Uropathogens and their Susceptibility Patterns in Children at Princess Rhmah Hospital, Jordan

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Abstract

Background: Knowledge of antimicrobial susceptibility patterns is required to prescribe empirical therapy and formulate guidelines for the treatment of urinary tract infections. This study assesses the etiology and antimicrobial susceptibility of the main uropathogens in Jordanian children.

Methods: A retrospective study was conducted on a positive urine cultures taken from children aged below 15 years, who attended as outpatient clinics or inpatient at Princess Rahmah Hospital between January and December/2008. The obtained data analysed and the results were tabulated.

Results: A total of 597 isolates were recovered from children with lower urinary tract infections. Uropathogens were isolated more in females (82%) than in males. The most frequent pathogen found was *Escherichia coli* (72.9%), followed by *Klebsiella spp.* (19.9%), *Proteus spp*. (3%), *Pseudomonas spp* (2%), *Staphylococcus aureus* (1%), *Streptococcus spp* (0.7%), and *Enterobacter spp*. (0.5%). The highest susceptibility rate of *E. coli* was 100% to both amikacin and ceftriaxone, followed by cefotaxime (89.4%), ciprofloxacin (85.5%), and gentamicin (83.9%). Whereas the lowest susceptibility rates were 27.5%, 21.6% and 16.0% to cotrimoxazole, amoxicillin-clavulanic acid and ampicillin respectively.

Conclusions: *E. coli* was the main uropathogen in children patients. The most of *E. coli* isolates were susceptible to amikacin, ceftriaxone, cefotaxime, ciprofloxacin and gentamicin. Overall cotrimoxazole, amoxicillin-clavulanic acid and ampicillin resistance rate was near 75% or more, and this rate was not affected according to the type of urinary infection. This information should be considered when empirical therapy is recommended or prescribed for children with Urinary Tract Infection (UTI) in Jordan.

Keywords: Urinary Tract Infection, Antimicrobials, Drug Resistance.

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Introduction

Urinary Tract Infection (UTI) is the second most common infectious presentation in community practice. Worldwide, about 150 million people are diagnosed with UTI each year, costing the global economy in excess of 6 billion US dollars. [1] Infection of the urinary tract occurs more frequently in girls than in boys. [2]

The most frequent uropathogen is *Escherichia coli*, accounting for 65%- 90% of urinary infections, [3, 4] and this may be due to contamination with colonic bacteria through urethra. [5] Other uropathogen isolates are *Proteus spp., Klebsiella spp., Enterobacter spp., Serratia spp. and Pseudomonas spp.* [6, 7]

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The most commonly used antibacterial drugs in the treatment of UTIs are trimethoprim/sulfamethoxazole, ciprofloxacin, cephalosporins, semi-synthetic penicillins with or without inhibitors, nitrofurantoin and fosfomycin. [8]

However, *E. coli* and other uropathogens are becoming increasingly resistant to commonly prescribed antimicrobials, which results in decreasing their effectiveness. [9] Increasing the rates of resistance among bacterial uropathogens has become a major public health problem in both developed and developing countries. [10] Several factors are associated with the rise of resistance rate of bacterial uropathogens including misuse of antimicrobials, [11] frequent oral use of wide-spectrum antimicrobials that may change the intestinal flora, (which is usually a common cause of UTI), [12, 13] and inappropriate dosages and duration of treatment. [14]

Sensitivity of bacterial uropathogens to antimicrobials shows great geographical and historical variability due to different antimicrobial treatments. Due to the above reasons, the treatment of UTI in children should be re-evaluated every five years according to the local resistance rates. [15]

Although there were many studies on uropathogens and their susceptibility patterns in children conducted in Jordan, it's necessary to re-evaluate the uropathogens resistant pattern. Therefore, this retrospective study was conducted to assess the changing susceptibility patterns of urinary pathogens isolated from urine cultures received from children inpatients and outpatients at Princess Rahmah Hospital during a period of 1 year (2008). This study is important for clinicians in order to facilitate the empiric treatment of children with symptoms of UTIs. Moreover, the data would also help the authorities to formulate antibiotic prescription policies.

Materials and Methods

This retrospective study was conducted on children patients (≤ 15 years of age) who attended as outpatients or inpatients with diagnosed Urinary Tract Infection (UTI) at Princess Rahmah Hospital located in Irbid, Jordan, between January and December/2008. The study protocol was approved by the Ethics Committee of the Ministry of Health (MOH) in Jordan (MOH, REC, 08, 0057).

