Original Investigation / *Özgün Araştırma*

DOI: 10.5578/ced.20239702 • *J Pediatr Inf 2023;17(3):e160-e165*

Antibiotic Resistance Rates of *Klebsiella pneumoniae* Strains Isolated from Urine Culture: A Five-Year Analysis

İdrar Kültüründen İzole Edilen Klebsiella Pneumoniae'nın Yıllara Göre Antibiyotik Direnç Değişimi

Harun Yıldız(İD), Aslı Çelebi Tayfur(İD)

Clinic of Pediatrics, Keçiören Training and Research Hospital, Ankara, Türkiye

Cite this article as: Yıldız H, Çelebi Tayfur A. Antibiotic resistance rates of *Klebsiella pneumoniae* strains isolated from urine culture: A five-year analysis. J Pediatr Inf 2023;17(3):e160-e165.

Abstract

Objective: The aim is to determine the frequently encountered microorganisms in urinary tract infections (UTIs) in children in our region, their antibiotic sensitivity and resistance patterns, and based on our findings, to identify empirical antibiotic treatment options for our region.

Material and Methods: Urine culture results and antibiotic susceptibility profiles of pediatric patients who were diagnosed and treated for urinary tract infections at Ankara Keçiören Training and Research Hospital Pediatric Clinic between the years 2015 and 2020 were retrospectively evaluated. Statistical analysis using the SPSS program was conducted to determine whether there was a significant relationship between resistance changes and the patient's complaints, symptoms, and demographic characteristics.

Results: A total of 416 cases (female/male= 246/170) were included in the study. Among the cases, 295 (70.9%) had cystitis, 107 (25.7%) had acute pyelonephritis, and 14 (0.2%) were diagnosed with urosepsis. Additionally, 31 cases (7.4%) had recurrent urinary tract infections. Among the patients, 43 (10.3%) showed no resistance to any antibiotics in urine culture antibiotic sensitivity tests, while 139 (33.4%) cases had resistance to one antibiotic, 169 (40.6%) cases had resistance to 2-5 antibiotics, and 65 (15.6%) cases had resistance to >5 antibiotics. In extended-spectrum beta-lactamase (ESBL) resistance, a statistically significant difference was observed especially in the year 2019 (p< 0.001), and this difference was prominent in patients with urogenital anomalies and/or vesicoureteral reflux.

Conclusion: *Klebsiella pneumoniae* has developed statistically significant resistance over the years, particularly against cephalosporins and many other types of antibiotics. The presence of urogenital anomalies like VUR is a significant risk factor for the development of resistance.

Keywords: Urinary tract infection, *Klebsiella pneumoniae*, antibiotic resistance

Öz

Giriş: Bölgemizdeki çocuklarda idrar yolu enfeksiyonlarında (İYE) sık rastlanan mikroorganizmalar, bunların antibiyotik duyarlılığı ve direnç paternlerinin saptanması ve bulgularımıza göre bölgemiz için ampirik antibiyotik tedavi seçeneklerinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: 2015-2020 yılları arasında Ankara Keçiören Eğitim ve Araştırma Hastanesi Pediyatri Kliniğinde idrar yolu enfeksiyonu tanısıyla takip ve tedavi edilen çocuk hastaların, idrar kültür sonuçları ve antibiyogramları retrospektif değerlendirildi. Direnç değişimleri ile hastanın şikayet, semptom ve demografik özellikleri arasındaki ilişkinin SPSS programıyla istatistiksel olarak anlamlı olup olmadığına bakıldı.

