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ORIGINAL ARTICLE

Distribution of urinary *Enterobacterales* isolates and antibiotic resistance profiles: Three-year data

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ABSTRACT

Objective: Urinary tract infections (UTIs) are one the most frequent human infections. Increasing trend of antimicrobial resistance (AMR) and difficult-to-treat resistance cases are of serious concern. This study aimed to investigate the order of *Enterobacterales* urinary isolates and AMR profiles for 3 years in a tertiary hospital.

Material and Methods: Clinical urinary cultures of patients obtained from January 2017 to December 2019 in Balıkesir Atatürk City Hospital were included in the study. Isolated *Enterobacterales* strains and their antibiotic susceptibilities were retrospectively evaluated. Antimicrobial susceptibility tests were performed by conventional and automated methods according to guidelines of The European Committee on Antimicrobial Susceptibility Testing.

Results: Among a total of 9297 urine isolates, 78.5% were members of order *Enterobacterales* (n=7300). The majority of strains were isolated from intensive care units (n=3979; 54.5%). Most of the patients were female (62.9%) and 52.4% of the patients had an indwelling urinary catheter (catheter-associated UTIs). The carbapenem resistance was 13.6% in *Klebsiella* spp., followed by *Morganella* spp. (7.5%). Extended-spectrum β-lactamases (ESBLs) were detected most frequently also in *Klebsiella* spp. (over 50%), followed by *Escherichia coli* (over 30%) and *Enterobacter* spp. (over 30%). *E. coli* and *Klebsiella* spp. showed significant change in resistance to ceftazidime, while *Proteus* and *Morganella* spp. showed a change in resistance to cefepime and fluoroquinolone, additionally. Alterations in Amoxicillin and Clavulanic acid and cefepime resistance of *Enterobacter* and other rare species were also significant.

Conclusion: Antibiotic consumption is strongly related to AMR and Türkiye seems to have a serious struggle with both antibiotic consumption and AMR. Local and/or national antimicrobial policies are effective in Türkiye, but further measures are required.

Keywords: Antibiotic resistance, carbapenems, *Enterobacterales*, *Enterobacteriaceae*, urinary tract infections.

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INTRODUCTION

Urinary tract infections (UTIs) are observed in both pediatric and adult populations and are one of the most common infections among healthcare-associated and community-associated ones. They had a wide spectrum, such as from asymptomatic cases to pyelonephritis, and they are mainly caused by gram-negative bacteria, including members of the order *Enterobacterales*. *Escherichia coli* causes almost 80% of UTIs and they are much more common in females. UTIs are not just a problem of the urinary tract, since more than a quarter of sepsis cases are admitted to emergency departments and nearly half of the sepsis cases in hospitalized patients are mainly sourced by UTIs. Accurate diagnosis and targeted treatment in support of antimicrobial susceptibility testing (AMST) and pharmacological evaluation are crucial; however, the increasing trend of antimicrobial resistance (AMR) created difficult-to-treat resistance (DTR) infections, which is unfortunately in growing condition among UTIs.[1]

Appropriate use of antibiotics is the most important interventable factor in fight against AMR.[2] Thus, antimicrobial stewardship programs and societies published guidelines for defining appropriate treatments in each stage of UTIs.[3–6] On the other hand, antibiotic consumption trends and policies vary among countries which cause different susceptibility patterns that may lead to variable therapies.[7] Recent data on AMR showing increasing ratios of *Enterobacterales* producing extended-spectrum β-lactamases (ESBL), AmpC β-lactamases, and carbapenemases along with other resistance mechanisms threaten public health.[8] The European Committee on Antimicrobial Susceptibility Testing (EUCAST) is the reference method to apply and interpret AMST results, which is strongly recommended to monitor years by even local facilities.[9,10] The aim of this study is to share AMR status of our tertiary center in urine isolates and to observe whether there is a significant alteration, or not.

