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Comparison of respiratory tract pathogens and antibiotic susceptibility profiles of patients diagnosed with COVID-19 with pre-COVID-19

Feray Ferda Şenol[1], İlkay Bahçeci[2], Nuray Arslan[2], Özlem Aytaç[1], Pınar Öner[1], Zülal Aşçı Toraman[3]

[1]Elazığ Fethi Sekin State of Hospital, Medical Microbiology, Elazığ, Turkey
[2]Recep Tayyip Erdoğan University, Faculty of Medicine, Medical Microbiology, Rize, Turkey
[3]Fırat University, Faculty of Medicine, Medical Microbiology, Elazığ, Turkey

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ABSTRACT

Objective: It is aimed to compare the respiratory tract agents and antibiotic resistance rates in patients with a diagnosis of COVID-19 with the non-COVID-19 period.

Material and Method: Patients diagnosed with bacterial respiratory tract infection between March 2019 and March 2021 were included in the study. Bacteria identification and antibiotic susceptibility were evaluated according to automated system and EUCAST standards.

Results: Between March 2019-March 2020 (before the pandemic), the most common bacterium was *Pseudomonas aeruginosa* (*P. aeruginosa*) 280 (15.5%) second *Acinetobacter baumannii* (*A. baumannii*) in a total of 1797 patients hospitalized in the service and intensive care units, and the resistance rates were the same. Between March 2020 and 2021, a total of 1357 COVID -19 patients were found in clinical and intensive care units, and the most common reproducing agent was *A. baumannii* 168 (12.3%), the second *P. aeruginosa* 164, and resistance rates were found to invrease.

Conclusion: The increase in the resistance rates of bacteria causing respiratory tract infection was remarkable. It was determined that *P. aeruginosa* and *A. baumannii*, which were the most common isolates before the pandemic and showed high resistance rates against all antibiotic groups, were the most common bacteria during the pandemic period.

Keywords: Antimicrobial susceptibility; COVID-19; respiratory infection

INTRODUCTION

Co-infection and secondary infections due to severe flu infections are common (1). Coronaviruses are single-stranded, enveloped, positive-sense RNA viruses. There are various subtypes (HKU1-CoV, HcoV-NL63, HCoV-OC43 and HCoV-229E) that can be easily transmitted from person to person. It is a large family of viruses that can cause severe acute respiratory syndrome ("severe acute respiratory syndrome" SARS) and Middle East respiratory syndrome ("Middle East respiratory syndrome" MERS) from a self-limiting mild infection picture that is very common in the community, such as the common cold (2). COVID-19 is a contagious disease that can cause death in rapidly progressing elderly and chronically ill people in the world. It can affect many organs such as the liver, brain, kidney, especially the lungs (3). In the pneumonia epidemic in Wuhan, China in December 2019, the name of the disease identified as SARS CoV-2 was accepted as coronavirus disease 2019 (COVID-19). The source of infection of the disease has not yet been clarified. From the available data, they are considered to be wild animals. Lung is the organ that is most affected and has an effect on mortality. The most common complications in patients with COVID-19 admitted to the hospital were pneumonia (79.1%), ARDS (3.37%), and shock (1%). Apart from these, disseminated intravascular coagulation, acute kidney injury, and rhabdomyolysis were observed less frequently (4). The diagnosis of COVID-19 is made by real-time reverse transcriptase polymerase chain reaction (RT-PCR) test, taken from oropharyngeal and nasopharyngeal swabs. False-negative results may be encountered due to the low sensitivity of the test. For this reason, patients should be evaluated together with clinical, thoracic computed

Corresponding Author: İlkay Bahceci, ilkay.bahceci@erdogan.edu.tr
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tomography (CT) and laboratory findings for the diagnosis (4,5). Lower respiratory tract infections are among the most common hospital-acquired infections in patients hospitalized in intensive care units, and the use of broad-spectrum antibiotics in the treatment has led to the emergence of antibiotic resistance in the agents that cause this type of infection (6). In this study, it was aimed to evaluate the infectious agents and antimicrobial resistance profiles of patients with respiratory tract infection in patients with a diagnosis of COVID-19, and to determine and compare the infectious agents and antimicrobial resistance profiles of patients with respiratory tract infections before the pandemic.

