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Antibiotic resistance pattern of uropathogenic *Escherichia coli* isolated from children with symptomatic urinary tract infection in Moscow, Russia

Souadkia Sarra, Mbarga Manga Joseph Arsene, Volina Elena Grigorievna, Podoprigora Irina Victorovna, Yashina Natalia Vyacheslavovna and Borechova Marina Nikolaïevna

Department of Microbiology and Virology, Institute of Medicine, RUDN University, Moscow, Russia.
Corresponding author: Mbarga Manga Joseph Arsene, e-mail: josepharsenembarga@yahoo.fr
Co-authors: SS: sarah1sdk@gmail.com, VEG: volina-eg@rudn.ru, PIV: podoprigora-iv@rudn.ru; YNV: yashina-nv@rudn.ru; BMN: borekhova-mn@rudn.ru
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Abstract

Background and Aim: Uropathogenic *Escherichia coli* (UPEC) is commonly involved in urinary tract infections (UTIs), which are generally treated with antibiotics. However, the emergence of multidrug-resistant (MDR) strains of UPEC has made the treatment difficult. There is thus a need to continuously assess their sensitivity to antibiotics. This study aimed to determine the antibiotic resistance patterns and MDR phenotypes of UPEC strains isolated from children diagnosed with UTIs at the Russian Children's Clinical Hospital in Moscow, Russia.

Materials and Methods: Kirby–Bauer's disc diffusion method was used to study the sensitivity to antibiotics of 106 UPEC isolates from urine specimens from children (aged from 9 months to 18 years old) diagnosed with UTIs. The results were interpreted in accordance with the Clinical and Laboratory Standards Institute guidelines and the correlations of variables with the degree to which each antibiotic inhibited the UPEC strains in terms of diameter on the disc were determined using Spearman's rank correlation test. A t-test and principal component analysis were performed to visualize the correlations of the susceptibility of UPEC to antibiotics with the age and sex of the patients. Statistical significance was set at $p \leq 0.05$.

Results: Among the 106 UPEC strains tested, none (0%) showed resistance to fosfomycin (FO), while 84 (79.2%) were resistant (R) to at least one antibiotic. The highest rates of resistance were observed to amoxicillin (69.8%), ampicillin (62.3%), cefazolin (39.6%), trimethoprim (TR) (37.7%), ceftriaxone (34.9%), and tetracycline (33.0%). Interestingly, 22 (20.8%) strains were R to imipenem. UPEC isolates from males aged 1-6 years were more R to antibiotics than those from the other groups, with the exception of TR, to which UPEC isolates from females aged 13-18 years old were less sensitive (S). The multidrug-resistance (MDR) index ranged between 0.00 and 0.75 and we found that more than a quarter of UPEC (31/106) had an MDR index ≥0.5 and only 22 (20.7%) strains were S to all antibiotics tested (MDR index=0). Finally, Spearman's rank correlation test showed that, with the exception of FO, there were correlations between the inhibition diameters of all other antibiotics.

Conclusion: FO is the only antibiotic to which all UPECs were S and may be suggested as the first line of treatment for UPEC. Further research is needed to continue monitoring antibiotic resistance and to investigate the genetic features associated with such resistance observed in this study.

Keywords: antibiotics, multidrug resistance, urinary tract infections, uropathogenic *Escherichia coli.*

Introduction

Urinary tract infections (UTIs) are among the most common bacterial infections, affecting around 150-250 million people each year worldwide [1]. These infections account for 75% of infections in community settings and 50-65% of those in health-care settings [2,3]. In uncomplicated UTIs (50-90%), strains of uropathogenic *Escherichia col*i (UPEC) are the most common organisms seen [4,5]. In such cases, these strains diverge from their status as part of the commensal intestinal flora and colonize the urinary tract, exhibiting various virulence factors, which allow them to infect that tract [6].

It is estimated that 40% of women and 12% of men experience a minimum of one symptomatic UTI episode during their lifetime, and 27-48% of affected women suffer from recurrent UTIs [7,8]. UPEC is the most common group of bacterial pathogens causing UTIs in children [9] and leads to the recurrence of infection in 10-30% of cases [10]. Infections caused by UPECs are generally treated with antibiotics. However, in recent years, several complications have been observed in the treatment and management of patients with this pathology due to the emergence and spread of antibiotic resistance [11,12].

Furthermore, multidrug-resistant (R) organisms can cause an increase in UTIs in children that are difficult to treat [13]. The increasing prevalence of R Enterobacteriaceae causing UTIs in children has been widely recorded [14].

