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The Antibiotic Resistance Patterns of *Pseudomonas Aeruginosa* Strains Isolated from Microbiological Specimens

Mikrobiyolojik Örneklerden İzole Edilen Pseudomonas Aeruginosa Suşlarının Antibiyotik Direnç Modelleri

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ABSTRACT

Objective: In this single-center retrospective study, which included samples isolated from humans, it was aimed to determine the antibiotic resistance rates of *Pseudomonas aeruginosa* strains isolated from samples sent to the microbiology laboratory for four years.

Material and Method: These were evaluated retrospectively in terms of *Pseudomonas* species that wound, blood, tracheal aspirate, abscess, vagina, serebrospinal fluid, sputum and urine culture samples of 789 patients from the service, intensive care and outpatient clinics between 2017 and 2021.

Results: Isolated Pseudomonas strains of the hospitalized patients were most commonly found in the chest diseases service (38.6%), urology department (14.3%) and palliative care unit (12.5%). The distribution of samples was followed by sputum (20.4%) cultures, most commonly urine (42.7%). In our study, according to antibiotic resistance rates, the highest drug resistance was observed against cefuroxime, levofloxacin and netilmicin and the lowest resistance was against amikacin. Gentamicin, cefepime, and aztreonam resistance levels significantly decreased with time (P=0.0004, 0.0038, and 0.0321, respectively), but levofloxacin and colistin resistance levels significantly rose (P=0.0407 and, P<0.0001 respectively). Over time, there have been appreciable reductions in resistance to ciprofloxacin, ceftazidime, and cefepime (P=0.0004, 0.0038, and 0.0321, respectively). Only cefepime showed a significant decline in resistance of bacteria isolated from urine culture over time (P=0.0003). Resistance to levofloxacin substantially increased in 2019 for bacteria isolated from cultures of respiratory secretions, urine, and, sputum whereas it increased in 2020 for strains isolated from wound cultures (P=0.0145).

Conclusion: Due to the regularly diverse usage of antimicrobials, changes in the antibiotic resistance pattern were found in patients over a period of years. The highest drug resistance was observed against ceforoxime, levofloxacin and netilmicin, and the lowest resistance was against amikacin. By choosing effective treatment protocols with the rational use of antibiotics; it was concluded that it is necessary to regularly determine the microorganisms and antibiotic resistances for each hospital.

Keywords: *Antibiotic Resistance, Culture, Pseudomonas aeruginosa , Strain*

ÖZET

Giriş: İnsanlardan izole edilen örnekleri içeren bu tek merkezli retrospektif çalışmada, dört yıl boyunca mikrobiyoloji laboratuvarına gönderilen örneklerden izole edilen *Pseudomonas aeruginosa* suşlarının antibiyotik direnç oranlarının belirlemesi amaçlanmıştır.

Materyal ve Metot: Servis, yoğun bakım ve polikliniklerden 2017-2021 yılları arasında gelen 789 hastaya ait yara, kan, trakeal aspirat, apse, vajina, beyin omurilik sıvısı, balgam ve idrar kültürü örnekleri *Pseudomonas* türleri açısından retrospektif olarak değerlendirilmiştir.

Bulgular: Yatan hastalardan izole edilen Pseudomonas suşların en sık göğüs Hastalıkları servisi (%38,6) olmak üzere üroloji bölümü (%14,3) ve palyatif bakım ünitesinden (%12,5) gelmiştir. Örneklerin dağılımı en sık idrar olmak üzere (%42.7) ikinci sıklıkla balgam(%20.4) kültürleriydi. Çalışmamızda antibiyotik direnç oranlarına gore en Yüksek direnç sefuroksim, levofloksasin ve netilmisine karşı; en düşük direnç amikasine karşı olduğu belirlendi. Aztreonam, sefepim ve gentamisine karşı dirençler yıllar içinde önemli ölçüde azalırken (sırasıyla P=0.0321, 0.0038 ve 0.0004), kolistin ve levofloksasine karşı dirençler önemli ölçüde arttı (P<0.0001 ve P=0.0407 sırası dahilinde). Yıllar içinde sefepim, seftazidim ve siprofloksasine karşı dirençlerde önemli düşüşler gözlendi (sırasıyla P=0.0321, 0.0038 ve 0.0004). Yıllar içinde sadece sefepim için idrar kültüründen izole edilen suşların direncinde önemli bir azalma gözlendi (P=0.0003). Balgam, idrar ve solunum sekresyonu kültürlerinden izole edilen suşların levofloksasine karşı direnci 2019 yılında önemli ölçüde artarken, 2020 yılında yara kültürünün direnci artmıştır (P=0.0145).

