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Enfeksiyon Etkeni Nonfermenter Gram Negatif İzolatlar ve Antibiyotik Dirençleri: Üç Yıllık Veri

Non-Fermenting Gram-Negative Isolates as Infecting Agents and Antibiotic Resistance: Three-Year Data

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ÖZ

Amaç: Bu çalışmanın amacı, üç yıllık dönemde bir üçüncü basamak hastanenin enfeksiyon etkeni nonfermenter gram negatif izolatlarını ve antibiyotik direnç profillerini belirlemektir.
Materyal ve Metot: Balıkesir Atatürk Şehir Hastanesi'ndeki çeşitli kültürlerden, Ocak 2017-Aralık 2019 arasında, toplamda 3817 nonfermenter gram negatif organizma izole edilmiştir ve retrospektif olarak incelenmiştir. Tanımlama ve antibiyotik duyarlılıkları konvansiyonel yöntemler ve Phoenix^{TM} 100 sistemi (Becton Dickinson, MA, ABD) ile yapılmıştır
Bulgular: Toplamda; 2201 (%57,7) *P. aeruginosa*, 1283 (%33,6) *A. baumannii-calcoaceticus* kompleks, 202 (% 5,3) *S. maltophilia* ve 131 (%3,4) *B. cepacia* kompleks suşu izole edildi. Suşların %54,5'i yoğun bakım ünitelerinden izole edildi ve bunu dahili branş (%33,4) ve cerrahi branş servisleri (%12,1) takip etti. Tüm *A. baumannii-calcoaceticus* kompleks suşlarında test edilen altı antibiyotiğin dördüne %70'in üzerinde direnç belirlendi. Beta-laktam antibiyotik direncinin yanında (genellikle % 30'dan fazla gözlendi), florokinolon direnci de (%30,4) yüksekti. *S. maltophilia* izolatlarında, kotrimaksazol direnci %10'un altında kaldı. *B. cepacia* kompleks izolatlarında, seftazidim direnci yıllar içinde artış gösterdi (2018, %22,2; 2019, %67,0).
Sonuç: Antibiyotik direnci sorunu yalnız yeni antibiyotiklerin geliştirilmesi ile değil, ayrıca bilinen antibiyotiklerin etkinliğinin arttırılması ile kazanılabilir. Bu amaca yönelik işlemlerde ilk basamak, yerel sürveyans çalışmaları gibi güncel durumun tespitidir.
Anahtar Kelimeler: Acinetobacter, antimicrobial resistance, Burkholderia, Pseudomonas, Stenotrophomonas

ABSTRACT

Objective: This study aimed to investigate clinical non-fermenting gram-negative isolates and antibiotic resistance profiles for three years in a tertiary hospital.
Materials and Methods: A total of 3817 non-fermenting gram-negative strains isolated from various cultures between January 2017 and December 2019 in Balıkesir Atatürk City Hospital were investigated retrospectively. Identification and antibiotic susceptibilities were performed using conventional methods and Phoenix^{TM} 100 system (Becton Dickinson, MA, USA).
Results: A total of 2201 (57.7%) *P. aeruginosa*, 1283 (33.6%) *A. baumannii-calcoaceticus* complex, 202 (5.3%) *S. maltophilia* and 131 (3.4%) *B. cepacia* complex strains were identified. The majority of strains were isolated from intensive care units (54.5%), followed by internal medicine (33.4%) and surgical services (12.1%). All *A. baumannii-calcoaceticus* complex species showed over 70% resistance to most antibiotics. In addition to β-lactam antibiotic resistance (generally over 30%), resistance to fluoroquinolones (30.4%) seemed to have particular importance. Co-trimoxazole showed below 10% resistance in *S. maltophilia* isolates. In *B. cepacia* complex, ceftazidime resistance increased in years (2018, 22.2%; 2019, 67.0%).
Conclusion: The issue of antibiotic resistance cannot be won by just developing novel antimicrobials, but also by increasing the efficiency of current ones. The first step is to "diagnose" the current condition, like local surveillance studies.
Keywords: Acinetobacter, antimicrobial resistance, Burkholderia, Pseudomonas, Stenotrophomonas