Data Collection

The microbiological and antibacterial susceptibility data of this study have been obtained from the records of clinical microbiology laboratory of Princess Rahmah Hospital. These data were filled in a prepared data sheet. However, clinical microbiology laboratory of Princess Rahmah Hospital applied the following procedure for sample processing and culture, bacterial identification and susceptibility testing.

Urine Specimens and Primary Inoculation

The urine samples were cultured in 5% sheep blood agar and MacConkey's media. Inoculation was done with the help of a 0.001ml calibration loop. All the sample plates were incubated for 48 hrs at 37oC in 5-10% carbon dioxide for anaerobic growth.

Isolation and Identification

Based on the Gram-staining characteristics of the bacteria, 2-3 colonies diluted in 4-5 ml normal saline in a sterile glass tube. Then a swab was dropped in the dilution and spread onto Mueller Hinton agar for antimicrobial susceptibility testing.

Antimicrobial Susceptibility Testing

All isolates were tested for their susceptibilities to at least eight out of 15 antimicrobials by using antimicrobials diffusion discs. [16]

Antimicrobials tested were amikacin, amoxicillin-clavulanic acid, ampicillin, cefaclor, cefixime, cefotaxime, ceftazidime, ceftriaxone, cephlexin, cephalothin, ciprofloxacin, cotrimoxazole, gentamicin, nalidixic acid and norfloxacin.

Statistical Analysis

Data were analyzed using SPSS (version15 for Windows) to calculate the frequencies and cross tables.

Results

During a 12 month period (January to December 2008), a total of 597 positive urine cultures of children aged below 15 years old were studied. There were 490 (82%) females and 107 (18%) males. The data show that the majority of uropathogen isolates were *Escherichia coli* (72.9%), *Klebsiella spp.* (19.9%), *proteus spp.* (3%), *Psedomonas spp* (2%) *Staphylococcus aureus* (1%), *Streptococcus spp*. (0.7%), and *Enterobacter spp.* (0.5%) table (1).

Table (1): Uropathogen isolates from children with UTI.

Bacteria	Sex		Total	%
	F	M		
1. E.coli	62	373	435	72.9
2. Klebsella	35	84	119	19.9
3. Protous	5	13	18	3
4. Pseudomonas	1	11	12	2
5. Staph. Aurous	2	4	6	1
6. Strepto coccus	1	3	4	0.7
7. Enterobacter	1	2	3	0.5
Total	107	490	597	100

Antimicrobial susceptibility to 15 selected antimicrobial of different classes for seven urine isolates are summarized in table (2).

The highest susceptibility rate of *Escherichia coli* was to both amikacin and ceftriaxone (100%), whereas the lowest susceptibility rate was to ampicillin (16%). The highest susceptibility rate of other uropathogen isolates i.e. *Klebsiella spp*. (100%) to amikacin, *proteus spp.* (100%) to both cefotaxime and ciprofloxacin, *Psedomonas spp* (100%) to both amikacin and ceftazidime, *Staphylococcus aureus* (100%) to ciprofloxacin, *Streptococcus spp*. (100%) to (ampicillin, cefotaxime, cephalothin and ciprofloxacin) and *Enterobacter spp.* (66.7%) to (ampicillin, cefaclor, cefotaxime, ciprofloxacin, nalidixic acid and norfloxacin). Whereas the lowest susceptibility rate for all the other uropathogen isolates i.e *Klebsiella spp*. (10%) to ampicillin, *proteus spp.* (16%) to amoxicillin-clavulanic acid, *Psedomonas spp* (0%) to both ampicillin and cotrimoxazole, *Staphylococcus aureus* (50%) to cefaclor, *Streptococcus spp*. (25%) to cefixime and *Enterobacter spp.* (33.3%) to cotrimoxazole. However, the highest susceptibility rate of all the different uropathogen isolates was (100%) to amikacin and ceftriaxone, whereas ampicillin exhibited the lowest susceptibility rate (14.9%) table (3).

Table (2): Susceptibility percentage (%) of uropathogens isolates to antimicrobial agents.

