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Comparison of the Infection Characteristics and Antimicrobial Use Among Patients Hospitalized in the Intensive Care Unit During and After the COVID-19 Pandemic Periods

COVID-19 Pandemisi ve Pandemi Sonrası Dönemde Yoğun Bakım Ünitelerinde Yatan Hastalarda Antimikrobiyal Tüketimi ve Enfeksiyonların Özelliklerinin Karşılaştırılması

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Abstract

Introduction: During the severe acute respiratory syndrome-Coronavirus-2 pandemic, intensive care units (ICUs) were pivotal in treating severe cases. In the ICU, invasive procedures and the use of immunosuppressive drugs have been associated with an increased risk of infection. We aimed to compare the antibiotic use, infection types, culture positivity, and resistance patterns among patients in the ICU during and after the pandemic period.

Materials and Methods: The patients who were followed up in the adult ICU at our hospital were retrospectively assessed after being divided into two groups. Group 1 included patients admitted between December 1, 2020, and May 5, 2021, (pandemic group). Group 2 consisted of patients admitted between June 1, 2021, and November 1, 2023 (post-pandemic).

Results: Antibacterial (100% vs. 92.7%, p=0.003), and antifungal (33.3% vs. 10.7%, p<0.001) use was significantly higher during the pandemic in comparison to the post-pandemic period. Additionally, multiple classes of antimicrobial drugs were used and antivirals were administered more commonly during the pandemic than after the pandemic (p<0.001). The interval from admission to antimicrobial therapy, duration of antimicrobial therapy, and total length of hospital stay were statistically longer during the pandemic than after the pandemic. The culture-positive endotracheal aspirates (ETAs) were more frequently observed during the pandemic than after it (56% vs. 42.1%, p=0.019). The proportion of patients in whom *Klebsiella* spp. were identified in the ETA was higher during the pandemic than after the pandemic (19.1% vs. 7.3%). Furthermore, the blood cultures yielded the growth of *Stenotrophomonas maltophilia, Klebsiella* spp., and *Candida* spp. more commonly in the pandemic group than in the post-pandemic period. There was no statistically significant difference in the proportion of patients who developed methicillin-resistant *Staphylococcus aureus* infection (p=0.473), methicillin-resistant coagulase-negative *Staphylococcus* infection (p=0.263), or third-generation cephalosporin-resistant (p=0.658) and carbapenem-resistant Gram-negative infections (p=0.214) between the two time periods.

Conclusion: In our study, a notable disparity was observed in the antibiotic usage rates and types between the two study groups. We hypothesize that this discrepancy may be attributed to the rigorous implementation of infection control measures and the enhanced effectiveness of the antibiotic stewardship committee, particularly during and following the period of reduced epidemic burden.

Keywords: COVID-19, intensive care unit, antimicrobials, infection

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Öz

Giriş: Yoğun bakım üniteleri, şiddetli akut solunum yolu sendromu Koronavirüs-2 pandemisi sırasında şiddetli vakaların tedavisinde önemli hale gelmiştir. Hem invaziv prosedürler hem de immünosüpresif ilaç kullanımı sekonder enfeksiyon riskinin artmasıyla ilişkilendirilmiştir. Bu çalışmada, pandemi dönemini pandemi sonrası dönemle, yoğun bakım ünitesindeki hastalarda antibiyotik kullanımını, enfeksiyonların tipini, kültür pozitifliği ve direnç paternlerini karşılaştırmayı amaçladık.

Gereç ve Yöntem: Hastanemizdeki yetişkin yoğun bakım ünitesinde takip edilen hastalar retrospektif olarak iki grupta değerlendirildi. Grup 1, COVID-19 pandemisi sırasında 01.12.2020 ile 01.05.2021 arasındaki hastaları içerirken, Grup 2, pandemi sonrası 01.06.2021 ile 01.11.2021 arasındaki hastaları içerdi.

