Annals of Medical Research
DOI: 10.5455/annalsmedres.2019.12.911 2020;(27)2:476-83

Original Article

Acinetobacter species and their antibiotic resistance profiles isolated from various clinical specimens between 2014 and 2018

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Abstract

Aim: *Acinetobacter* species have emerged as an important cause of nosocomial pneumonia and bloodstream infections, especially in immunocompromised patients with underlying pathologies. Worldwide, there has been a marked increase in resistance to most antimicrobial agents in recent years. The aim of this study was to evaluate *Acinetobacter* spp., their antimicrobial resistance rates and changes in resistance rates isolated from a tertiary hospital in a five-year period.

Material and Methods: In this study, *Acinetobacter* strains isolated from inpatients or outpatients between January 2014 and December 2018 were included in the Medical Microbiology Laboratory of our hospital. BD Phoenix 100 (Becton Dickinson, USA) was used for identification and antibiotic susceptibility of the isolates.

Results: *Acinetobacter* baumannii and A. baumannii - *A. calcoaceticus* complex constituted 91% of all isolates. *Acinetobacter* strains were mostly isolated from inpatients with pneumonia (37%) and soft tissue infections (22.5%). Colistin resistance was not observed between 2014 and 2016, but it was detected in 2017 and 2018. Colistin resistance was 2.5% and 12.6% in A. baumannii and 2.9% and 13.5% in A.baumannii-calcoaceticus complex in 2017 and 2018, respectively, and this increase was statistically significant. Colistin and tigecycline were the most effective agents in all isolates. The resistance rates of tigecycline in A.baumannii and A.baumannii-calcoaceticus complex strains were 11% and 14.3%, respectively. Extensively drug-resistant isolates were 91.7% and pan drug-resistant isolates were 2.3%.

Conclusion: It has been observed that resistance to all used drugs including colistin in *Acinetobacter* species increased and the rate of pan drug-resistant isolates were also elevated. Especially the significant increase in colistin resistance observed in recent years raises concern. In order to prevent and cope with the development of multiple resistance, each laboratory should determine the distribution of resistance in *Acinetobacter* species and in particular resistance to colistin.

Keywords: *Acinetobacter* species; antibiotic resistance; epidemiology; PDR; XDR

INTRODUCTION

Acinetobacter species are immobile, non-fermentative, non-pigmented, Gram-negative coccobacilli, commonly found in nature, moist soil, water and sewage systems. *Acinetobacter* genus has more than 60 species and most of them are non-pathogenic microorganisms in the environment (1). It is reported that the most common species causing infections are *A. baumannii*, followed by *A. calcoaceticus* and *A. lwoffii* (2). Closely related species with similar phenotypic and biochemical properties are grouped into *A. calcoaceticus-A. baumannii* complex and firstly consisted of four species: *Acinetobacter* calcoaceticus, *Acinetobacter* baumannii, *Acinetobacter* pittii and *Acinetobacter* nosocomialis. Recently two new species, *Acinetobacter* seifertii and *Acinetobacter* dighoorniae, have also been incorporated into the *A.calcoaceticus-A.baumannii* complex. Among the *A.calcoaceticus-A.baumannii* complex, *A. baumannii* is the clinically most important species responsible for 80% of infections. *A. pittii* and *A. nosocomialis* species are considered clinically important as they cause community and hospital-acquired infections. *A. seifertii* and *A. digjhoorniae* species were also isolated from human clinical specimens. *A. calcoaceticus*, on the other

Received: 31.12.2019 **Accepted:** 14.02.2020 **Available online:** 09.03.2020
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hand, is considered as a non-pathogenic environmental microorganism isolated from soil and rarely causes diseases (3).