Drug	E.coli n = 435		Klebsella n = 119		Protous n = 18		Pseudomonas n = 12		Staph. Aurous n = 6		Streptococcus n = 4		Enterobacter n = 3	
	N	S %	N	S %	N	S %	N	S %	N	S %	N	S %	N	S %
AK	22	100	7	100	0	0	5	100	0	0	0	0	0	0
AMC	346	25.4	96	21.0	13	38.4	4	0	5	80.0	3	100	3	66.6
AMP	337	16.0	95	9.8	10	20	7	0	0	0	3	100	3	100
CAZ	113	77.5	28	71.4	6	83	3	100	0	0	0	0	0	0
CEC	380	67.2	105	52.3	14	50	8	25	6	50	0	0	3	100
CFX	304	79.2	82	58.7	10	70	9	11.1	2	50	3	33.3	0	0
CF	174	71.8	72	58.5	10	90	5	40	0	0	4	25	0	0
CIP	398	85.5	112	92.8	16	100	10	80	3	100	4	100	3	100
CLT	193	59.0	44	55.5	7	57.1	4	0	2	100	3	66.6	1	0
COT	368	28.8	98	37.7	14	35.7	11	0	6	50	3	33.3	3	33.3
CTR	10	100	0	0	0	0	0	0	0	0	0	0	0	0
CTX	371	89.4	104	71.1	16	100	11	81	5	60	4	100	3	100
GEN	348	83.9	93	74.7	13	84	12	83	5	80	3	66.6	0	0
NAL	401	52.6	116	66.3	18	77	9	11	0	0	3	66.6	3	33.3
NOR	411	83.5	115	86.3	0	0	9	77	0	0	4	50	3	66.6

Number of isolates (N), Sensitive (S), amikacin (AK), amoxicillin-clavulanic acid (AMC), ampicillin (AMP), ceftazidime (CAZ), cefaclor (CEC), cephlexin (CFX), cefixime (CF), ciprofloxacin (CIP), cephalothin (CLT),

cotrimoxazole (COT), ceftriaxone (CTR), cefotaxime (CTX), gentamicin (GEN), nalidixic acid (NAL), norfloxacin (NOR).

Table (3): Susceptibility percentage (%) of all different uropathogen isolates to antimicrobial agents.

Drug	Bacteria		
	N	S	%
AK	34	34	100
CTR	10	10	100
CIP	546	477	87.3
CTX	514	440	85.6
NOR	542	457	84.3
CAZ	150	112	74.6
GEN	474	338	71.3
CFX	410	299	72.9
CF	265	179	67.5
CEC	520	328	63.0
NAL	550	305	55.4
CLT	254	126	49.6
COT	503	153	30.4
AMC	470	123	26.1
AMP	455	68	14.9

Number of isolates (N), Sensitive (S), amikacin (AK), amoxicillin-clavulanic acid (AMC), ampicillin (AMP), ceftazidime (CAZ), cefaclor (CEC), cephlexin (CFX), cefixime (CF), ciprofloxacin (CIP), cephalothin (CLT), cotrimoxazole (COT), ceftriaxone (CTR), cefotaxime (CTX), gentamicin (GEN), nalidixic acid (NAL), norfloxacin (NOR).

Discussion

This current study provides information regarding the main etiological agent *Escherichia coli* that causes UTI in children (inpatient and outpatient setting), and its antimicrobial susceptibility patterns. The occurrence ratio between female to male patients was (4.3:1) which agrees with those reported in Jordan. [17-22]

Many studies in Jordan [17-23] and elsewhere [24] reported that *E.coli* and *Klebsiella spp* were the leading pathogens. This current study showed similar findings.

Results of this study are in agreement with other studies which reported that *E. coli* was the most common uropathogen isolated from urine of children. [3,4,19,21,25-27]

An increase in the occurrences of *E. coli* as causative of UTI is likely related to contamination with colonic bacteria through urethra. [5]

The majority of commonly encountered pathogen isolates from urine were *Escherichia coli*, *Klebsiella spp.*, *proteus spp.*, *Psedomonas spp*, *Staphylococcus aureus*, *Streptococcus spp*. and *Enterobacter spp.* which are not too different from that reported in the literature.

The most effective antimicrobial agent for *Escherichia coli* was amikacin and ceftriaxone (100%), followed by cefotaxime (89.4%), ciprofloxacin (85.4%), gentamicin (83.9%), and norfloxacin (82.2%). Whereas the lowest susceptibility rate observed with ampicillin (16.0%), amoxicillin-clavulanic acid (25.4%) and cotrimoxazole (28.8%).

Almost similar findings were reported in the literature. [17, 19, 21- 23, 28] High resistance rate to ampicillin, amoxicillin-clavulanic acid and cotrimoxazole is due to the widely used of these antibacterial drugs in the world including Jordan.
In this study, *Klebsiella spp* and *Pseudomonas spp.* (the second and forth common cause of UTI in children, respectively), showed high sensitivity rate of 100% to amikacin. Whereas ampicillin showed the lowest susceptibility rate of 9.8% and 0% for *Klebsiella spp.* and *Pseudomonas spp*, respectively. Similar low susceptibility pattern for *Klebsiella spp. and Pseudomonas spp* was reported in Jordan. [17, 22]

Other uropathogens that have been found in this study were *Proteus spp.*, *Staphylococcus aureus* and *Streptococcus spp*. which showed a high sensitivity rate of 100% to ciprofloxacin. Whereas the lowest susceptibility rate of 20% *for Proteus spp* to amoxicillin-clavulanic acid, 50% for *Staphylococcus aureus* to cotrimoxazole and 25% for *Streptococcus spp*. to cefixime.