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INTRODUCTION

During the 20th century, antibiotics created an up-and-coming trend in the fight against infectious diseases, which led to extensive consumption of them. Consequently, this has resulted in antimicrobial resistance (AMR) issues. AMR and mortality have a strong correlation in infections. Furthermore, new antibiotic developments can not catch up with the resistance velocity. This condition forced communities to take proactive steps. The first one is continuous surveillance studies on AMR, even at the local level, and guiding (or limiting/restricting) clinical usage of antibiotics (stewardship programs), which is a huge necessity.[1] Recently, all international and national organizations endorse laboratories to make such surveillance, and as a result, studies like The Turkish National Antimicrobial Resistance Surveillance System (UAMDSS), The Canadian Ward Surveillance Study (CANWARD), Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR), The SENTRY Antimicrobial Surveillance Program and The European Antimicrobial Resistance Surveillance Network (EARS-Net) were performed.[1-6]

The emerging problem of AMR and diminishing treatment options have alarmed not only microbiology societies, but also worldwide organizations, including political communities. According to The Centers for Disease Control and Prevention (CDC), carbapenem-resistant *Acinetobacter* spp. stands at the top of threat list as "urgent", whereas Multidrug-resistant (MDR) *Pseudomonas aeruginosa* defined as a "serious" threat.[7] In addition, World Health Organization (WHO) declared carbapenem-resistant *Acinetobacter baumannii* and *P. aeruginosa* in critical priority category of new antibiotic requirements.[8] Despite rare isolation, *Burkholderia cepacia* complex is strongly associated with fatal infections (particularly pulmonary infections in cystic fibrosis patients) and outbreaks due to contaminated medical equipment.[9] *Stenotrophomonas maltophilia* is a commensal organism with relatively low virulence. However, the similar capability of contaminated medical devices and solutions, colonizations in the healthcare settings and in addition, intrinsic resistance to various antibiotics make the organism an important concern.[10]

National and local antimicrobial stewardship policies require all laboratories and infection control boards a continuous follow-up and endorse healthcare facilities to take action. This study aimed to investigate infection-causative non-fermenting gram-negative isolates and their antibiotic resistance profile for three years in a state (tertiary) hospital.

MATERIALS AND METHODS

Ethics Committee Approval: Our study was approved by Balıkesir University, Faculty of Medicine Ethics Committee (Date: 21.11.2020, decision no: 2020/196). It was conducted by the international declaration, guidelines, etc.

Sample Size: Clinical cultures from January 2017 to December 2019 in Balıkesir Atatürk City Hospital (tertiary center) were included in the study. Isolated strains and their antibiotic susceptibilities were evaluated, retrospectively. A total of 3817 isolates causing infections from various sites (blood, urinary tract, upper and lower respiratory, wound, abscess, external auditory, and other) were included in the study.

Methods: All sample results except the first causative one were excluded for same-patient repetitious samples. Cultures were performed with conventional methods (Urine cultures: 35-37°C, 48h, ambient atmosphere with 5% sheep blood agar, eosin methylene blue agar; other samples: 35-37°C, 48h, 5% CO_2 atmosphere with 5% sheep blood agar, eosin methylene blue agar, chocolate agar) (RTA Laboratories, Kocaeli, Turkey). Gram staining features such as hemolysis, morphology, etc., catalase and oxidase tests, biochemical analysis (triple sugar iron agar, indole, simmon citrate agar, urease positivity, etc.), and Phoenix^{TM} 100 automated system (Becton Dickinson, MA, USA) were used for identifications.

Antibiotic susceptibilities were performed by Phoenix^{TM} 100 automated system (Becton Dickinson, MA, USA) according to The European Committee on Antimicrobial Susceptibility Testing (EUCAST, valid from 01.01.2019, v.11) guideline. Since only broth microdilution is required for colistin susceptibility, resistance could not be shared.[11] Susceptibilities for the *B. cepacia* complex were applied according to The Clinical and Laboratory Standards Institute (CLSI).[12] *P. aeruginosa* ATCC 27853 and *E. coli* ATCC 25922 were used as quality control strains.

Statistical Analysis: Statistical analysis was performed with SPSS 22.0 (IBM Inc, Chicago, IL, USA). Annual antimicrobial resistance ratios were compared by Chi-squared distribution test. p levels<0.05 were accepted as statistically significant.