MATERIAL AND METHOD

The study was carried out with the permission of the Fırat University Non-Interventional Research Ethics Committee (Decision No: 2021/04-31 Date: 18.03.2021). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Between March 1, 2020 and March 1, 2021, respiratory tract infection agents and antimicrobial resistance profiles of patients diagnosed with COVID-19 were evaluated by retrospectively comparing the infectious agents and antimicrobial resistance profiles of patients with pre-pandemic respiratory tract infections. In more than one respiratory tract sample belonging to the same patient, only one growth of the same bacteria showing the same antimicrobial susceptibility pattern was evaluated. The first samples of the patients were taken into account and studied. Microbiological analyzes of sputum and DTA samples taken from a total of 3154 adult patients with respiratory tract infection and inpatient treatment, 1797 before the pandemic and 1357 with a diagnosis of COVID-19 were performed and the results were evaluated. Appropriately taken sputum and DTA samples were cultivated according to conventional culture methods and culture plates were incubated for 18-24 hours at 35-37°C in an environment with 5-10% CO2 and growth was evaluated at the end of the incubation. Identification of bacterial isolates was carried out according to the manufacturer's instructions using the automated system Vitek 2 (bioMérieux, France). Antimicrobial susceptibility test was evaluated by Vitek 2 (bioMérieux, France) automated system according to EUCAST (The European committee on antimicrobial susceptibility testing) criteria (7). Colistin resistance for *A. baumannii* species was studied by liquid microdilution method. The rates of the first bacteria isolated as causative agents and the antimicrobial resistance rates of these bacteria were analyzed and compared retrospectively as Pre-Pandemic Period (PPP) and Pandemic Period (PP).

Statistical Analysis

In the study, which was planned as a retrospective cross-sectional study, to reveal the difference between the rates of respiratory tract infection agents and antimicrobial resistance in the pandemic and pre-pandemic period, the difference between the rates of the pre- and post-COVID period was investigated using the Z test for dependent and independent rates. In addition, chi-square and/or Fisher's exact test were used for comparisons between gender and other sociodemographic characteristics. Obtained results were expressed with frequency distributions and percentages and $p<0.05$ value was considered statistically significant. IBM SPSS Statistics for Windows, Version 23.0 Armonk, NY: IBM Corp. (IBM Corp. Released 2015) was used for statistical analyzes used in the research.

RESULT

Yeast pathogen was isolated in 61 patients and bacterial pathogen in 818 patients from 626 sputum (34.8%) and 1171 DTA (65.1%) cultures of 1797 patients (1041 males, 756 females) before the pandemic. Of the isolated pathogens, 740 (90.4%) were Gram-negative and 78 (9.5%) were Gram-positive bacteria. *P. aeruginosa* (34.2%), *A. baumannii* (22.2%), *K. pneumoniae* (10.7%), (4.2%) and *E. coli* (3.5%) were most commonly isolated. 15.4% of the detected bacteria are other Gram-negative bacteria (*Stenotrophomonas maltophilia*, *Enterobacter cloacae*, *Enterobacter aerogenes*, *Proteus mirabilis*, *Serratia marcescens*, *Providencia rettgeri*, *Citrobacter freundii*). The distribution of bacterial agents detected before the pandemic is given in **Table 1**. During the pandemic period, yeast in 101 patients and bacterial pathogen in 608 patients were isolated from 245 sputum (18%) and 1112 DTA (82%) cultures of 1357 patients (752 men, 605 women). Of the isolated pathogens, 554 (91.1%) were Gram-negative and 54 (8.8%) were Gram-positive bacteria. *A. baumannii* (27.6%), *P. aeruginosa* (27%), *K. pneumoniae* (15%), *E. coli* (4.2%) and *P. putida* (4.1%) were most commonly isolated. 13.15% of the detected bacteria are other Gram-negative bacteria. (*Stenotrophomonas maltophilia*, *Enterobacter cloacae*, *Enterobacter aerogenes*, *Proteus mirabilis*, *Serratia marcescens*, *Providencia rettger*, *Citrobacter freundii*) The distribution of bacterial agents detected during the pandemic period is given in **Table 2**.