Acinetobacter spp are among the most resistant microorganisms encountered in clinical practice in initiating effective empirical treatment. *A. baumannii* is naturally resistant to penicillins and has acquired resistant genes against almost all antibiotics that can treat Gram-negative bacteria, including fluoroquinolones, aminoglycosides, and cephalosporins (1). Major resistance mechanisms are; beta-lactamases inactivating beta-lactam drugs, loss or mutations in porin or OMP (outer membrane protein), presence of efflux pumps, changes in PBP (4). Today, a significant proportion of these isolates are called carbapenem-resistant *A. baumannii*, extensively drug-resistant (XDR), or pan drug-resistant (PDR) *A. baumannii* (5).

The most common clinical manifestations of *Acinetobacter* spp. are nosocomial pneumonia and bacteremia. Furthermore, they cause opportunistic nosocomial infections such as urinary tract infections, endocarditis, skin and soft tissue infections, peritonitis and meningitis (2). *A. baumannii* is the most common species responsible for nosocomial infections (4). In recent years, multidrug-resistant *A. baumannii* infections have been associated with increased mortality (6). Therefore, monitoring of the antimicrobial resistance of *Acinetobacter* species consistently is crucial for the selection of appropriate empirical treatment for serious patients. The aim of this study was to evaluate the *Acinetobacter* spp., their antibiotic resistance rates and resistance status in years isolated from clinical samples of inpatients and outpatients.

MATERIAL and METHODS

Acinetobacter species isolated from samples sent from various clinics to the University of Health Sciences University, Okmeydani Training and Research Hospital, between January 2014 and December 2018 were examined retrospectively in this study. The hospital has 796 beds and approximately 55000 hospitalizations per year. The total number of intensive care beds is 61 adults and 37 children and newborns. The first reproduction of the same material and reproduction of different materials belonging to the same patient were included in the study. This study was approved by the Ethics Committee of University of Health Sciences University, Okmeydani Training and Research Hospital (27.08.2019 / 1420).

Clinical specimens were cultured in 5% sheep blood agar, McConkey agar and chocolate agar (bioMérieux-SA, France) according to the sample type and incubated at 37 °C for 18-24 hours. After incubation, microorganisms were evaluated for colony morphology and gram staining. For the identification of isolates and determination of antibiotic susceptibility, Phoenix™ - 100 (Becton Dickinson, Diagnostic Instrument System, Sparks, USA) panels of the automated system were used. Antibiotic susceptibility results were determined according to the recommendations of Clinical and Laboratory Standards Institute (CLSI) between 2014 and 2015 and European Antimicrobial Susceptibility Testing Committee (EUCAST) between 2016 and 2018. CLSI criteria were continued to be applied for the agents other than carbapenem, aminoglycoside, fluoroquinolones and trimethoprime-sulfamethoxazole (TMP-SXT). For Tigecycline, the US Food and Drug Administration (FDA) limit values were applied. The XDR *Acinetobacter* isolate was defined as any isolate non-susceptible of the 1-3 drug groups including aminoglycosides, carbapenems, fluoroquinolones, and polymyxin. Any isolate non-susceptible to all tested antimicrobials of four classes was identified as PDR isolate (1). Escherichia coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27853 were used as quality control strains.

Statistical Analyses

Statistical analyzes were performed using SPSS 21 (SPSS Inc, Chicago, IL, USA) program. The suitability of the variables to normal distribution was examined by visual methods (histogram and probability graphs) and Kolmogorov-Smirnov test. Variables were compared using Student's t test or Mann-Whitney U test. Pearson Chi-Square or Fisher exact tests were used for qualitative variables. Kruskal-Wallis test was used to compare more than two groups with non-normal distribution and ordinal variables. A p value of less than 0.05 was considered statistically significant.

RESULTS

One thousand four hundred and eighteen *Acinetobacter* strains included in the study were isolated from various clinical specimens of 849 patients. The median age of the patients was 65 years (range: 0-97) and 58.2% of the patients were male. The median age of female patients (68 years) was higher than that of the male patients (63 years) ($p < 0.001$). Among the patients, 91.1% were inpatients and 64.1% were in the intensive care units. The clinical specimens where species were isolated most frequently were respiratory tract (37%), skin and soft tissue (22.5%), blood (19.3%) and urine (17.8%) samples. Demographic data of the patients are shown in Table 1.