MATERIAL AND METHODS

Ethical Approval

Approved by The Ethical Board of Balıkesir University, Faculty of Medicine (date: 21 October 2020, desicion number: 2020/190). This study was conducted in accordance with ethical principles of the Declaration of Helsinki (revised version of 2013).

Materials

Enterobacterales strains isolated from urine cultures of patients in all age groups admitted to Balıkesir Atatürk City Hospital between 2017 and 2019 were included. Contaminations, untreated cases, and cultures with insufficient colony-forming units/mL were excluded, and only samples that were accepted as infectious agents were included.

Methods

Urine cultures were quantitatively inoculated onto 5% sheep blood agar, eosin methylene blue (EMB) agar (RTA Laboratories, Kocaeli, Türkiye) (35–37°C, 48 h, ambient atmosphere). The only first sample was included for repetitious samples from the same patient. Grown colonies were identified by gram staining, hemolysis feature, colorimetric change in EMB agar, catalase, and oxidase tests, Phoenix™ 100 automated system (Becton Dickinson, MA, USA).

Antimicrobial susceptibility tests were performed by Phoenix™ 100 automated system (Becton Dickinson, MA, USA) and Kirby–Bauer disk diffusion method according to guidelines of The European Committee on Antimicrobial Susceptibility Testing (EUCAST, valid from 01.01.2019, v.9). Extended-spectrum β-lactamase (ESBL)-producing and carbapenemase-producing *Enterobacterales* strains were screened according to EUCAST guidelines. Ciprofloxacin resistance was reported as resistant to all fluoroquinolones.[9] *E. coli* ATCC 25922 was used for quality control.

Statistical Analysis

SPSS 22.0 (SPSS Inc., Chicago, IL, USA) program was used. Annual AMR ratios were compared by Chi-squared distribution test. P levels <0.05 were accepted as statistically significant.

RESULTS

Among a total of 9297 urine isolates (non-fermenter gram negatives n=518, Coagulase-negative staphylococci n=1282, *Enterococcus* spp. n=101, fungi n=42, other species n=54), 78.5% were members of order *Enterobacterales* (n=7300). The majority of strains were isolated from intensive care units (ICUs) (n=3979; 54.5%), followed by surgical (n=1708; 23.4%) and internal medicine (n=1613; 22.1%) services.

The majority of the patients were female (62.9%), 37.2% of patients were <18 years of age (age 43±11 years). The outpatients were only 28.0% of *Enterobacterales* (n=2044). All cultures from ICUs and 56.6% of cultures from inpatients were obtained from urinary catheters, of which 52.4% were catheter-associated UTIs. Over 85% of cultures of outpatients were obtained by midstream urine, 11.8% were provided by pediatric U-Bags and the rest of them were from catheters. Only nine samples were suprapubic aspiration.

Antibiotic resistance profiles of various members of order *Enterobacterales* are presented in Tables 1–3. Resistance to amoxicillin and clavulanic acid varied from 26.7% to 100% but remained high (over 50%) generally. As shown in Table 1, significant alterations in ceftazidime resistance were detected for *E. coli* and *Klebsiella* spp. (p<0.001). Fluoroquinolone and cephalosporin resistance were generally over 30% for both these species, while carbapenem resistance was 13.6% in *Klebsiella* spp., followed by *Morganella* spp. (7.5%), but it was <2% in *E. coli.* ESBLs were detected most frequently also in *Klebsiella* spp. (over 50%), followed by *E. coli* (over 30%) and *Enterobacter* spp. (over 30%) (Table 3). As shown in Table 2, alongside ceftazidime resistance, *Proteus* spp. showed additional increasing ratios of cefepime and fluoroquinolone resistance. As shown in Table 3, alterations in amoxicillin and clavulanic acid and cefepime resistance of *Enterobacter* and other species were also significant (p<0.001). Trimethoprim-sulfamethoxazole resistance was over 30% in majority of all species (Table 1, 2). No other significant alterations were observed.

