Pathogens Causing Urinary Tract Infection and Their Resistance Patterns among Pediatric Patients in Chong Hua Hospital (January 2003 to June 2005)

AUTHORS: Arlene Rodriguez-Encarnacion, M.D
Chong Hua Hospital, Cebu
CORRESPONDENCE:
Dr. Arlene Rodriguez-Encarnacion
Email: arlene_r_e@yahoo.com
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ABSTRACT

The management of urinary tract infection (UTI) is fraught with challenges, especially, in an era of increasing antimicrobial resistance. Antibiograms that make use of local and population-based data aid clinicians in their treatment strategies.

Objectives: This study aims to determine the common organisms isolated in the urine culture and the organism's sensitivity pattern to antibiotics among inpatients and outpatients aged 0-18 years old at Chong Hua Hospital from January 1, 2003 to June 30, 2005.

Methods: Data from inpatients and outpatients aged 18 years old and below with a urine culture of ≥ 100,000 CFU of a single pathogen were collected from the Chong Hua Hospital Microbiology Laboratory within a 30-month period. The organisms cultured were identified and the resistance pattern of the 5 most common isolates was determined. The medical charts of inpatients were reviewed to determine the initial antibiotics started.

Results: 140 patients were included in the study. UTI was most common in the >28 days to 1 year age group. UTI was more frequent in males aged >28 days to 1 year and in females aged 1 to 5 years. The common isolates were: *Escherichia coli* (75%), *Proteus mirabilis* (6%), *Pseudomonas aeruginosa* (6%), *Enterobacter* sp (5%), and *Klebsiella pneumoniae* (4%). Antibiotic susceptibility testing revealed that there was resistance to ampicillin (76%) and cotrimoxazole (64.15%). Less than 10% resistance was found with ceftriaxone, imipenem, gentamicin, ciprofloxacin, netilmicin, amikacin and cefepime. Cefuroxime was the most common antibiotic started in hospitalized patients.

Conclusion: The most common etiologic agents of UTI were *E. coli, P. mirabilis, P. aeruginosa, Enterobacter sp. and K. pneumoniae.* There was high resistance to the recommended first-line antibiotics cotrimoxazole and ampicillin.

INTRODUCTION

Urinary tract infection (UTI) is one of the most common causes of hospital admissions and outpatient consultations in pediatric practice. Its clinical spectrum ranges from asymptomatic infection to cystitis to pyelonephritis.[1] Repeated infections may even cause complications leading to renal scarring; it may also signify an underlying anatomic abnormality. Although frequently encountered and well-researched, diagnosis and management of UTI continue to be a controversial issue with many challenges for the clinician.[2] Increasing resistance to antibiotics complicates its treatment by increasing patient morbidity, cost of reassessment and retreatment, rates of hospitalization, and use of broader-spectrum antibiotics.[3]

Knowledge of the current, most common pathogens and their resistance patterns will aid clinicians in the judicious use of antimicrobials. Adequate treatment in the outpatient department will lessen the number of admissions, thus decreasing the financial burden to the family of the patients. In the hospital setting, appropriate and early antibiotic coverage upon admission of patients will result in their faster recovery and prevention of further complications.

An updated database of the local antibiotic resistance patterns is a valuable clinical tool. Hospital antibiograms usually reflect inpatient data on resistance patterns that cause UTI. These data tend to overestimate drug resistance and may mislead clinicians about the prevalence of local resistance.[4] Inclusion of outpatient data, therefore, increases the accuracy of such antibiograms. It is the aim of this research to determine the common organisms causing UTI and their resistance patterns to antibiotics among inpatients and outpatients aged 0-18 years old at Chong Hua Hospital from January 1, 2003 to June 30, 2005. Frequencies of UTI in different age groups were also determined.

MATERIALS AND METHODS

Study Population

The study population were patients 0-18 years old who were admitted in the Chong Hua Hospital or were seen as outpatients and had urine cultures done at the Chong Hua Hospital between January 1, 2003 and June 30, 2005. Their data were included in the study if the urine culture showed ≥100,000 CFU of a single pathogen. Patients who were re-admitted due to recurrent UTI were excluded.