RESULTS

Among 3817 isolates, a total of 2201 (57.7%) *P. aeruginosa*, 1283 (33.6%) *A. baumannii-calcoaceticus* complex, 202 (5.3%) *S. maltophilia* and 131 (3.4%) *B. cepacia* complex strains were identified. Distributions of species regarding sample type were presented in Table 1. The majority of strains were isolated from intensive care units (ICUs) (n=2079; 54.5%), followed by internal medicine (IMSs) (n=1276; 33.4%) and surgical services (SSs) (n=462; 12.1%). *P. aeruginosa* showed just a slightly higher isolation rate (n=973) from *A. baumannii-calcoaceticus* complex (n=907) in ICUs, while it showed a strong predominance in other services (IMSs, n=852; SSs, n=376).

Table 1. Distribution of isolated species according to sample type.

Sample / Species	***Acinetobacter baumannii-calcoaceticus* complex (n=1283, 33.6%)**	***Pseudomonas aeruginosa* (n=2201, 57.7%)**	***Burkholderia cepacia* complex (n=131, 3.4%)**	***Stenotrophomonas maltophilia* (n=202, 5.3%)**	**Overall (n)**
Sputum	284	551	12	83	930
Urine	96	411	-	11	518
Blood	150	133	17	18	318
Lower Respiratory Samples (Bronchoalveolar lavage-BAL, Deep Tracheal Aspirate-DTA)	522	520	98	71	1211
Wound/Abscess	217	430	-	11	658
Other (Sterile body fluids, cerebrospinal fluid, etc.)	14	21	4	8	47
External auditory	-	135	-	-	135
Total	1283	2201	131	202	3817

All antibiotic resistance profiles and comparisons among years were presented in Table 2 and Table 3. Except for co-trimoxazole and amikacin, all *A. baumannii-calcoaceticus* complex species showed more than 70% resistance to antibiotics. Significant alterations of resistance in aminoglycosides (particularly for amikacin) were observed (Gentamicin, 63.2% to 77.0%; amikacin 29.1% to 66.6%). For *P. aeruginosa,* interestingly, an opposed significant decrease was found in amikacin (24% to 9.6%). In addition to β-lactam antibiotic resistance (generally over 30%), resistance to fluoroquinolones (30.4%) seemed to have particular importance. Co-trimoxazole is the only recommended antibiotic for testing of *S. maltophilia* by EUCAST, and it showed promisingly below 10% resistance overall. For *B. cepacia* complex, in particular, ceftazidime resistance massively increased over the years (2018, 22.2%; 2019, 67.0%), which was statistically significant. A similar pattern was also observed for co-trimoxazole.

Surveillance studies that include Turkish data like UAMDSS and CAESAR data directly show the general position of Turkey.[2,3] In addition, other comprehensive studies such as EARS-Net, SENTRY and CANWARD show resistance profiles.[1,4-6] To gain an overlook opinion about our data and their concordance with comprehensive studies, Table 4 was presented that included UAMDSS, CAESAR and EARS-Net data.[2,3,6]

DISCUSSION AND CONCLUSION

The A. baumannii-calcoaceticus complex is increasingly important, especially for ICUs, and its infectious spectrum is wide. Nosocomial outbreaks and their high antibiotic resistance rates (Multi-drug resistance, MDR; extensive-drug resistance, XDR and pan-drug resistance, PDR) are major concerns. Several mechanisms were identified for resistance, such as enzymatic inactivation (e.g., carbapenem-hydrolyzing β-lactamases, carbapenemases), drug efflux, and/or by target site modifications.[13] Carbapenem-resistant *Acinetobacter* spp. is declared a top priority that requires novel antibiotics, and such resistance shows an increasing trend also for other gram-negative bacteria. Recently, tigecycline and colistin resistance have become urgent conditions.[7,8,14] In this study, most *A. baumannii-calcoaceticus* complex strains were isolated from respiratory samples (upper and lower) and from ICUs, which indicated colonization and infections as nosocomial conditions like ventilator-associated pneumonia. Wound samples followed these rates that note the biofilm formations. Aminoglycosides can be used as a part of combined therapies since EUCAST does not recommend them as monotherapies. However, this study showed a clear increase in resistance for both gentamicin and amikacin.[11] Similar change was also observed in a 10-year bloodstream infections (BSIs) study from Turkey, despite reported higher rates from UAMDSS and CAESAR.[2,3,15] Our resistance rates were notably higher from the 20-year worldwide panorama of SENTRY, but seem closer to 20-Year SENTRY BSI surveillance.[16,17] Of note, carbapenem resistance remains a problem in Turkey, including our facility, even though the results of our study showed a lower rate

Table 2. Antibiotic resistance profiles of *Acinetobacter baumannii-calcoaceticus* complex[a] and *Pseudomonas aeruginosa*[b], respectively.