Sonuç: Antimikrobiyallerin irrasyonel kullanımına bağlı olarak hastalarda antibiyotik direnç profilinde yıllar içinde değişiklikler olduğu tespit edildi. En Yüksek ilaç direnci sefuroksim, levofloksasin ve netilmisine, en düşük direnç amikasine karşı olduğu gözlemlendi. Antibiyotiklerin akılcı kullanımı ile etkili tedavi protokollerini seçerek; her hastane için mikroorganizmaları ve antibiyotik dirençlerini düzenli olarak belirlemek gerektiği kanaatine varıldı.

Anahtar kelimeler: *Antibiyotik direnç, Kültür, Pseudomonas aeruginosa , Suş*

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INTRODUCTION

In hospitalized patients, one of the most prevalent Gram-negative bacteria responsible for hospital and other healthcare-associated illnesses is *Pseudomonas aeruginosa* (Raman et al., 2018).

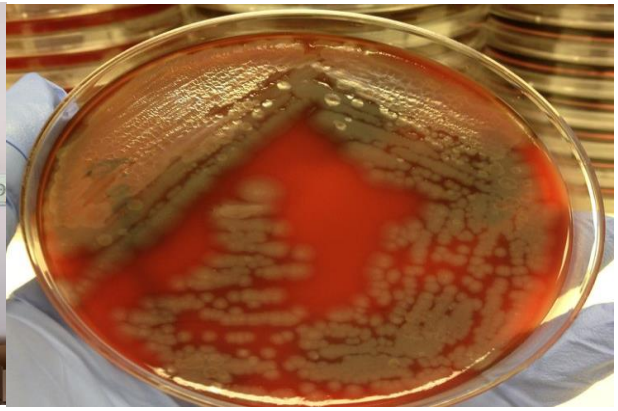
P. aeruginosa is of particular importance as it is one of the most common nosocomial infections in hospitalized patients and has multi-drug resistance due to its nature, leading to death and morbidity in immunocompromised individuals. (Stoveruet al., 2000; Matheeuet al., 2008; Frimmersdorfuet al., 2010).

In last decade, the antibiotic resistance rates have increased due to the unconscious use of inappropriate and broad-spectrum antibiotics and the lack of appropriate disinfection methods (Frimmersdorf et al., 2010). Each year, more than 2.8Million antibiotic-resistant illnesses occur in the United States, and these infections cause more than 35,000 fatalities (Nelson et al., 2021). According to a recent study conducted in Turkey, the total fatality rates due to *P. aeruginosa* infections in a clinic was found as 46% and as 68% due to carbapenem-resistant colistin susceptible *P.aeruginosa* infections among patients hospitalized in the intensive care unit (Vatansever et al., 2020). Although common prevention and infection control efforts reduced deaths from antibiotic-resistant infections in hospitals (Nelson et al., 2021), there is limited amount of data on this issue for Turkish population (Adejobi et al., 2021).

Therefore, in this study, it was aimed to determine the frequency of antibiotic resistance among *P. aeruginosa* strains isolated from samples collected over a period of four years in the microbiology laboratory of a single center in order to generate scientific data.

MATERIAL AND METHOD

This single-center retrospective study involved the data of human participants and its protocol was in compliance with the 1964 Helsinki Declaration and its later revisions or equivalent ethical standards, as well as the ethical requirements of the institutional and national research committee. Ethical permission was provided by Non-Interventional Research Ethics Committee of Bandırma Onyedi Eylül University Health Sciences (Project no: 2020-51, Date: 28th Jan 2021).