Enterobacter spp (the lowest common cause of UTI in children in this study), showed highest susceptibility rate of 66.7% to ampicillin, cefaclor, cefotaxime, ciprofloxacin, nalidixic acid and norfloxacin. The lowest susceptibility rate of 33.3% for *Enterobacter spp* was to cotrimoxazole. Close findings for gram negative bacteria were reported in Jordan. [22]

This study shows that the highest susceptibility rate (100%) for all uropathogen isolates was to amikacin and ceftriaxone followed by ciprofloxacin (87.3%), cefotaxime (85.6%) and norfloxacin (84.3.5%). The comparatively low susceptibility rate for all uropathogen isolates of 28.9%, 22.6% and 14.9% was to cotrimoxazole, amoxicillin-clavulanic acid and ampicillin, respectively. Due to the high rate of resistant shown by UTI isolates to amoxicillin-clavulanic acid, ampicillin, and cotrimoxazole. Therefore, these drugs should not be the drug of choice for the treatment of UTI.

These results have also revealed a decrease in the susceptibility rate for most of the antimicrobial used in this study than that reported previously in the literatures. [18, 29] These results are in agreement with other studies, [9, 10] that showed increasing resistant rate of uropathogens to commonly prescribed antimicrobials by the time, and as a consequence decreasing their effectiveness.

Conclusion

UTI in children is mainly caused by *Escherichia coli* organisms, which are developing resistance to commonly used antimicrobials. This emergence of multiple drug resistance calls for a continuous monitoring and reviewing of antimicrobial policy in Princess Rahmah Hospital and in the country at large. Therefore, this study is important for clinicians in order to facilitate the empiric treatment of children with urinary pathogens. Moreover, the data would also help the authorities to formulate antibacterial prescription policies.

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مسببات عدوى الجهاز البولي ونمط حساسيتها عند الأطفال في مستشفى الأميرة رحمة، الأردن

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الملخص

إن معرفة حساسية البكتريا للمضادات البكتيرية ضرورية وهامة وذلك ليتمكن الطبيب من وصف العلاج المناسب وتجنب وصف الأدوية الغير فعالة لعلاج أمراض الجهاز البولي عند الأطفال. لذلك فان هذه الدراسة هدفت للتعرف على العامل المسبب لعدوى الجهاز البولي وحساسية للمضادات البكتيرية المستخدمة في علاج أمراض الجهاز البولي.

طريقة البحث: لقد قام الباحث بجمع معلومات الدراسة المتعلقة بالعزولات البكتيرية من عينات البول للأطفال الذين تقل أعمارهم عن 15 سنة من سجلات مختبر مستشفى الأميرة رحمة للأطفال في اربد في خلال العام 2008، وقد تم تحليل النتائج بالطرق الإحصائية المناسبة.

النتائج: بينت النتائج انه تم عزل (597) عترة بكتيرية وكانت نسبة العزولات من الإناث (82%) أكثر مقارنة مع تلك المعزولة من الذكور. لقد لوحظ إن معظم العزولات كانت لعصيات القولونية بنسبة (72%) ثم تلتها الكلبسيلا (19,9%)، البروتيس (3%)، البسيدوموناس (2%)، المكورات العنقودية الذهبية (1%)، المكورات العقدية (0,7%)، وأخيرا البكتيريا الداخلية بنسبة (0,5%). لقد فحصت حساسية البكتيريا لعدة مضادات بكتيرية مستخدمة في علاج أمراض الجهاز البولي وقد تباينت حساسية العصيات القولونية للأدوية على النحو التالي: الاميكاسين وسيفترايكسون (100%)، سيفوتاكسيم (89,4%)، سيبروفلوكساسين (85,5%)، جنتاميسين (83,9%). ثم تناقصت الحساسية تدريجيا لتصل إلى (16%) للامبيسللين.

الاستنتاج: إن نتائج هذه الدراسة تشير بوضوح إلى ضرورة اختبار حساسية البكتيريا للأدوية المستخدمة في علاج أمراض الجهاز البولي عند الأطفال قبل وصفها للعلاج.

الكلمات الدالة: عدوى الجهاز البولي، المضادات البكتيرية، مقاومة الأدوية.