Bulgular: Pandemi sırasında pandemi sonrasına göre antibakteriyel (%100'e karşı %92,7, p=0,003) ve antifungal kullanım (%33,3'e karşı %10,7, p<0,001) oranları istatistiksel olarak daha yüksek idi. Ek olarak, birden fazla sınıf antimikrobiyal ilaç kullanımı ve antiviral tüketimi pandemi sırasında pandemi sonrasına göre daha yaygın olarak bulunmuştur (p<0,001). Hastaneye kabulden antimikrobiyal tedaviye geçen süre, antimikrobiyal tedavi süresi ve toplam hastanede kalış süresi pandemi sırasında pandemi sonrasına göre istatistiksel olarak daha uzun olarak gözlemlendi. Kültür pozitif endotrakeal aspiratlar (ETA) pandemi sırasında pandemi sonrasına göre daha yaygın olarak bulunmuştur (%56'ya karşı %42,1, p=0,019). Pandemi döneminde ETA'da *Klebsiella* spp. üreten hastaların oranı pandemi sonrası dönemdeki hastalardan daha yaygın olarak bulunmuştur (%19,1'e karşı %7,3). Kan kültürlerinde *Stenotrophomonas maltophilia*, *Klebsiella* spp. ve *Candida* spp. pandemi döneminde pandemi sonrası döneme göre daha yaygın olarak bulunmuştur. İki zaman dilimi arasında metisiline dirençli *Staphylococcus aureus* enfeksiyonu (p=0,473), metisiline dirençli koagülaz negatif *Staphylococcus* enfeksiyonu (p=0,263) veya üçüncü nesil sefalosporin dirençli (p=0,658) ve karbapenem dirençli Gram-negatif enfeksiyonları (p=0,214) olan hastaların oranında istatistiksel olarak anlamlı bir fark gözlenmemiştir.

Sonuç: Çalışmamızda, antibiyotik kullanım oranlarında ve tiplerinde belirgin bir farklılık gözlemlendi. Bu farklılığın, enfeksiyon kontrol önlemlerinin titizlikle uygulanmasına ve özellikle salgın insidansının azaldığı dönemde ve sonrasında antibiyotik yönetim komitesinin artan etkinliğine atfedilebileceğini varsayıyoruz.

Anahtar Kelimeler: COVID-19, yoğun bakım ünitesi, antimikrobiyaller, enfeksiyon

Introduction

Infections in intensive care units (ICUs) are often caused by more resistant agents than those in other hospital areas, posing serious consequences with an increased frequency. Factors contributing to this heightened risk include endotracheal intubation or tracheostomy for mechanical ventilation and frequent invasive procedures such as intravenous or bladder catheterization[1].

Infections in ICUs can result in extension of hospital stay, increase in costs, and increase in mortality risk. Furthermore, the potential for the spread of infections originating in ICUs poses a threat to other patients[2-4].

Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2), a novel strain of coronavirus, has been globally spreading since December 2019, leading to the Coronavirus disease-2019 (COVID-19) pandemic. Although the clinical course is generally self-limiting, approximately 5% of patients experience severe respiratory failure. Thus, ICUs are pivotal in the treatment of severe cases of COVID-19 requiring respiratory support.

Both invasive procedures (e.g., intubation and catheterization) and the use of steroids and immunomodulatory agents (e.g., tocilizumab) during the disease have been associated with an increased risk of infections[5]. The most common bacterial complications of COVID-19 infection include secondary pneumonia, including ventilator-associated pneumonia (VAP), and bloodstream infections (BSI)[5].

Due to the high risk of secondary infections, antibiotics are frequently administered to patients in ICUs. Approximately 43% of patients are treated with inappropriate antibiotics, leading to the emergence of resistant agents[6]. This increases the risk of secondary bacterial infections in viral epidemics, which was also observed in and contributed to the increased use of antibiotics during the COVID-19 pandemic[7].

