Causative agents and antibiotic susceptibilities in children with urinary tract infection

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ABSTRACT

Objectives: Nowadays, it has become more difficult treatment of the urinary tract infections because of developing high antibiotic resistance. The aim of this study was to investigate the most common causative microorganisms, their susceptibility to antibiotics in childhood urinary tract infections (UTI).

Materials and methods: In this study, data belonging to urinary culture of 111 children with the diagnosis of UTI at Dicle University Medical School, Department of Pediatrics, throughout 1.5 years.

Results: Of all cases 97 (87.4%) were female and 14(12.6%) were male. The most common complaints of children were dysuria, fever, flank pain and pollakiuria. Isolated microorganisms according to decreasing frequency were E.coli (75.7%), Klebsiella sp (7.2%), Proteus sp (6.3%) and Enterobacter sp (1.8%). The resistance rates against trimethoprim-sulfamethoxazole was 71.3%, ampicillin 82.4%, amoxicillin-clavulanate 54.7% and tetracycline 68.3%, and the least resistance rates were for ceftriaxone (16%) and amikacin (8.1%).

Conclusion: In conclusion, the most common causative agent was E.coli and the highest resistance ratios were against trimethoprim-sulfamethoxazole, ampicillin and amoxicillin-clavulanate in children with UTI that presented in this study. Fewest ratio of resistance was found against amicasin and cephtriaxone. J Microbiol Infect Dis 2011;1(1):17-21.

Key words: Childhood, urinary tract infections, causative organisms, antibiotic sensitivity, resistance

Çocuklarda idrar yolu enfeksiyonu etkenleri ve antibiyotik duyarlılıklarını

ÖZET

Amaç: Günümüzde gelişen yükselen antibiyotik direnci nedendeyi idrar yolu enfeksiyonlarının tedavisini giderek zorlaşmaktaadir. Bu çalışmanın amacı çocukluk çağı idrar yolu enfeksiyonlarında (İYE) en sık görülen mikroorganizmalar, antibiyotik duyarlılıklarını ve direnç durumunu araştırmaktır.

Gereç ve yöntem: Bu araştırmada 1.5 yıllık bir süre içinde Dicle Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı’nda İYE tanısıyla izlenen çocuklara ait idrar kültürlerinde üreme saptanan 111 idrar örneğine ait veriler incelendi. Hastaların klinik muayene bulguları, idrar tetkik sonuçları ve idrar kültürleri gözden geçirildi. İdrar toplama yöntemi olarak koopere olan çocuklarda orta akım idrarı, daha küçük çocuklarda steril idrar torbası yöntemi uygulandı. Kültürlerde İYE demek için klinik bulgulara ek olarak 100.000 koloni/ml tek tip bakteri üremesi esas alındı. Hastalara kültür antibiyogram sonuçlarına uygun antibiyotikler 10-14 gün süreyle verildi. Idrar yolu enfeksiyonu geçiren çocuklara kontrolleri arquivo izlemde tutuldu.

Bulgular: Olguların 97’si kız (%87.4), 14’ü erkek (%12.6). Olgularında en sık başvuru şikayetleri idarda yanma, ateş, yan ağrısı ve sik idrara çıkma idi. Siklik sırasına göre izole edilen etkenler E.coli (%75.7), Klebsiella sp (%7.2), Proteus sp (%6.3) ve Enterobacter sp (%1.8) olarak saptandı. Idrar kültür antibiyogramda saptanan direnç oranları trimetoprim/sulfametoksazol için %71.3, ampsilin için %82.4, amoksilin-klavunik asit için %54.7 ve tetrasiklin için %68.3 olarak yüksek oranlarda görülürken, en az dirençli (s-ftisakron (%16), Amikasin’de (%8.1) ve ceftriaxone (%16) gibi karşılaşılmamış olduğu görüldü.

Sonuç: Sonuç olarak incelediğimiz İYE geçiren çocuklarda en sık rastlanan etken E.coli olup en yüksek direnç oranları trimetoprim/sulfametoksazol, ampsilin ve amoksilin-klavunik asitne karşı saptandı. En az direnç olanları ise amikasin ve ceftriaxone karşı saptandi.