Bulgular: Çalışmaya 416 olgu (kız/erkek= 246/170) dahil edildi. Olguların 295 (%70.9)'inde sistit, 107 (%25.7)'sinde akut piyelonefrit ve 14 (%0.2)'ünde ürosepsis tanısı mevcuttu. Ayrıca olguların 31 (%7.4)'inde tekrarlayan İYE vardı. Hastaların 43 (%10.3)'ünün idrar kültürü antibiyotik duyarlılık testlerinde hiçbir antibiyotiğe direnç bulunmazken, 139 (%33.4) olguda bir tane antibiyotiğe, 169 (%40.6) olguda 2-5 antibiyotiğe ve 65 (%15.6) olguda >5 antibiyotiğe karşı direnç saptandı. Genişletilmiş spektrumlu beta-laktamaz (GSBL) direncinde, yıllar arasında özellikle 2019 senesinde istatistiksel anlamlı fark saptandı (p< 0.001) ve bu fark ürogenital anomalisi olan ve/veya vezikoüretral reflüsü olan hastalarda belirgindi.

Sonuç: Başta sefalosporinlere karşı olmak üzere birçok antibiyotik türüne karşı *Klebsiella pneumoniae* yıldan yıla istatistiksel olarak anlamlı direnç geliştirmiştir. VUR gibi üregenital anomalilerin olması direnç gelişimi için anlamlı bir risk faktörüdür.

Anahtar Kelimeler: İdrar yolu enfeksiyonu, *Klebsiella pneumoniae*, antibiyotik direnci

Correspondence Address/Yazışma Adresi

Harun Yıldız

Keçiören Eğitim ve Araştırma Hastanesi,
Pediyatri Kliniği,
Ankara-Türkiye

E-mail: harunyildiz14@gmail.com

Received: 01.11.2022 **Accepted:** 05.01.2023 **Available Online Date:** 08.09.2023

Introduction

Urinary tract infection is the presence of significant bacteriuria and pyuria in a symptomatic child (1). Urinary tract infections are the second most common disease in children after upper respiratory tract infections. These infections are sometimes symptomatic and sometimes asymptomatic. Causative agents of UTIs are bacteria found especially in the colon. *Escherichia coli*, *Klebsiella*, *Proteus*, *Enterococcus*, *Pseudomonas* and *Enterobacter* spp. of the *Enterobacteriaceae* family are the most frequently isolated bacterial species in UTIs. Today, in the current treatment approach, empirical antibiotic therapy is started without waiting for the urine culture result, which can lead to ineffective treatment. Both ineffective empirical treatments and the use of unnecessary or inappropriate doses and duration of antibiotics increase antibiotic resistance rates, which cause difficulties in choosing empirical treatment in UTI. Failure to initiate appropriate antibiotic therapy within the first 48 hours, especially in children under two years of age with febrile UTI, may cause renal parenchymal damage, recurrent acute pyelonephritis infections, hypertension, proteinuria, and chronic kidney failure. Therefore, antibiotic susceptibility studies should be considered when planning empirical treatment in UTI.

The most common cause of end-stage renal disease in our country is chronic pyelonephritis, and this irreversible mortal complication is a parameter that shows how important effective treatment is (2,3). In addition, *K. pneumoniae*, which we investigated in our study, can produce ESBL by acquiring plasmid-mediated genes and gain resistance to many antibiotics. Therefore, it may cause complications (4).

Both the prevalence of UTIs in our country and the severity of complications make effective antibiotic selection and regional antibiotic resistance studies even more important. In our study, it was aimed to determine the antibiotic resistance change of *K. pneumonia*, one of the most frequently encountered microorganism in urinary tract infections in children in our region, by years and to determine empirical antibiotic treatment options for our region in the light of results.

Materials and Methods

Demographic characteristics, symptoms, clinical findings, laboratory findings, urinary system imaging results, and other accompanying diseases were reviewed retrospectively in children aged 0-18 years, who were admitted to Ankara Keçiören Training and Research Pediatrics Clinic with symptoms and signs of UTI and with positive nitrite, leukocyturia and/or bacteriuria in urine analysis and *K. pneumoniae* growth in urine culture between 2015 and 2020. Colony growth of ≥100.000 cfu/mL in urine culture taken by sterile bag, midstream or capture method, ≥1 bacteria in urine culture taken by suprapubic aspiration, and ≥50.000 cfu/mL in urine culture taken with transurethral catheter were considered significant (5). The growth of two different microorganisms in the urine culture was accepted as contamination (6).

