Original Investigation/ *Özgün Araştırma*

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Microbiological and Antimicrobial Profile of Urinary Tract Infection in Children from A Teaching Hospital in South India

Güney Hindistan'da Bir Eğitim Hastanesindeki Çocuklarda Üriner Sistem Enfeksiyonlarının Mikrobiyolojik ve Antimikrobiyal Profili

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Abstract

Objective: Urinary tract infections are an important healthcare issue and are responsible for nearly 3% of all infections among the pediatric population. There are increasing reports on rising antibiotic resistance and these reports stress the continual surveillance of antimicrobial efficacy, particularly in countries with wide antibiotic abuse. This retrospective study aims to analyze the resistance of bacterial isolates to commonly used antibiotics in pediatric populations.

Material and Methods: In this study, records of all urine isolates and their antibiotic susceptibility profile from pediatric patients (1 month to 15 years) visiting a teaching hospital in south India in between June 2012 and December 2012 were evaluated.

Results: Of 342 samples tested, 62 (18.1%) showed significant growth, and 42(67.8%) were from children under 5 years of age, with male predominate. *Escherichia coli* (48.4%) the most prevalent urinary pathogen, resistant to cephalosporin (87.5%) and fluroquinolones (81.7%) and lowest resistance to nitrofurantoin (30%) and aminoglycoside (38.3%), **Conclusion:** The uropathogens causing UTI in the pediatric population are highly resistant to most of the antibiotics recommended for empiric use in the therapy of UTI. Development of regional surveillance programs is necessary for implementation of national UTI guidelines.

Keywords: Antibiotic susceptibility, children, *Escherichia coli*, India, resistance

Özet

Giriş: İdrar yolu enfeksiyonları önemli bir sağlık sorunu olmakla birlikte pediatrik popülasyon arasında görülen bütün enfeksiyonların %3'ünden sorumludur. Yükselen antibiyotik direnci ile ilgili her geçen gün sayısı artan raporlar özellikle antibiyotik suistimalinin yaygın olduğu ülkelerde antimikrobiyal etkinliğin devamlı takibinin yapılmasının gerekliliğinin altını çizmektedir. Bu retrospektif çalışma, bakteriyel izolatların pediatrik popülasyonda yaygın biçimde kullanılan antibiyotiklere karşı direncini incelemeyi amaçlamaktadır.

Gereç ve Yöntemler: Bu çalışmada, Haziran 2012 ile Aralık 2012 tarihleri arasında güney Hindistan'da bir eğitim hastanesini ziyaret eden pediatrik hastaların (1 aylıktan 15 yaşa kadar) idrar izolatları ve onların antibiyotik duyarlılıklarına ait kayıtlar değerlendirildi.

Bulgular: Test edilen 342 örnekten 62'sinde (%18.1) önemli ölçüde üreme görüldü ve bunların 42 (%67.8)'si beş yaş altı ağırlıklı olarak erkek popülasyonda elde edildi. En yaygın üriner patojeni olan *Escherichia coli* (%48.4) sefalosporin (%87.5) ve florokinolonlara (%81.7) en yüksek direnci gösterirken en düşük direnci nitrofurantoin (%30) ve aminoglikozite (%38.3) gösterdi.

Sonuç: Pediatrik popülasyonda idrar yolu enfeksiyonuna (İYE) yol açan üriner patojenler, İYE tedavisinde ampirik kullanım için önerilen antibiyotiklerin birçoğuna karşı yüksek oranda dirençliler. Bölgesel denetleme programlarının geliştirilmesi ulusal İYE kılavuzunun uygulamaya konmasında gereklidir.

Anahtar Kelimeler: Antibiyotik duyarlılığı, çocuklar, *Escherichia coli*, Hindistan, direnç

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Introduction

An urinary tract infection (UTI) is the common bacterial infection in the pediatric population. The estimated incidence of UTI is 1% in boys and 3% in girls during the first ten years of life (1). After the initial UTI, the prevalence of UTI during the first 6-12 months is upto 30% in infants and children (2). Timely evaluation and treatment are very important as, untreated UTI can result in serious complications such as recurrent infection, pyelonephritis with sepsis, pre-term birth and renal damage in young children (3). It is recommended to prescribe the appropriate dosage (often in the reduced amount) with antimicrobials and preferred drugs in selected periods of chronic renal failure (CRF) (4). Inappropriate and widespread use of antibiotics has led to the emergence of multidrug resistance (MDR) pathogens (5).

