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# Antibiotic susceptibility of escherichia coli strains isolates determined as a cause of urinary tract infection in pediatric patients

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**Abstract**

Urinary tract infections (UTIs) are bacterial infections that are most commonly encountered by physicians in all age groups both in the Nasocomial hospital and community acquired hospital. International guidelines are used for the selection of antibiotics. However, it is recommended to adopt the international guidelines into local epidemiological data before using it to select the routine treatment. In this study, it was aimed to determine the antimicrobial susceptibility of Escherichia coli (E.Coli) strains isolated from urinary tract infections in children applied due to urinary system infections and treated accordingly. It was designed to be examined to be raised from 249 children, with sales route design and sale to the pediatric and urinary outpatient clinic between July 1, 2019 and July 1, 2020. 210 patients with n≥105 cfu/ml bacteria. Patients with vesicourethral reflux and neurogenic patients were excluded from the study. At the same time, people who can be displayed in the products that have been in use in the last six months and people who have grown Klebsiella, Proteus mirabilis, Candida and ESBL positive bacteria. 98 cultures included in the study were evaluated The mean age of totally 98 patients including 84 females and 14 males diagnosed with urinary tract infection was 37 (1-192) months. There was a statistically significant difference between each group with respect to age and they were as F:49 month and M: 9 respectively ($p<0.001$). Amoclavin-claviculinate 33.6%, ampicillin 20.4%, cefuroxime 25.5%, trimethoprimsulfamethoxazole (TMP-SMX) 19.4%, ciprofloxacin 7.1%, ceftriaxone 19.3% by disc diffusion and / or automated system tests in 141 isolated E. coli strains, 6.1% and 11.2% nitrofurantoin resistance rates were determined. ESBL was found positive in 7 (4.96%) of 141 E. coli isolated and these patients were excluded from the study. Recently, antibiotics are given empirically before performing urine culture and antibiograms and this situation causes the problem of resistance to widely preferred antibiotics. Cefixime, ampicillin or trimethoprim-sulfamethoxazole can be used as the first option in empirical treatment of pediatric urinary tract infections. However, urine culture and antibiogram should be performed if possible before antibiotics are given. It should not be ignored that the rates of resistance may change over time according to the frequent preference of antibiotics initiated empirically in that region or country.

**Keywords:** Children, urinary tract infections, urine culture, E.coli, antibiotics

## Introduction

Urinary tract infections (UTIs) are bacterial infections that are most encountered by physicians in all age groups both in the hospital environment and outside the hospital [1].

UTI occurs in approximately 3-5% of girls and 1% of boys [2]. The cause of more than 80% of community-acquired UTIs is E. coli, followed by other Enterobacteriaceae members and gram-positive cocci [3]. Recurring urinary tract infections eventually cause kidney damage, and thus hypertension and kidney failure may develop [4].

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Recently, empirical antibiotics treatment is initiated without a urinary culture antibiogram, which causes resistance to commonly used antibiotics [5]. The only cause of antibiotic resistance is not the empirical antibiotic treatment in urinary tract infection, otherwise, every unnecessary antibiotic and even antibiotics used in prophylaxis of urinary tract infection also contribute to the development of resistance.

International guidelines are used for the selection of antibiotics. However, it is recommended to adopt the international guidelines into local epidemiological data before using it to select the routine treatment [6].

## Materials and Methods

The urinary culture results of 249 pediatric patients who were admitted to the pediatric and urology outpatient clinics between

1 July 2019 and 1 July 2020 with suspicion of outpatient urinary tract infection, and whose urine samples were positive, were evaluated retrospectively. The data of 141 children whose urine cultures were positive for E.coli (≥105 cfu/ml) were examined. It was found that the cultures from 7 patients were positive for ESBL. The clean-catch urine samples from children with toilet training, and the urine samples from children without toilet training which were collected in urine bag or taken with a urethral catheter, were cultivated in blood agar and EMB agar and then incubated at 35°C for 18-24 hours. The urine samples were examined in Thoma slide under a microscope before centrifuging and the samples with >10 leukocyte/m3 were considered as pyuria. The identification of all detected microorganisms was performed using conventional biochemical methods as well as AutoSCAN®-4 System (Siemens/ Dade Behring). The finding of ≥103 cfu/mL was considered significant in gram-negative bacteria in terms of growth density. The antibiotic susceptibilities were determined with the disc diffusion method according to "Clinical and Laboratory Standards Institute (CLSI)" standards. Escherichia coli ATCC 25923 was used as a control strain. The double-disc synergy test was performed to show the presence of GSBL in enteric bacteria. The ESBL-producing strains were confirmed by ATB G-5 (bioMeri´eux). The patients who had a recurring UTI, a hospitalization history in the last 6 months, an underlying kidney disease, or a bladder and ureter problem were excluded from the study.

**Statistical Analysis**

The results are presented as mean±SD. The descriptive statistics were calculated using frequencies and percentages.

The crosstabs and Chi-square test was used to compare the categorical parameters. The Mann Whitney U test was used for the comparison of age between two gender. Statistical analysis was carried out with Statistical Package of Social Science (SPSS), version 20.0 (SPSS Inc., Chicago, IL). A p value of <0.05 was considered statistically significant.