The percentages of resistance to antibiotics in antibiogram results were compared according to years and it was checked whether there was a statistically significant change in resistance. In addition, the effect of the presence of additional urological anomaly, age and sex on antibiotic resistance was also examined.

Sterile urine samples taken from the patients were quantitatively inoculated on 5% sheep blood agar and eosin methylene blue (EMB) agar media using 0.01 µL standard loop at the Health Sciences University Ankara Keçiören Training and Research Hospital Microbiology Laboratory and were incubated for 24-48 hours in an oven at 37°C. Pure colonies evaluated as gram-negative were passaged into triple sugar iron (TSI), Simmon's citrate agar, urea, indole, and action media and were identified according to fermentation of lactose and other sugars, indole production, urea hydrolysis and citrate use. Identification of strains that could not be identified by this method was performed with the VITEK 2 Compact (bioMerieux, France) device in accordance with the manufacturer's instructions. Antibiotic susceptibilities were evaluated on Mueller-Hinton agar by Kirby-Bauer disc diffusion method and were evaluated in accordance with the data of the European Committee on Antimicrobial (7).

Statistical Analysis

Statistical analysis was prepared with SPSS 22.0 (Statistical Program Social Sciences) package program. First, in the evaluation of the data, the demographic characteristics of the cases included in the study, urinary tract infection types, recurrent urinary tract infections, complaints and symptoms, urological diseases, radiological imaging results, BUN, creatinine and CRP results, and their distribution of resistance to antibiotics were given. Then, the frequency and percentage of the patients' resistance to antibiotics were evaluated according to their year of presentation, sex, age, clinical and urological findings, USG and voiding cystourethrography, and the results were compared using chi-square, Yates correction or Fisher's exact test. In addition, the results of sex, year of admission, urological disease and vesicoureteral reflux (VUR) rates according to ESBL were evaluated with frequency and percentage, and the results were compared using chi-square, Yates correction or Fisher's exact test. In terms of years of admission, the results of the determination of the change in the resistance status according to the applied antibiotics were also evaluated with their frequency and percentages and were compared using the chi-square, Yates correction or Fisher's exact test. All statistical calculations were evaluated at 95% confidence interval and at $p< 0.05$ significance level.

Results

Of the 416 cases included in the study, 246 (59.1%) were females and 170 (40.9%) were males (F/M= 1.44). Of the cases, 14 (3.4%) were in the neonatal period, 30 (7.2%) were younger than one year, 196 (47.1%) were in the 1-5 years age range, and 176 (42.3%) were older than five years. Eighty-seven (20.9%) patients were admitted in 2015, 104 (25%) in 2016, 83 (20%) in 2017, 64 (15.4%) in 2018, and 78 (18.8%) in 2019. Cystitis was diagnosed in 295 (70.9%) cases, acute pyelonephritis in 107 (25.7%) and urosepsis in 14 (0.2%) cases. Thirty-one (7.4%) of the cases had a history of recurrent UTI.

When comorbidities of the patients were investigated, 112 of the cases were evaluated with urinary USG and three with MR-urography. Urinary cystourethrography was performed in 43 patients, and static kidney scintigraphy (TcDMSA) was performed in 28 patients. Radiological imaging findings were normal in 391 (94.5%) cases. VUR was detected in 43 cases (10.33%). Of the cases detected to have VUR, 23 had grade I VUR, 13 had grade II VUR, five had grade III VUR and two had Grade IV VUR.

Renal parenchymal scar was found in five cases (1.2%), urinary stones in five cases (1.2%), ureteropelvic stenosis in three cases (0.7%), hydronephrosis in three cases (0.7%), nephrocalcinosis in three cases (0.7%), diverticula in the bladder in three cases (0.7%), double collecting system in two cases (0.5%), multicystic dysplastic kidney in one case (0.2%), horseshoe kidney in one case (0.2%), polycystic kidney in one case (0.2%), renal hypoplasia in one case (0.2%), and renal hypoplasia in one case. One patient only had one kidney (0.2%) and one patient had nutcracker syndrome (0.2%).