In this study, we aimed to compare the pandemic period with the post-pandemic period in terms of the characteristics of the infections and antimicrobials used among patients admitted to the ICU.

Materials and Methods

Patients who were followed up in the adult ICUs at İstanbul Medeniyet University, Göztepe Prof. Dr. Süleyman Yalçın City Hospital, which houses 815 beds and 105 ICU beds, were retrospectively assessed after being divided into two groups. Group 1 included patients admitted between December 01, 2020, and May 01, 2021 (during the COVID-19 pandemic), and group 2 included patients admitted between June, 06, 2021, and November 01, 2023 (post-pandemic). The following data, spanning the 5-month periods, were obtained from the hospital's electronic database: patient demographics (e.g., age, sex, and underlying comorbidities), infection types, antimicrobials used empirically or targeted therapy for infections, cultured agents and their resistance patterns, length of stay in the ICU, and clinical outcomes. Patients who had consumed prophylactic antibiotics and had a positive SARS-CoV-2 test were not

included in the study. Antibiotic use was calculated on the basis of the number of days a patient was hospitalized in the ICU. The study was approved by the Ethics Committee of İstanbul Medeniyet University, Göztepe Prof. Dr. Süleyman Yalçın City Hospital (no: 2021/0111, date: 10.02.2021), and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Descriptive statistics are presented as numbers and percentages (n, %), mean±standard deviation, or median with its 25-75% percentile. Normality was assessed using histograms and the Shapiro-Wilk test. In the comparison of the pandemic and post-pandemic groups, we used the Mann-Whitney U test for non-normally distributed continuous variables and the chi-square or Fisher's exact test for categorical variables. A p value <0.05 was considered statistically significant. R (version 4.2.3; https://www.r-project.org/) was used for all statistical analyses.

Results

The mean age of the study patients was 65.0±16.5 years, and 154 patients (48.3%) were female. Patients in the pandemic group were younger than those in the post-pandemic group (62.5±13.2 vs. 67.1±18.5, p=0.011). The median delay between symptom onset and hospital admission was longer in the pandemic group than in the post-pandemic group (six days vs. two days, p<0.001). All the patients in the pandemic group (n=141) received antimicrobial therapy. Empiric antibiotic therapy was initially administered. Subsequently, the antibiotics were revised according to the culture results. Antimicrobials (100% vs. 93.3%, p=0.004), antibiotics (100% vs. 92.7%, p=0.003), and antifungals (33.3% vs. 10.7%, p<0.001) were used more in the pandemic group than in the post-pandemic group. Additionally, multiple classes of antimicrobials were used more commonly in the pandemic group than in the post-pandemic group (p<0.001). Among the patients who received antimicrobial therapy (n=307), the time from admission to antimicrobial therapy (median six days vs. two days, p<0.001), duration of antimicrobial therapy (median 17 days vs. 11 days, p<0.001), and length of hospital stay (median 18 days vs. 11 days, p<0.001) were statistically significantly longer in the pandemic group than in the post-pandemic group. There was no difference in the end-of-treatment mortality between the two groups (Table 1). Table 2 shows the comparison of the antibiotic classes that were used in the pandemic and post-pandemic groups. Penicillin (68.1% vs. 51.1%, p=0.003) and cephalosporin (71.6% vs. 40.4%, p<0.001) group of antibiotics were used more commonly in the pandemic group than in the post-pandemic group. Furthermore, linezolid (51.1% vs. 20.8%, p<0.001) and tigecycline (39.0% vs. 23.0%, p=0.003) were used more frequently in the pandemic group than in the post-pandemic group. The polymyxin (30.5% vs. 19.1%; p=0.026) and aminoglycoside (24.8% vs. 10.7%; p=0.001) group of antibiotics were used statistically significantly more in the pandemic group than in the post-pandemic group. Furthermore, clindamycin was used more frequently in the pandemic group than in the post-pandemic group (24.8% vs. 7.8%, p<0.001). Antivirals were used more in the pandemic group than in the post-pandemic group (p<0.001). The positivity rate of the endotracheal aspirate (ETA) cultures was high among patients in the pandemic group than among those in the post-pandemic group (56% vs. 42.1%, p=0.019). However, the positivity rate of urine cultures was higher in the post-pandemic group than in the pandemic group (40.4% vs. 28.4%, p=0.033). The proportion of patients in whom *Klebsiella* spp. was identified in the ETA cultures was higher in the pandemic group than in the post-pandemic group (19.1% vs. 7.3%). *Stenotrophomonas maltophilia, Klebsiella* spp., and *Candida* spp. were identified in the blood cultures more frequently in the pandemic group than in the post-pandemic group (Table 3).

