Isolation and antimicrobial resistance patterns of *Escherichia coli* causing urinary tract infections in children aged 1 to 12 years.

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Abstract

Background: Urinary tract infection is a common problem worldwide. *Escherichia coli* are the greatest cause of primary urinary tract infections (UTI). Antimicrobial susceptibility testing provides information that allows physicians to select the most appropriate antimicrobial agents for treating a specific infection.

Objective: This study aimed to assess the current status of drug resistance among urinary *Escherichia coli* isolates.

Methodology and Results: A total of 512 urine samples were collected from out patients of age between 1 to 12 years of both sex of children at Serum Analysis Center Pvt. Ltd. (Referral Laboratory); Howrah; West Bengal; India between December 2016 to November 2017. The urine samples were cultured on HiCrome UTI Agra media and Eosin Methylene Blue Agar media (EMB) and the bacterial isolates were identified by Gram staining and conventional biochemical methods. Antimicrobial susceptibility testing was performed by Kirby Bauer disk diffusion method according to the current National Committee for Clinical Laboratory Standards (NCCLS) guidelines.

Among the 512 urine samples examined (1 to 12 years of children), included 276 (54.0%) in Male child and 236 (46.0%) in Female child and 220 (42.9%) of urinary pathogens are isolated. *Escherichia coli* isolated 50.0% from male child and 72.4% from female child. 41.9% of ESBL stains were isolates from 1 to 12 years of children (both sex).

Resistance rates of *Escherichia coli* (1 to 12 years of children) isolates were 83.8% to Amoxicillin/clavulanic acid, 70.5% to Cefixime, 23.5% to Fosfomycin, 26.5% to Nitrofurantoin, 63.2% to Ofloxacin, 66.1% to Ceftriaxone, 67.6% to Cefotaxime, 22.0% to Gentamicin, 89.7% to Cefpodoxime, 63.2% to Ciprofloxacin, 19.2% to Tobramycin, 80.8% to Cefprozil, 63.2% to Co-trimoxazole, 92.6% to Cefaclor, 70.5% to Doxycycline, 4.5% to Amikacin, 57.4% to Levofloxacin, 58.9% to Tetracycline and 89.8% to Cefalexin.

Conclusion: Considering the relatively increase rates of UTI and drug resistance observed in this study, continued local, regional, and national surveillance is warranted. Antibiotics should only be issued when prescribed by physicians.

Keywords: Urinary tract infections, Antibiotic resistance, Pediatrics, Antibiogram, *Escherichia coli.*

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Introduction

Urinary tract infections (UTIs) are a common problem in pediatric patients. Resistance to common antibiotic agents appears to be increasing over time, although resistance rates may vary based on geographic region or country. Prior antibiotic exposure is a pertinent risk factor for acquiring resistant organisms during a first UTI and recurrent UTI. Judicious prescribing of antibiotics for common pediatric conditions is needed to prevent additional resistance from occurring. Complex pediatric patients with histories of hospitalizations, prior antibiotic exposure, and recurrent UTIs are also at high risk for acquiring UTIs due to extended spectrum beta-lactamase-producing organisms. Data regarding the impact of *in vitro* antibiotic susceptibility testing interpretation on UTI treatment outcomes is lacking.

Urinary tract infections (UTIs) are among the most common infections with an increasing resistance to antimicrobial agents [1]. These ailments affect patients in all age groups and both sexes [2]. *Escherichia coli* have been documented as the most important pathogen associated with urinary tract infections in many countries [1].

Acute urinary tract infections are relatively common in children, with 8% of girls and 2% of boys having at least one episode by seven years of age, and between 30% and 40% will have another episode within two years [3,4]. Several studies have demonstrated that the geographical variability of pathogen occurrence in cases of UTI among inpatient and outpatient populations is limited by the predominance of Gram-negative bacterial organisms such as *Escherichia coli* and *Enterobacter aerogenes* in various regions of the world [5,6].

The most common pathogen is *Escherichia coli*, accounting for approximately 85% of urinary tract infections in children. Renal parenchyma defects are present in 3 to 15% of children within one to two years of being diagnosed with urinary tract infection. Clinical signs and symptoms of a urinary tract infection depend on the age of the child, but all febrile children two to 24 months of age with no obvious cause of infection should be evaluated for urinary tract infection (with the exception of circumcised boys older than 12 months). Evaluation of older children may depend on the clinical presentation and symptoms that point toward a urinary source (e.g., leukocyte esterase or nitrite present on dipstick testing; pyuria of at least 10 white blood cells per high-power field and bacteriuria on microscopy).