In laboratory examination of the patients, elevated serum creatinine levels were found in seven (1.7%) cases, elevated blood urea levels in six (1.4%) cases, and elevated serum C-reactive protein levels in 33 (4.9%) cases.

While no antibiotic resistance was found in the antibiotic susceptibility tests of 43 (10.3%) of the 416 subjects included in the study, 139 (33%) had one antibiotic, 169 (40.6%) had 2-5 antibiotics and 65 (15.6%) had >5 antibiotics resistance.

Table 1. Change in antibiotic resistance between 2015 and 2020

	2015		2016		2017		2018		2019		
	(+) n/N	(%)	(+) n/N	(%)	(+) n/N	(%)	(+) n/N	(%)	(+) n/N	(%)	p
Ampisilin	77/87	88.5%	84/104	80.8%	58/83	69.9%	30/64	46.9%	64/78	82.1%	**<0.001**
Amikacin	2/79	2.5%	1/96	1.0%	0/83		0/57		0/77		0.384
AKA	21/83	25.3%	29/99	29.3%	14/79	17.7%	9/60	15.0%	18/76	23.7%	0.206
SAM	19/62	30.6%	22/78	28.2%	3/65	4.6%	0/50		2/49	4.1%	**<0.001**
Gentamycin	15/86	17.4%	6/101	5.9%	2/79	2.5%	0/57		1/70	1.4%	**<0.001**
Imipenem	0/79		0/96		0/75		0/56		0/67		-
Levofloxacin	0/60		0/77		0/56		0/37		0/52		-
Meropenem	0/84		0/89		0/77		0/59		0/72		-
Nitrofurantoin	25/81	30.9%	38/89	42.7%	19/74	25.7%	6/56	10.7%	19/67	28.4%	**0.001**
Norfloxacin			3/88	3.4%	0/73		0/56		0/66		0.054
Ofloxacin	5/58	8.6%	3/75	4.0%	2/54	3.7%	0/35		0/50		0.142
PİP	14/63	22.2%	6/79	7.6%	0/65		0/50		0/49		**<0.001**
PTZ	3/81	3.7%	4/97	4.1%	0/76		0/57		0/68		0.085
Cefazolin	26/86	30.2%	18/102	17.6%	13/79	16.5%	16/59	27.1%	30/75	40.0%	**0.003**
Cefepime	8/79	10.1%	7/88	8.0%	11/72	15.3%	6/54	11.1%	21/59	35.6%	**<0.001**
Cefoxitin	9/78	11.5%	9/87	10.3%	11/71	15.5%	7/52	13.5%	22/56	39.3%	**<0.001**
Cefotaxime	6/80	7.5%	7/88	8.0%	10/71	14.1%	5/52	9.6%	19/56	33.9%	**<0.001**
Ceftazidime	7/64	10.9%	6/81	7.4%	10/66	15.2%	4/50	8.0%	20/48	41.7%	**<0.001**
Ceftriaxone	7/83	8.4%	7/89	7.9%	9/74	12.2%	4/55	7.3%	19/65	29.2%	**<0.001**
Cephalothin	9/64	14.1%	8/79	10.1%	10/57	17.5%	8/37	21.6%	20/50	40.0%	**<0.001**
Cefuroxime	10/65	15.4%	10/80	12.5%	10/58	17.2%	8/37	21.6%	21/49	42.9%	**0.002**
Ciprofloxacin	2/76	2.6%	2/85	2.4%	0/69		0/51		0/63		0.431
TMP/SMX	17/86	19.8%	23/101	22.8%	19/78	24.4%	19/56	33.9%	42/68	61.8%	**<0.001**

AKA: Amoxicillin clavulanic acid, SAM: Ampisilin sulbactam, PİP: Piperacillin, PTZ: Piperacillin tazobactam, TMP/SMX: Trimethoprim-sulfamethoxazole.