Table 1: Antibiotic resistance profiles of *E. coli* and *Klebsiella* species

Organism	*E. coli*										*Klebsiella* species									
Years	2017		2018		2019		Overall			p	2017		2018		2019		Overall			p
Antibiotics	R (n)	%	R (n)	%	R (n)	%	S (n)	R (n)	%		R (n)	%	R (n)	%	R (n)	%	S (n)	R (n)	%	
Imipenem	8	0.6	28	1.3	24	1.2	5617	60	1.1	0.816	52	13.4	58	11.9	50	9.5	1243	160	11.4	0.650
Meropenem[2]	23	1.6	39	1.8	38	1.9	5540	100	1.8	0.864	57	14.8	74	15.3	59	11.2	1208	190	13.6	0.636
Ertapenem	152	11.6	204	9.4	212	10.7	4902	568	10.8	0.903	124	34.4	151	31.9	147	28.0	936	422	31.1	0.648
Gentamicin[3,5]	281	19.3	452	20.2	421	20.9	4548	1154	20.2	0.980	161	41.5	139	28.3	158	29.6	955	458	32.4	0.076
Amikacin[3,5]	9	0.7	25	1.1	14	0.7	5570	48	0.9	0.776	41	10.9	40	8.4	44	8.3	1261	125	9.0	0.693
Ciprofloxacin[2]	332	22.9	662	29.7	642	32.0	4045	1636	28.8	0.333	153	40.5	204	41.7	222	41.8	819	579	41.4	0.946
Trimethoprim-sulfamethoxazole	549	38.1	819	37.2	787	39.3	3491	2155	38.2	0.958	170	44.7	222	45.9	245	46.1	758	637	45.7	0.987
Amoxicillin-clavulanic acid[1]	664	45.6	1009	45.2	885	44.2	3134	2558	44.9	0.987	255	66.2	306	62.6	332	62.1	516	893	63.4	0.829
Piperacillin-tazobactam	174	11.9	261	11.8	218	10.9	5014	653	11.5	0.968	159	41.3	187	38.5	178	33.5	878	524	37.4	0.591
Ceftazidime[4]	328	22.8	701	31.9	692	70.8	2610	1721	37.3	<0.001	198	51.8	233	48.3	293	86.9	477	724	60.3	<0.001
Ceftriaxone[2,4]	462	31.9	748	33.5	694	34.6	3780	1904	33.5	0.901	227	59.7	258	52.6	283	52.9	638	768	54.6	0.516
Cefepime	428	29.7	731	33.2	123	31.2	2758	1282	31.7	0.897	221	57.6	246	51.0	49	51.6	445	516	53.7	0.562
Cefixime[1]	360	37.7	796	37.4	760	39.1	3110	1916	38.1	0.958	190	63.9	259	56.8	299	59.1	511	748	59.4	0.582

1: Uncomplicated UTI only; 2: Indications other than meningitis; 3: Infections orgininating from urinary tract; 4: Reported with an alert indicating "Monotherapy with cefotaxime, ceftriaxone or ceftazidime as well as combination therapy of these agents with an aminoglycoside should be avoided against *Klebsiella aerogenes*"; 5: Reported with an alert indicating "Aminoglycosides should always be used in combination," *E. coli*: *Escherichia coli*.