Of the 1418 *Acinetobacter* strains isolated from 849 patients, 46.2% was *A.baumannii*, 44.8% was *A.baumannii-calcoaceticus* complex, 0.8% was *A.woffii / haemolyticus* and 8.3% was non-typeable *Acinetobacter spp*. There was no significant difference between the median ages of the cases regarding the *Acinetobacter* species (p: 0.22). Table 2 presents the demographic characteristics of the cases according to the *Acinetobacter* species isolated. *A.baumannii* was the most frequently isolated from respiratory tract, skin and soft tissue samples, cerebrospinal fluid and catheter samples, while *A.baumannii-calcoaceticus* complex was the most frequently isolated from blood and urine samples.

Antibiotic resistance rates of *Acinetobacter* species are shown in Table 3. The most effective antibiotics for *A.baumannii* were colistin, tigecycline, and TMP-SXT, whereas resistance rates were 2.5%, 11% and 73.9%, respectively. Resistance rates to other antibiotics ranged from 86.1% to 97.6%. The most effective antibiotics for *A.baumannii*-calcoaceticus complex strains were colistin, tigecycline, and TMP-SXT and their resistance rates were 4.2%, 14.3%, and 74.8%, respectively.

Table 1. Demographic characteristics of the study population

		N (%)
		849
Total number of patients		1418
Age (median)		65
Gender	Female	355 (41.8)
	Male	494 (58.2)
Application type	Outpatient	69 (8.1)
	Inpatient	780 (91.9)
Wards	Intensive care unit	544 (64.1)
	Internal Medicine	67 (7.9)
	Plastic surgery	48 (5.7)
	Hematology/oncology	37 (4.4)
	General surgery	31 (3.7)
	Orthopedics	29 (3.4)
	Urology	24 (2.8)
	Neurochirurgia	11 (%1.3)
	Infectious diseases	10 (%1.2)
	Pediatrics	9 (%1.1)
	Outpatients	19 (%2.2)
	Others	20 (%2.4)
Sample type	Respiratory system	314 (%37)
	Skin and soft tissue	191 (%22.5)
	Blood	164 (%19.3)
	Urine	151(%17.8)
	Brain cerebrospinal fluid	14 (%1.6))
	Catheter	8 (%0.9)
	Other sterile body fluids	7 (%0.8)

Resistance to other antibiotics in these isolates ranged between 82.7% and 95.9%. Eleven A.lwoffii / haemolyticus strains isolated from clinical specimens were found to have lower antibiotic resistance rates (14.3% - 57.1%) than other *Acinetobacter* species; and there was no resistance to colistin, tigecycline and netilmycin antibiotics. Any *Acinetobacter* spp. was not resistant to colistin, while tigecycline was found to be the most effective antibiotic with a resistance rate of 5.4% after colistin. Resistance to other antibiotics in these isolates ranged from 76.1% to 97.4%.