Table 2. Number and rate of extended spectrum beta-lactamase (ESBL) positive *K. pneumonia* between 2015 and 2020

Years	Positive number	Positive %
2015	11	(17.7%)
2016	12	(19.4%)
2017	11	(17.7%)
2018	7	(11.3%)
2019	21	(33.9%)

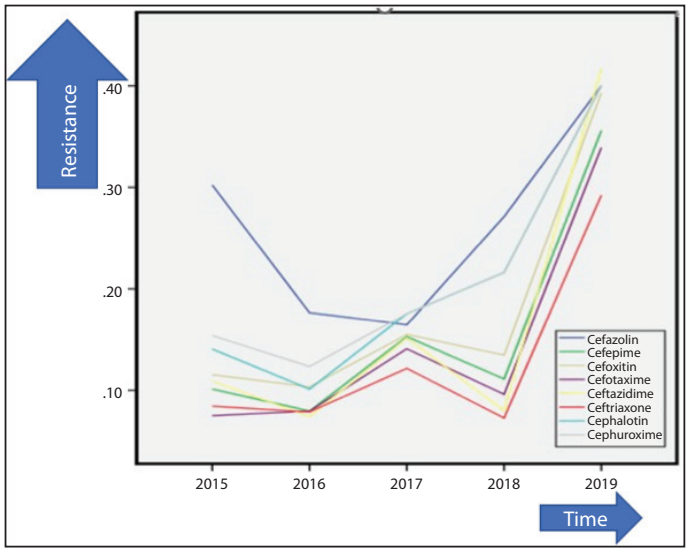

Table 3. Change in cephalosporin resistance over the years.

As seen in Table 1, a statistically significant difference was found in the rates of resistance development against drugs in *K. pneumoniae* including resistance to ampicillin (p< 0.001), sulbactam ampicillin (SAM) (p< 0.001), gentamicin (p< 0.001), nitrofurantoin (p< 0.001), piperacillin (PIP) of *K. pneumoniae* by year of application (p< 0.001), cefazolin (p< 0.003), cefepime (p< 0.001), cefoxitin (p< 0.001), cefotaxime (p< 0.001), ceftazidime (p< 0.001), ceftriaxone (p< 0.001), cephalothin (p< 0.001), cefuroxime (p< 0.002), and trimethoprim-sulfamethoxazole (TMP/SXT) (p< 0.001). While there was a decrease in the resistance rates against ampicillin, SAM, gentamicin, nitrofurantoin and PIP by years, an increase was observed in the resistance rates against cefazolin, cefoxitin, cephalothin, cefuroxime, cefotaxime, ceftazidime, ceftriaxone, cefepime and TMP-SXT. There was no statistically significant difference in the resistance rates of amoxicillin clavulanate (AKA), amikacin, levofloxacin, norfloxacin, ofloxacin, ciprofloxacin, piperacillin tazobactam, imipenem and meropenem by years.

Table 2 shows the changes in extended-spectrum beta-lactamase (ESBL) resistance rates between years. There was a statistically significant increase in ESBL resistance, especially in 2019 (p< 0.001).

As can be seen in Table 3, due to the increase in ESBL resistance, a significant increase in resistance to cephalosporins was observed, especially in 2019.

No statistically significant correlation was observed between ESBL and sex, but ESBL resistance was found to be statistically significantly higher in cases with VUR (p< 0.001) and other urological diseases (p< 0.04) as seen in Table 4.

As seen in Table 5, as a result of univariate logistic regression analysis, anatomical pathology on USG (OR= 4.663, 95% CI= 2.659-8.180, p≤ 0.001), urological disease (OR= 2.765, 95% CI= 1.146-6.674, p= 0.024), presence of recurrent UTI (OR= 2.563, 95% CI= 1.120-5.865, p= 0.026), and vesicourethral reflux (OR= 12.613, 95% CI= 6.298-25.259, p≤ 0.001) were found to be effective on ESBL resistance. Anatomical pathology on USG increases the risk of ESBL resistance 4663 times, urological disease 2765 times, recurrent UTI 2563 times and vesicourethral reflux 12.613 times. As a result of the univariate logistic regression analysis, the factors with p< 0.25 were included in the multivariate logistic regression analysis. The enter model was applied in multivariate logistic regression analysis. According to the results of multivariate logistic regression analysis and to the results of the established model, VUR (OR= 11.537, 95% CI= 4.249-31.325, p≤ 0.001) was found to be effective on ESBL resistance. Presence of VUR increases the risk of ESBL resistance 11.537 times.