Antibiotics are medicines used to prevent and treat bacterial infections. Antibiotic resistance occurs when bacteria change in response to the use of these medicines. Bacteria, not humans or animals, become antibiotic-resistant. These bacteria may infect humans and animals, and the infections they cause are harder to treat than those caused by non-resistant bacteria. Antibiotic resistance leads to higher medical costs, prolonged hospital stays, and increased mortality (Table 1).

Antimicrobial resistance among urinary tract isolates has recently been reported with an increased frequency all over the world [7-10]. The world urgently needs to change the way it prescribes and uses antibiotics. Even if new medicines are developed, without behavioral change, antibiotic resistance will remain a major threat. Behavior changes must also include actions to reduce the spread of infections through vaccination, hand washing, practicing safer sex, and good food hygiene.

For more than half a century, antibiotic drugs have ensured that potentially life-threatening bacterial infections are treatable. Today, however, more and more bacterial infections fail to respond to antibiotic treatment. A federal task force recently warned that antibiotic resistance is “a growing menace to all people” and concluded that if nothing is done, treatments for common infections will become “increasingly limited and expensive- and, in some cases, nonexistent”.

The present study was carried out to isolate *Escherichia coli* from urine samples. Knowledge of antimicrobial susceptibility pattern in *Escherichia coli*, the predominant pathogen associated with urinary tract infection is important as a guide in selecting empirical antimicrobial therapy.

Materials and Methods

Study population, design, and setting

The current study was conducted in the Department of Microbiology, Serum Analysis Center Pvt. Ltd. (Referral Laboratory); Howrah; West Bengal; India; from December 2016 to November 2017.

Table 1. *Age distribution of sampled population.*

Age Group	Total Population	Male child	Female child
1 to 12 years	512	276 (54.0%)	236 (46.0%)
1 to 5 years	312	170 (54.5%)	142 (45.5%)
>5 to 12 years	200	106 (53.0%)	94 (47.0%)

Patient evaluation

A prospective analysis was done on 512 of outpatients. All patients were within ages 1 to 12 of children, comprising of both male and female patients. All samples received consisted 276 (54.0%) of male children and 236 (46.0%) of female children.

Categories age group

- Preschool aged Children: 1to 5 Years.
- School aged Children: >5 to 12 Years.

Collection of urine sample

Early morning mid-stream urine samples were collected using sterile, wide mouthed container with screw cap tops [11]. On the urine sample bottles were indicated name, age, sex, and time of collection along with requisition forms.

Sample processing

A calibrated sterile micron wire loop for the semi-quantitative method was used for the plating and it has a 4.0 mm diameter designed to deliver 0.01 ml. A loopful of the well mixed urine sample was inoculated on HiCrome UTI Agar media and EMB (Eosin Methylene Blue) Agar media. The plate was incubated aerobically at 37° C for overnight. The plates were then examined macroscopically and microscopically (colony Gram stain) for bacterial growth. The bacterial colonies were counted and multiplied by 100 to give an estimate of the number of bacteria present per milliliter of urine. Culture results were interpreted according to the standard criteria and a growth of $>10^5$ colony forming unit (CFU) /ml was considered as significant *bacteriuria* [12]. The urine samples were analyzed bacteriological using the methods [11,13,14].

Identification of isolates

The isolates were identified using colony morphology, Gram staining, Motility test, Indole test, Citrate test (Simmons Citrate Agar media), Urease test (Urease Agar media + 40% Urea), Triple Sugar Iron Agar media, ONPG (Ortho-nitrophenyl beta-D-galactopyranoside) and Oxidase test [11,14].

Antimicrobial susceptibility testing

All isolates were tested for antimicrobial susceptibility on Muller Hinton Agar by the standard Bauer et al. disc diffusion method [15] recommended by the Clinical and Laboratory Standards institute (CLSI) [16]. Antibiotic agents (disks) were obtained from Hi Media Laboratories, Pvt. Ltd; Mumbai. Appropriate quality control strains were used to validate the results of the antimicrobial disk. *Escherichia coli*, ATCC 25922, and *Pseudomonas aeruginosa*, ATCC 27853 was used as quality control strains [14]. Susceptibility test results will be interpreted according to criteria established by the CLSI [17].