Retrospective testing for *Pseudomonas* species was done on samples of wound, sputum, cerebrospinal fluid (CSF), vagina, abscess, tracheal aspirate, blood, and urine culture isolated from 789 individuals who were hospitalized in the service, ICU, and outpatient services of our hospital between 2017 and 2021. Patients' urine samples were obtained and inoculated on 5% sheep blood agar (RTA Laboratories, Gebze, Turkey) and eosin-methyleneblue (EMB) agar media (RTA Laboratories, Gebze, Turkey). Other clinical samples were plated and maintained at 37°C for one day with 5% EMB agar, sheep blood agar, and chocolate (CHOC) agar (RTA Laboratories, Gebze, Turkey) inocula. At the end of incubation, the bacterial growths were evaluated by the presence and type of colony and the culture samples considered appropriate to be included in the antibiogram were selected for the study for the bacterial identification. Samples taken from the patients which were contaminated, the patients whose culture findings could not be reached, and who were younger than 18 years of age were not included in this research (Since it is predicted that antibiotic resistance rates in pediatric patients may vary widely according to the frequency of drug use.)

Blood samples were inoculated into the blood culture bottles (Render C/Horacio Lengo N 18, Malaga, Spain) and incubated in an automated system (RENDER BC128, Automated Blood Culture Systems, Jinan, Shandong, China). Samples that produced a growth signal within five days were pre-identified by a gram staining. After pre-identification, the samples were inoculated on 5% sheep blood agar, chocolate agar and EMB agar media and incubated between 35.5°C - 37°C for 18-24 hours.

At the end of 24 hours of incubation of all specimens belong to 801 patients, the conventional methods (gram staining, oxidase test, fermentation feature)

were used to identify the *Pseudomonas* isolates at species-level in the growths detected, and the antibiotic susceptibility tests were evaluated using the Phoenix 100 automatic system. (Becton Dickinson, Sparks, Md, BD). Drug susceptibilities were categorized by the automated device after 24 hours. The outcomes were assessed in accordance with the "European Committee on Antimicrobial Susceptibility Testing (EUCAST)" guidelines.

Statistical Method

For the statistical analysis, NCSS (Number Cruncher Statistical System) 2007 program (USA, Utah, Kaysville) was employed. The variables were analyzed by using the descriptive statistical methods (Maximum, Minimum, Ratio, Frequency) and to examine the qualitative data, the Pearson ChiSquare test was utilized.

RESULTS

P. aeruginosa strains isolated from 789 participants who applied to our hospital between 2017-2021 were included in the research. 63.5% of the participants were male (n=501) and 36.5% were female (n=288). The participants' ages was recorded between 18 and 103 years, with an average of 68.90 ± 15.12 years. The distribution of units sending the culture samples showed that 35.5% of patients were hospitalized in the service (n=280), 22.7% applied to the polyclinic units (n=179), and 41.8% were hospitalized in the ICUs (n=330).

According to the distribution of microbiological culture types, urine (42.7%) and sputum (20.4%)samples were obtained most frequently. The least frequent types of cultures were the catheter tip culture (0.4%), peritoneal fluid culture (0.4%) and CSF culture (0.3%). Only one vaginal secretion and only one pleura fluid were cultured for the microbiological examination (Table 1).

Table 1. The distribution of types of microbiological cultures

Type of culture	N	%
Abscess culture	10	1.3
Sputum culture	161	20.4
Urine culture	337	42.7
Blood culture	35	4.4
Catheter tip culture	3	0.4
Ear culture	15	1.9
Peritoneal fluid culture	3	0.4
Pleural fluid culture	1	0.1
CSF culture	2	0.3
Quantitative cultures of respiratory secretions	121	15.3
Vaginal secretion culture	1	0.1
Wound culture	100	12.7
TOTAL	789	100.0

CSF: Cerebrospinal fluid

Table 2 represents the units where the microbiological samples were collected in detail. The majority of the participants applied to the service were transferred mainly from three departments: 38.6% from the chest diseases department, 14.3% from the urology department and 12.5% from the unit of palliative care. The majority of patients who applied to the polyclinics were sent from the department of urology (42.5%), or the department of chest diseases (14%) or the home care unit (11.7%). The percentage of ICU patients whose microbiological samples were collected was 41.8% of all patients.