Data Collection

The urine culture results were obtained from the Chong Hua Hospital Microbiology Laboratory Inpatient and Outpatient logbooks. The isolated organisms were identified and ranked according to the most frequently isolated bacteria. The resistance patterns of the five most common isolates to common antibiotics were determined. A chart review of inpatients was done to determine the initial antibiotics started. The method of urine collection was not specified in the culture results.

Data Analysis

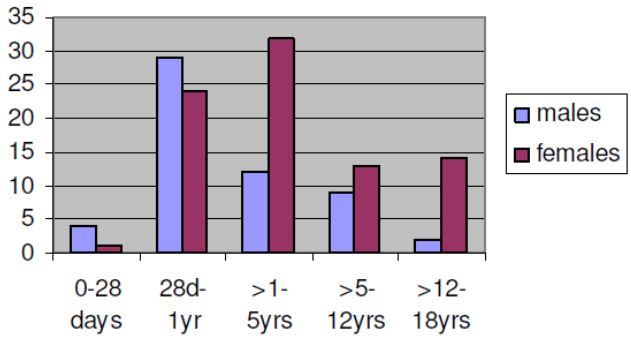
Data was analyzed using Microsoft Excel 2002 from Microsoft Office XP. The sex and age distributions were analyzed and were expressed in percentages. The resistance patterns to antibiotics and the proportion of common antibiotics used were also expressed in percentages.

RESULTS

A total of 1,417 patients, 0-18 years, old submitted specimens for urine culture; 790 were inpatients and 627 were outpatients. Only 140 9.8%) patients were eligible for inclusion in this study, 69 (49%) were inpatients and 71 (51%) were outpatients. Most of the patients (37%) belonged to the >28 days to 1 year age group. Females comprised 60%, while males comprised 40% of the study population. UTI was found to be common in males older than

28 days to 1 year age group and in females in the 1-5 years old age group (Fig. 1).

Figure 1. Sex distribution of UTI Cases in Different Age Groups



Escherichia coli was the most common organism isolated, which accounted for 106 (75.7%) of the pathogens. *Proteus mirabilis* and *Pseudomonas aeruginosa* were seen in 8 cases (5.7%). *Enterobacter* sp. was isolated in 7 patients (5%), *Klebsiella pneumoniae* in 5 patients (3.6%), *Morganella morganii* in 3 patients (2.1%), Coagulase negative *Staphylococcus* in 2 patients (1.4%), and *Micrococcus* sp. in 1 patient (0.7%).

Antibiotic susceptibility testing revealed that *E. coli* had a high resistance rate to amoxicillin (75%), ampicillin (67.5%) and cotrimoxazole (59%).

Proteus mirabilis was resistant to nitrofurantoin (100%), cefalothin (75%), ampicillin (62.5%), and cotrimoxazole (45%). There was some resistance against aztreonam (25%), cefalothin (25%), amikacin (14.5%), and ceftazidime (8.5%). There was no resistance noted against the other antibiotics tested.

Pseudomonas aeruginosa was 100% resistant to ampicillin, ampicillin-sulbactam, cefuroxime, cotrimoxazole, and co-amoxiclav (Table 3) as expected. Unfortunately for imipenem (25%), aztreonam (20%), and ciprofloxacin (10%) resistant isolates were seen.

Enterobacter sp. was 100% resistant to cefoxitin and co-amoxiclav and 50% resistant to ceftazidime, cefuroxime, and ampicillin. There was 16.5% resistance to cotrimoxazole.

Klebsiella pneumoniae was 100% resistant to ampicillin and cotrimoxazole. No resistance was noted in the other antibiotics tested.

Over-all, among the antibiotics used in the study, cefepime, amikacin, netilmicin, ciprofloxacin, gentamicin, imipenem, and ceftriaxone were highly effective against all the uropathogens. On the average, there was less than 10% resistance against these antibiotics. There was 64.15% and 76% resistance to cotrimoxazole and ampicillin, respectively.

Only 61 charts of the 69 inpatients were retrieved. Cefuroxime was the most common antibiotic used as first-line IV antibiotic for UTI (Fig 5) (where is Figure 5?); it was used in 24 patients (39.3%). This was followed by ampicillin in 12 patients (19.7%), amikacin in 11 patients (18%), ampicillin-sulbactam and co-amoxiclav in 3 patients (4.9%), and ofloxacin in 2 patients (3.3%). Cefepime, cefotaxime, ciprofloxacin, ceftizoxime, ceftriaxone and amoxicillin were used in 1 patient each (1.6%).