Table 4 shows the comparison of the resistance patterns of the isolated microorganisms in the pandemic and post-pandemic groups. There was no statistically significant difference in the proportion of patients with methicillin-resistant *Staphylococcus aureus* (MRSA) infection (p=0.473), methicillin-resistant coagulase-negative *Staphylococcus* infection (p=0.263), or third-generation cephalosporin-resistant (p=0.658) and carbapenem-resistant Gram-negative infections (p=0.214) between the two groups.

Empirical antifungal therapy was administered to patients in whom fungal infection was suspected, and the antifungal was revised according to the culture results. Five patients in the pandemic group developed fluconazole-resistant fungal infections. No fungal infections were observed in the post-pandemic group (p=0.016).

All patients in the pandemic group who were admitted to the ICU and 25 patients in the post-pandemic group (n=178) were administered steroid therapy. In the pandemic group, 54, 15, 3, 4, 60, and 5 patients developed bacterial pneumonia, bacteremia/sepsis, urinary tract infection, candidemia, viral pneumonia, and other infections, respectively. In the post-pandemic group, 48, 44, 32, 4, and 50 patients were diagnosed with bacterial pneumonia, bacteremia/sepsis, urinary tract infection, candidemia, and other infections, respectively. In the pandemic group, the rates of VAP, catheter-associated BSI, and urinary catheter-associated infections (CAUTI) in the ICU were 1, 3, and 1, respectively. In the post-pandemic group, 1 patient developed VAP, 13 developed BSI, and 4 developed CAUTI.

Table 1. Comparison of the demographic variables, clinical variables, and antimicrobial use between the pandemic and post-pandemic groups

Characteristics	Pandemic group (n=141)	Post-pandemic group (n=178)	p
Sex			0.009
Female	56 (39.7)	98 (55.1)	
Male	85 (60.3)	80 (44.9)	
Age, mean±SD	62.513.2±	67.118.5±	0.011
Comorbidities			0.211
No	29 (20.6)	26 (14.6)	
Yes	112 (79.4)	152 (85.4)	
Time from symptom onset to admission	6 (4-9)	2 (1-3)	<0.001
Antimicrobial drug use			0.004
No	0 (0)	12 (7.3)	
Yes	141 (100)	166 (93.3)	
Antibiotic use			0.003
No	0 (0)	13 (7.3)	
Yes	141 (100)	165 (92.7)	
Antifungal use			<0.001
No	94 (66.7)	159 (89.3)	
Yes	47 (33.3)	19 (10.7)	
Antiviral use			<0.001
No	13 (9.2)	142 (79.8)	
Yes	128 (90.8)	36 (20.2)	
Use of multiple classes of antimicrobial drugs			<0.001
No	23 (16.3)	112 (62.9)	
Yes	118 (83.7)	66 (37.1)	
Time from admission to antimicrobial therapy (n=307)	6 (3-8)	2 (1-4)	<0.001
Duration of antimicrobial therapy (n=307)	17 (12-25)	11 (5-20)	<0.001
Fever*, (n=307)			0.032
No	99 (70.2)	135 (81.3)	
Yes	42 (29.8)	31 (18.7)	
Intubation*, (n=307)			<0.001
No	138 (97.9)	105 (63.3)	
Yes	3 (2.1)	61 (36.7)	
SPO_2*, (n=243)	88 (80.2-91)	85 (77-90)	0.123
WBC count*, (n=307)	7400 (5300-10700)	11550 (7900-16875)	<0.001
Length of hospital stay, median (25-75%)	18 (13-28)	11 (6-21.8)	<0.001
Mortality			0.165
No	47 (33.3)	74 (41.6)	
Yes	94 (66.7)	104 (58.4)	