Ethics Committee Approval: Approval was obtained for this study from the Umraniye Training and Research Hospital Ethics Committee on 29.04.2021/132.

**Results**

Of 210 patients diagnosed with urinary tract infection, 141 were included in the study. In the study sample consisting of 112 girls and 29 boys, the average age was 22 (1-192) months. There was a significant difference in age between the two groups (G:49 months old and B: 9 months old) (p=0.001).

Of 249 patients whose urinary cultures were positive for bacteria growth (≥105 cfu/ml), 20 had vesicourethral reflux and 12 had neurogenic bladder so that they were excluded from the study. Also, 25 patients were excluded from the study due to hospitalization history caused by an infection in the last six months. Of these 210 patients, 20 had Klebsiella in their cultures, 12 had Proteus mirabilis, 6 had Staphylococcus aureus, 7 had Enterobacter aerogenes, 6 had Candida, 7 had ESBL (%4.96). All of these detected cases were E.coli isolates. The cultures of 141 patients included in the study were taken into evaluation.

The most common presenting symptoms (in children who can express themselves) were urinary burning (75.5%), frequent urination (66.8%), fever (30%) and stomach pain (25%). The small children mainly had a loss of appetite and discomfort. The antibiotic susceptibility rates of isolated E. coli were found as; 66.4% for amoxicillin-clavulanic acid, 79.6% for ampicillin, 74.5% for cefuroxime, 91.9% cefotaxime, 74.5% for cefixime, 80.7% for ceftriaxone, 88.8% for cefoxitin, 89.8 for cefepime, 92.9% for gentamicin, 100% for amikacin, 92.9% for ciprofloxacin, 88.8% for nitrofurantoin, 80.6 for trimethoprim-sulfamethoxazole, 93.9% for phosphomycine, 99% for piperacillin/tazobactam, 100% ertapenem, 76.5% for aztreonam (Table 1). Amoxicillin-clavulanic acid (33.6%), cefuroxime (25.5%), cefixime (25.5%) and ampicillin (20.4%) were found to be the most resistant antibiotics.

**Table 1.** Antibiotic susceptibility rates

| Fisher's Exact test | Female | Male | P | % |
|---|---|---|---|---|
| Amoxicillin-clavulanate (Sensitive/ Resistance ) | 57/27 | 8/6 | 0.545 | 33.6 |
| Ampicillin | 68/16 | 10/4 | 0.475 | 20.4 |
| Cefuroxime | 62/22 | 11/3 | 1 | 25.5 |
| Cefotaxime | 75/9 | 14/0 | 0.350 | 9.1 |
| Cefixime | 64/20 | 9/5 | 0.339 | 25.5 |
| Ceftriaxone | 67/17 | 12/2 | 1 | 19.3 |
| Cefoxitine | 74/10 | 13/1 | 1 | 11.2 |
| Cefepime | 76/8 | 12/2 | 0.632 | 10.2 |
| Gentamycine | 77/7 | 14/0 | 0.589 | 7.1 |
| Amikacin | 84/0 | 14/0 | - | 0 |
| Ciprofloxacin | 77/7 | 14/0 | 0.589 | 7.1 |
| Nitrofurantoin | 77/7 | 10/4 | 0.049 | 11.2 |
| Trimethoprim-sulfamethoxazole | 66/18 | 13/1 | 0.292 | 19.4 |
| Fosfo | 78/6 | 14/0 | 0.589 | 6.1 |
| Piperacilline_tazobactam | 83/1 | 14/0 | 1 | 1 |
| Ertapenem | 83/0 | 14/0 | 1 | 0 |
| Aztreonam | 64/20 | 11/3 | 1 | 23.5 |

**Discussion**

Urinary tract infections (UTIs) are one of the most common bacterial infections in children and an important cause of hospitalization for them [7].

The causing factors of UTI vary by age and sex. In all periods of life, except for the first three months, girls have more urinary tract infections than boys. After one-year-old, girls are approximately 10-15 times more likely to have UTI than boys [8].

In community-acquired and hospital-acquired (nosocomial) infections, the resistance to various antimicrobial agents has been increasing rapidly. This causes problems in the selection of antibiotics and the efficiency of treatment. The most important resistance mechanism in gram-negative enteric bacteria is the production of beta-lactamase, and approximately 500 types of beta-lactamase have been identified so far [9-11].

A study found that 78.8% of the patients, whose urine samples

were positive, were a girl. In our study, of the patients, whose urine samples were positive, 85.7% were a girl and 14.3% were a boy [12]. In our study, the rates of microorganisms grown in urinary cultures were 46.6% for E.Coli, 9.5% for Kleb.pneumoniae, 5.7% for Proteus, 2.8% for Staf. aureus, 3.3% for Enterobacteria and 2.8% for Candida. We obtained similar results with the study by Yüksek et al. in terms of 2 microorganisms first grown in cultures (57.4% for E. coli and 9.7% for Kleb.pneumoniae) [13]. Differently, the growth of Candida was noted in our study. It was found that these patients had genital candidiasis. Candida infection is seen in the urinary system in the adult age group and in patients who use antibiotics for a long time. In a study with adults, E.coli (57%), coagulase-negative staphylococcus (12%), K.pneumoniae (5%), Enterococcus and Candida spp. (4%) and Staphylococcus aureus (3%) microorganisms were isolated [13]. An important susceptibility factor that is responsible for the dominance of E. coli is the ability to bind to urinary tract urothelium.