Years/ Antibiotics[1,a]	2017			2018			2019			Overall			p
	S	R	R-Rate	S	R	R-Rate	S	R	R-Rate	S	R	R-Rate	
	(n)	(n)	(%)	(n)	(n)	(%)	(n)	(n)	(%)	(n)	(n)	(%)	
Imipenem	69	178	72.1	124	431	77.7	110	368	77	303	977	76.3	0.639
Meropenem	71	175	71.1	125	430	77.5	113	365	76.4	307	970	75.8	0.579
Gentamicin	91	156	63.2	116	442	79.2	110	368	77	317	966	75.3	0.021*
Amikacin[3]	173	71	29.1	202	342	62.8	159	317	66.6	534	730	57.8	<0.001*
Ciprofloxacin	60	184	75.4	94	461	83.1	104	375	78.3	258	1020	79.8	0.378
Colistin	NA[2]												NA[2]
Co-trimoxazole	104	136	56.7	178	362	67	180	294	62	675	792	63.2	0.277
Years/ Antibiotics[1,b]	**2017**			**2018**			**2019**			**Overall**			p
	S	**R**	**R-Rate**	**S**	**R**	**R-Rate**	**S**	**R**	**R-Rate**	**S**	**R**	**R-Rate**	
	(n)	**(n)**	**(%)**	**(n)**	**(n)**	**(%)**	**(n)**	**(n)**	**(%)**	**(n)**	**(n)**	**(%)**	
Imipenem	494	95	16.1	654	198	23.2	593	133	18.3	1741	426	19.7	0.43
Meropenem	487	96	16.5	676	193	22.2	600	144	19.4	1763	433	19.7	0.557
Amikacin[3]	535	28	24	776	72	8.5	653	69	9.6	1964	169	7.9	0.001*
Ciprofloxacin	452	119	20.8	599	271	31.1	469	273	36.8	1810	663	30.4	0.039*
Piperacillin	348	121	25.8	398	233	35.9	47	24	33.8	811	378	31.8	0.27
Piperacillin-Tazobactam	486	98	16.8	621	251	28.8	574	171	23	1681	520	23.6	0.123
Cefepime	439	128	22.6	551	323	37	454	197	30.3	1444	648	31	0.067
Ceftazidime	456	127	21.8	594	277	31.8	525	219	29.4	1575	623	28.3	0.242
Aztreonam	356	162	31.3	497	329	39.8	93	51	35.4	946	542	36.4	0.495
Co-trimoxazole	ID												NA

[1]: Resistance data according to EUCAST guidelines; [2]: Not Applicable due to lack of broth microdilution results; [3]: Aminoglycoside results were reported with a warning indicating not to be used as a monotherapy agent; NA: Not applicable; ID: Insufficient Data.

Table 3. Antibiotic resistance profiles of *Burkholderia cepacia* complex[a] and *Stenotrophomonas maltophilia*[b], respectively.

Years/ Antibiotics[1,a]	2017			2018			2019			Overall			p
	S	R	R-Rate	S	R	R-Rate	S	R	R-Rate	S	R	R-Rate	
	(n)	(n)	(%)	(n)	(n)	(%)	(n)	(n)	(%)	(n)	(n)	(%)	
Ceftazidime	2	0	None	49	14	22.2	22	44	67.0	73	58	44.3	<0.001*
Meropenem	1	2	67	46	5	9.8	60	7	10.4	107	14	11.6	0.809
Minocycline	1	0	None	10	0	None	13	0	None	24	0	None	NA
Co-trimoxazole	ID[2]			13	1	7.1	30	7	18.9	43	8	15.7	0.019*
Levofloxacin	2	0	None	57	1	1.7	58	3	4.9	117	4	33.0	0.174
Years/ Antibiotics[3,b]	**2017**			**2018**			**2019**			**Overall**			p
	S	**R**	**R-Rate**	**S**	**R**	**R-Rate**	**S**	**R**	**R-Rate**	**S**	**R**	**R-Rate**	
	(n)	**(n)**	**(%)**	**(n)**	**(n)**	**(%)**	**(n)**	**(n)**	**(%)**	**(n)**	**(n)**	**(%)**	
Co-trimoxazole	ID[2]			61	6	9.0	86	7	7.5	147	13	8.8	0.602

[1]: Resistance data according to CLSI guidelines; [2]: Data could not be reached. Excluded from statistical analysis; [3]: Resistance data according to EUCAST guideline; NA: Not applicable; ID: Insufficient Data.