Extended-spectrum Beta-lactamase (ESBL) detection by the CLSI phenotype method

The CLSI ESBL confirmatory test with cefotaxime (30 mcg) and Cefotaxime/Clavulanic acid (30+10 mcg) were performed for all isolates using the disc diffusion method on Mueller-Hinton Agar plates. Susceptibility test results were interpreted according to criteria established by the CLSI [17].

Results

For the twelve months of this study, 512 patient urine samples were received and cultured. There were 276 (54.0%) male child and 236 (46.0%) female child giving a total of 512 children who enrolled in this study. Their age ranged from 1 to 12 years. Among the cultures screened, bacteriuria of 10^5 cfu/ml of urine was found in 220 (42.9%) of the samples. A total of 292 (57.0%) of the urine samples were culture negative. 104 (37.7%) were isolated from male child and 116 (49.2%) from female child. *Escherichia coli* isolated 50.0% from male child and 72.4% from female child (Tables 1-11).

Discussion

In the community, bacterial infection of the urinary tract is one of the common causes for seeking medical attention. Demonstration of bacteria by appropriate culture methods is one of the methods in diagnosis of UTI. Traditionally, $>10^5$ bacteria/ml of urine showing a single isolate is taken to indicate bacteriuria and distinguishes infection from contamination in asymptomatic patients [18,19]. The pathogens causing UTIs are almost always predictable, with *Escherichia coli* being the primary etiological agent among both outpatient and inpatients [2,20-22]. Despite the widespread availability of antibiotics,

Table 2. *Prevalence of UTI in different age groups.*

Age Group	Total Population	Positive culture	Negative culture
1 to 12 years	512	220 (42.9%)	292 (57.0%)
1 to 5 years	312	148 (47.4%)	164 (52.6%)
>5 to 12 years	200	72 (36.0%)	128 (64.0%)

Table 3. *Prevalence of UTI in different age groups with male and female child.*

Age Group	Total Population in Male child	Positive culture in Male child	Total Population in Female child	Positive culture in Female child
1 to 12 years	276	104 (37.7%)	236	116 (49.2%)
1 to 5 years	170	74 (43.6%)	142	74 (52.2%)
>5 to 12 years	106	30 (28.3%)	94	42 (44.7%)

Table 4. *Escherichia coli isolated on urine culture with age group of 1 to 12 years.*

Pathogen	Male child [No.: 104]	Female child [No.: 116]
Escherichia coli	52 (50.0%)	84 (72.4%)

Table 5. *Escherichia coli isolated on urine culture with age group of 1 to 5 years.*

Pathogen	Male child [No.: 74]	Female child [No.: 74]
Escherichia coli	36 (48.6%)	54 (73.0%)

Table 6. *Escherichia coli isolated on urine culture with age group of >5 to 12 years.*

Pathogen	Male child [No.: 30]	Female child [No.: 42]
Escherichia coli	16 (53.3%)	30 (71.4%)

Table 7. *Extended-spectrum beta-lactamases (ESBL) isolated of UTI in different age groups [both sex].*

Age Group	Total Positive Culture	ESBL in *Escherichia coli*
1 to 12 years	220	92 (41.9%)
1 to 5 years	148	58 (39.2%)
>5 to 12 years	72	34 (47.3%)

Table 8. *Percentage of resistant and susceptibility of isolated Escherichia coli to tested antibiotic.*

Total Isolates : 136				
Antibiotics	**R (No.)**	**R (%)**	**S (No.)**	**S (%)**
Amoxicillin/Clavulanic acid	**114**	**83.8**	**22**	**16.2**
Amikacin	6	4.5	130	95.5
Gentamicin	30	22	106	78
Tobramycin	26	19.2	110	80.8
Fosfomycin	32	23.5	104	76.5
Ciprofloxacin	86	63.2	50	36.8
Ofloxacin	86	63.2	50	36.8
Levofloxacin	78	57.4	58	42.6
Nitrofurantoin	36	26.5	100	73.5
Trimethoprim/ Sulfamethoxazole	**86**	**63.2**	**50**	**36.8**
Doxycycline Hydrochloride	96	70.5	40	29.5
Tetracycline	80	58.9	56	41.1
Cefixime	**96**	**70.5**	**40**	**29.5**
Ceftriaxone	90	66.1	46	33.9
Cefotaxime	92	67.6	44	32.4
Cefpodoxime	**122**	**89.7**	**14**	**10.3**
Cefprozil	**110**	**80.8**	**26**	**19.2**
Cefaclor	126	92.6	10	7.4
Cefalexin	**122**	**89.8**	**14**	**10.2**