Anahtar kelimeler: Çocukluk çağı, idrar yolu enfeksiyonu, patojenler, antibiyotik duyarlılığı, direnç.

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INTRODUCTION
Urinary tract infection (UTI) is the most common disease of the genitourinary system in children, and it is the second most common infection after respiratory tract infections during childhood. UTI may be asymptomatic or symptomatic and may cause mortality due to sepsis, and pyelonephritis at early childhood. Especially recurrent UTI may cause serious long term complications such as hypertension and end-stage renal failure.

The most common causative agents of UTI are *E.coli*, Klebsiella, Pseudomonas, other Gram (-) enteric bacilli (such as Proteus) and other agents such as group B streptococci, staphylococci, *Candida albicans* and microorganisms belonging to flora of vagina and periurethral region.

Nowadays, resistance is increasing and resistance pattern is changing because of careless and irregular use of antibiotics especially in children with frequently recurrent UTI and re-infection. The importance of infectious agent determination and susceptibility to antibiotics and the detection of resistance status are key factors in the diagnosis and properly treatment of UTI because of the increasing antibiotic resistance.

Especially, regional studies should be considered for choosing empiric antibiotics before obtaining results of culture results since antibiotic susceptibilities may change from region to region. International studies may weakly guides about different regional characteristics.

In present study, we aimed to investigate the most common microorganisms, antibiotic susceptibility and resistance pattern and generate a basis for the empiric antibiotic treatment of childhood UTI for our region.

MATERIALS AND METHODS
In this study, 111 consecutive children with positive urine cultures were investigated. Patients were selected among children who admitted to Department of Pediatrics, Dicle University Medical Faculty Hospital, Diyarbakir, Turkey between July 2003 and May 2005. Cases’ age was between one month and 13 years. Their files were reviewed retrospectively. Data about age, gender, urine culture results were included.

Approximately 50 ml urine samples which were taken from urine bag or by suprapubic aspiration of urine or midstream urine after standard cleaning of the genital area were sent to the laboratory within thirty minutes. Urine samples were inoculated dishes which containing Eosin methylene Blue (EMB) agar and blood agar (Oxoid @) by 0:01 ml calibrated with a standard loop, and were incubated at 37°C in aerobic conditions in the oven for 1-2 days. Then; 15 ml urine sample after 3000 rpm centrifuge in the centrifuge tube for 5 minutes were investigated a drop of sample from the sediment of dip part of the tube for bacteria, leukocyte and epithelial on the x40 zoom. Also other cell structures such as erythrocytes, epithelial cells and yeasts were recorded to be evaluated with the results of culture during microscopic examination.

The number of bacteria in the in urine was calculated by taking into consideration the amount planted and the number of the colony in the culture medium. Quantities of breeding colonies of bacteria per milliliter were determined. The number of bacteria per milliliter was calculated $10^3-10^4$/ml, if 10-100 colonies were counted in the blood agar, and was calculated as $10^4$ n/ml, if 100 colonies were counted in the blood agar. The under $10^4$ presence of bacteria per milliliter have not been evaluated. When the presence of bacteria counted $10^4-5$ per milliliter, factors such as the patient’s age, gender, clinical symptoms, characteristics of isolated bacteria, using antimicrobial agents etc. were evaluated together. The presence of bacteria more than $10^5$ per milliliter was accepted as UTI. The presence of two or more types of microorganism or the presence of bacteria less than $10^3$ per milliliter was accepted as contamination. In addition, each bacteria determined in the urine sample which taken by suprapubic aspiration were evaluated significant. Colony morphology, Gram staining characteristics, motion characteristics and biochemical properties of reproducing microorganisms were investigated and were made for their identification. Conventional methods, and when necessary automated trading systems (Bio Mérieux @) were used to identify the species level of bacteria. Different antibiotic susceptibility panels which accordance with the recommendations of NCCLS were selected depending on the nature of each group of bacteria. Consisting inhibition zones after an overnight incubation at 37°C was evaluated as
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moderately susceptible to susceptible and resistant according to their types of antimicrobials.

Statistical analysis
The data were presented as the number and percentages. The mean age of the patients were presented as mean plus / minus the standard deviation. Descriptive statistics were used.