Table 2: Antibiotic resistance profiles of *Proteus* and *Morganella* species

Organism	*Proteus* species										*Morganella* species									
Years	2017		2018		2019		Overall			p	2017		2018		2019		Overall			p
Antibiotics	R (n)	%	R (n)	%	R (n)	%	S (n)	R (n)	%		R (n)	%	R (n)	%	R (n)	%	S (n)	R (n)	%	
Imipenem[4]	0	0	4	7.0	15	10.8	185	19	9.3	0.004	1	7.1	1	5.9	2	22.2	36	4	10.0	
Meropenem[2]	7	8.1	4	2.8	2	1.4	358	13	3.5	0.034	0	0	1	5.9	2	22.2	37	3	7.5	
Ertapenem	20	26.3	28	19.6	34	24.6	275	82	22.9	0.564	0	0	3	18.8	3	33.3	33	6	15.4	
Gentamicin[3,5]	27	31.0	40	27.2	46	32.4	263	113	30.1	0.717	1	7.1	4	23.5	3	33.3	32	8	20.0	
Amikacin[3,5]	5	6.2	16	10.9	9	6.4	338	30	8.2	0.308	0	0	0	0	0	0	39	0	0	
Ciprofloxacin[2]	15	17.9	52	35.6	63	44.7	241	130	35.0	<0.001	1	7.1	6	35.3	3	33.3	30	10	25.0	
Trimethoprim-sulfamethoxazole	28	32.2	68	46.6	68	47.9	211	164	43.7	0.037	2	14.2	7	43.8	3	33.3	27	12	30.8	NA
Amoxicillin-clavulanic acid[1]	22	25.6	38	25.8	40	28.2	275	100	26.7	0.934	13	100	16	100	9	100	0	38	100	
Piperacillin-tazobactam	6	6.9	7	4.8	6	4.3	355	19	5.1	0.630	1	7.1	2	11.8	0	0	37	3	7.5	
Ceftazidime	4	4.7	14	9.7	17	41.5	237	35	12.9	<0.001	2	14.3	1	6.3	2	50.0	29	5	14.7	
Ceftriaxone[2]	20	22.9	36	24.7	47	33.1	272	103	27.5	0.242	0	0	2	11.8	3	33.3	34	5	12.8	
Cefepime	14	16.7	25	17.2	9	39.1	204	48	19.1	<0.001	0	0	1	6.3	0	0	31	1	3.1	
Cefixime[1]	29	46.8	51	37.5	64	48.1	187	144	43.5	0.293	6	54.6	11	73.3	7	87.5	10	24	70.6	

1: Uncomplicated UTI only; 2: Indications other than meningitis; 3: Infections orgininating from urinary tract; 4: Reported with an alert indicating "The intrinsically low activity of imipenem against *Morganella morganii*, *Proteus* spp. and *Providencia* spp. requires the high exposure of imipenem"; 5: Reported with an alert indicating "Aminoglycosides should always be used in combination"; NA: Not applicable.

Table 3: Antibiotic resistance profiles of *Enterobacter* and other species (including *Citrobacter*, *Serratia*, etc.)

Organism	*Enterobacter* species										Other species									
Years	2017		2018		2019		Overall			p	2017		2018		2019		Overall			p
Antibiotics	R (n)	%	R (n)	%	R (n)	%	S (n)	R (n)	%		R (n)	%	R (n)	%	R (n)	%	S (n)	R (n)	%	
Imipenem	2	3.2	4	4.5	3	10.7	170	9	5.03	0.034	1	2.9	2	7.7	2	13.3	60	5	7.7	
Meropenem[2]	3	4.8	4	4.5	2	7.1	170	9	5.03	0.630	1	2.9	2	7.7	2	13.3	60	5	7.7	
Ertapenem	15	27.3	19	21.8	8	29.6	127	42	24.9	0.431	5	27.8	2	8.3	4	28.6	45	11	19.6	
Gentamicin[3,5]	10	16.1	13	14.4	4	14.3	153	27	15.0	0.899	3	12.5	4	14.3	4	26.7	56	11	16.4	
Amikacin[3,5]	1	1.7	3	3.5	0	0	171	4	2.3	0.241	1	5.6	0	0	2	13.3	55	3	5.2	
Ciprofloxacin[2]	9	15.0	18	20.0	8	28.6	143	35	19.7	0.050	1	4.3	4	14.3	2	14.3	58	7	10.8	
Trimethoprim-sulfamethoxazole	16	26.2	14	15.9	7	25	140	37	20.9	0.174	2	10.0	3	12.0	1	6.7	54	6	10.0	
Amoxicillin-clavulanic acid[1]	60	100	74	83.6	21	75	22	155	87.6	<0.001	17	70.8	22	84.6	10	66.7	16	49	75.4	NA
Piperacillin-tazobactam	16	25.8	24	26.9	10	35.7	129	50	27.9	0.234	2	8.3	4	14.8	3	20.0	57	9	13.6	
Ceftazidime[4]	19	31.2	29	32.9	14	82.4	104	62	37.5	<0.001	3	13.6	6	25.0	7	100	37	16	30.2	
Ceftriaxone[2,4]	24	38.7	41	45.6	15	53.6	100	80	44.4	0.104	7	29.2	7	25.0	7	46.7	46	21	31.3	
Cefepime	21	34.4	21	24.1	2	33.3	110	44	28.6	0.238	5	22.7	4	16.7	2	100	37	11	22.9	
Cefixime[1]	31	67.4	56	68.3	19	70.4	49	106	68.4	0.898	6	35.3	9	42.9	8	53.3	30	23	43.4	

