

ORIGINAL ARTICLE

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 and resistance 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 amikacin and ceftriaxone. *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 duyarlılıkları

ÖZET

Amaç: Günümüzde gelişen yüksek antibiyotik direnci nedeniyle idrar yolu enfeksiyonlarının tedavisi giderek zorlaşmaktadır. Bu çalışmanın amacı çocukluk çağı idrar yolu enfeksiyonlarında (İYE) en sık görülen mikroorganizmalar, antibiyotik duyarlılıkları 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. İdrar yolu enfeksiyonu geçiren çocuklar kontrollere çağrılarak izlemde tutuldu.

Bulgular: Olguların 97'si kız (%87.4), 14'ü erkekti (%12.6). Olgularda en sık başvuru şikayetleri idrarda yanma, ateş, yan ağrısı ve sık idrara çıkma idi. Sıklık sırasına göre izole edilen etkenler *E.coli* (%75.7), *Klebsiella* sp (%7.2), *Proteus* sp (%6.3) ve *Enterobacter* sp (%1.8) olarak saptandı. İdrar kültür antibiyogramda saptanan direnç oranları trimetoprim/sulfametoksazol için %71.3, ampicilin için %82.4, amoksisilin-klavunik asit için %54.7 ve tetrasiklin için %68.3 olarak yüksek oranlarda görülürken, en az direncin seftriakson (%16) ve Amikasin'e (%8.1) karşı gelişmiş olduğu görüldü.

Sonuç: Sonuç olarak incelediğimiz İYE geçiren çocuklarda en sık rastlanan etken *E.coli* olup en yüksek direnç oranları trimetoprim/sulfametoksazol, ampicilin ve amoksisilin-klavunik asite karşı saptandı. En az direnç oranları ise amikasin ve seftriaksona karşı saptandı.

Anahtar kelimeler: Çocukluk çağı, üriner sistem enfeksiyonu, patojenler, antibiyotik duyarlılığı, direnç.

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Received: 15.05.2011, Accepted: 25.06.2011

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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.^{2, 3, 4}

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.⁵

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, Diyarbakır, 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 aspi-

ration 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 Mériex ®) were used for 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

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 polakiuria (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-sulphamethoxazol, 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 leucocyturia 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	%
<i>E. Coli</i>	84	75.7
Klebsiella	8	7.2
Enterobacter sp	2	1.8
Enterobacteriaceae	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)
Ceftriaxone	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-sulphamethoxazole

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

Study	Year	<i>E.coli</i> (%)	Klebs. sp (%)	Proteus sp (%)	Enterobacter sp (%)	Pseu. sp (%)	Staph. sp (%)	Enteroc. sp (%)
Alpay et al. ⁷⁹	1995	66.4	4.7	16.4	-	5.5	-	-
Yüce et al. ⁸⁰	1995	43	13.2	14.7	5.9	3.4	9	1.8
Ayata et al. ⁸¹	1998	63	18	10	-	-	-	-
Gündüz et al. ⁸²	1998	51	14	6	26	3	-	-
Ulubay et al. ⁸³	1998	65.7	-	8.5	5.7	2.8	-	5.7
Ergür et al. ⁸⁴	1999	66.6	-	-	20.8	5	7.5	-
Gürgöze et al. ⁸⁵	2002	57	21	12	6	-	2	-
Hacı et al. ⁸⁶	2003	62.7	8.9	8.9	16.5	-	-	-
Tosun et al. ⁸⁷	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.^{1,6,7} 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%).^{8, 9,10, 11,12,13} 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).^{14,15}

Antimicrobial resistance may develop in different ways against microorganisms; Antimicro-

bial 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.¹⁶⁻¹⁸ 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 to 16%), cephazoline (14%) and cefuroxime (range, 4.4 to 40%) in children.^{9,12,13,19,20} 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-sulphamethoxazole ampicillin, amoxicillin-clavulanate, cefuroxime and tetracycline, and have high susceptibility rates to amikacin and ciprofloxacin in children (Tablo 5).

In Conclusion, our study demonstrated that urinary tract pathogens have high resistance ratios against trimethoprim/sulfamethoxazole, 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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