NOTE *– Children 1 -12 Years*

Table 9. *Percentage of resistant and susceptibility of isolated Escherichia coli to tested antibiotic.*

Total Isolates : 90				
Antibiotics	**R (No.)**	**R (%)**	**S (No.)**	**S (%)**
Amoxicillin/Clavulanic acid	**80**	**88.9**	**10**	**11.1**
Amikacin	4	4.4	86	95.6
Gentamicin	22	24.5	68	75.5
Tobramycin	12	13.4	78	86.6
Fosfomycin	26	28.9	64	71.1
Ciprofloxacin	56	62.2	34	37.8
Ofloxacin	54	60	36	40
Levofloxacin	52	57.8	38	42.2
Nitrofurantoin	24	26.7	66	73.3
Trimethoprim/ Sulfamethoxazole	**58**	**64.4**	**32**	**35.6**
Doxycycline Hydrochloride	68	75.5	22	24.5
Tetracycline	60	66.6	30	33.4
Cefixime	**62**	**68.8**	**28**	**31.2**
Ceftriaxone	58	64.5	32	35.5
Cefotaxime	58	64.5	32	35.5
Cefpodoxime	**80**	**88.8**	**10**	**11.2**
Cefprozil	**70**	**77.8**	**20**	**22.2**
Cefaclor	82	91.1	8	8.9
Cefalexin	**82**	**91.1**	**8**	**8.9**

NOTE *– Category-I: Pre School aged Children [1 -5 Years]*

UTIs remain the most common bacterial infections in human populations [23]. In studies performed in various regions of the world mostly *Escherichia coli* has been isolated in UTI [24-29]. Our findings are consistent with these reports. In our study confirmed *Escherichia coli* are major urinary pathogen and urinary tract infection was more common among females than male child.

Table 10. *Percentage of resistant and susceptibility of isolated Escherichia coli to tested antibiotic.*

Total Isolates : 46				
Antibiotics	**R (No.)**	**R (%)**	**S (No.)**	**S (%)**
Amoxicillin/Clavulanic acid	**34**	**74**	**12**	**26**
Amikacin	2	4.3	44	95.7
Gentamicin	8	17.4	38	82.6
Tobramycin	14	30.5	32	69.5
Fosfomycin	6	13	40	87
Ciprofloxacin	30	65.3	16	34.7
Ofloxacin	32	69.5	14	30.5
Levofloxacin	26	56.5	20	43.5
Nitrofurantoin	12	26	34	74
Trimethoprim/ Sulfamethoxazole	**28**	**60.8**	**18**	**39.2**
Doxycycline Hydrochloride	28	60.8	18	39.2
Tetracycline	20	43.4	26	56.6
Cefixime	**34**	**74**	**12**	**26**
Ceftriaxone	32	69.5	14	30.5
Cefotaxime	34	74	12	26
Cefpodoxime	**42**	**91.3**	**4**	**8.7**
Cefprozil	**40**	**87**	**6**	**13**
Cefaclor	44	95.7	2	4.3
Cefalexin	**40**	**87**	**6**	**13**

NOTE *– Category-II: School aged Children [>5 - 12 Years]*

Table 11. *Antibiotics commonly used to treat urinary tract infection in children.*

Antibiotic	Dosing	Common adverse effects
Amoxicillin/ clavulanate (Augmentin)	25 to 45 mg per kg per day, divided every 12 hours	Diarrhea, nausea/vomiting,rash
Cefixime (Suprax)	8 mg per kg every 24 hours or divided every 12 hours	Abdominal pain, Diarrhea, flatulence,rash
Cefpodoxime	10 mg per kg per day, divided every 12 hours	Abdominal pain, Diarrhea,nausea,rash
Cefprozil (Cefzil)	30 mg per kg per day, divided every 12 hours	Abdominal pain, Diarrhea, elevated results on liver function tests, nausea
Cephalexin (Keflex)	25 to 50 mg per kg per day, divided every 6 to 12 hours	Diarrhea,headache, nausea/ vomiting, rash
Trimethoprim/ sulfamethoxazole (Bactrim, Septra)	8 to 10 mg per kg per day, divided every 12 hours	Diarrhea, nausea/vomiting, photosensitivity, rash