1: Uncomplicated UTI only; 2: Indications other than meningitis; 3: Infections orgininating from urinary tract; 4: Reported with an alert indicating "Monotherapy with cefotaxime, ceftriaxone or ceftazidime as well as combination therapy of these agents with an aminoglycoside should be avoided against *Enterobacter* spp., *Citrobacter freundii* and *Hafnia alvei*"; 5: Reported with an alert indicating "Aminoglycosides should always be used in combination"; NA: Not applicable.

DISCUSSION

AMR in clinically significant bacteria, such as members of *Enterobacterales*, is of ongoing concern. Monitoring of alterations in AMR levels by prospective/retrospective, regional/national/multi-national, surveillance programs and performing standardized procedures to determine antimicrobial susceptibility are crucial steps in fight.[11,12] UTIs, no doubt, are one of the most frequent human infections, that lead to huge amount of antibiotic consumption. Even the non-complicated and community-acquired ones can be caused by resistant microorganisms and in treatment, *in vitro* susceptibility results have a key point alongside with pharmacological distribution of the drug.[12] Therefore, periodic monitoring is important to observe AMR status.

Both community-acquired and nosocomial UTIs should be considered as important morbidity and mortality factors with serious burden on the health-care systems. The most common causative agents of UTIs are the order of *Enterobacterales* (More than 60% of UTIs are caused by two species - *E. coli* and *Klebsiella* spp.), followed by particular Gram positives (*Enterococcus* spp. *Staphylococcus* spp., etc.) and other species (*Mycoplasma* spp., *Ureoplasma* spp., other gram negatives and fungi). Recommended first-line treatment consists of nitrofurantoin, fosfomycin, and sulfamethoxazole/trimethoprim, and β-lactam antibiotics (third-generation cephalosporins, carbapenems), fluoroquinolones and aminoglycosides are alternatives to such treatment. On the other hand, for particular patient populations (children, pregnant women, patients with liver/kidney failure, etc.,) β-lactam antibiotics take the first line, which makes them very important.[12] However, multidrug resistance (MDR) in Gram-negative bacteria is a growing threat causing the treatment of UTIs as a compelling issue. In a 10-year survey from Hungary, such a significant increase to particularly 3rd generation cephalosporins, arising amounts of ESBL producers were observed in UTI cases. The authors also noted that even though Hungary is a low-prevalence country in carbapenem resistance, such cases were sourced from UTIs. They additionally noticed high levels of fluoroquinolone resistance, which threatens the first-line treatment, and regarding this, they referred to their antibiotic consumption habits.[12] In another survey from Central Europe, resistance to amoxicillin/clavulanic acid was over 10% for *E. coli* and *Proteus* spp. and ranged between 20.4% and 58.9% for *Klebsiella* spp. with a significant increasing trend among years. Unfortunately, ampicillin was out of scope for gram negatives, since resistance rates were too high. Similar to our study, over 30% of the *Klebsiella* spp. isolates were resistant to cephalosporins, except cefepime showing above 25% and 50% resistance rates for *E. coli* and *Klebsiella* spp., respectively. Besides, their cephalosporin resistance to *E. coli* and *Proteus* spp. was below 10%, which was significantly lower than our data. They reported similar ratios (approx. 40%) of fluoroquinolone resistance with our data, however, despite our results, a dwindling trend was noticed for *Proteus* spp.[13] A tertiary center from Romania reported threatening data since it was stated that over 35% of isolates were MDR with a mortality rate of 24%, and among these, over 60% were *E. coli*. When it comes to extensive drug-resistant (XDR) and pan drug-resistant isolates, *Klebsiella* spp. seemed to take the front-runner position, but its overall amount was below 10%.[14] Conversely, in our study, *Klebsiella* spp. took all first lines for all categories with an MDR rate of 10.4%. For *E. coli*, this rate was nearly 10-fold below that may indicate an epidemiologic shift towards drug-resistant *Klebsiella* spp. Miftode et al.,[14] also stated antibiotic consumption ratios, which indicates "the fear factor," that in case of any encounter to ESBL or DTR cases, clinicians usually preferred advanced treatments like carbapenems. Interestingly, there is a wide spectrum of DTR-case variance, since the results of the studies Miftode et al.[14] (7% of all isolates, mostly *Klebsiella* spp.) and Gianella et al,[15] indicated high numbers of DTR cases from Italy (11% of all isolates, mostly *Klebsiella* spp.), while researchers from France, Hungary, and the USA stated a much lower prevalence (max 1%).[11,14–17]

