive, 35% gram-negative, and 4.3% *Candida* spp. in the pre-pandemic period (3). Studies have reported methicillin resistance in CNS between 40% and 90.7% (3,10). Vancomycin and teicoplanin are the most preferred antibiotics for treating methicillin-resistant staphylococcal infections. However, strains with decreased susceptibility to glycopeptide group antibiotics have been reported recently (11). Aytac et al. stated that CNSs were 100% sensitive to vancomycin and teicoplanin before and during the pandemic (3). In our study, 71.3% gram-positive bacteria, 21.6% gram-negative bacteria, and 7.1% yeast were isolated in the population. Consistent with the literature, CNS was most frequently isolated in the pre-pandemic period (62.4%) and during the pandemic period (60.6%). There was no significant difference in CNS reproduction rates in the pre-pandemic and pandemic periods. While no change was observed in vancomycin sensitivity for CNS, a significant decrease was observed in teicoplanin and linezolid sensitivity. There may be a decrease in teicoplanin and linezolid sensitivity due to the high rate of secondary bacterial infections observed during the COVID-19 pandemic and the antibiotic therapy applied to CNS in our ICU. The microorganism differences reported between centers may be due to conditions such as the characteristics of the patients followed in ICUs, ICU bed capacity, different antibiotic treatment protocols applied, and whether the cause of bacteremia is community or hospital origin.

Contamination can be seen due to improper skin antisepsis during sample collection for blood culture. In only one of the blood cultures sent from the same patient simultaneously, CNS belonging to the skin flora, *Bacillus* species (other than *B.anthracis*), *Micrococcus* spp., *Corynebacterium* spp., *Propionibacterium* spp. reproduction is considered as contamination (3,12). Studies show that CNS strains are the most common contamination factor (13-14). As a good quality indicator, the contamination rate is required to be below 3% (1). In studies from Turkey, contamination rates have been reported between 8.6% and 17.8% (1,15). In our study, 11.9% of contamination was observed in the pre-pandemic period and 12.4% in the pandemic period. There was no significant difference between the contamination rates before and after the pandemic. High contamination rates may be due to insufficient skin antisepsis, such as not paying attention to hand hygiene and not using gloves. Staphylococcus aureus and CNS usually constitute the majority of Gram-positive bacteria isolated from blood cultures. Karlowsky et al. CNS and Staphylococcus aureus rates 42% and 16.5%, respectively (16). In our study, CNS and *Staphylococcus aureus* was isolated at a rate of 62.4% and 2% in the pre-pandemic period and 60.6% and 4.7% during the pandemic period. According to global surveillance data, *Staphylococcus aureus* strains may differ in countries, hospitals, and even in different units (17). A surveillance study covering European countries reported that MRSA rates ranged from 5-100% and decreased in some countries over the years (18). In Staphylococcus aureus, methicillin resistance has been reported between 15.3% and 60.4% (9-12,19). Aytaç et al. reported methicillin resistance at a rate of 50% in the pre-pandemic period and 75% in the pandemic period (3). In our study, *Staphylococcus aureus* was found to be 50% (n=2) before and 20% (n=3) during the pandemic. Studies from Turkey have reported that no vancomycin resistance was found in methicillin-resistant and susceptible strains (20-21). Aytac et al. said that CNS was 100% sensitive to vancomycin and teicoplanin before and during the pandemic (3). In our study, *Staphylococcus aureus* was 100% sensitive to vancomycin in the pre-pandemic period, while 13.3% resistance was detected during the pandemic. *Enterococci* are among the leading causes of nosocomial infections. Sirin et al. (1) 13.6%, and Çetin et al. (22) reported that *enterococci* grew at 8%. In our study, *Enterococcus* spp. was significantly less isolated during the pandemic (8.4% vs. 4.1%). Due to the severe prognosis of COVID-19 patients followed in the ICU during the pandemic, the shorter duration of stay in the ICU and the less cross-contamination because they often stay in isolated rooms may cause a decrease in the number of enterococci. The most crucial problem in *enterococci* is the increasing resistance to glycopeptide antibiotics. Sirin et al. reported no glycopeptide resistance in *E. faecalis,* whereas 15.5% vancomycin and 13.8% teicoplanin resistance were in *E. faecium* (1). In our study, before the pandemic, vancomycin and teicoplanin resistance in *Enterococcus spp.* was 11.8% and 17.6%, respectively. During the pandemic period, it was found to increase to 23.1% in both vancomycin and teicoplanin. However, no significant difference was observed between the periods (Table 4). It is important to determine risk factors for vancomycin-resistant enterococcal colonization and infection, to screen patients at risk with rectal swab sampling, and to take isolation precautions.