RESULTS
The study included 111 children [97 (87.4%) female and 14 (12.6%) male] who had positive urine cultures. Patients' ages ranging was from one month to 13 years. Females' mean age was 5.8 ± 3.5 years and males' mean age was 4 ± 2.5 years. The diagnoses of children with UTI were pyelonephritis in 66 (59.5%), cystitis in 31 (27.9%) and non-specified as pyelonephritis or cystitis in 14 (12.6%). The most common complaints were dysuria, fever, chest pain, and pollakiuria (Table 1).

The most commonly determined microorganism was Escherichia coli (75.7%) according to urine culture results (Table 2).

The highest ratios for antibiotic resistance were found against trimethoprim-sulphametoxazol, ampicillin, amoxicillin-clavulanate and tetracycline in urine antibiograms (Table 3).

Frequency of isolated microorganisms in children with urinary tract infection in the previous studies and our study was shown in (Table 4).

Urinalysis showed nitrite positivity in 43 (38.7%), bacteriuria in 19 (17.1%) and leukocyturia in 90 (90%).

Table 1. Symptoms of children with urinary tract infection

| Complaints          | n | %  |
|---------------------|---|----|
| Vomiting            | 20| 18 |
| Dysuria             | 65| 58.6|
| Fever               | 41| 36.9|
| Urgency             | 14| 12.6|
| Weight loss         | 20| 18 |
| Restlessness        | 30| 27 |
| Pollakuria          | 24| 21.6|
| Flank pain          | 49| 44.1|
| Incontinence        | 24| 21.6|
| Color / smell changes| 21| 18.9|
| Low urinary         | 6 | 5.4 |
| Constipation        | 13| 11.7|
| Abnormal flow       | 6 | 5.4 |

Table 2. The frequency of isolated microorganisms from urine culture

| Microorganisms      | n  | %  |
|---------------------|----|----|
| E.Coli              | 84 | 75.7|
| Klebsiella          | 8  | 7.2 |
| Enterobacter sp     | 2  | 1.8 |
| Enterobacteriacea   | 1  | 0.9 |
| Proteus             | 7  | 6.3 |
| Others              | 9  | 8.1 |
| Total               | 111| 100.0|

Table 3. Antibiotic susceptibility of isolated microorganisms.

| Tested antimicrobials | Bacteria n (%) | Resistant n (%) | Middle susceptible n (%) | Susceptible n (%) |
|-----------------------|----------------|-----------------|--------------------------|-------------------|
| Ampicillin            | 91 (82)        | 75 (82.4)       | 1 (1.1)                  | 15 (16.5)         |
| Amoxicillin-clavulanate| 86 (77.5)     | 47 (54.7)       | 13 (15.1)                | 26 (30.2)         |
| Aztreonam             | 67 (60.4)      | 25 (37.3)       | 3 (4.5)                  | 39 (58.2)         |
| Amikacin              | 99 (89.2)      | 8 (8.1)         | 4 (4)                    | 87 (87.9)         |
| Gentamicin            | 97 (87.4)      | 26 (26.8)       | 2 (2.1)                  | 69 (71.1)         |
| Cefotaxime            | 80 (72.1)      | 14 (17.5)       | 2 (2.5)                  | 64 (80)           |
| Ceftazidime           | 67 (60.4)      | 15 (22.4)       | 3 (4.5)                  | 49 (73.1)         |
| Cefuroxime            | 68 (61.3)      | 26 (38.2)       | 3 (4.4)                  | 39 (57.4)         |
| Ceftriazone           | 50 (45)        | 8 (16)          | -                        | 42 (84)           |
| Ciprofloxacin         | 90 (81.1)      | 19 (21.1)       | -                        | 71 (78.9)         |
| Levofloxacin          | 58 (52.3)      | 18 (31)         | -                        | 40 (69)           |
| TMP-SXT               | 94 (84.7)      | 67 (71.3)       | 1 (1.1)                  | 26 (27.7)         |
| Tetracycline          | 63 (56.8)      | 43 (68.3)       | -                        | 20 (31.7)         |