Studies on pregnant women, childs, and adolescents generally show slight differences in epidemiology and AMR. In a wide meta-analysis of Bryce et al.,[18] in *E. coli*, high resistance rates in first-line β-lactam antibiotics (over 60%), and relatively lower rates to fluoroquinolones (26.8%) and nitrofurantoin (17%) can be observed, alongside with an inference that previous antibiotic usage was a predisposing factor for AMR. They noted that Türkiye had the highest ampicillin resistance isolates (67%) among OECD countries.[18] Although there was not any data on ampicillin in our study, such high rates can be estimated from AMR data of other β-lactam antibiotics. Studies like Hanna–Wakim et al.[19] Also found additional independent risk factors for AMR in pediatric age groups, such as vesicoureteral reflux. Asian and African data on pregnant women actually did not show epidemiologic differences, however, higher fluoroquinolone and nitrofurantoin resistance along with relatively lower β-lactam resistance were noticeable.[20] This picture is slightly different in American data, with lower fluoroquinolone and nitrofurantoin resistance, which we believe that it is actually concordant with antibiotic consumption habits.[2] Turkish pediatric data were strictly concordant with Eastern European data, and indicated similarly, serious rates of β-lactam resistance, fluoroquinolone, and sulfamethoxazole/trimethoprim resistance.[21–25] Our data were not divided into age groups but in general, compatible levels of AMR were observed.

There were some limitations of this study. First, we could not reach the data before 2017 because of hospital software changes. Furthermore, it was unable to discriminate resistance ratios according to types of clinics, especially ICUs. The difference in AMR between in- and out-patients was out of the scope of our study, however, there were only a few isolates (n=31) out of *E. coli* and *Klebsiella* species. Among these two species, the major difference was observed in resistance to trimethoprim-sulfamethoxazole in outpatients, which was 22.2% and 27.8% for *E. coli* and *Klebsiella* species, respectively. Resistance to amoxicillin–clavulanic acid was over 30% and resistance to cephalosporins was over 25% in outpatients, generally. As expected, carbapenem resistance in *Klebsiella* species was significantly lower in outpatients (4.8%), of whom the majority had a urinary catheter (elders, etc.) (92.3%). Even though significant changes were observed in *Proteus* and *Enterobacter* spp. for carbapenems, the sample sizes were too low to make a meaningful comment. *Morganella* spp. and other species had the same sample size issue, which prevented to make the statistical evaluation. In addition, cefepime resistance in *Enterobacter* spp. did not show any significant difference, however, amoxicillin-clavulanic acid resistance showed a statistically decreasing trend. On the other hand, we believe this condition is because of isolated species since *Enterobacter cloacae* complex generally shows resistance to this antibiotic and in time, different *Enterobacter* spp. were isolated and