Table 2. The detailed distribution of units according to the medical departments

Department	Service (n=280)		Polyclinic (n=179)		Intensive Care Unit (n=330)	
	n	%	N	%	N	%
General surgery	18	6.4	15	8.4	0	0
Urology	40	14.3	76	42.5	0	0
Chest diseases	108	38.6	25	14.0	0	0
Intensive care unit	0	0	0	0	330	100
Home health care	0	0	21	11.7	0	0
Internal diseases	25	8.9	4	2.2	0	0
Orthopedics	11	3.9	13	7.2	0	0
Palliative care	35	12.5	0	0	0	0
Otorhinolaryngology	1	0.4	12	6.7	0	0
Infectious diseases	5	1.8	7	3.9	0	0
Neurology	11	3.9	0	0	0	0
Cardiology	5	1.8	1	0.6	0	0
Emergency	5	1.8	0	0	0	0
Gynecological diseases	0	0	4	2.2	0	0
Cardiovascular surgery	5	1.8	0	0	0	0
Neurosurgery	5	1.8	1	0.6	0	0
Hemodialysis	3	1.1	0	0	0	0
Physiotherapy	2	0.7	0	0	0	0
Psychiatry	1	0.4	0	0	0	0

The distribution of findings of antibiotics resistance tests performed for the *P. aeruginosa* compared by years is shown in Table 3. Totally, the highest resistance rates of the organisms to the antibiotics evaluated were against the netilmicin, levofloxacin and cefuroxime. The lowest rate of resistance was against the amikacin. The resistance of the organism against amikacin was highest in 2019 and lowest in 2020 (P=0.0107). The resistance rates of the organisms against aztreonam, cefepime and gentamicin drastically dropped over time (P=.0321, .0038 and .0004, respectively) and on the other hand, the resistance rate against colistin and levofloxacin considerably increased (P<.0001 and P=.0407, respectively). The resistance rate against piperacillin/ tazobactam was highest in 2018 and lowest in 2020 (P=0.0148). The resistances to the other antibiotics, namely ciprofloxacin, imipenem, meropenem and netilmicin did not change significantly over years (Table 3).

Table 3. The distribution of antibiotics resistance findings of the *Pseudomonas aeruginosa* organism presented by years

Antibiotic type	2017		2018		2019		2020		*P value*	TOTAL	
	n/Total	%	n/Total	%	n/Total	%	n/Total	%		n/Total	%
Amikacin	9/177	5.1	13/215	6.0	29/242	12.0	8/169	4.7	*0.0107*	59	7.3
Aztreonam	63/145	43.4	83/183	45.4	6/30	20.0	0/0	0.0	*0.0321*	152	42.5
Cefepime	69/174	39.7	85/212	40.1	35/136	25.7	24/96	25.0	*0.0038*	213	34.5
Cefuroxime	89/89	100.0	98/98	100.0	101/101	100.0	81/81	100.0	-	369	100.0
Ciprofloxacin	75/175	42.9	107/214	50.0	108/243	44.4	75/169	44.4	*0.5819*	365	45.6
Colistin	10/150	6.7	24/71	33.8	11/11	100.0	3/3	100.0	*<0.0001*	48	20.4
Gentamicin	57/181	31.5	62/214	29.0	57/242	23.6	23/170	13.5	*0.0004*	199	24.7
Imipenem	44/171	25.7	48/209	23.0	47/241	19.5	42/166	25.3	*0.4102*	181	23.0
Levofloxacin	2/12	16.7	0/0	0.0	106/205	51.7	92/168	54.8	*0.0407*	200	51.9
Meropenem	40/170	23.5	45/210	21.4	48/240	20.0	30/167	18.0	*0.6304*	163	20.7
Netilmicin	51/97	52.6	44/101	43.6	7/20	35.0	0/0	0.0	*0.2413*	102	46.8
Piperacillin/ Tazobactam	43/180	23.9	58/215	27.0	45/245	18.4	28/168	16.7	*0.0148*	174	21.5