Table 4. Relation between ESBL resistance and sex, VUR and urological disease

		Extendes spectrum beta-lactamase				
		Positive (n= 62)		Negative (n= 354)		
		n	(%)	n	(%)	p
Sex	Male	23	(37.1%)	147	(41.5%)	0.513
	Female	39	(62.9%)	207	(58.5%)	
Urological disease	Absent	54	(87.1%)	336	(94.9%)	**0.040**
	Present	8	(12.9%)	18	(5.1%)	
VUR	Absent	37	(59.7%)	336	(94.9%)	**<0.001**
	Present	25	(40.3%)	18	(5.1%)	

ESBL: Extended spectrum beta lactamase, VUR: Vesicourethral reflux.

Table 5. Results of univariate and multivariate logistic regression analysis regarding all possible factors that could be effective on cases in whom pathological findings were detecetd on CT

	Univarite logistic regression				Multivariate logistic regression			
	Wald	**p**	**OR**	**%95 GA**	**Wald**	**p**	**OR**	**%95 GA**
Age, year	3.070	0.080	0.941	(0.880-1.007)	1.584	0.208	0.952	(0.882-1.028)
Sex (ref: female)	0.427	0.513	1.204	(0.690-2.102)	-	-	-	-
USG	28.839	<0.001	4.663	(2.659-8.180)	1.622	0.203	1.716	(0.747-3.942)
Presence of urological disease	5.121	**0.024**	2.765	(1.146-6.674)	0.327	0.567	0.725	(0.241-2.181)
Recurrent UTI	4.962	**0.026**	2.563	(1.120-5.865)	1.431	0.232	0.518	(0.176-1.523)
UTI type (ref: cystititis)	1.723	0.189	2.521	(0.623-10.023)	0.425	0.514	1.717	(0.338-8.713)
VUR	51.169	**<0.001**	12.613	(6.298-25.259)	23.028	**<0.001**	11.537	(4.249-31.325)

Wald: Test statistics, OR: Hazard radio.
Statistically significant p-values are in bold.
USG: Ultrasonography, UTI: Urinary tract infection, VUR: Vesicouretral reflux.

Discussion

There may be differences in patient diversity in each geographical region, and antibiotic resistance rates vary depending on factors such as patient compliance with treatment and previous antibiotic choices. For this reason, it is necessary to conduct regional studies on antibiotic resistance rates in order to prevent the development of resistance.

In this study, the rate of resistance to nitrofurantoin was found to be 25.7%. In the literature, the resistance rate of *K. pneumoniae* to nitrofurantoin has been reported between 10-23% (8). The fact that the drug is prescribed frequently, not used properly and preferred in the treatment of long-term UTI prophylaxis explains the high rate of resistance to nitrofurantoin in this study. Determining the drug to be used in UTI prophylaxis according to the results of frequently updated regional antibiotic resistance studies will both increase the efficacy of the treatment and decrease resistance rates.

The resistance rates of patients with urogenital anomalies to cephalosporins (cefepime, cefoxitin, cefuroxime, cephalothin, cefotaxime, ceftazidime and ceftriaxone) were found to be statistically significantly higher than patients with uncomplicated UTI ($p< 0.04$). Again, the rates of resistance to piperacillin, piperacillin/tazobactam, cephalosporins and TMP-SXT in patients with VUR were found to be statistically significantly higher than patients without VUR ($p< 0.001$). It is known that the presence of urogenital anomaly and VUR increases the risk of UTI (9,10). Observation of high cephalosporin resistance in patients with urogenital anomaly or VUR who have frequent UTIs in our study, and similarly, higher cephalosporin resistance in patients with recurrent UTIs emphasize the importance of the role of wrong or ineffective treatment approaches in the development of resistance. It was also an expected result that more resistance was observed in VUR patients against TMP-SMX, one of the most frequently used agents in our region for antibiotic prophylaxis. It is necessary to carry out studies on the effectiveness of regional prophylaxis in these patients to prevent complications.