A study found that 13 (7.8%) of 165 patients were positive for ESBL (7 E.coli and 6 K.pneumoniae), which was 2 times of the ESBL positive cases in our study [12].

(Also, half of all causative bacteria strains (49.3%) had GSBL positivity, and the ESBL (+) E.coli accounted for 39.4% of all the infections. As stated before, UTI caused by ESBL (+) has become a growing problem around the world [14].

Childhood urinary system infection isolates have ampicillin resistance varying from 40% to 100%, trimethoprim-sulfamethoxazole resistance varying from 27% to 67%. In our study, ampicillin resistance was 20.4%, trimethoprim-sulfamethoxazole resistance was 19.4%, while in the study by Yüksel et al., ampicillin resistance was 61.9% and trimethoprim-sulfamethoxazole resistance was 56.4% [13].

It was thought that the difference might be caused by that the alternatives of these antibiotics are more preferred by physicians. In a study by Erdoğan et al., the antibiotic resistance rates of E.coli strains were found as; 71.7% for ampicillin, 54.3% for trimethoprim-sulfamethoxazole, 43.5% for amoxicillin-clavulanic acid, 21.7% for cefazolin, 15.2% for cefuroxime, 6.5% for nitrofurantoin, 4.3% for cefixime, 4.3% for ceftriaxone, 4.3% for gentamicin, 2.2% for amikacin and 2.2% for ciprofloxacin [3]. While the resistance pattern in patients has been like this about 15 years ago, it has been changed today as a result of changes in drug selection.

Çatal et al. found the antibiotic resistance rates of E.coli strains were 40% for ampicillin and 60% for trimethoprim-sulfamethoxazole, which are similar to our study; however, they found that the resistance has increased over the years, and the resistance to ampicillin reached to 70% after 6 years [15].

In our study, the antibiotic susceptibility rates of isolated E. coli were found as; 66.4% for amoxicillin-clavulanic acid, 79.6% for ampicillin, 74.5% for cefuroxime, 91.9% cefotaxime, 74.5% for cefixime, 80.7% for ceftriaxone, 88.8% for cefoxitin, 89.8 for cefepime, 92.9% for gentamicin, 100% for amikacin, 92.9% for ciprofloxacin, 88.8% for nitrofurantoin, 80.6 for trimethoprim-sulfamethoxazole, 93.9% for phosphomycine, 99% for piperacillin/tazobactam, 100% ertapenem, 76.5% for aztreonam (Table 1). Amoxicillin-clavulanic acid (33.6%), cefuroxime (25.5%), cefixime (25.5%) and ampicillin (20.4%) were found to be the most resistant antibiotics. In the study by Aydemir et al., the susceptibility rates were found as 60.7% for amoxicillin-clavulanic acid, 31.8% for ampicillin, 90.4% for cefuroxime, 95.9% for cefepime, 90.4% for ceftriaxone, 92.5% for gentamicin, 96.6% for amikacin, 91.8% for ciprofloxacin, 94.5% for nitrofurantoin, 45.5 for trimethoprim-sulfamethoxazole, which are similar to our study; however, it was thought that the reason why the susceptibility rates of ampicillin and trimethoprim-sulfamethoxazole were low might be the excessive and unnecessary use to these two agents [16].

The studies conducted in Turkey contain limited information about cefixime. The study by Gökçe et al. reported that the cefixime resistance was 1% [17].

The second- and third-generation oral cephalosporins may be preferred in the empirical treatment of simple cystitis due to their relatively low resistance rates [17]. It was reported that oral cefixime treatment showed similar efficacy to parenteral treatment in preventing renal scar and reduce fever in cases with pyelonephritis [3]. We think that we found the cefixime resistance as 25.5% due to the excessive use of these drugs in recent years as well as the fact that oral cefixime treatment was effective as much as 2nd and 3rd generation cephalosporins as reported by Erdoğan et al.

## Conclusion

Recently, antibiotics are given empirically before performing urine culture and antibiograms and this situation causes the problem of resistance to widely preferred antibiotics. Cefixime, ampicillin or trimethoprim-sulfamethoxazole can be used as the first option in empirical treatment of pediatric urinary tract infections. However, urine culture and antibiogram should be performed if possible before antibiotics are given. It should not be ignored that the rates of resistance may change over time according to the frequent preference of antibiotics initiated empirically in that region or country.

**Conflict of interests**
*The authors declare that there is no conflict of interest in the study.*

**Financial Disclosure**
*The authors declare that they have received no financial support for the study.*

**Ethical approval**
*Approval was obtained for this study from the Umraniye Training and Research Hospital Ethics Committee on 29.04.2021/132.*

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