Microorganisms and antibiotic resistance rates isolated during the Pre-Pandemic Period (PPP) and Pandemic Period (PP) in sputum samples are given in **Table 3**, and the rates of microorganisms and antibiotic resistance isolated during PPP and PP in Aspirate samples are given in **Table 4**. *P. aeruginosa* strains isolated from sputum samples were most sensitive to the antibiotic colistin (COL) (71.2%) during the PPP period, while the antibiotic to which it was most resistant was Amikacin (AK) (69.2%); It

was determined that COL (92.4%) was the most sensitive antibiotic in the PP period and Piperacillin/Tazobactam (PRP) (69.2%) was the most resistant antibiotic. The PPP period of *A. baumannii* strains was the most sensitive antibiotic for COL (100%), the most resistant antibiotic for Meropenem (MEM) (97.5%); It was determined that COL (100%) was the most sensitive antibiotic in the PP period, and Gentamicin (G), AK, CIP (Ciprofloxacin), CAZ (Ceftazidime), IPM (Imipenem), MEM (83.3%) were the most resistant antibiotics. The antibiotic COL, IMP (92.9%) to which *K. pneumoniae* strains are most sensitive during PPP period, while the antibiotic to which they are most resistant is Ampicillin/sulbactam (SAM) (100%); It was determined that the most sensitive antibiotic in the PP period was IMP (71.5%), and the most resistant antibiotic was SAM (100%). The antibiotic to which *E. coli* strains are most sensitive during PPP period is COL, IMP (100%), and the antibiotic to which they are most resistant is SAM (100%); It was determined that COL, IMP, MEM (100%) was the most sensitive antibiotic in the PP period, and SAM (100%) was the most resistant antibiotic. It was determined that the antibiotic COL (63.7%) was the most sensitive of *P. putida* strains during the PPP period, and the antibiotic to which it was most resistant was MEM (90.9%). The most sensitive and most resistant antibiotic distribution of sputum samples according to bacteria is given in **Table 5**. *P. aeruginosa* strains isolated from DTA samples were most sensitive to COL (81.6%) during PPP period, and to PRP (96%); It was determined that COL (93.3%) was the most sensitive antibiotic in the PP period, and PRP (84%) was the most resistant antibiotic. *A. baumannii* strains are most sensitive to COL (89.5%) during PPP, most resistant to antibiotics IMP, MEM, SAM, CAZ, CIP (100%); It was determined that COL (89.5%) was the most sensitive antibiotic in the PP period, and IMP, MEM, SAM, CAZ, CIP (100%) were the most resistant antibiotics. *K. pneumoniae* strains are most sensitive to COL(54%) during PPP, and SAM,CAZ(100%); It was determined that the most sensitive antibiotic in the PP period was IMP (44.1%), and the most resistant antibiotic was SAM (100%). The most sensitive antibiotics of *E. coli* strains during PPP period are MEM and IMP (100%), while the most resistant antibiotics are SAM, CAZ, FEP (100%); It was determined that COL, IMP, MEM (100%) were the most sensitive antibiotics in the PP period, and SAM (100%) was the most resistant antibiotic. The antibiotic COL (70.9%) to which *P. putida* strains are most sensitive during the PPP period, and the antibiotics to which they are most resistant are AK, CAZ, FEP (100%); It was determined that COL (84%) was the most sensitive antibiotic in the PP period, and CAZ, FEP, PTZ (84%) were the most resistant antibiotics. The most sensitive and most resistant antibiotic distribution of DTA samples according to bacteria is given in **Table 6**.

The comparison of bacteria growing in sputum and DTA is given in **Table 7**, and no significant difference was observed between the batteries.

Table 1. Distribution of Commonly Isolated Pathogenic bacteria in Sputum and DTA cultures before the pandemic

Common isolates	Sputum		Deep tracheal Aspirate		Total	
	n	%	n	%	n	%
Pseudomonas aeruginosa	52	18.5	228	81.4	280	45.6
Acinetobacter baumannii	40	22	142	78	182	29.6
Klebsiella pneumoniae	14	16	74	84	88	14.3
Pseudomonas putida	11	31.4	24	68.5	35	5.7
Escherichia coli	18	62	11	38	29	4.7

Table 2. Distribution of Commonly Isolated Pathogenic bacteria in Sputum and DTA cultures during the pandemic period

Common isolates	Sputum		Deep tracheal Aspirate		Total	
	n	%	n	%	n	%
Acinetobacter baumannii	6	3.57	162	96.42	168	35.4
Pseudomonas aeruginosa	13	8	151	92	164	34.5
Klebsiella pneumoniae	7	7.7	84	92.3	91	19.19
Escherichia coli	4	15.38	22	84.61	26	5.48
Pseudomonas putida	-	-	25	100	25	5.27

Table 3. Microorganisms and antibiotic resistance rates isolated in sputum samples during the Pre-pandemic period and the Pandemic period