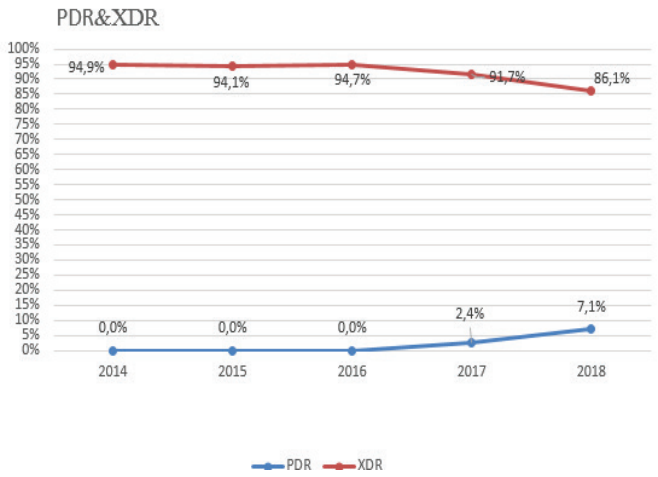


Figure 1. Distribution of PDR and XDR isolates between 2014 and 2018

Of the total 1418 isolates, 2.3% were PDR and 91.7% were XDR. There were no significant differences regarding age and sex between 21 cases with PDR and 751 cases with XDR (p: 0.70 and p: 0.46). All of the PDR isolates and 94.5% of the XDR isolates were inpatients. PDR strains were the most frequently isolated from respiratory, blood, urine, and cerebrospinal fluid samples, whereas XDR strains were the most frequently isolated from respiratory, blood, urine and skin / soft tissue samples. All of the PDR isolates and 66.2% of the XDR isolates were intensive care unit patients (Table 4). As shown in Figure 1, there was a statistically significant change in the distribution of PDR and XDR isolates between 2014 and 2018 (p <0.001). While PDR isolates were not detected between 2014 and 2016, they increased by 2.4% in 2017 and 7.1% in 2018. While XDR isolates ranged between 91.7% and 94.9% in 2014-2017, a decrease to the 86.1% was observed in 2018.

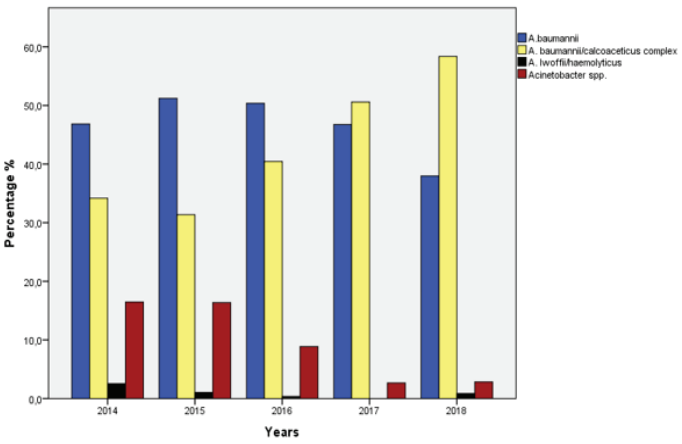


Figure 2. Distribution of *Acinetobacter* species by years

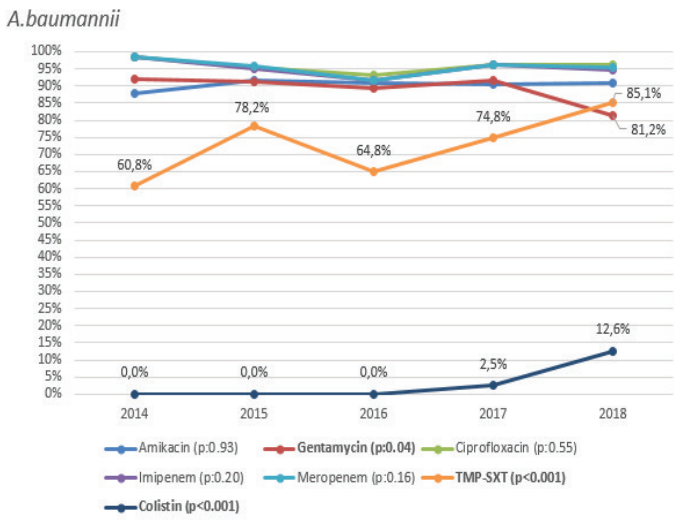
Figure 2 shows the distribution of *Acinetobacter* species between 2014 and 2018. No statistically significant difference was observed in the distribution of species between years (p: 0.12). When the changes in antibiotic

Table 2. Demographic characteristics of patients according to Acinetobacter species