their resistance profiles were also reported. The lack of resistance data on nitrofurantion is another issue since it was not able to obtain from hospital software. Colistin resistance could not also be tested, since it requires broth microdilution method only. Acquired AmpC β-lactamase screening could not be interpreted due to the lack of cefoxitin susceptibility results in panel; however, it is assumed that it is below 30% since it is observed fewer than ESBL in Europe.[26] Finally, we could not reach antibiotic consumption data of our area to compare with resistance ratios.

CONCLUSION

Antibiotic consumption is strongly related to AMR. In the multi-nationality OECD report, Türkiye had a bad position on AMR but recently achieved limited success in the fight against it.[27] We believe, these regional differences in terms of AMR clearly show a condition, that "microbiology and/or healthcare" is not the only way to fight, the socioeconomic status of the countries, health-care policies, agricultural interventions, etc. are all major factors, which must be considered while determining policies.

Statement

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Ethics Committee Approval: The Balıkesir University Faculty of Medicine Clinical Research Ethics Committee granted approval for this study (date: 21.10.2020, number: 2020/190).

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REFERENCES

1. Klein RD, Hultgren SJ. Urinary tract infections: Microbial pathogenesis, host–pathogen interactions and new treatment strategies. Nat Rev Microbiol 2020;18:211–26.
2. Sanchez GV, Babiker A, Master RN, Luu T, Mathur A, Bordon J. Antibiotic resistance among urinary isolates from female outpatients in the United States in 2003 and 2012. Antimicrob Agents Chemother 2016;60:2680–3.
3. Okarska-Napierała M, Wasilewska A, Kuchar E. Urinary tract infection in children: Diagnosis, treatment, imaging–Comparison of current guidelines. J Pediatr Urol 2017;13:567–73.
4. Kang CI, Kim J, Park DW, Kim BN, Ha US, Lee SJ, et al. Clinical practice guidelines for the antibiotic treatment of community-acquired urinary tract infections. Infect Chemother 2018;50:67–100.
5. Nicolle LE, Gupta K, Bradley SF, Colgan R, DeMuri GP, Drekonja D, et al. Clinical practice guideline for the management of asymptomatic bacteriuria: 2019 update by the Infectious Diseases Society of America. Clin Infect Dis 2019;68:e83–110.
6. Bonkat G, Bartoletti R, Bruyère F, Cai T, Geerlings SE, Köves B, et al; European Association of Urology. EAU Guidelines on Urological Infections. Available at: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Urological-Infections-2022.pdf. Accessed Feb 23, 2023.
7. Aykan SB, Ciftci IH. Antibiotic resistance patterns of *Escherichia coli* strains isolated from urine cultures in Turkey: A meta-analysis. Mikrobiyol Bul [Article in Turkish] 2013;47:603–18.
8. Bassetti M, Garau J. Current and future perspectives in the treatment of multidrug-resistant gram-negative infections. J Antimicrob Chemother 2021;76(Suppl 4):iv23–37.
9. European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 9.0. Available at: https://www.eucast.org. Accessed June 15, 2021.
10. Frieri M, Kumar K, Boutin A. Antibiotic resistance. J Infect Public Health 2017;10:369–78.
11. Gajdács M, Bátori Z, Ábrók M, Lázár A, Burián K. Characterization of resistance in gram-negative urinary isolates using existing and novel indicators of clinical relevance: A 10-year data analysis. Life 2020;10:16.