The antibiotics may not be saving us from UTIs for very much longer. Scientists tracking UTIs from 2000 to 2010 found a dramatic uptick in cases caused by *Escherichia coli* that do not respond to the drugs that are our first line of defense. In examining more than 12 million urine analyses from that period, they found that cases caused by *Escherichia coli* resistant to ciprofloxacin grew five-fold, from 3% to 17.1% of cases. *Escherichia coli* resistant to the drug trimethoprim-sulfamethoxazole jumped from 17.9% to 24.2%. These are two of the most commonly prescribed antibiotics used to treat UTIs. When they are not effective, doctors must turn to more toxic drugs, and the more those drugs are used, the less effective they in turn become. When those drugs stop working, doctors will be left with a drastically reduced toolkit with which to fight infection (Figure 1).

Some of this growing resistance in *Escherichia coli* and other bacteria are due to the fact that antibiotics are being overprescribed, handed out to patients who have no bacterial infections. There is also evidence that the genes that give bacteria resistance to drugs are being spread in livestock farming operations, where antibiotics are a common ingredient in animal feed. Ciprofloxacin is one of those antibiotics, and researchers have found that *Escherichia coli* resistant to it are thriving in poultry farms. Very closely related strains of drug-resistant *Escherichia coli* have been found in people, suggesting that the bugs spread from the birds to humans.

People suffered from UTIs long before antibiotics were discovered in the early twentieth century, of course. Should these drugs cease to be effective, we'll have to go back to what we were doing before. The truth is, though, before antibiotics we had no real treatment. Sicknesses resembling UTIs have been described in medical texts for thousands of years, by everyone from the ancient Greeks and Chinese to the pioneers of evidence-based medicine in the early 1900s. Some of these doctors prescribed various tinctures, ointments, and special diets to deal with the symptoms, but in cases in which the infection spread to the bladder and kidneys and beyond, they were fairly helpless. As a last-ditch effort, they operated to drain puss from the infected kidneys and hoped the patient would survive. Treatment did not fundamentally change until antibiotics arrived on the scene.

Extended-spectrum beta-lactamases (ESBL) are enzymes that confer resistance to most beta-lactam antibiotics, including penicillins, cephalosporins, and the monobactam aztreonam. Infections with ESBL-producing organisms have been associated with poor outcomes. Community and hospital-acquired ESBL-producing Enterobacteriaceae are prevalent worldwide [30]. Reliable identification of ESBL-producing organisms in clinical laboratories can be challenging, so their prevalence is likely underestimated. Carbapenems are the best antimicrobial agent for infections caused by such organisms.

Beta-lactamases are enzymes that open the beta-lactam ring, inactivating the antibiotic. The first plasmid-mediated beta-lactamase in gram-negative bacteria was discovered in Greece in the 1960s. It was named TEM after the patient from whom it was isolated (Temoniera) [31]. Subsequently, a closely related enzyme was discovered and named TEM-2. It was identical in biochemical properties to the more common TEM-1 but differed by a single amino acid with a resulting change in the isoelectric point of the enzyme.

These two enzymes are the most common plasmid-mediated beta-lactamases in gram-negative bacteria, including Enterobacteriaceae, Pseudomonas aeruginosa, Haemophilus influenzae, and Neisseria gonorrhoeae. TEM-1 and TEM-2 hydrolyze penicillins and narrow spectrum cephalosporins, such as cephalothin or cefazolin. However, they are not effective against higher generation cephalosporins with an oxyimino side chain, such as cefotaxime, ceftazidime, ceftriaxone, or cefepime. Consequently, when these antibiotics were first introduced, they were effective against a broad group of otherwise resistant bacteria. A related but less common enzyme was termed SHV, because sulfhydryl reagents had a variable effect on substrate specificity.