Table 4: Data comparison of *Acinetobacter* spp and *P.aeruginosa* with UAMDSS, CAESAR, and EARS-Net reports (%).

Years / Antibiotics	Present Study[d]		UAMDSS (R-Rate-%)[e]												CAESAR[e,f] (R-Rate-%)		EU/EEA Country Range (R-Rate-%) (EARS-Net; 2015-2019)[e]	
			2011[c]		2012[c]		2013[c]		2014[c,d]		2015[c,d]		2016[c,d]		2020[c,d]		2019[d]	
	PA	ABC	PA	AS	PA	AS	PA	AS	PA	AS	PA	AS	PA	AS	PA	AS	PA	AS
Imipenem[b]	19.7	76.3	28.9	ID	30.6	ID	33.4	ID	30.0	90.0	37.0	90.0	46.1	92.3	38.0	90.0	0.0-55.4	0.0-92.3
Meropenem[b]	19.7	75.8	21.2		27.0		26.1											
Gentamicin	7.9	75.3	15.0		19.3		19.2		18.0	74.0	17.0	80.0	26.1	77.3	21.0	80.0	0.3-48.9	0.0-92.1
Amikacin	30.4	57.8	8.4		9.8		ID		ID	ID	ID	ID	23.2	72.4	14.0	70.0	ID	ID
Fluoroquinolone[a]	19.7	79.8	16.8		23.3		20.3		19.0	89.0	24.0	89.0	37.7	91.2	35.0	91.0	4.5-52.2	0.0-95.8
Piperacillin	31.8	NA	36.4	NA	35.2	NA	41.7	NA	ID	NA	ID	NA	ID	ID	ID	NA	ID	NA
Piperacillin-Tazobactam	23.6		22.7		25.2		20.6		21.0		30.0		30.1		34.0		2.3-52.8	
Cefepime	31		ID		ID		ID		15.0		26.0		30.5		31.0		ID	
Ceftazidime	28.3		30.2		37.2		39.8		19.0		24.0		23.5		28.0		3.5-52.2	
Aztreonam	36.4		ID		ID		ID		ID				ID		ID		ID	
Co-trimoxazole	NA	63.2																

UAMDSS: Turkish National Antimicrobial Resistance Surveillance System; CAESAR: Central Asian and European Surveillance of Antimicrobial Resistance report; EARS-Net: Antimicrobial Surveillance in the European Union and European Economic Area; ID: Insufficient Data, NA: Not Applicable; PA: *Pseudomonas aeruginosa*; ABC: *Acinetobacter baumannii-calcoaceticus* complex; AS: *Acinetobacter* spp.; [a]: Including ciprofloxacin and levofloxacin; [b]: Some surveillance reports stated carbapenems as one data including imipenem and meropenem; [c]: CLSI results, [d]: EUCAST results; [e]: Included results of all *Acinetobacter* species; [f]: Data of Turkey.

profile. This might have caused because of sample types since comprehensive surveillance studies mainly depend on only severely invasive manifestations, including cerebrospinal fluid (CSF) and blood cultures (BCs).[2,3]

Interestingly, there was an opposing condition in amikacin with *P. aeruginosa.* A statistically significant decrease was observed, which is also contrary to UAMDSS. We believe this might have been because the physicians preferring to prescribe other antibiotics since their susceptibility patterns are not as high-resistant as *Acinetobacter* spp. In a comprehensive study from Turkey focused on lower respiratory samples, these two pathogens, *P. aeruginosa* and *A. baumannii-calcoaceticus* complex, were the leading causes of hospital-acquired infections. Susceptibility patterns were catastrophic, since carbapenem, fluoroquinolone and cephalosporin resistance was over 90%, aminoglycoside resistance was over 75%, and colistin resistance was over 10% in *A. baumannii-calcoaceticus* complex. For *P. aeruginosa*, carbapenem, fluoroquinolone and cephalosporin resistance were all above 30%, amikacin resistance was 19.9% and colistin resistance was 7.5%.[18] These rates seem to be more compatible with our results, since our strains were mainly isolated from respiratory samples, as stated before. As shown in Table 4, analysis of EARS-Net indicated a wide resistance-rate spectrum according to the data-sourced country, but obviously, Turkey stands at "the high-rate position" for these two pathogens.[6] Despite statistical insignificance, a slightly rising trend of resistance can be observed for many antibiotics, which might support "prescription" hypothesis. More data on antibiotic consumptions are required to explain this. Of note, antimicrobial consumption and resistance in bacteria from humans and animals reported by The European Centre for Disease Prevention and Control (ECDC) showed a direct association with consumption and resistance.[19]