In our study, it was determined that the resistance to cephalosporins increased significantly in 2019, and there was a statistically significant difference in the rate of resistance development between years. Cephalosporins are the agents of choice for both upper respiratory tract infections and pneumonias, which explains antibiotic resistance. Failure to choose broad-spectrum cephalosporins in the selection of antibiotics in upper respiratory tract infections may reduce these resistance rates. Again, the increase in resistance in 2019 shows that there can be a significant increase in resistance in a short time like a year. Therefore, antibiotic resistance studies should be performed at frequent intervals.

In our study, the rate of infection with ESBL (+) *K. Pneumoniae* was observed significantly in 2019, which correlated with a statistically significant increase in resistance to cephalosporins. In our country, third generation cephalosporins are preferred for parenteral treatment in children hospitalized with bacterial infections such as upper respiratory tract infection, lower respiratory tract infection, urinary tract infection, and meningitis (11). Cephalosporin group drugs are frequently prescribed to outpatients (11). For this reason, all branches should avoid broad-spectrum antibiotics in the first step, and antibiotic studies should be carried out at least not in the branch but hospital-wide.

Reducing unnecessary hospitalization is another factor that will reduce antibiotic resistance. Many studies indicate that the efficacy of oral or intravenous therapy is similar. The criterion that will determine whether a patient will receive inpatient or outpatient treatment is the patient's clinic. If the patient is incompatible with oral therapy, vomits, has a complicated UTI, is dehydrated or has a septic appearance, inpatient

IV therapy will be appropriate (5). In a similar regional study, EBSL positivity rate has been found to be 18%, and oral gentamicin and amikacin treatment for *Klebsiella*-induced UTI has been reported as a suitable option for outpatient treatment in children with good oral intake. Again, in the same study, carbapenem sensitivity has been found to be 100% similar to our study (12). However, it has been reported in the literature that serious resistance to carbapenems can develop with the effect of increased carbapenemases (13).

Klebsiella pneumoniae infections are also an important cause of hospital-acquired infections. It has been reported in the literature that biofilm-forming bacteria such as *Klebsiella* develop antibiotic resistance more rapidly (14). Measures to be taken to prevent hospital-acquired infections will also reduce the development of resistance against *Klebsiella pneumoniae*.

It has also been reported in the literature that the efficacy of blueberry in the prophylaxis of recurrent UTIs is similar to trimethoprim and is safe (5). If prophylaxis can be done with non-antibiotic agents, it is another alternative that can reduce resistance especially to antibiotics used in prophylaxis. However, more work is needed in this regard.

The shortcomings of our study are as follows: Since there was no pediatric intensive care unit in our hospital and there were no hospital-acquired *Klebsiella* infections in our study, the resistance rates may have been found to be lower than they were. The absence of resistance to imipenem and meropenem in our study was attributed to the lack of pediatric intensive care in our hospital, the fact that most of the patients included in our study did not have a long-term hospitalization history, and urethral catheterization was not applied. In addition, the fact that carbapenems are not the first choice in empirical treatment explains the absence of resistance to carbapenems and shows that resistance rates may decrease if empirical and unnecessary use of cephalosporins is avoided.

Conclusion

Significant development of resistance against *Klebsiella pneumoniae* has been observed over the years. Along with the increase in ESBL resistance, the increase in resistance especially to cephalosporin group antibiotics was evident. ESBL resistance was more common in patients with VUR and urogenital anomalies. Conducting local antibiotic susceptibility studies and updating these results periodically will guide the effective treatment of urinary tract infections in children and the choice of empirical antibiotics.

Ethics Committe Approval: This study was approved by Ankara Keçiören Training and Research Hospital Ethics Committee (Decision no: 2115, Date: 12.08.2020).

Informed Consent: Patient consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - AÇT, HY; Design- AÇT, HY; Supervision - AÇT, HY; Resource- HY; Data Collection and/or Processing - HY; Analysis and/ or Interpretation - HY; Literature Search- HY; Writing - HY; Critical Review - AÇT, HY.