Antibiotic resistance is an important issue affecting public health, and rapid detection in clinical laboratories is essential for the prompt recognition of antimicrobial-resistant organisms. Infection-control practitioners and clinicians need the clinical laboratory to rapidly identify and characterize different types of resistant bacteria efficiently to minimize the spread of these bacteria and help to select more appropriate antibiotics. This is particularly true for ESBL-producing bacteria. The epidemiology of ESBL-producing bacteria is becoming more complex with increasingly blurred boundaries between hospitals and the community. *Escherichia coli* that produce CTX-M βlactamases seem to be true community ESBL producers with different behaviors from Klebsiella spp, which produce TEM-derived and SHV-derived ESBLs. These bacteria have become widely prevalent in the community setting in certain areas of the world and they are most likely being imported into the hospital setting. A recent trend is the emergence of community-onset bloodstream infections caused by ESBL-producing bacteria, especially CTX-M-producing *Escherichia coli*. These infections are currently rare, but it is possible that, in the near future, clinicians will be regularly confronted with hospital types ofbacteria causing infections in patients from the community.β–lactums contribute a measure class of safer antibiotics. They are widely used as broad spectrum antibiotics for all the type of infections. New generation of antibiotics is predominantly preferred in clinical use. Many more new β- lactums are expected for the clinical use and many new β- lactums are expected in future. There is a better scope, prosperity for the discovery and development of new and safer β-lactums. The structure of β- lactams, their nature, classification, chemistry to be well studied. β- lactums, their mode of action, their bactericidal properties and their future growth is seen with new hopes. In this study, in the age group of 1 to 5 years, ESBL found 39.2% in both sex of child and the age group of >5 to 12 years, ESBL found 47.3% in both sex of child (Table 7).

Nursing-home patients may be an important reservoir of ESBL-producing multidrug-resistant *Escherichia coli* and *K. pneumoniae* [31-34]. In our study, resistance to more than one antibiotic was rather common and the spread of ESBL-producing isolates was quite alarming. The resistance rate to fluoroquinolones observed in this study was quite high, particularly in *Escherichia coli*, and poses some concerns about their use in empirical treatment of UTIs. Resistance to fluoroquinolones is known to be associated with the previous use of antibiotics, particularly fluoroquinolones, and previous reports have demonstrated that underlying urinary tract diseases predispose patients to repeated UTIs and, in turn, to exposure to antibiotics such as fluoroquinolones [35-37].

In a world without antibiotics, many peoples' UTIs would doubtless subside under attack from the immune system. But some fraction of them would not, and those people would find themselves in dire straits. And about the common idea that cranberry juice can prevent or treat UTIs: evidence is pretty spotty. Better to try to reduce the irresponsible use of antibiotics than rely on juice (Figures 2-4).

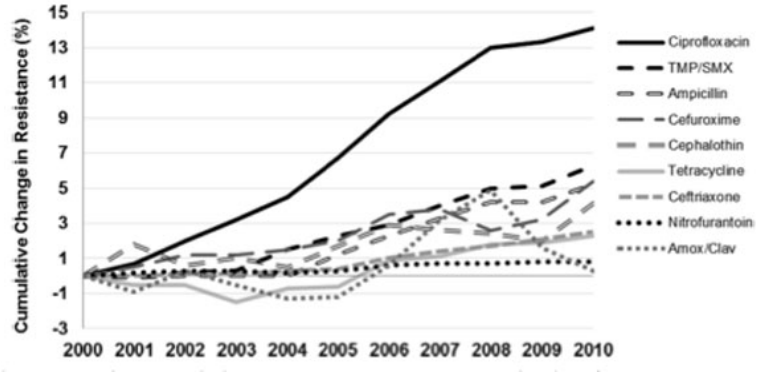

Figure 1. *The trends in antibiotics resistance.*

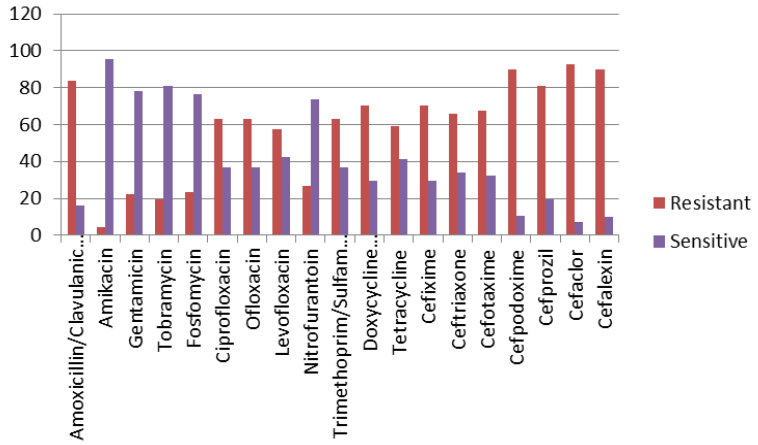

Figure 2. *Pattern of Escherichia coli resistant and sensitive (children: 1 - 12 years).*