Consequently, it has become necessary to regularly assess the antibiotic sensitivity of UPEC strains to establish their resistance profile and to monitor the evolution of antibiotic resistance in specific geographical areas. Thus, this study was conducted to evaluate the antibiotic sensitivities of UPEC strains isolated from children diagnosed with UTIs at the Russian Children's Clinical Hospital in Moscow.

Materials and Methods

Ethical approval and informed consent

After retrieval of relevant information from the referral, all isolates were anonymized, with only the age and sex being retained. Therefore, no ethical approval was necessary.

Study period and location

This study was performed from November 2017 to June 2018 at the Russian children's clinical hospital, Moscow, Russia, and in the Department of Microbiology and Virology of the People's Friendship University of Russia.

Collection of isolates

The 106 strains of *E. coli* used in the present study were isolated from urine specimens taken from patients (children aged 9 months to 18 years old) with symptomatic and laboratory-confirmed UTIs. The bacteria were not repetitive since only one bacterium was considered per patient. These bacteria were isolated and identified in the laboratory of the Russian Children's Clinical Hospital and transferred to the research laboratory of the Department of Microbiology and Virology of People's Friendship University of Russia, where they were kept frozen at −80°C.

Culture conditions

All of the cultures were performed on Brain Heart Infusion Broth (BHIB) (HiMedia™ Laboratories Pvt. Ltd., India) and Muller Hinton Agar (MHA HiMedia™) and incubated aerobically at 37°C for 18-24 h.

Antimicrobial susceptibility testing

The antimicrobial resistance pattern was determined by the modified Kirby–Bauer's disc diffusion method, as described by Manga *et al*. [15]. Briefly, after bringing the bacteria at room temperature, they were cultured at 37°C for 24 h in sterile BHIB. A total of 1.5 mL of each overnight culture was centrifuged (Eppendorf Centrifuge 5415 R) for 10 min at 3000 RCF and the pellet was collected, washed 3 times with phosphate-buffered saline, and resuspended in 5 mL of physiological water to obtain a concentration equivalent to 0.5 McFarland. Then, 100 µL of the culture was plated on Muller Hinton Agar and the antibiotic discs were placed aseptically using a dispenser. The following 12 antibiotics were used: Amoxicillin (AMC), 30 µg/disc; ampicillin (AMP), 25 µg/disc; cefazolin (CZ), 30 µg/disc; CZ/clavulanic acid (CAC), 30/10 per disc; ceftazidime (CAZ), 30 µg/disc; ceftriaxone (CTR), 30 µg/disc; ciprofloxacin (CIP), 30 µg/disc; fosfomycin (FO), 200 µg/disc; imipenem (IMP), 10 µg/disc; nitrofurantoin (NIT), 200 µg/disc; tetracycline (TE), 30 µg/disc; andtrimethoprim (TR), 30 µg/disc.

Interpretation of results and data analysis

After 18-24 h of incubation at 37°C, the inhibition diameters were measured and interpreted in accordance with the Clinical and Laboratory Standards Institute [16]. R, intermediate (I), and sensitive (S) interpretations were obtained automatically using algorithms written in Excel software (Microsoft Office 2016 MSO version 16.0.13628.20128[32 bits], USA) with the parameters described in Table-1 [15,16]. The software Minitab 18 was used to perform Spearman's rank correlation test between inhibition diameters and the statistical significance was set at $p \leq 0.05$. A t-test and principal component analysis (PCA) were carried out using XLSTAT 2020 statistical software (Addinsof Inc., New York, USA). PCA was used to visualize the correlations of the susceptibility of UPEC to antibiotics with the age and sex of the patients from whom the bacteria were isolated.

Results

In this study, the 106 UPEC tested were previously isolated from the urine of children (n=106) aged 9 months to 18 years old with laboratory-confirmed UTIs. The median age was 5.5 years and the male-to-female ratio was 0.68:1. To facilitate data analysis and interpretation of the results, the subjects were divided into six groups based on sex and age ranges of 1-6 years, 7-12 years, and 12-18 years. All results involving sex and age were expressed as intragroup prevalence, that is, as a percentage relative to the group considered.