Isolations of *S. maltophilia* and *B. cepacia* complex are generally rare, similar to our study (totally 8.7%). The 20-year SENTRY study did not report any of these pathogens among BSIs and CANWARD surveillance only reported *S. maltophilia* which were 1.6% of all isolates.[4,16] The multicenter study of lower respiratory samples in Turkey notified 3.0% (total), and 10-year BSI study from Turkey stated 1.3% (*S. maltophilia)* and 0.3% (*B. cepacia* complex) isolation rates.[15,18] Like our data, *S. maltophilia* takes the third line of non-fermenting gram-negative agents causing healthcare-associated infections. It has capabilities of biofilm formation and attaching to surfaces, including medical devices. Long-term hospitalization in ICUs, corrupted immune status, cystic fibrosis, major surgeries, mechanic ventilation and previous administration of broad-spectrum antibiotics are major risk factors for *S. maltophilia* infections.[10] EUCAST only recommends testing of co-trimoxazole, since it is suggested as the first-line therapeutic agent; however, minocycline and doxycycline were also recommended.[10,11] In this study, the co-trimoxazole resistance rate was 8.8%, which was slightly higher than SENTRY study (4%) and the Turkish multicenter respiratory study (6.5%).[17,18] However, some reports indicate significantly higher results (>15%), confirming a potential growing problem.[20,21] For *B. cepacia* complex, ceftazidime resistance in this study showed a significantly increasing trend (in total, 44.3%, $p<0,001$). In several reports, rates of *B. cepacia* complex strains that were found to be susceptible to doxycycline, minocycline, and ceftazidime were 46.4%, 45.9% and 35-36%, respectively.[9] Comparing to the Turkish multicenter respiratory study, it was found that only meropenem showed a lower resistance in this study.[18] Despite being a tertiary center, diseases like cystic fibrosis are rarely diagnosed in our facility; nevertheless, our resistance rates indicated a great concern. Our facility is in the phase of becoming "a training and research hospital," which might cause the beginning of closer and long-term follow-up programs in such cases. So it is possible to encounter much more cases and isolate more strains. Thus, it seems to be crucial to take action immediately against antibiotic resistance even for such rarely isolated strains.

There were some limitations of this study. First, our susceptibility results were mainly based on EUCAST methodology except for the *B. cepacia* complex. Studies like SENTRY and UAMDSS were depended on CLSI guidelines, and some discrepancies were reported between the results of the two methods.[22] Both EUCAST and CLSI are reference methods, and so, as long as one reference method was used, it is important to observe general trends of resistance. Since their comparison is beyond the scope of this study, we believe these discrepancies created just a minor effect. Secondly, colistin resistance could not be determined due to the incapability of using the broth microdilution method as EUCAST recommended. Colistin resistance is a growing concern worldwide, but the compatibility of automated devices and manual susceptibility techniques are very poor, which makes it hard to test.[23] Thirdly, the retrospective character of the study might have caused data insufficiency to consider. It was unable to gain any information before 2017, and in addition, we could not reach to co-trimoxazole resistance data of *S. maltophilia* and *B. cepacia* complex in 2017. Finally, to observe the possible relationship with resistance, we could not reach to antibiotic consumption data of our facility and/or area.

In conclusion, despite recent increasing awareness worldwide, the conflict between humankind and resistant microorganisms is on the page of the negative side. As stated by many antimicrobial stewardship programs, this conflict cannot be won by just developing novel antimicrobials, but also by increasing the efficiency of older ones.[8] The first step of this approach is to "diagnose" the current condition since surveillance studies indicate such data. Still, it is also the continuity of this step via a standardized methodology. CLSI and EUCAST seem to fill this gap, and with these guidelines, it is crucial to report resistance data to observe both current conditions and particular changes after interventions. It should be in mind that this contestation starts with local data.

Ethics Committee Approval: Our study was approved by the Balıkesir University, Faculty of Medicine Ethics Committee (Date: 21.11.2020, decision no: 2020/196). The study was carried out by international declaration, guidelines, etc.

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

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