		N	A.baumannii		A.baumannii/ calcoaceticus complex		A.lwoffii/ haemolyticus		Acinetobacter spp.	
			N	%	N	%	N	%	N	%
Number of isolates		1418	655	46.2	635	44.8	11	0.8	117	8.3
Age year	(median)		63		63		62		67	
Gender	Female	613	295	45	265	41.7	2	18.2	51	43.6
	Male	805	360	55	370	58.3	9	81.8	66	56.4
Age groups	<18	47	17	36.2	35	53.2	2	4.3	3	6.4
	19-40	215	97	45.1	97	45.1	2	0.9	19	8.8
	41-60	360	181	50.3	156	43.3	1	0.3	22	6.1
	61-80	538	244	45.4	245	45.5	5	0.9	44	8.2
	>80	258	116	45	112	43.4	1	0.4	29	11.2
Admission type	Outpatient	84	29	4.4	41	6.5	2	18.2	12	10.3
	Inpatient	1334	626	95.6	594	93.5	9	81.8	105	89.7
Sample type	Respiratory system	419	208	49.6	169	40.3	2	0.5	40	9.5
	Skin and soft tissue	262	134	51.1	104	39.7	0		24	9.2
	Blood	374	165	44.1	178	47.6	6	1.6	25	6.7
	Urine	261	95	36.4	142	54.4	1	0.4	23	8.8
	Brain cerebrospinal fluid	31	17	54.8	10	32.3	2	6.5	2	6.5
	Catheter	44	22	50	19	43.2	0		3	6.8
	Other sterile body fluids	27	14	51.9	13	48.1	0		0	
Wards	Intensive care unit	962	457	47.5	432	44.9	3	0.3	70	7.3
	Internal Medicine	87	36	41.4	42	48.3	2	2.3	7	8
	Plastic surgery	87	42	48.3	35	40.2	0		10	11.5
	Hematology/oncology	56	27	48.2	24	42.9	0		5	8.9
	General surgery	57	26	45.6	24	42.1	0		7	12.3
	Orthopedics	44	18	40.9	21	47.7	1	2.3	4	9.1
	Urology	28	10	35.7	12	42.9	1	3.6	5	17.9
	Neurochirurgia	15	8	53.3	7	46.7	0		0	
	Infectious diseases	16	8	50	6	37.5	0		2	12.5
	Pediatrics	11	4	36.4	4	36.4	2	18.2	1	9.1
	Outpatients	28	8	28.6	17	60.7	0		3	10.7
	Others	27	11	40.7	11	40.7	2	7.4	3	11.1

resistance of *Acinetobacter* species between 2014-2018 were examined; as shown in Figure 3, the rates of resistance to amikacin, ciprofloxacin, imipenem, and meropenem in *A.baumannii* strains did not change significantly over the years (p: 0.93, p: 0.55, p: 0.20 and p: 0.16, respectively). While the resistance to gentamycin in these isolates was 91.7% in 2017, the resistance rate decreased to 81.2% in 2018 and the difference between two years was statistically significant (p: 0.04). There was a significant change in TMP-SXT resistance rates over the years; resistance rate increased from 60.8% in 2014 to 85.1% in 2018 (p <0.001).

While colistin resistance in *A.baumannii* strains was not detected between 2014 and 2016, resistance rates were increased by 2.5% in 2017 and 12.6% in 2018 (p <0.001).



Figuru 3. Antibiotic resistance rates of *A.baumannii* strains between 2014 and 2018

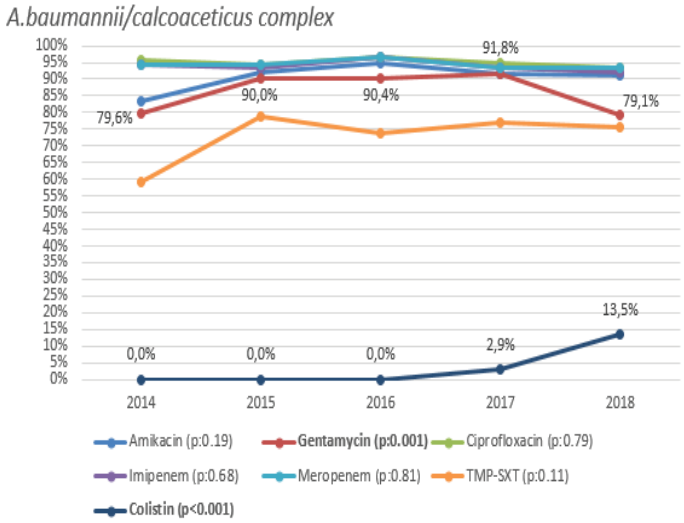


Figure 4. Antibiotic resistance rates of *A.baumannii*-calcoaceticus complex strains between 2014 and 2018