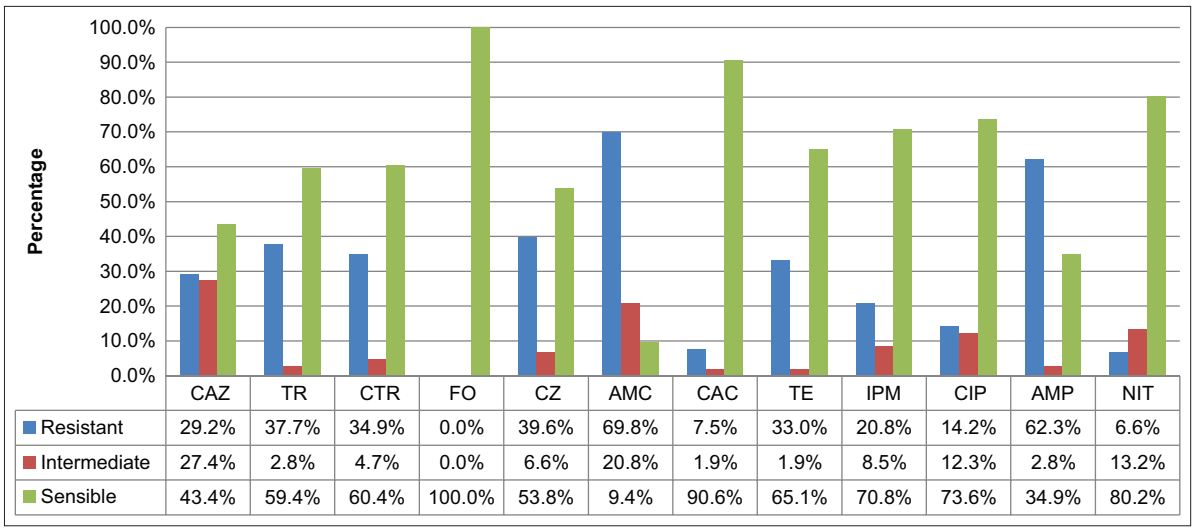
Figure-1 shows the sensitivity of the isolated UPEC to antibiotics. Out of the 1272 antibiograms performed, we observed 77 (29.6%) R cases, 109 (8.6%) I cases, and 786 (61.8%) S cases. Isolated UPECs exhibited the highest resistance to AMC (69.8%), AMP (62.3%), CZ (39.6%), TR (37.7%), CTR (34.9%), and TE (33.0%). Interestingly, no UPEC was R to FO and, unlike cefazoline, CZ/CAC was highly active in 90.6% of UPEC. In addition, antibiotics such as NIT, CIP, and IMP were also very active, with susceptibility rates of 80.2%, 73.6%, and 70.8%, respectively. Furthermore, Figures-2 and 3 present the overall prevalence of the susceptibility of UPEC to antibiotics depending on the age and sex of the children from whom the bacteria were isolated.

As presented in Figure-2, UPEC isolated from males aged 1-6 years were more R to AMP, amoxicillin, CAZ, and cefazoline. Those isolated from males aged 13-18 years were also R to AMP and amoxicillin,

Table 1: Interpretation criteria for antibiotic sensitivity of enterobacteria [15,16].

Interpretation	Antibiotics/limits of inhibition diameters (mm)											
	CIP	CZ	CAZ	AMC	CTR	TR	TE	NIT	AMP	IMP	CAC	FO
R	d≤15	d≤14	d≤14	d≤13	d≤13	d≤13	d≤14	d≤13	d≤13	d≤13	d≤14	d≤12
I	16-20	15-17	15-17	14-17	14-20	14-15	15-18	14-17	14-16	14-15	15-17	13-15
S	d≥21	d≥18	d≥18	d≥18	d≥21	d≥16	d≥19	d≥18	d≥17	d≥16	d≥18	d≥17

AMC=Amoxycillin, AM=Ampicillin, CZ=Cefazolin, CAC=Cefazolin/clavulanic acid, CAZ=Ceftazidime, CTR=Ceftriaxone, CIP=Ciprofloxacin, FO=Fosfomycin, IMP=Imipenem, NIT=Nitrofurantoin, TE=Tetracyclin, TR=Trimethoprim



	CAZ	TR	CTR	FO	CZ	AMC	CAC	TE	IPM	CIP	AMP	NIT
Resistant	29.2%	37.7%	34.9%	0.0%	39.6%	69.8%	7.5%	33.0%	20.8%	14.2%	62.3%	6.6%
Intermediate	27.4%	2.8%	4.7%	0.0%	6.6%	20.8%	1.9%	1.9%	8.5%	12.3%	2.8%	13.2%
Sensible	43.4%	59.4%	60.4%	100.0%	53.8%	9.4%	90.6%	65.1%	70.8%	73.6%	34.9%	80.2%

Figure-1: Sensitivity to antibiotics of the 106 uropathogenic *Escherichia coli* isolated. R=Resistant, I=Intermediate, S=Sensitive, AMC=Amoxycillin, AMP=Ampicillin, CZ=Cefazolin, CAC=Cefazolin/clavulanic acid, CAZ=Ceftazidime, CTR=Ceftriaxone, CIP=Ciprofloxacin, FO=Fosfomycin, IMP=Imipenem, NIT=Nitrofurantoin, TE=Tetracyclin, TR=Trimethoprim.