SPUTUM													
Microorganism	**Period**	**n**	**AMC**	**SAM**	**G**	**AK**	**SXT**	**CİP**	**CAZ**	**FEP**	**PTZ**	**IMP**	**MEM**	**COL**
A. baumannii	PPP	40	-	87.5	87.5	87.5	90	95	95	-	-	85	97.5	0
A. baumannii	PP	6	-	66.6	83.3	83.3	50	83.3	83.3	-	-	83.3	83.3	0
p			NA	0.4718	0.7151	0.7151	0.0531	0.8448	0.8448	NA	NA	0.6162	0.6053	NA
P. aeruginosa	PPP	52	-	-	61.5	69.2	-	61.5	61.5	50	63.4	48	50	28.8
P. aeruginosa	PP	13	-	-	15.3	30.7	-	61.5	53.8	30.7	53.8	61.5	53.8	7.6
p			NA	NA	0.0075	0.0256	NA	0.7500	0.8490	0.3485	0.7508	0.5750	0.9482	0.2194
K. pneumoniae	PPP	14	78.5	100	35.7	35.7	78.5	57.1	85.7	85.7	71.4	7.1	50	7.1
K. pneumoniae	PP	7	71.4	100	28.5	28.5	71.4	85.7	85.7	57.1	71.4	28.5	71.4	28.5
p			0.8425	NA	0.8720	0.8720	0.8547	0.4125	0.5085	0.3645	0.6085	0.5088	0.6409	0.5088
E. coli	PPP	18	66.6	100	44.4	27.7	44.4	77.7	83.3	72.2	33.3	0	5.5	0
E. coli	PP	4	75	100	25	25	25	75	75	50	25	0	0	0
p			0.7895	NA	0.8794	0.6092	8794	0.5875	0.7436	0.7881	0.7863	NA	0.3935	NA
P. putida	PPP	11	-	-	63.6	72.7	-	81.8	81.8	81.8	81.8	72.7	90.9	36.3
P. putida	PP	-	-	-	-	-	-	-	-	-	-	-	-	-
p														

AMC: Amoxicillin/clavulanic acid, SAM: Ampicillin sulbactam, CN: Gentamycin, AK: Amikasin, SXT: Sulfamethoxazole/Trimethoprim, CIP:Ciprofloxacin, CAZ: Ceftazidime, FEP: Cepepim, TPZ: Piperacillin/Tazobactam, IPM: imipenem, MEM: Meropenem COL: Colistin

Table 4. Microorganisms and antibiotic resistance rates isolated in DTA samples during the Pre-pandemic period and the Pandemic period

Microorganism	Period	n	AMC	SAM	G	AK	SXT	CİP	CAZ	FEP	PTZ	IMP	MEM	COL
A. baumannii	PPP	142		100	82.3	98.5	83.8	100	100	-	-	100	100	10.5
A. baumannii	PP	162		100	90.7	95	93.8	100	100	-	-	100	100	9.2
P			NA	NA	0.0469	0.1708	0.0091	NA	NA	NA	NA	NA	NA	0.8517
P. aeruginosa	PPP	228	-	-	75	67.5	-	63.1	60	73.6	96	80.7	85	18.4
P. aeruginosa	PP	151	-	-	51.6	51	-	61	49.6	58.2	84	74.8	66.8	6.62
P			NA	NA	<0.001	0.0018	NA	0.7606	0.0587	0.0025	0.001	0.2157	0.001	0.0019
K. pneumoniae	PPP	74	85.1	100	78.3	71.6	94	90.5	100	94.5	81.08	68.9	93.3	46
K. pneumoniae	PP	84	85.7	100	63.1	57.1	83.3	90.4	89.2	94	79.4	55.9	61.9	79.7
P			0.9051	NA	0.0561	0.0841	0.0657	0.8027	0.0102	0.8357	0.9487	0.1296	<0.001	<0.001
E. coli	PPP	11	36.3	100	81.8	-	72.7	72.7	100	100	36.3	0	0	18.8
E. coli	PP	22	50	100	50	-	63.6	77.2	77.2	77.2	40.9	0	0	0
P			0.7082	NA	0.1662	NA	0.8957	0.8836	0.2280	0.2280	0.9021	NA	NA	0.1806
P. putida	PPP	24	-	-	80	100	-	95.8	100	100	95.8	95.8	95.8	29.1
P. putida	PP	25	-	-	79.1	80	-	80	84	84	84	80	80	16
P			NA	NA	0.7824	0.0658	NA	0.2113	0.1278	0.1278	0.3727	0.2113	0.2113	0.4493