Table 3. Antibiotic resistance rates of Acinetobacter species

	A.baumannii (655)		A.baumannii-calcoaceticus complex (635)		A.lwoffii/haemolyticus (11)		Acinetobacter spp. (117)
	R/N	%	R/N	%	R/N	%	R/N
Amikacin	594/655	90.7	581/635	91.5	3/11	27.3	89/115
Gentamycin	581/653	89	547/635	86.1	3/11	27.3	89/117
Netilmycin	301/325	92.6	336/365	92.1	0/7	0	13/15
Ampicillin-sulbactam	186/216	86.1	110/133	82.7	3/7	42.9	69/73
Piperacillin-Tazobactam	242/248	97.6	154/163	94.5	3/7	42.9	89/96
Ticarcilin-clavulanate	159/163	97.5	100/105	95.2	1/5	20	9/10
Sefepim	238/244	97.5	155/163	95.1	4/7	57.1	83/87
Ceftazidime	238/246	96.7	156/165	94.5	4/7	57.1	87/90
Ceftriaxone	136/141	96.5	94/98	95.9	3/7	42.9	75/77
Ciprofloxacin	589/616	95.6	593/627	94.6	3/10	30	33/39
Levofloxacin	187/201	93	104/113	92	1/7	14.3	75/92
Imipenem	620/653	94.9	595/635	93.7	3/11	27.3	111/116
Meropenem	619/650	95.2	597/634	94.2	3/11	27.3	108/115
TMP-SXT	482/652	73.9	474/634	74.8	3/11	27.3	89/117
Tigecycline	24/218	11	19/133	14.3	0/7	0	4/74
Colistin	15/604	2.5	24/567	4.2	0/9	0	0/115

R:Resistance, N: Number

As shown in Figure 4, the resistance rates of *A.baumannii*-calcoaceticus complex strains to amikacin, ciprofloxacin, imipenem, meropenem, and TMP-SXT did not show significant changes between years (p: 0.19, p: 0.79, p: 0.68, p: 0.81, and p = 0.11, respectively). Gentamycin resistance rates in these isolates were 79.6% in 2014, 90-93.6% between 2015 and 2017, while gentamycin resistance rate decreased to 79.1% in 2018 (p <0.001). While colistin resistance was not detected in *A.baumannii-calcoaceticus* complex strains between 2014 and 2016, there was a significant increase in resistance rates of 2.9% in 2017 and 13.5% in 2018 (p <0.001).

Table 4. Demographic characteristics of cases with XDR and PDR isolates

			XDR		PDR	
		N	N	%	N	%
Number of isolates		1418	1301	91.7	33	2.3
Number of patients		849	751	88.5	21	2.5
Age year	(median)		66		64	
Gender	Female	318	311	41.4	7	33.3
	Male	454	440	58.6	14	66.7
Age groups	<18	17	16	2.1	1	4.8
	19-40	90	89	11.9	1	4.8
	41-60	184	176	23.4	8	38.1
	61-80	320	314	41.8	6	28.6
	>80	161	156	20.8	5	23.8
Admission type	Outpatient	41	41	5.5	0	0
	Inpatient	731	710	94.5	21	2.9
Sample type	Respiratory system	414	403	31	11	33.3
	Skin and soft tissue	245	244	18.8	1	3
	Blood	349	338	26	11	33.3
	Urine	228	223	17.1	5	15.2
	Brain cerebrospinal fluid	29	26	2	3	9.1
	Catheter	42	41	3.2	1	3
	Other sterile body fluids	27	26	2	1	3
Wards	ICU	518	497	66.2	21	100
	Internal Medicine	51	51	6.8	0	0
	Plastic surgery	42	42	5.6	0	0
	Hematology/oncology	35	35	4.7	0	0
	General surgery	34	34	4.5	0	0
	Orthopedics	25	25	3.3	0	0
	Urology	15	15	2	0	0
	Neurochirurgia	11	11	1.5	0	0
	Infectious diseases	8	8	1.1	0	0
	Pediatrics	6	6	0.8	0	0
	Outpatients	11	11	1.5	0	0
	Others	16	16	2.1	0	0