Continuous variables are presented as mean±standard deviation or median (25-75%). Categorical variables are presented as number and percentage (n, %).*At the time of initiation of antimicrobial therapy.

SPO_2: Oxygen saturation, WBC: White blood cell, SD: Standard deviation

Table 2. Comparison of antibiotic use between the pandemic and post-pandemic groups

Antibiotics used	Pandemic group (n=141)	Post-pandemic period (n=178)	p
Penicillin			0.003
No	45 (31.9)	87 (48.9)	
Yes	96 (68.1)	91 (51.1)	
Cephalosporin			<0.001
No	40 (28.4)	106 (59.6)	
Yes	101 (71.6)	72 (40.4)	
Carbapenem			0.142
No	51 (36.2)	80 (44.9)	
Yes	90 (63.8)	98 (55.1)	
Glycopeptide			0.057
No	77 (54.6)	117 (65.7)	
Yes	64 (45.4)	61 (34.3)	
Linezolid			<0.001
No	69 (48.9)	141 (79.2)	
Yes	72 (51.1)	37 (20.8)	
Tigecycline			0.003
No	86 (61.0)	137 (77.0)	
Yes	55 (39.0)	41 (23.0)	
Polymyxin			0.026
No	98 (69.5)	144 (80.9)	
Yes	43 (30.5)	34 (19.1)	
Tetracycline			<0.001
No	70 (49.6)	165 (92.7)	
Yes	71 (50.4)	13 (7.3)	
Quinolone			0.076
No	104 (73.8)	147 (82.6)	
Yes	37 (26.2)	31 (17.4)	
Aminoglycoside			0.001
No	106 (75.2)	159 (89.3)	
Yes	35 (24.8)	19 (10.7)	
Clindamycin			<0.001
No	106 (75.2)	164 (92.2)	
Yes	35 (24.8)	14 (7.8)	
SXT			<0.001
No	106 (75.2)	173 (97.2)	
Yes	35 (24.8)	5 (2.8)	
Macrolide			0.079
No	135 (95.7)	160 (89.9)	
Yes	6 (4.3)	18 (10.1)	

Table 2. Comparison of antibiotic use between the pandemic and post-pandemic groups

Antibiotics used	Pandemic group (n=141)	Post-pandemic period (n=178)	p
Fosfomycin			>0.999
No	133 (94.3)	169 (94.9)	
Yes	8 (5.7)	9 (5.1)	
Metronidazole			0.019
No	141 (100)	173 (96.1)	
Yes	0 (0)	7 (3.9)	
Daptomycin			0.657
No	138 (97.9)	178 (98.9)	
Yes	3 (2.1)	2 (1.1)	

Categorical variables are presented as number and percentage (n, %).

SXT: Trimethoprim-sulfamethoxazole

Table 3. Comparison of the culture positivity rates and bacteria grown between the pandemic and post-pandemic groups