E.coli, Klebsiella spp., *Pseudomonas* spp., and *Acinetobacter* spp. were reported to be the most frequently isolated gram-negative bacteria in patients followed up in the ICU (1,3,8,16,18). Our study's most frequently isolated gram-negative bacteria were *Klebsiella* spp., *Acinetobacter* spp., and *E.coli*, respectively. There was a significant increase in the reproduction rate of *Klebsiella* spp, during the pandemic period compared to the pre-pandemic period (3.9% vs. 10.8%, p=0.006) (Table 2). It is known that COVID-19 is more common and severe in immunocompromised patients. *Klebsiella spp*. may have been isolated more frequently during the pandemic since it can cause infections such as surgical wounds, pneumonia, bacteremia, and urinary and respiratory system infections, especially in individuals with weakened immune systems. It has been reported that bacteremia caused by *Pseudomonas aeruginosa* and *Acinetobacter* spp. is challenging to treat. Resistance development and mortality are high in ICUs where patients with weakened immunity are high (23). Sirin et al. reported that Acinetobacter spp. and *Pseudomonas aeruginosa* were isolated at a rate of 13.1% and 4.8%, respectively, from blood culture samples (1). In our study, *Acinetobacter* spp. was detected in 8.4% of the population before and 4.4% during the pandemic. *Pseudomonas* spp. was lower than the literature before the pandemic (1%) and during the pandemic (1.6%). In recent years, the increased carbapenemase production in these bacterial species has led to increasing resistance to carbapenem group antibiotics. In the literature, imipenem susceptibility has been reported between 51-82% in *Pseudomonas aeruginosa* and 14-61% in *Acinetobacter baumannii* (22,24). In our study, while the susceptibility to imipenem in *Acinetobacter* spp. and *Pseudomonas* spp. was 11.8% and 100% in the pre-pandemic period, it decreased to 7.1% and 20% during the pandemic period. However, the decrease in sensitivity during the pandemic period was insignificant (Table 3).

It has been emphasized that aminoglycosides, generally used with another antimicrobial, are the most effective antibiotics after colistin in *Acinetobacter* spp. and Pseudomonas aeruginosa (1). Turk Dagi et al. reported that gentamicin and amikacin resistance in *Acinetobacter baumannii* were 79% and 59%, respectively (25). In our study, gentamicin and amikacin resistances for *Acinetobacter* spp. were 76.5% and 71.6% before the pandemic. Consistent with the literature, aminoglycosides, except colistin, were the most sensitive antibiotics for *Acinetobacter* spp. However, although not significant, a decrease in sensitivities was observed during the pandemic (Table 3).

Different members of the *Enterobacteriaceae* family, especially *E. coli* and *K. pneumoniae*, can resist broad-spectrum beta-lactam antibiotics with their ability to produce extended-spectrum beta-lactamases (ESBL). Sirin et al. reported that *E. coli* and *Proteus* species were relatively more susceptible among ESBL-producing species, while *Klebsiella* species had higher antibiotic resistance rates (1). In our study, following the literature, the antibiotic susceptibility of *Klebsiella* spp. was lower than *E.coli*. Although insignificant during the pandemic, a sensitivity decrease was observed in both *Klebsiella* spp. and *E.coli* against beta-lactam group antibiotics. Although colistin has been reported to be the most effective antimicrobial against *A. baumannii* isolates, it has been reported that colistin resistance has increased in recent years (26). Our study did not detect colistin resistance for *Klebsiella* spp. and *Acinetobacter* spp. both before and during the pandemic (Table 3).

It has been reported that the frequency of hospital-acquired candidemia has increased in recent years, and it is isolated between 6-10% in ICUs (1,3). In a study from Brazil, a ten-fold increase in the frequency of candidemia was reported in COVID-19 patients receiving high-dose steroids (27). Rapid diagnosis and treatment are important in invasive yeast infections since higher mortality has been reported in COVID-19 cases that do not receive treatment than those who receive antifungal treatment. In our study, *Candida* spp. was detected at a rate of 6.4% before and 7.6% during the pandemic period. During the pandemic period, 57.6% of our patients followed in the ICU were found to be positive for COVID-19. The rates of *Candida* spp. isolated from the blood cultures of COVID-19-positive patients were significantly higher than those of COVID-19-negative patients (p=0.022).

Limitations

The study's limitations are retrospective, single-center, and the patient sample is small.

CONCLUSION

In conclusion, we think that the severe course of COVID-19 infection in patients with weakened immune systems may have caused a significant increase in secondary infections, which may have contributed to the increase in Klebsiella strains isolated from patients in the pandemic period, as well as the decrease in susceptibility to gram-positive and negative microorganisms. The decrease in cross-contamination in these patients, who are frequently followed in isolated rooms in our ICU, may have played a role in the significantly lower detection of *Enterococcus* strains. The increase in candidemia in COVID-19-positive patients may be due to the prolonged hospital stay and high-dose steroid use in treatment, and more effective infection control programs and rational antibiotic use policies should be implemented in similar pandemic periods that may occur in the future.

Conflict of Interest: No conflict of interest was declared by the authors.

Ethics: For this retrospective cross-sectional study, approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, Istanbul, Turkey (date:22.06.2022 number:152)

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