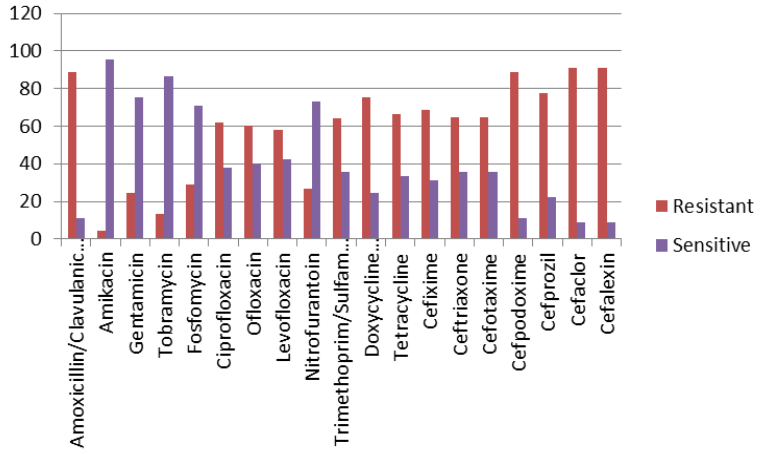

Figure 3. *Pattern of Escherichia coli resistant and sensitive (pre-school aged children [1 - 5 years]).*

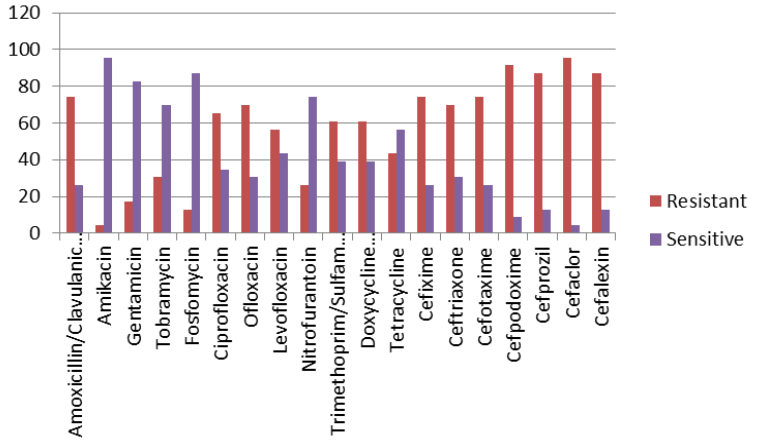

Figure 4. *Pattern of Escherichia coli resistant and sensitive (school aged children [>5 - 12 years]).*

Conclusion

The study detected increasing resistance of *Escherichia coli* strains to commonly use oral antibiotics in UTI of children. The present results in increasing commonly use of oral antibiotic resistance trends in UTI patients indicate that it is imperative to rationalize the use of antimicrobials and to use these conservatively. Considering the relatively increase rates of UTI and drug resistance observed in this study, continued local, regional, and national surveillance of antimicrobial resistance among urinary pathogens causing UTI, so as to increase positive outcomes of clinical interventions. Antibiotics should only be issued when prescribed by physicians.

Antibiotic resistance is a growing problem in pediatric urology as highlighted by the significantly increased urinary pathogen resistance to commonly use of oral antibiotics. Poor empiric prescribing practices, lack of urine testing, and nonselective use of prophylaxis exacerbate this problem. However, three small changes in practice patterns may curb the growing resistance rates: use of urine testing in order to only treat when indicated and tailor broad-spectrum therapy as able; selective application of antibiotic prophylaxis to patients; and use of local antiobiograms, particularly pediatric-specific antiobiograms, with inpatient versus outpatient data.

This study will provide novel, clinically important information on the diagnostic features of childhood UTI and the cost effectiveness of a validated prediction rule, to help primary care clinicians improve the efficiency of their diagnostic strategy for UTI in children. Regular monitoring is required to establish reliable information about resistance pattern of urinary pathogens for optimal empirical therapy of patients with UTIs. Finally, we suggest that empirical antibiotic selection should be based on the knowledge of local prevalence of bacterial organisms and antibiotic sensitivities rather than on universal guidelines.

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