Culture characteristics	Pandemic group (n=141)	Post-pandemic period (n=178)	p
Positive endotracheal aspirate culture			0.019
No	62 (44.0)	103 (57.9)	
Yes	79 (56.0)	75 (42.1)	
Acinetobacter spp.			0.222
No	127 (90.1)	151 (84.8)	
Yes	14 (9.9)	27 (15.2)	
Klebsiella spp.			0.003
No	114 (80.9)	165 (92.7)	
Yes	27 (19.1)	13 (7.3)	
Stenotrophomonas maltophilia			0.440
No	130 (92.2)	169 (94.9)	
Yes	11 (7.8)	9 (5.1)	
Pseudomonas aeruginosa			0.543
No	128 (90.8)	166 (93.3)	
Yes	13 (9.2)	12 (6.7)	
Haemophilus spp.			0.069
No	141 (100)	173 (97.2)	
Yes	0 (0.0)	5 (2.81)	
Aspergillus			0.037
No	137 (97.2)	178 (100)	
Yes	4 (2.8)	0 (0.0)	
Positive blood culture			0.176
No	45 (31.9)	71 (39.9)	
Yes	96 (68.1)	107 (60.1)	
Acinetobacter spp.			0.561
No	131 (92.9)	161 (90.4)	
Yes	10 (7.1)	17 (9.6)	

Table 3. Continued

Culture characteristics	Pandemic group (n=141)	Post-pandemic period (n=178)	p
Positive endotracheal aspirate culture			0.019
Stenotrophomonas maltophilia			0.017
No	120 (85.1)	167 (93.8)	
Yes	21 (14.9)	11 (6.2)	
Pseudomonas aeruginosa			>0.999
No	137 (97.2)	173 (97.2)	
Yes	4 (2.8)	5 (2.8)	
Klebsiella spp.			0.032
No	131 (92.9)	175 (98.3)	
Yes	10 (7.1)	3 (1.7)	
Staphylococcus aureus			0.470
No	139 (98.6)	173 (97.2)	
Yes	2 (1.4)	5 (2.8)	
Candida spp.			0.030
No	127 (90.1)	172 (96.6)	
Yes	14 (9.9)	6 (3.4)	
KNS			0.926
No	76 (53.9)	98 (55.1)	
Yes	65 (46.1)	80 (44.9)	
Positive urine culture			0.033
No	101 (71.6)	106 (59.6)	
Yes	40 (28.4)	72 (40.4)	
Escherichia coli			0.164
No	133 (94.3)	159 (89.3)	
Yes	8 (5.67)	19 (10.7)	
Klebsiella spp.			0.521
No	138 (97.9)	171 (96.1)	
Yes	3 (2.13)	7 (3.9)	
Acinetobacter spp.			0.442
No	140 (99.3)	178 (100)	
Yes	1 (0.7)	0 (0.0)	
Pseudomonas aeruginosa			0.139
No	140 (99.3)	172 (96.6)	
Yes	1 (0.7)	6 (3.4)	
Enterococcus spp.			0.120
No	139 (98.6)	169 (94.9)	
Yes	2 (1.4)	9 (5.1)	

Table 4. Comparison of the of culture positivity rates and resistance patterns between the pandemic and post-pandemic groups

Resistance patterns	Pandemic group (n=141)	Post-pandemic group (n=178)	p
Methicillin-resistant coagulase-negative *Staphylococcus* infection			0.377
No	126 (89.4)	152 (85.4)	
Yes	15 (10.6)	26 (14.6)	
Methicillin-resistant *Staphylococcus aureus* infection			0.474
No	139 (98.6)	172 (96.7)	
Yes	2 (1.4)	6 (3.3)	
Third-generation cephalosporin resistance in Gram-negative bacteria			0.755
No	92 (65.2)	112 (62.9)	
Yes	49 (34.8)	66 (37.1)	
Carbapenem resistance in Gram-negative bacteria			0.158
No	96 (68.1)	135 (75.8)	
Yes	45 (31.9)	43 (24.2)	
Levofloxacin-resistant *Stenotrophomonas maltophilia*			0.195
No	139 (98.6)	178 (100)	
Yes	2 (1.4)	0 (0)	
SXT-resistant *Stenotrophomonas maltophilia*			0.195
No	139 (98.6)	178 (100)	
Yes	2 (1.4)	0 (0)	
Ampicillin-resistant *Enterococcus*			0.233
No	140 (99.3)	173 (97.2)	
Yes	1 (0.7)	5 (2.8)	
Fluconazole-resistant fungi			0.016
No	136 (96.5)	178 (100)	
Yes	5 (3.5)	0 (0)	
Amphotericin-B-resistant fungi			0.505
No	141 (100)	176 (98.9)	
Yes	0 (0)	2 (1.1)	

Categorical variables are presented as number and percentage (n, %).