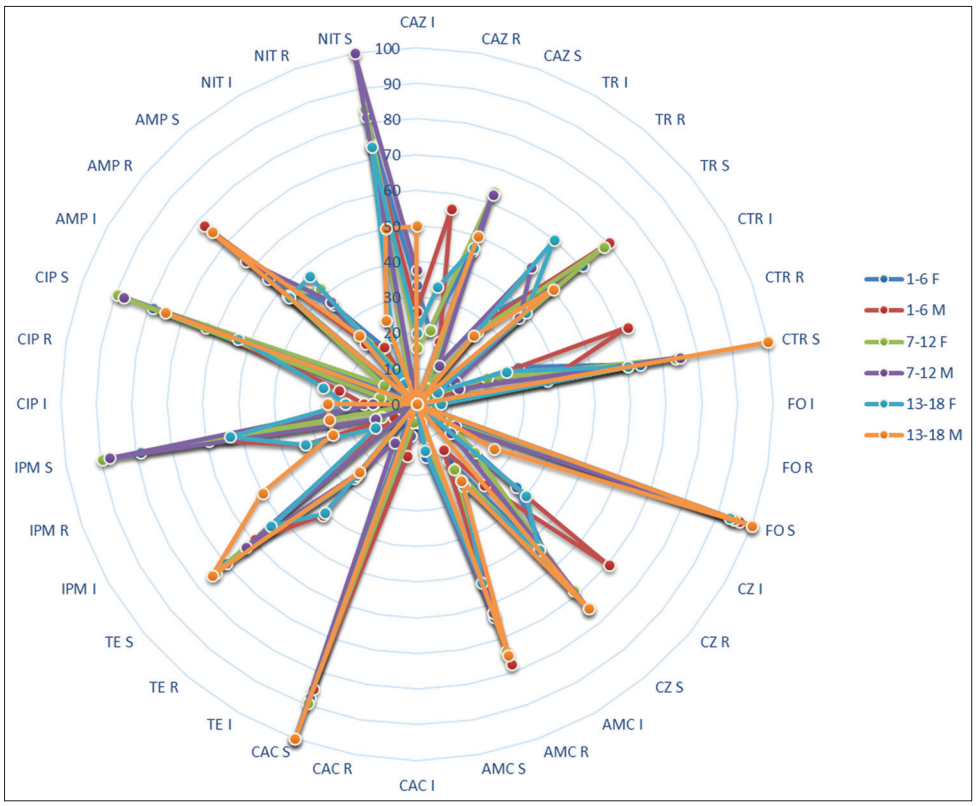


Figure-2: Overall prevalence of the susceptibility of uropathogenic *Escherichia coli* to antibiotics depending on the age and sex of the children from whom the bacteria were isolated. R=Resistant, I=Intermediate, S=Sensitive, AMC=Amoxycillin, AMP=Ampicillin, CZ=Cefazolin, CAC=Cefazolin/clavulanic acid, CAZ=Ceftazidime, CTR=Ceftriaxone, CIP=Ciprofloxacin, FO=Fosfomycin, IMP=Imipenem, NIT=Nitrofurantoin, TE=Tetracycline, TR=Trimethoprim.

but very S to CTR and CZ/CAC. Moreover, UPEC isolated from children aged 7-12 years were all S to IMP, CIP, NIT, and FO. As shown in Figure-3, UPEC strains isolated from females aged 13-18 years old were the most R to TR.

In addition, as observed in Table-2, Spearman's rank correlation test showed that, with the exception of FO, there were strong correlations among the sensitivities of UPEC to 11 other antibiotics, with probabilities ranging from 0.000 to 0.035 ($p \leq 0.05$) and Spearman's coefficients ranging from 0.241 to 0.917. The strongest correlation was observed between susceptibility to IMP and susceptibility to CIP ($p < 0.000$ and Spearman's coefficient=0.917).