XDR: Extensively drug-resistant, PDR: Pan drug-resistant

DISCUSSION

In many countries, multi-drug resistant, non-fermentative Gram-negative pathogens including *Acinetobacter* species are increasing, posing a serious global health threat (7). Long-term hospitalization patients, especially in intensive care units and burn units, are at risk for colonization and infection (4). In this study, it has been investigated 1418 *Acinetobacter* strains isolated from various clinical specimens in a period of 5 years in a tertiary hospital in Turkey. 91% of isolates were identified as *A. baumannii* or *A.baumannii-A.calcoaceticus* complex.

Acinetobacter species are naturally resistant to many antibiotics. However, they can develop resistance with many mechanisms. Therefore, there are difficulties in the

treatment of infections caused by *Acinetobacter* species. Although carbapenem is an important treatment option against isolates with multiple drug resistance, the increase in carbapenem resistance in *Acinetobacter* species poses an important problem all over the world (1,8). In recent studies, although different mechanisms such as changes in the efflux pump or outer membrane proteins have been identified, it has been stated that the main mechanism in carbapenem resistance is the acquisition of genes encoding oxacillinase which hydrolyzed carbapenem (9). Maraki et al. (8) reported that carbapenem resistance in A. baumanii isolates was 93%. In the SENTRY study, imipenem and meropenem resistance rates according to EUCAST criteria in 13752 *A.calcoacetius – A.baumannii* complex isolates between 1997-2016 for Europe, North America, Asia-Pacific Region, Latin America were reported as %55.5-%53.9, %27-%32.6, %54.0-%55.5, %51.5-%51.3, respectively (1). In a systematic review and meta-analysis from Iran, it was reported that carbapenem resistance was 4.5% until 2005, reached 100% in 2016 (10). In a study conducted in our country, only seven (5.6%) of the *Acinetobacter* strains isolated from 124 patients with pneumonia were found to be susceptible to carbapenem (11). In another study conducted in 2012-2013 in Turkey, both meropenem and imipenem resistance in *A. baumannii* strains was reported to be 94.9% (12). It appears that different resistance rates have been reported in the literature for carbapenems from different geographical regions. In our study, resistance rates to imipenem and meropenem in *A.baumannii-calcoaceticus* complex strains were found to be 93.7% and 94.2% and did not change significantly over the years. Although our results were similar to the studies conducted in Turkey, this rate of resistance remained in very high compared to resistance rates detected in the SENTRY study, including Europe, the USA, and the Asia-Pacific region. The fact that the SENTRY study was conducted over a wide range of dates and the lower carbapenem resistance rates in the 90s may have led to lower overall resistance rates.