Figure 2.Organisms Isolated from Urine cultures.

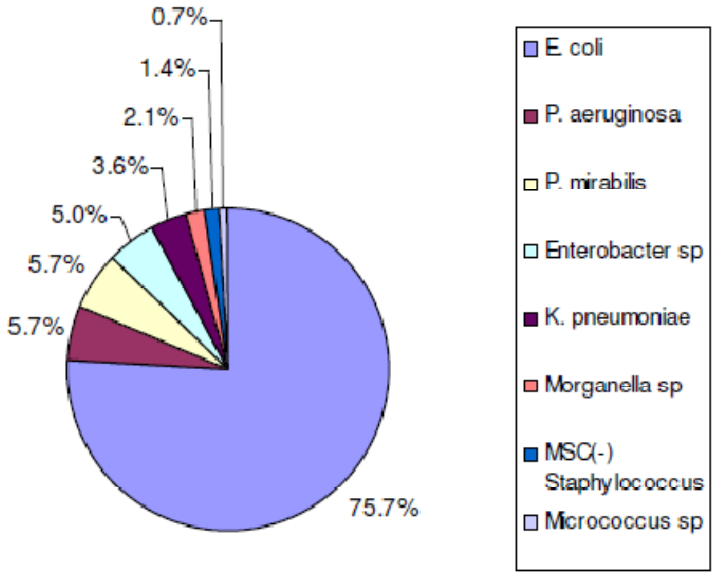


Figure 2. Bacteria Isolated from Urine Specimens

Table 1. Percent Resistance of Bacteria Isolated from Urine Specimens

Antibiotic	**Per cent Resistant**			
	Escherichia coli N=106	Proteus mirabilis N=8	Enterobacter spp. N=7	Pseudomonas aeruginosa N=8
Amoxicillin	75	-	-	-
Ampicillin	67.5	62.5	50	100
Cotrimoxazole	59	45	16.5	100
Cefalothin	22.5	25	75	-
Cefuroxime	15.5	0	50	100
Co-amoxiclav	14.5	0	100	100
Gentamicin	11.5	0	0	0
Nitrofurantoin	10.5	100	0	-
Netilmicin	10	0	-	0
Nalidixic acid	9.5	-	50	-
Ceftazidime	8.5	8.5	50	0
Piperacillin-tazobactam	7.5	0	0	0
Amikacin	5	14.5	0	0
Aztreonam	4	25	-	20
Cefoxitin	3.5	0	100	-
Cefepime	2.5	0	0	0
Ceftriaxone	2	0	0	37.5
Imipenem	1	0	-	25
Ciprofloxacin	1	0	0	10

DISCUSSION

UTI occurs in as many as 5% of girls and 1%-2% of boys but it occurs more frequently in boys than in girls before the age of 1.[1,12] This finding was also true in our study. Females are said to be more susceptible to UTI after the age of 6 months due to their shorter urethra which provides easy access of the bacteria to the bladder.[22] Consistent with foreign studies, *E. coli* was the most common cause of UTI, followed by *Proteus mirabilis*[3, 5]. However, we cultured Pseudomonas in 8 patients (6%): 3 of them were inpatients, 2 of whom had a history of instrumentation as in catheterization and one had prolonged stay in the hospital (45 days). Ladhani in 2003 noted that *Pseudomonas* sp. were more prevalent among urine isolates of children with renal problems[16]. The other organisms—*Enterobacter, Klebsiella* and *Staphylococcus* were among the usual pathogens.

An increasing resistance to *E. coli*, as seen in other studies in other countries[11-17] is mirrored in our study. Of particular importance were the high resistance of *E. coli* against amoxicillin, ampicillin and cotrimoxazole. Another local study by Caylao, et al, also noted increasing resistance of uropathogens to ampicillin (41.07%), cotrimoxazole (26.79%), gentamicin (10.7%), amikacin (8.93%), and nalidixic acid (5.3%) [9]. Miller and Tang stated that in the empirical treatment of uncomplicated UTI, cotrimoxazole was recommended unless resistance exceeds 10%-20%. If such antibiotic was used, there was suboptimal clinical (outcome) translating to <60% clinical cure[4]. Since ampicillin and cotrimoxazole had resistance rates that exceeded 20% in our study, using them in the empiric treatment of UTI in our setting needs further review.