TMP-SXT: trimetoprim-sulphametoxasole

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Table 4. Frequency of isolated microorganisms in children with urinary tract infection in the previous studies and our study

| Study          | Year | E. coli (%) | Klebs. sp (%) | Proteus sp (%) | Enterobacter sp (%) | Pseu. sp (%) | Staph. sp (%) | Enteroc. sp (%) |
|----------------|------|-------------|---------------|----------------|---------------------|--------------|--------------|-----------------|
| Alpay et al.  | 1995 | 66.4        | 4.7           | 16.4           | -                   | 5.5          | -            | -               |
| Yüce et al.   | 1995 | 43          | 13.2          | 14.7           | 5.9                 | 3.4          | 9            | 1.8             |
| Ayata et al.  | 1998 | 63          | 18            | 10             | -                   | -            | -            | -               |
| Gündüz et al. | 1998 | 51          | 14            | 6              | 26                  | 3            | -            | -               |
| Ulubay et al. | 1998 | 65.7        | -             | 8.5            | 5.7                 | 2.8          | -            | 5.7             |
| Ergür et al.  | 1999 | 66.6        | -             | -              | 20.8                | 5            | 7.5          | -               |
| Gürgeþe et al.| 2002 | 57          | 21            | 12             | 6                   | -            | 2            | -               |
| Hacı et al.   | 2003 | 62.7        | 8.9           | 8.9            | 16.5                | -            | -            | -               |
| Tosun et al.  | 2004 | 65.5        | 10            | 10             | 0.7                 | 0.2          | 0.9          | 0.9             |
| Our study     | 2005 | 75.7        | 7.2           | 6.3            | 1.8                 | -            | 8.1          | 0.9             |

DISCUSSION

Urinary tract infections, especially in early childhood, if not treated with suitable antibiotics can cause serious problems such as hypertension and renal failure, and continues to be a very important health problem. UTIs are more common in boys in the neonatal period however more common in girls after neonatal period. In our study, most (87.4%) of the cases were girls. Clinical manifestations of patients with urinary tract infection may be varied according to age groups. Most of our patients had abdominal pain, dysuria and fever.

Each country or region having its own epidemiological data, the frequency of isolation agents and antibiotic resistance patterns, therefore this knowledge is important for prevention complications, treatment and prophylaxis of UTIs. Previous studies from outside Turkey demonstrated that most frequent UTIs’ agents in children were Escherichia coli (89.9-57.2%), Klebsiella sp (2.1-10%), P.mirabilis (1.2-10.9%), Enterobacter sp (1.2-12.7%), Pseudomonas sp (1-7%), Staphylococcus sp (% 1.2-6.3) and Enterococcus sp (3.7-13.7%). Previous studies from various regions of Turkey and our study demonstrated that most frequently ITUs’ agents in children were E.coli and other Gram-negative bacteria (Table 4).

Antimicrobial resistance may develop in different ways against microorganisms; Antimicrobial resistance is developing rapidly depending on the transfer of resistance genes, due to the R plasmids against E.coli and other many gram-negative bacteria. Previous studies were demonstrated quite different resistance rates against various antibiotics in our country and abroad; Previous studies from outside Turkey demonstrated that resistance rates in E.coli isolates to ampicillin (range, 39 to 72% ), trimethoprim-sulfamethoxazole (range, %23 to 40%), ciprofloxacin (8.9%), amoxicillin-clavulanate (range, 6.5 to16%), cephaloxine (14%) and cefuroxime (range, 4.4 to 40%) in children. Previous studies from various regions of Turkey and our study demonstrated similar results to abroad studies; Especially E.coli and other urinary tract pathogens have high resistance rate against trimetoprim-sulphametoxazole ampicillin, amoxicillin-clavulanate, cefuroxime and tetracycline, and have high susceptibility rates to amikacin and ciprofloxacin in children.

In Conclusion, our study demonstrated that urinary tract pathogens have high resistance ratios against trimetoprim/sulphamethoxazole, ampicillin, amoxicillin-clavulanate and cefuroxime which frequently prescribe for treatment of UTI in children. Therefore these higher resistance status should be taken into consideration while prescribing antibiotics for empirical use before obtaining urine culture and antibiotic susceptibility results.
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