In the present retrospective study, we investigated the microbiological profile and antibiotic sensitivity pattern of urine isolates documented from a pediatric population visiting a teaching hospital for treatment of UTI.

Materials and Metods

A systematic retrospective analysis was performed on culture positive urine isolates collected between June 2012 to December 2012 from both the inpatient and the outpatient sections of a hospital in south India. The pathogen/s grown from the first sample of urine was considered for the analysis.

Sample processing, isolation and identification of pathogens was as per standard protocol (6,7) and also been described elsewhere (5). Briefly, a loopful of the well mixed urine sample was inoculated on 5% sheep blood and Cystine Lactose Electrolyte-Deficient (CLED) agar medium. Sample showing significant growth that is $\geq 10^4$ colony forming units (CFU/mL) were considered significant and processed for further identification and susceptibility testing. Susceptibility testing was done by Kirby-Bauer disk diffusion method and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines-2012. Repeated sample (from same patient who was already included), samples that grew more than two types of organism or evidence of perineal contamination were not included for analysis.

Statistical analyses were performed using SPSS version 16 (SPSS, Inc., Chicago, IL, USA). Chi-square test (χ^2) and z-test were used to identify statistically significant differences between gender sub-groups at 95% confidence. Probability factor (P) less than 0.05 was regarded as statistically significant.

Results

During the study period, a total number of 342 urine specimens were received for culturing and 62 (18.1%) showed significant growth. Of the 62 isolates, 42 (67.8%) were from children < 5 years of age and male to female ratio was 1.5:1 (Table 1). Median age was 3 years (IQR 1, 6), and overall 56.5% were males.

Gram-negative bacteria represented 79% of the isolates and *E. coli* (54.8%) was the most common pathogen. There was no significant difference in the rate of isolation among genders (χ^2 = 7.696 (8), p= 0.4637) (Table 2).

The antimicrobial susceptibility pattern showed that most of the isolates were resistant to cephalosporin, and nitrofurantoin; sensitive to aminoglycoside and less sensitive to fluroquinolones antibiotics. Trends of antibacterial resistance for individual uropathogens are presented in (Table 3).

Discussion

As urinary tract infection is a very common pediatric condition, its diagnosis and treatment have important implications for childhood health, development of antibiotic resistance, and health care costs (3,8,9). The prevalence and antimicrobial susceptibility of uropathogens may vary with time and geographical area. Therefore monitoring the local etiology of UTI would be beneficial to guide empiric treatment (10,11).

The present retrospective study highlights the age and gender-wise distribution of UTI and antibiotic resistance patterns of uropathogens in the pediatric population seeking healthcare services in south India. Similar to others studies (10,12), proportion of affected males was higher in our cohort. Earlier report has suggested that uncircumcised infant boys are more likely to have UTI since microorganisms may develop under the prepuce

Table 1. Age and gender-wise distribution of the culture positive urine samples

Age	Male (%) n= 35	Female (%) n= 27	Total (%) n= 62	Z test	p
1 Month to 1 years	13 (37.1)	10 (37.0)	23 (37.1)	0.0082	0.9935
2 to 5 years	12 (34.3)	7 (25.9)	19 (30.6)	0.7	0.4769
6 to 10 years	5 (14.3)	8 (29.6)	13 (21.0)	1.5	0.1422
11 to 15 years	5 (14.3)	2 (7.4)	7 (11.3)	0.9	0.3947
χ^2= 2.698 (3), p= 0.4406. Numbers in parentheses indicate percent composition.					

Table 2. Frequency distribution of isolates among patients gender

Isolates	Male (% n= 35	Female (%) n = 27	Total (%) n = 62	Z test	p
Citrobacter spp.	1 (2.9)	0	1 (1.6)	0.9	0.3723
Escherichia coli	17 (48.6)	13 (48.1)	30 (48.4)	0.0	0.9688
Enterobacter spp.	5 (14.3)	1 (3.7)	6 (9.7)	1.4	0.1617
Klebsiella spp.	3 (8.6)	2 (7.4)	5 (8.1)	0.2	0.8635
NFGNB	3 (8.6)	1 (3.7)	4 (6.5)	0.8	0.4366
Proteus spp.	0	2 (7.4)	2 (3.2)	1.6	0.1019
Pseudomonas aeruginosa	0	1 (3.7)	1 (1.6)	1.1	0.2513
Enterococcus spp.	4 (11.4)	4 (14.8)	8 (12.9)	0.4	0.6919
Candida spp.	2 (11.4)	3 (11.1)	5 (8.1)	0.0	0.9705

χ^2= 7.696 (8), p= 0.4637. NFGNB: Non-fermenting gram-negatif basili.
Numbers in parentheses indicate percent composition.