SXT: Trimethoprim-sulfamethoxazole

Discussion

In our study, we observed a higher consumption of antimicrobials in patients hospitalized in ICUs during the pandemic period than in those hospitalized during the post-pandemic period. Furthermore, we observed an increase in the use of multiple antibiotics, longer duration of antibiotic use, and longer hospital stay in the pandemic period than in the post-pandemic period.

Approximately 70% of patients admitted to the ICU are administered prophylactic, preemptive, empirical, or targeted antibiotic therapy. However, up to 30% of patients treated with antibiotics in the ICU do not have an active infection[8]. An analysis of antibiotic use revealed notable factors such as unnecessary combination therapy involving two or more antibiotics, prolonged prophylaxis, or extended antibiotic treatment beyond the recommended periods[8]. The challenge of diagnosing infections in patients admitted to the ICU also reportedly contributes to inappropriate antibiotic use.

Although routine antibiotic use was not recommended during the COVID-19 pandemic, studies conducted in various countries, including our own[6–12], have reported an increase in antibiotic use during this period. In patients admitted to the ICU, antibiotics that were started prophylactically/empirically were revised according to the culture results. In our study, we observed a significant increase in the use of antibiotic (ceftriaxone, linezolid, tetracycline, and clindamycin), antifungal, and antiviral drugs during the pandemic than during the post-pandemic period. A study conducted in Egypt revealed an increase in the use of carbapenem, vancomycin, linezolid, trimethoprim-sulfamethoxazole, and azithromycin, as well as a decrease in the

use of fluoroquinolones, lincosamides, and third- and fourth-generation cephalosporins in ICUs during the COVID-19 period[13].

Malik and Mundra[14] reported that antibiotics were administered to 78% of the patients during the COVID-19 period, with ceftriaxone and azithromycin being the most commonly administered antibiotics. Similarly, Grau et al.[15] found an increase in the antibiotic use in Spain during the first wave of the COVID-19 pandemic. Meta-analysis studies on antibiotic use during the COVID-19 period revealed usage rates ranging from 72% to 75%, with coinfection rates ranging from 3.5% to 8.6%. At the onset of the COVID-19 pandemic, factors such as uncertainty regarding the disease's treatment, overwhelmed hospitals, inadequate functioning of antibiotic control committees, shortage of physicians dedicated to COVID-19, observations of secondary bacterial infections in previous epidemics, and the initial recommendation for broad-spectrum antibiotic use in patients admitted to the ICU contributed to the excessive and inappropriate use of antibiotics[14-17].

In Turkey, Menekşe and Deniz[18] reported that antibiotics were administered to 91% of the patients admitted to the ICU due to COVID-19, and the most commonly used antibiotics were piperacillin-tazobactam, carbapenems, tigecycline, and methicillin-resistant Gram-positive resistant groups. In our study, although there was no difference between the two periods in the use of carbapenems and tigecycline, there was a significant increase in the use of linezolid during the pandemic.

Intensive care units represent environments where nosocomial infections are most frequently encountered. In a meta-analysis study, the rate of secondary infections in patients hospitalized in ICUs due to COVID-19 ranged from 7% to 51%. Pneumonia was identified as the most common secondary infection, with Gram-negative bacteria, primarily *Pseudomonas aeruginosa*, *Enterobacter* spp., and *Escherichia coli*, emerging as the predominant causative agents[3,19,20].