In our study, the most effective antibiotics for *A.baumannii* and *A.baumannii-calcoaceticus* complex strains were found to be colistin and tigecycline, the resistance rates were 2.5%-4.2% and 11%-14.3%, respectively. Colistin resistance in *A.baumannii* and *A.baumannii-calcoaceticus* complex strains was not detected between 2014 and 2016, whereas resistance rates were increased by 2.5% and 2.9% in 2017 and 12.6% and 13.5% in 2018, respectively. In a study conducted by Maraki et al. (8) in 914 *A.baumannii* isolates between 2010 and 2014, multidrug resistance was reported to be 92.9% and colistin resistance was 7.9% in 2014. Gao et al. (13) reported that susceptibility of colistin was high (97%) in the period from 2009 to 2014. In a multicenter study conducted by Boral et al. (14) from different geographical regions of our country, 164 clinical and 12 environmental *A.baumannii* isolates were included. In this study, colistin resistance was reported to be 1.2%, tigecycline resistance was 1.7%, and resistance rates to all other antimicrobial agents were above 90%. In a study by Cetinkol et al (15) conducted with 50 multi-drug resistant *A.baumannii* strains isolated from various clinical samples, all strains (100%) were susceptible to colistin, 96% were susceptible to TMP-SXT and only 36% were susceptible to tigecycline. Because of the increasing resistance to colistin and tigecycline, treatment options for resistant *Acinetobacter* strains are decreasing. New antibiotic regimens are needed to treat infections caused by *Acinetobacter* spp.

In our study, 2.3% of total 1418 isolates were found to be PDR and 91.7% were XDR. While PDR isolates were not detected between 2014 and 2016, they increased by 2.4% in 2017 and 7.1% in 2018. While XDR isolates ranged between 91.7% and 94.9% in 2014-2017, a decrease to 86.1% was observed in 2018. The decrease in XDR isolates in 2018 may be due to the increase in PDR isolates. Mortality has been reported to be higher in patients infected with *A.baumannii* strains with multiple drug resistance (16). In a multicentre study by Gales et al. (1) involving different geographical regions, 13752 *A.baumannii-calcoaceticus* complex strains isolated between 1997 and 2016 years were investigated and multidrug resistance was 66.4% in Europe, 61.5% in Latin America, 56.9% in Asia-Pacific and 38.8% in North America. Significant reductions in susceptibility to all antimicrobial agents were observed in *A.baumannii-calcoaceticus* complex isolates during the study period in all geographical regions. XDR rate (91.7%) detected in our study was higher. We believe that the most important reason for this was because the study of Gales et al included strains isolated since 1997. In a study conducted in the intensive care unit from 2014 to 2015 by Ziółkowski et al. (17), multi-drug resistance in 187 *A.baumannii* strains was found over 90%. All of these strains have been reported to be susceptible to colistin in that study. Muntean et al. (18) investigated multidrug resistance in Gram-negative bacilli between 2000 and 2015 and reported a statistically significant increase in the rate of those with multidrug resistance in *A.baumannii* strains. In the study of Rebic et al (19), the multidrug-resistance rate in 622 *Acinetobacter* isolates was reported to be 78.4% and the PDR rate was 17.24%. PDR strains were found to be associated with high mortality rates in patients with *Acinetobacter* infection. Intensive usage of carbapenem antibiotics and increase in interventional procedures has been reported as factors leading to an increase in multiple or pan drug resistant cases (20). In our study, all patients with PDR - were intensive care unit patients. In 2017, the first evidence of *A.baumannii*'s PDR environmental isolate was reported (21). Therefore, in the coming years, PDR strains are seen as a serious health problem not only in hospital infections but also in community-acquired infections. Therefore, it has recently come to the schedule to determine the combinations of antibiotics using in vitro synergy tests (22).

The large number of patients and their long-term outcomes are the strengths of our study. However, this study has some limitations. It is a single-centered study. It could not be performed by broth dilution for colistin antibiotic susceptibility. Other limitation include that it could not be made genetically discrimination at the species level and agent-contamination discrimination.

CONCLUSION

In conclusion; recently, there is a significant increase in resistance rates of *Acinetobacter* spp to colistin and tigecycline. Moreover, pan drug-resistant isolates are increasingly common. New antibiotic regimens are needed to treat infections caused by *Acinetobacter* spp. In order to prevent the development of multiple resistances and cope with these isolates, each laboratory should determine the distribution of resistance in Acinetobacter species and in particular resistance to colistin.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: This study was approved by the Ethics Committee of University of Health Sciences, Okmeydani Training and Research Hospital (27.08.2019 / 1420).

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