AMC: Amoxicillin/clavulanic acid, SAM: Ampicillin sulbactam, CN: Gentamycin, AK: Amikasin, SXT: Sulfamethoxazole/Trimethoprim, CIP:Ciprofloxacin, CAZ: Ceftazidime, FEP: Cepepim, TPZ: Piperacillin/Tazobactam, IPM: imipenem, MEM: Meropenem COL: Colistin

Table 5. Distribution of sputum samples to which they are most susceptible and most resistant to bacteria

Microorganism	Period	Most Sensitive	%	Most Resistant	%
A. baumannii	ppp	COL	100	MEM	97.5
A. baumannii	pp	COL	100	G/AK/CİP/CAZ/IPM/MEM	83.3
P. aeruginosa	ppp	COL	71.2	AK	69.2
P. aeruginosa	pp	COL	92.4	CİP,IMP	61.5
K. pneumoniae	ppp	COL/IMP	92.9	SAM	100
K. pneumoniae	PP	IMP	71.5	SAM	100
E. coli	ppp	COL/IMP	100	SAM	100
E. coli	pp	COL/IMP/MEM	100	SAM	100
P. putida	ppp	COL	63.7	MEM	90.9
P. putida	pp	-		-	-

Table 6. Distribution of DTA samples to which they are most sensitive and resistant to bacteria

Microorganism	Period	Most Sensitive	%	Most Resistant	%
A. baumannii	ppp	COL	89.5	SAM/CİP/CAZ/IPM/MEM	100
A. baumannii	pp	COL	90.8	SAM/CİP/CAZ/IPM/MEM	100
P. aeruginosa	ppp	COL	81.6	PTZ	96
P. aeruginosa	pp	COL	93.3	PTZ	84
K. pneumoniae	ppp	COL	54	SAM/CAZ	100
K. pneumoniae	pp	IMP	44.1	SAM	100
E. coli	ppp	IMP/MEM	100	SAM/CAZ/FEP	100
E. coli	pp	IMP/MEM/COL	100	SAM	100
P. putida	ppp	COL	70.9	AK/CAZ/FEP	100
P. putida	pp	COL	84	CAZ/FEP/PTZ	84

Table 7. Comparison of bacteria growing in sputum and DTA

Bacterium	Sputum [Pre-Post] p value	DTA [Pre-Post] p value
Pseudomonas aeruginosa	0.0039	0.0037
Acinetobacter baumannii	<0.0001	<0.0001
Klebsiella pneumoniae	0.1362	0.1370
Escherichia coli	0.0012	0.0012
Pseudomonas putida	0.0058	0.0056

DISCUSSION

The COVID-19 pandemic is a viral pneumonia pandemic. Interpersonal transmission occurs through direct contact or through droplets spread by sneezing or coughing from an infected person. The most common initial symptoms in patients found to be infected with COVID-19 are cough, fever, and fatigue. Other symptoms and signs are headache, hemoptysis,

diarrhea, sputum, dyspnea and lymphopenia (8). Although the clinical course of people infected with COVID-19 is mild at a rate of 81%, 14% require severe care and 5% require intensive care (9). In the elderly, the mortality rate between the ages of 70 and 79 is 8 percent, and the mortality rate at the age of 80 and above is 14.8% (10). Zhou et al. reported that in the current coronavirus disease 2019 (COVID-19) pandemic, 50% of COVID-19 patients who died had secondary bacterial infections (11). In a systematic review of eleven case series, including 2002 patients, it was found that the risk of severe disease is quadrupled in patients with COVID-19 accompanied by COPD, and this risk is approximately doubled in active smokers; In addition, it was found that the need for intensive care, mechanical ventilation and mortality were statistically significantly higher in patients with COPD (12).