In our study, the interval between symptom onset, hospital admission, and initiation of antibiotic therapy was significantly longer in the pandemic group than in the post-pandemic group. Pneumonia was the most prevalent infection during this time, as evidenced by the increased number of tracheal aspirate cultures and significantly extended intubation durations. In the post-pandemic period, the most common infections were bacterial pneumonia, sepsis/bacteremia, and urinary tract infections, in that order. The absence of a significant difference in mortality between the two periods in our study may be attributed to the consistent profiles of infectious agents and antimicrobial resistance across both periods.

In our study, no significant difference was observed in the types of infectious agents isolated from the patients admitted to the ICU during and after the pandemic. Blood cultures revealed comparable rates of methicillin-resistant coagulase-negative *Staphylococci*, MRSA, carbapenem-resistant Gram-negative bacteria, and cephalosporin-resistant Gram-negative agents across both time periods (Table 3). However, ETA cultures were more prevalent during the pandemic than after the pandemic (56% vs. 42.1%, p=0.019). Conversely, positive urine cultures were more frequently identified after the pandemic than during the pandemic (40.4% vs. 28.4%, p=0.033).

During the pandemic, *Klebsiella* spp. and *Stenotrophomonas maltophilia* were the most commonly identified causative agents of pneumonia in tracheal aspirate cultures. In the post-pandemic period, nosocomial infections were predominantly caused by Gram-negative bacteria, particularly *Acinetobacter* and *Pseudomonas* species. Similar findings were reported by Costa et al.[21], who identified *Acinetobacter baumannii*, *P. aeruginosa*, and *Klebsiella pneumoniae* as the most common agents causing secondary infections in patients with COVID-19 who were admitted to the ICU. Chen et al.[22] observed that community-acquired pathogens such as *Mycoplasma*, *Haemophilus influenzae*, and *Streptococcus pneumoniae* were the most common causes of secondary infections in patients with mild and moderate diseases. However, nosocomial pathogens such as *S. maltophilia*, *K. pneumoniae*, *P. aeruginosa*, and *Enterobacter aerogenes* were the most common cause of secondary infection in patients with critical and severe diseases. These findings are consistent with those of our study.

In a study from the Czech Republic that compared nosocomial infection agents before and during the pandemic, a significant decrease in *E. coli*, *Proteus mirabilis*, and *S. aureus* was observed during the pandemic[23]. However, infections due to *Enterococcus faecium*, *Klebsiella variicola*, and *Serratia marcescens* were higher in the pre-pandemic period[23].

Study Limitations

The primary limitation of our study lies in its retrospective nature. Furthermore, it was a single-center study that evaluated the most common infections. Furthermore, the antibiotic consumption rate was calculated according to the day of treatment rather than the World Health Organization standard.

Conclusion

In our study, although there was no statistically significant difference in the microbiological agents detected in the cultures between both time periods, there was a notable difference in the rates and types of antibiotics administered. This suggests that certain antibiotics were initially overutilized at the onset of the pandemic, which may have been due to their anticipated effectiveness against the virus. We propose that this disparity may be attributed to the rigorous implementation of infection control measures and the enhanced efficacy of the antibiotic

stewardship committee, particularly during and following the period when the epidemic rate declined.

Footnote

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of İstanbul Medeniyet University, Göztepe Prof. Dr. Süleyman Yalçın City Hospital and the study was conducted in accordance with the principles of the Helsinki Declaration (ethics committee no: 2021/0111, date: 10.02.2021).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: H.Ç., F.Y.İ., Concept: H.Ç., Y.Ç., Design: H.Ç., Y.Ç., Data Collection or Processing: H.Ç., B.B., F.Y.İ., R.G., S.G.O., Analysis or Interpretation: H.Ç., A.N.E., Y.Ç., Literature Search: H.Ç., A.N.E., B.B., F.Y.İ., R.G., S.G.O., Writing: H.Ç., A.N.E., B.B., Y.Ç.

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