Over-all, among the antibiotics used in the study, ceftriaxone, imipenem, gentamicin, ciprofloxacin, netilmicin, amikacin and cefepime were highly effective against all the uropathogens, but majority were in parenteral form and are quite expensive. To be able to use an antibiotic for outpatient treatment, an antibiotic should also have an oral preparation which attains good levels in the urine.

Cefuroxime had good activity against the pathogens, except, *Pseudomonas aeruginosa* (100% resistance) and *Enterobacter* sp. (50% resistance). It is has an oral preparation and with twice-daily, which increases patient compliance. Baskinas, et al, also found in their study that cefuroxime can be an alternative antibiotic (with oral form) to which *E. coli* and *K. pneumoniae* were sensitive[18]. In our study, *Pseudomonas* and *Enterobacter* only accounted for 10.7% of the isolates.

Co-amoxiclav also has an oral preparation, with twice-to-thrice-daily dosing depending on the preparation. It has good activity against *E. coli* based on the results of this study.

Ciprofloxacin is another antibiotic which has an oral form. Its resistance rate against all the isolates was only 2.2%. However, it is not recommended for use in the pediatric population because of its arthropathic effects in immature animals. In developed countries, there is an increasing use of this antibiotic in children for a variety of conditions like 1) cystic fibrosis in children, who are prone to respiratory infections caused by *Pseudomonas aeruginosa;* 2) children who are immunocompromised from chemotherapy regimens; 3) children with complex genitourinary anomalies who are prone to complicated UTI; 4) children with Salmonella infections; and 5) children with severe bacterial infections that fail to respond to initial antibiotic therapy[23]. The International Society of Chemotherapy suggests that fluoroquinolones can be used in pediatric patients with UTIs when alternative and effective therapy is not available[24]. Clinical observations surrounding their use suggest that quinolone antibiotics might be safer in children than in animals. In a well-defined pediatric population, i.e. children who are prone to complicated urinary tract infections,

fluoroquinolone antibiotics may still be useful[25].

This study showed that attending physicians were becoming aware of the increasing resistance to the first-line antibiotics, particularly ampicillin, as evidenced by the more frequent use of cefuroxime as the initial IV antibiotic of choice. However, ampicillin was still used in 19.7% of the time; Ciprofloxacin, ofloxacin and ceftizoxime were used by internists, cefotaxime was used in the neonatal age group.

Of the 12 in-patients who were started on ampicillin, 6 of the isolates were resistant. Five of these patients were given another antibiotic to which the isolated organism was sensitive, 4 were shifted to cefuroxime, and 1 was shifted to amikacin. There was 1 patient who was not shifted to another antibiotic after the urine culture and sensitivity result showed that the organism was resistant to ampicillin. This patient at the time of discharge was afebrile and asymptomatic and was advised to have a repeat urine culture on an outpatient basis. It is important to follow-up patients after treatment to determine if there will be clinical cure even if there was resistance to the antibiotic in vitro.

A limitation to this study is that the method of urine collection was not known, thus cannot be assured that all bacterial isolates were true pathogens.

CONCLUSIONS

This study showed that from January 2003 to June 2005 in Chong Hua Hospital were most common in patients aged 28 days to 1 year old; in males less than one year old; and in females >1-5 years old. *Escherichia coli* was the most common cause of UTI, followed by *Proteus mirabilis, Pseudomonas aeruginosa, Enterobacter sp.,* and *Klebsiella pneumoniae*.

Escherichia coli isolates were resistant to amoxicillin, ampicillin, cotrimoxazole, and cefalothin. The following antibiotics have good activity against all uropathogens: ceftriaxone, imipenem, gentamicin, ciprofloxacin, netilmicin, amikacin, and cefepime. The most common IV-antibiotic initially used to treat UTI in inpatients was cefuroxime.

RECOMMENDATIONS

It is recommended that antibiotic resistance surveillance be continually monitored for trends in resistance. Likewise, the clinical outcomes of the UTI after completion of treatment should also be studied.

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