Opportunistic pathogens reproduce especially in respiratory tract samples and have intense antibiotic resistance (13). Although the distribution of ventilator-associated pneumonia (VAP) factors varies according to regions, as in other nosocomial infections, Gram-negative bacteria such as *K. pneumoniae*, *P. aeruginosa*, *A. baumannii* are mostly isolated. However, in recent years, it has been observed that Gram-positive agents, especially *S. aureus*, have increased gradually (14). Clark D Russell et al found *S. aureus* and *Haemophilus influenzae* as the most common secondary respiratory tract infections in patients diagnosed with COVID-19, and Enterobacter spp. and *S. aureus* as coinfection agents (15). In the study of Koçak et al. 641 bacteria considered pathogenic were isolated from 245 sputum and 396 DTA cultures taken from 442 patients in total. The most commonly isolated agents are *A. baumannii* (25%), *P. aeruginosa* (12.6%), Klebsiella spp (14.7%), *E. coli* (10%), *H. influenzae* (6.9%), *S. aureus* (5.5%)) and *Streptococcus pneumoniae* (5.1%) (16). From the Bronchoalveolar lavage (BAL) cultures of 13 COVID-19 patients who were followed up intubated in the study of Araç E. et al.; They detected *K. pneumoniae* in five (55.5%), *A. baumannii* in one (11.1%), *E. coli* in one (11.1%), *P. aeruginosa* in one (11.1%) and *Burkholderia cepacia* in one (11.1%)(17). In our study, the most common bacterial agents before the pandemic; *P. aeruginosa* 280(15.5%), *A. baumannii* 182(10.1%), *K. pneumoniae* 88(4.89%), *P. putida* 35(1.9%), *E. coli* 29(%) 1.6). During the pandemic period, the most common *A. baumannii* 168 (12.3%), *P. aeruginosa* 164 (12%), *K. pneumoniae* 91 (6.7%), *E. coli* 26 (1.9%), *P. putida* 25 (1.8%). Gazi et al. examined the lower respiratory tract samples of 835 intensive care patients and reported that antibiotic resistance rates in Pseudomonas and A. baumanni species were higher than isolates isolated from other services (18). In our study, aspirate samples before and during the Pandemic period increase the resistance rate in all isolated bacteria compared to sputum samples. In the aspirate samples, the resistance rates of *A. baumannii* to G, SXT increased during the PP. The resistance rate of *P. aeruginosa* to G, AK, FEP, PTZ, MEM, COL decreased during the pandemic period, and the resistance rate to CAZ, MEM, COL during the pandemic period of *K. pneumoniae* decreased. In sputum samples, the resistance rate of *P. aeruginosa* decreased in G and AK during the pandemic period.

Carbapenems are known as the most effective beta-lactam antibiotics against bacterial resistance (19). Carbapenems are mostly used in the empirical treatment of serious bacterial infections (20). According to the research in Europe in the 2007 MYSTIC program; It has been reported that the most effective antibacterial group against nonfermentative gram-negative bacteria is carbapenems, but there is an increase in Acinetobacter strains which showing multi-antibiotic resistance and Pseudomonas strains which showing imipenem-resistance (21). Baumgart et al., in their study, found carbapenem resistance in Acinetobacter species to be 80% (22).In our study, carbapenem resistance in sputum samples was 83.3%-97.5% for *A. baumannii*, 48-61.5% for *P. aeruginosa*, 7.1-71.4% for *K. pneumoniae*, 0-5.5% for *E. coli*, and 72.7-90.9% for *P. putida*. Carbapenem resistance in our aspirate samples was 100% for *A. baumannii*, 66.8-85% for *P. aeruginosa*, 55.9-93.3% for *K. pneumoniae*, 0% for *E. coli* and 80% for *P. putida*.

Colistin resistance occurs especially in people who take colistin therapy for a long time. Its combination with other antimicrobials is the most commonly used option in empirical treatment (23). In a multicenter study conducted in Southern Europe (Italy, Greece and Spain), the colistin resistance of *A. baumannii* strains obtained from respiratory samples of patients with VAP was reported to be 47.7% (24). In our study, colistin resistance for *A. baumannii* was 0% in PPP and PP period in sputum samples and 10.5% in PPP period in Aspirate samples. 9.2% in the PP period. The emergence of multidrug-resistant and carbapenem-resistant *P. putida* has become a cause for concern. Carbapenem-resistant *P. putida* and *P. aeruginosa* isolates are increasingly reported in areas other than tracheal aspiration, urinary system and blood (25,26). The fact that it was seen among the most frequently isolated bacteria in our study and that it showed serious antimicrobial resistance signals that it will cause important problems in the future. In addition, increased yeast growth due to intensive antibiotic use and duration of hospitalization (27), which has been shown in various studies, also increased in our study.

CONCLUSION

Respiratory tract infections are the second most common cause of death worldwide. The use of broad-spectrum antibiotics causes the development of much more resistant strains in the respiratory tract. We think that if each hospital determines the microorganisms isolated in their own laboratory and their antimicrobial resistance patterns at regular intervals, shares these data with the relevant clinics and determines the appropriate empirical treatment choices, it can be effective in the control of nosocomial infections.

In addition, off-label use of antibiotics in COVID-19 infections has increased antibiotic resistance and accelerated the development of fungal infections.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the Fırat University Non-Interventional Research Ethics Committee (Decision No: 2021/04-31 Date: 18.03.2021).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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