12. Gajdács M, Ábrók M, Lázár A, Burián K. Comparative epidemiology and resistance trends of common urinary pathogens in a tertiary-care hospital: A 10-year surveillance study. Medicina 2019;55:356.
13. Hrbacek J, Cermak P, Zachoval R. Current antibiotic resistance trends of uropathogens in central Europe: Survey from a tertiary hospital urology department 2011–2019. Antibiotics 2020;9:630.
14. Miftode IL, Pasare MA, Miftode RS, Nastase E, Plesca CE, Lunca C, et al. What doesn't kill them makes them stronger: The ımpact of the resistance patterns of urinary enterobacterales isolates in patients from a tertiary hospital in eastern Europe. Antibiotics 2022;11:548.
15. Giannella M, Bussini L, Pascale R, Bartoletti M, Malagrinò M, Pancaldi L, et al. Prognostic utility of the new definition of difficult-to-treat resistance among patients with gram-negative bloodstream infections. Open Forum Infect Dis 2019;6:ofz505.
16. Diallo OO, Baron SA, Dubourg G, Chaudet H, Halfon P, Camiade S, et al. Major discrepancy between factual antibiotic resistance and consumption in south of France: Analysis of 539,037 bacterial strains. Sci Rep 2020;10:18262.
17. Kadri SS, Adjemian J, Lai YL, Spaulding AB, Ricotta E, Prevots DR, et al. Difficult-to-treat resistance in gram-negative bacteremia at 173 US hospitals: Retrospective cohort analysis of prevalence, predictors, and outcome of resistance to all first-line agents. Clin Infect Dis 2018;67:1803–14.
18. Bryce A, Hay AD, Lane IF, Thornton HV, Wootton M, Costelloe C. Global prevalence of antibiotic resistance in paediatric urinary tract infections caused by *Escherichia coli* and association with routine use of antibiotics in primary care: Systematic review and meta-analysis. BMJ 2016;352:i939.
19. Hanna-Wakim RH, Ghanem ST, El Helou MW, Khafaja SA, Shaker RA, Hassan SA, et al. Epidemiology and characteristics of urinary tract infections in children and adolescents. Front Cell Infect Microbiol 2015;5:45.
20. Belete MA, Saravanan M. A systematic review on drug resistant urinary tract infection among pregnant women in developing countries in Africa and Asia; 2005–2016. Infect Drug Resist 2020;13:1465–77.

21. Catal F, Bavbek N, Bayrak O, Karabel M, Karabel D, Odemis E, et al. Antimicrobial resistance patterns of urinary tract pathogens and rationale for empirical therapy in Turkish children for the years 2000–2006. Int Urol Nephrol 2009;41:953–7.
22. Samancı S, Çelik M, Köşker M. Antibiotic resistance in childhood urinary tract infections: A single-center experience. Turk Pediatri Ars 2020;55:386–92.
23. Idil N, Deniz Candan E, Yousefi Rad A. A retrospective study on urinary tract infection agents isolated from children and their antibiotic susceptibility. Hacettepe J Biol Chem 2020;48:265–74.
24. Cag Y, Haciseyitoglu D, Ozdemir AA, Cag Y. Antibiotic resistance and bacteria in urinary tract infections in pediatric patients. Medeni Med J 2021;36:217–24.
25. Demir M, Kazanasmaz H. Uropathogens and antibiotic resistance in the community and hospital-induced urinary tract infected children. J Glob Antimicrob Resist 2020;20:68–73.
26. European Committee on Antimicrobial Susceptibility Testing. EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance. Available at: https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Resistance_mechanisms/EUCAST_detection_of_resistance_mechanisms_170711.pdf. Accessed March 3, 2023.
27. Isler B, Keske Ş, Aksoy M, Azap ÖK, Yilmaz M, Yavuz SŞ, et al. Antibiotic overconsumption and resistance in Turkey. Clin Microb Infect 2019;25:651–3.