Table 3. Antibiotic resistance patterns % of bacterial pathogens isolated from pediatric population

Isolates	n	Amp	Cz	Ctx	Cpz	Caz	PT	Gn[a]	Net	AK	Cot	Nit	Nx	Cip	Lef	Mrp	Cpm
Citrobacter spp.	1	100	100	100	100	100	100	100	0.0	0.0	100	100	100	100	100	0.0	100
Escherichia coli	30	100	90.0	86.7	86.7	86.7	46.7	76.7	40.0	36.7	80.0	30.0	86.7	86.7	76.7	20.0	80.0
Enterobacter spp.	1	100	100	100	100	100	0.0	0.0	100	0.0	100	100	100	0.0	0.0	0.0	0.0
Klebsiella spp.	7	100	71.4	71.4	71.4	71.4	42.9	71.4	28.6	42.9	71.4	85.7	57.1	57.1	28.6	0.0	57.1
NFGNB	4	-	-	-	50.0	50.0	0.0	25.0	0.0	25.0	-	-	-	50.0	-	25.0	-
Proteus spp.	2	100	100	100	100	100	0.0	50.0	100	100	100	100	100	100	50.0	0.0	100
Pseudomonas aeruginosa	4	-	-	-	50.0	25.0	25.0	75.0	25.0	25.0	-	-	-	75.0	-	25.0	-
Enterococcus spp.	8	87.5	-	-	-	-	-	62.5	-	-	-	12.5	87.5	75.0	-	-	-
Overall	57	97.9	92.3	91.6	79.7	76.2	30.6	57.6	41.9	32.8	90.3	71.4	88.6	68.0	51.0	10.0	67.4

n: No of isolates, Amp: Ampicillin, Cz: Cefazolin, Ctx: Cefotaxime, Cpz: Cefoperazone, Caz: Ceftazidime, PT: Piperacillin + Tazobactam, Gn: Gentamicin, Net: Netilmicin, AK: Amikacin, Cot: Co-trimoxazole (trimethoprim-sulfamethoxazole), Nit: Nitofurantoin, Nx: Norfloxacin, Cip: Ciprofloxacin; Lef: Levofloxacin, Mrp: Meropenem, Cpm: Cefepime, NFGNB: Non-fermenting gram negative bacilli, [a]: High level gentamicin for *Enterococcus* spp., – : Not tested.

and enter the urinary tract (13). Concurrent to several previous reports (5,10,14), *E. coli* was the most frequently encountered species in our study. However, studies from some other parts of the country have shown different isolation rates, probably either due to variation in sample size, geographical location or population.

Antibiotic resistance has become a major clinical problem worldwide and has increased over the years (15). The antimicrobial susceptibility pattern of the pathogens varies widely by region, the patient population and the type of healthcare facility (9,16). Most of the isolates at our setting were MDR. Resistance to ampicillin and the cephalosporins (first, second, third and fourth generation) was seen more commonly among Gram negative bacilli. Sixty one percent of the isolates showed resistance to fluoroquinolones; which are the mainstay for treating UTI. These trends suggest the prior antimicrobial therapy in these sick children, more antibiotic consumption due to increase in different types of infections, self-medication which are often consumed for shorter than the clinically-accepted time length (17,18). The lack of uniform antibiotic policy and ignorance of hospital infection control practices would lead to the emergence and spread of resistance genes among bacteria (17-19). Resistance to carbapenems was commonly observed in extended spectrum beta-lactamase (ESBL) producers (25%). Since, carbapenems are often the last line of defense against resistant Gram-negative infections, resistance to these antibiotics could result in greater morbidity, mortality, costs, and prolonged hospital stay (20). Good clinical practice should guide the use of limited antibiotics left. The regional surveillance programs would be necessary to update the treatment guidelines of UTI in India.

The limitations of the study are that, the retrospective study precluded the available data of UTI, only patients visiting in hospital were included, and the UTI in the community was not well assessed, non-uniformity in collecting urine samples, lack of data on clinical response and outcome.

Conclusion

E. coli was the most common pathogen responsible for UTI in children. The uropathogens causing UTI in the pediatric population are highly resistant to most of the antibiotics recommended for empiric use in the therapy of UTI. Good clinical practice and regional surveillance programs would be necessary to update the treatment guidelines.

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