Chi-squared Test for Independence

The antibiotic resistance distribution of *P. aeruginosa* organism in different culture types by years is presented in Table 4. Significant declines in the resistance profile against cefepime, ceftazidime, and ciprofloxacin over time were seen (P=0.0003, 0.0422 and 0.0335, respectively) when *P. aeruginosa* strains isolated from cultures of sputum, wound, and respiratory secretions were taken into account. Only the resistance profile against cefepime over time (P=.0003) did strains isolated from urine cultures show a significant decline in antimicrobial resistance. Resistance to levofloxacin in bacteria separated from cultures of respiratory secretions, sputum, and urine substantially increased in 2019, whereas resistance in strains isolated from cultures of wounds significantly increased in 2020 (P=.0145). The distribution of antibiotic resistance of organisms against the amikacin, aztreonam, colistin, gentamicin, imipenem and piperacillin/tazobactam did not alter according to the different culture types by years.

Table 4. The distribution of antibiotic resistance of *Pseudomonas Aeruginosa* organism in different culture types presented by years

		Sputum culture		*Urine culture*		*Quantitative culture of respiratory secretions*		*Wound culture*		*P.value*
Antibiotics	***Years***	n	%	n	%	n	%	n	%	
Amikacin	***2017***	4	22.2	2	9.5	2	20.0	1	20.0	*0.8406*
	2018	5	27.8	4	19.0	1	10.0	2	40.0	
	2019	7	38.9	11	52.4	6	60.0	2	40.0	
	2020	2	11.1	4	19.0	1	10.0	0	0.0	
Aztreonam	***2017***	18	46.2	18	33.3	11	40.7	7	41.2	*0.7177*
	2018	19	48.7	35	64.8	14	51.9	9	52.9	
	2019	2	5.1	1	1.9	2	7.4	1	5.9	
Cefepime	***2017***	18	35.3	20	32.8	15	34.9	8	25.0	*0.0003*
	2018	15	29.4	39	63.9	12	27.9	12	37.5	
	2019	12	23.5	1	1.6	11	25.6	6	18.8	
	2020	6	11.8	1	1.6	5	11.6	6	18.8	
Ceftazidime	***2017***	21	38.2	15	15.0	15	31.3	9	33.3	*0.0422*
	2018	17	30.9	29	29.0	15	31.3	8	29.6	
	2019	13	23.6	34	34.0	13	27.1	5	18.5	
	2020	4	7.3	22	22.0	5	10.4	5	18.5	
Ciprofloxacin	***2017***	23	34.8	18	12.9	15	22.7	8	17.0	*0.0335*
	2018	19	28.8	47	33.6	16	24.2	13	27.7	
	2019	18	27.3	42	30.0	20	30.3	15	31.9	
	2020	6	9.1	33	23.6	15	22.7	11	23.4	
Colistin	***2017***	2	14.3	4	36.4	2	18.2	2	20.0	*0.3074*
	2018	7	50.0	7	63.6	7	63.6	3	30.0	
	2019	4	28.6	0	0.0	2	18.2	3	30.0	
	2020	1	7.1	0	0.0	0	0.0	2	20.0	
Gentamicin	***2017***	18	36.0	12	17.4	13	37.1	6	27.3	*0.3649*
	2018	15	30.0	27	39.1	7	20.0	8	36.4	
	2019	12	24.0	24	34.8	11	31.4	5	22.7	
	2020	5	10.0	6	8.7	4	11.4	3	13.6	
Imipenem	***2017***	13	31.7	10	17.9	11	28.2	5	25.0	*0.3763*
	2018	10	24.4	19	33.9	12	30.8	3	15.0	
	2019	12	29.3	12	21.4	11	28.2	5	25.0	
	2020	6	14.6	15	26.8	5	12.8	7	35.0	
Levofloxacin	***2017***	2	8.0	0	0.0	0	0.0	0	0.0	0.0145
	2019	16	64.0	44	54.3	21	56.8	11	40.7	
	2020	7	28.0	37	45.7	16	43.2	16	59.3	
Piperacillin/ Tazobactam	***2017***	13	29.5	13	19.7	5	19.2	6	33.3	0.1577
	2018	13	29.5	22	33.3	10	38.5	9	50.0	
	2019	15	34.1	15	22.7	6	23.1	2	11.1	
	2020	3	6.8	16	24.2	5	19.2	1	5.6	

Chi-squared Test for Independence

DISCUSSION

P. aeruginosa is an important pathogen that frequently causes multidrug-resistant nosocomial infections, especially in hospitalized patients (Gysin et al., 2021).