Conflict of Interest: All authors declare that they have no conflicts of interest or funding to disclose.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. *Shaikh N, Morone NE, Lopez J, Chianese J, Sangvai S, D'Amico F, et al. Does this child have a urinary tract infection? JAMA 2007;298(24):2895904. https://doi.org/10.1001/jama.298.24.2895*
2. *Sirin A, Emre S, Alpay H, Nayir A, Bilge I, Tanman F. Etiology of chronic renal failure in Turkish children. Pediatr Nephrol 1995;9:549-52. https://doi.org/10.1007/BF00860926*
3. *Mir S. Recurrent urinary tract infection in Turkey: Epidemiology and prevalance. In First Annual Aegean Pediatric Nephrology Seminars. 16-17 May 1994.*
4. *French GL, Shannon KP, Simmons N. Hospital outbreak of Klebsiella pneumoniae resistant to broad-spectrum cephalosporins and beta-lactam-beta-lactamase inhibitor combinations by hyperproduction of SHV-5 beta-lactamase. J Clin Microbiol 1996;34(2):358-63. https://doi.org/10.1128/jcm.34.2.358-363.1996*
5. *Döven SS. Çocuklarda idrar yolu enfeksiyonlarına güncel yaklaşım. Mersin Üniv Sağlık Bilim Derg 15(Özel Sayı-1) 21. Mersin Pediatri Günleri Bildiri Kitabı), 7-12.*
6. *Şenel U, Tanrıverdi Hİ. Ürolojik sorunlu pediyatrik hasta grubundaki idrar kültür antibiyogramların değerlendirilmesi. Konuralp Medical Journal 2014;6(3):27-30. https://doi.org/10.18521/ktd.96587*
7. *Matuschek E, Brown DF, Kahlmeter G. Development of the EUCAST disk diffusion antimicrobial susceptibility testing method and its implementation in routine microbiology laboratories. Clin Microbiol Infect 2014;20(4):O255-66. https://doi.org/10.1111/1469-0691.12373*
8. *Li G, Zhao S, Wang S, Sun Y, Zhou Y, Pan X. A 7-year surveillance of the drug resistance in Klebsiella pneumoniae from a primary health care center. Ann Clin Microbiol Antimicrob 2019;18(1):34. https://doi.org/10.1186/s12941-019-0335-8*
9. *Kim W, Lee S, Seo JM. Vesicoureteral reflux increases the risk of urinary tract infection prior to corrective surgery in newborn males with anorectal malformation. Pediatr Surg Int 2020;36(12):1495-500. https://doi.org/10.1007/s00383-020-04761-6*
10. *Nicolle LE. A practical guide to the management of complicated urinary tract infection. Drugs 1997;53(4):583-92. https://doi.org/10.2165/00003495-199753040-00004*
11. *Cosgrove SE, Kaye KS, Eliopoulous GM, Carmeli Y. Health and economic outcomes of the emergence of third-generation cephalosporin resistance in Enterobacter species. Arch Intern Med 2002;162(2):185-90. https://doi.org/10.1001/archinte.162.2.185*
12. *Celep G , Özçelik HB, Güçkan R. İkinci basamak bir sağlık kuruluşunda mikrobiyoloji laboratuvarı ve pediatri kliniği işbirliği. J Contemp Med 2020;10(1):114-21. https://doi.org/10.16899/jcm.603548*
13. *Effah CY, Sun T, Liu S, Wu Y. Klebsiella pneumoniae: An increasing threat to public health. Ann Clin Microbiol Antimicrob 2020;19(1):1. https://doi.org/10.1186/s12941-019-0343-8*
14. *Caneiras C, Lito L, Melo-Cristino J, Duarte A. Community- and hospital-acquired Klebsiella pneumoniae urinary tract infections in Portugal: Virulence and antibiotic resistance. Microorganisms 2019;7(5):138. https://doi.org/10.3390/microorganisms7050138*