The success of treatment is seriously challenged by the adaptive and intrinsic resistance of organisms against almost all antipseudomonal antibiotics commonly used. Therefore, understanding the antibiotic resistance profile of *P. aeruginosa* in a population is crucial and the combination therapy is suggested in the medication of diseases triggered by the microorganism to hinder the emergence of resistance (Varışlı et al., 2017; Horcajada et al., 2019). In this research, we investigated the bacterial isolates that were repeatedly produced by 789 participants treated or hospitalized in our clinic to study how antibiotic treatment affects the antimicrobial susceptibility over time. For all *P. aeruginosa* isolates analyzed for four years, we observed quite high rates of drug resistance to the cefuroxime, levofloxacin and netilmicin and lowest resistance rate was against the amikacin. In addition, the resistances of the organism against the gentamicin, cefepime and aztreonam significantly reduced over years while the rates against the colistin and levofloxacin considerably increased.

In a very recent study in Switzerland, when the antimicrobial susceptibility profiles of respiratory gram-negative bacterial isolates from COVID-19 patients were examined, it was observed that a significant number of *P. aeruginosa* isolates were resistant to the common antibiotics cefepime (56.3%), meropenem (50.0%), and ceftazidime (46.9%) (Gysin et al., 2021).

The resistance to piperacillin/tazobactam (65.6%) was observed as the highest value for any of the relevant medicine in the research (Gysin et al., 2021). Resistance to the ciprofloxacin was comparatively low in P. *aeruginosa* isolates (15.6%). We found lower rates of the resistance to the cefepime (34.5%), meropenem (20.7%) and piperacillin/tazobactam (21.5%) which decreased in a time dependent manner while the resistance rate to ciprofloxacin (45.6%) was higher than the above-mentioned study but did not change significantly by years.

Of the numerous aminoglycosides known to date, the tobramycin, paromomycin, kanamycin, streptomycin, neomycin, gentamicin, and amikacin are recognized by the US Food and Drug Administration (FDA) for the clinical care (Chandrika and Garneau-Tsodikova, 2016). Amikacin is a semi-synthetic aminoglycoside antibiotic which has been widely used and is effective against a variety of Gram-negative species, such as *Pseudomonas* and several Gram-positive species (Ramirez and Tolmasky, 2017). In studies, the resistance rate against amikacin was found to be between 1-30% (Eyigör et al., 2009; Varışlı et al., 2017). In a study by TozluKeten et al., (2010), this rate to amikacin (30%) was found to be less than resistance to ciprofloxacin (48%) and piperacillin tazobactam (32%). In this research, the total amikacin resistance degree of *P. aeruginosa* was measured as 7.3%, and the rate was highest in 2019 (12%). One main reason for the low antibiotic resistance against the amikacin may be that it is not frequently preferred in the empirical treatment.

The resistance of *P. aeruginosa* to the gentamicin owing to enzymatic N-acetylation has been known for a long time (Holmes et al., 1974). The gentamicin resistance among various hospitals is examined, a resistance profile varying between 4 and 51% was observed in the literature (Gayyurhan et al., 2008; Eyigör et al., 2009; Varışlı et al., 2017). In a study by Varışlı et al., (2017), the gentamicin resistance rates of *P. aeruginosa isolates* increased from 13.2% to 21% in the wound samples of patients who applied to the outpatient clinics. In our study, the gentamicin resistance rates of these isolates significantly decreased in four years from 31.5% to 13.5%, probably due to the less frequent usage in the clinic.

Fluoroquinolones including the ciprofloxacin and levofloxacin are frequently used in the empirical management of *P. aeruginosa infections*. In a research by Varışlı et al., (2017), the antibiotic resistance levels of *P. aeruginosa strains* obtained from the clinical specimens were also examined by years and no increase was observed in the ciprofloxacin resistance of abscess cultures in outpatients between 2011 and 2015, while the resistance rate in urine cultures increased from 14.2% to 20.3% in the same years. They also found that the ciprofloxacin resistance rate of *P. aeruginosa* was between 22-25% in the abscess culture and between 22-25.4% in the wound culture. In a research by Eyigör et al., (2009), the highest resistance rate was found against the ciprofloxacin (16%). Another study by Öztürk et al. (2011) found this rate as 15%. Other studies performed in Turkish population showed that the ciprofloxacin resistance rates were in the range of 7.2-47% (Duman et al., 2012; Durmaz and Özer 2015). In this research, the total antimicrobial resistance rate of *P. aeruginosa to* the ciprofloxacin was 45.6% and our data are compatible with the literature. The resistance of strains obtained from the sputum cultures significantly decreased by years, but total resistance profile did not change. On the other hand, resistance to levofloxacin has greatly grown in bacteria isolated from cultures of secretions of respiratory, urine, and sputum in 2019, whereas it has significantly increased in strains identified from cultures of wounds in 2020. The cause of this result may be the frequent usage of quinolone group antibiotics in the empirical treatment of urinary tract infections among outpatients since the most frequent microbiological samples were acquired from the urine cultures. The relatively high rates of ciprofloxacin resistance suggest that it would be appropriate to apply these

fluoroquinolones in combination with a beta-lactam antibiotic.

The overall mortality rate due to the infections of *P. aeruginosa in* the hospitals was found to increase in the carbapenem-resistant colistin susceptible *P. aeruginosa* infections (Vatansever et al., 2020). Varışlı et al., (2017) reported that the *P. aeruginosa* resistance level strains against the imipenem and meropenem determined by the EUCAST criteria in the hospitalized patients decreased significantly from 31% to 29% in years. Tozlu Keten et al., (2010) found the imipenem resistance rate determined by same criteria as 31%, and the meropenem resistance rate as 27%. Determined by the EUCAST criteria, we found the imipenem resistance rate of all *P. aeruginosa* isolates as 23%, and the meropenem resistance rate as 20.7% both of which did not change significantly in years. Out data were in agreement with the literature.

For the treatment of *P. aeruginosa* infections in critically sick patients, piperacillin-tazobactam is widely employed (Lodise et al., 2007). In a study, the rate of piperacillin-tazobactam resistance of *P. aeruginosa* isolates was observed to be 39% according to EUCAST criteria (Varışlı et al., 2017). In our study, the total resistance rate against piperacillin-tazobactam was 21.5% which was lower than before-mentioned study, suggesting a difference in the patient populations and type of diseases.

Continuous variations in the antimicrobial drug resistance for *P. aeruginosa strains* isolated from patients complicate the empirical treatment options. Therefore, in order to determine the effective treatment protocols, it is necessary to regularly examine the microorganisms and their antibiotic resistance for each hospital. As a result of the evaluations in our clinic, an alteration in the antibiotic resistance profile was detected in the patients over the years due to the frequently varied use of antimicrobials. The combination of aminoglycosides with antipseudomonal beta-lactams or quinolones may be considered appropriate in outpatients for the empirical treatment of *P. aeruginosa infections*. As a result, timely and accurate interpretation of the antibiotic susceptibility tests has been found to be extremely crucial for the success of antimicrobial treatments.

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

The author contributed to the study conception and design. The data collection and analysis were performed by DKT. The first draft of the manuscript was written by DKT and DKT commented on previous versions of the manuscript. DKT read and approved the final manuscript.

Ethics approval and consent to participate

The protocol of this retrospective study involving the data of human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethical approval was granted by Non-Interventional Research Ethics Committee of Bandırma Onyedi Eylül University Health Sciences (Project no: 2020-51, Date: 28th Jan 2021).

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