To visualize the associations among age, sex, and susceptibility of UPEC to antibiotics, PCA was performed. Figure-4 shows the distribution of the susceptibility to antibiotics of the tested UPEC, age, and sex in an F1×F2 system. UPEC isolated from 13 to 18-year-old females and 1-6-year-old children were globally strongly correlated with resistance to TE, CAZ, amoxicillin and to IMP, TR, cefazoline, while those from 7 to 12-year-old children were more correlated with sensitivity to most antibiotics used. Finally, as shown in Table-3, the multidrug resistance (MDR) index was obtained for each strain. We found that more than a quarter of UPEC (31/106) had an MDR index ≥0.5 and only 22 (20.7%) strains were S to all of the antibiotics tested (MDR index=0).

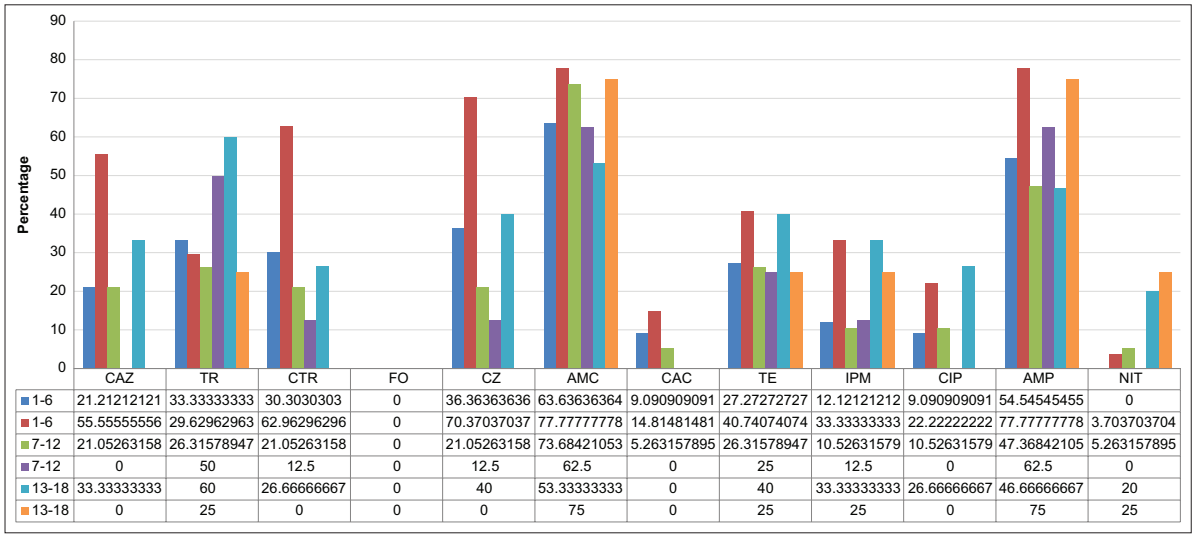
Discussion

Due to limited resources, this study focused only on analyzing the phenotype of antibiotic sensitivity of UPEC isolated from children diagnosed with UTIs. The selected antibiotics were those commonly used for treating UTIs in Russia.

In this study, the high resistance observed against AMP and amoxicillin was in accordance with previously reported results [17-19]. This high rate can be explained by the fact that these antibiotics are regularly used as first-line treatments as well as self-medication in the treatment of common bacterial infections [20,21]. These practices lead to the recurrent exposure of normal microbiota (including *E. coli*) to these antibiotics, which may prompt adaptation of the strains and thus antibiotic resistance [20,22-24]. Paschke *et al*. [22] reported that recent antimicrobial exposure is associated with antimicrobial-R UTIs among pediatric outpatients and that the magnitude of this association decreases with time since exposure. In their study, out of 533 children who had a first UTI, those exposed to amoxicillin within 30 days and 31-60 days before the UTI were associated with both AMP and amoxicillin-clavulanate resistance [22]. They also reported that there was no association between exposure to other antimicrobial agents and resistance to any of the antimicrobial agents [22]. Therefore, the high resistance to AMP and amoxicillin in UPEC isolated from children aged 1-6 years compared with the levels of other groups, which seemed unusual, could be explained by the previous study [22]. Unfortunately, in our study, information on the drugs taken by these children before their infection was not available, limiting our ability to perform comparisons with the data reported in the literature.

Otherwise, contrary to many studies [12,25,26], 20.8% of our isolates were R to IMP. Shirani *et al*. [17] reported that certain UPEC acquire genes encoding extended-spectrum beta-lactamases. These enzymes destroy the β-lactam ring in the antibiotic structure of many antibiotics including carbapenems [17]. The emergence of carbapenem-R UPEC makes treatment of these infections increasingly challenging [26,27].

Moreover, we found that UPEC strains isolated from females aged 13-18 years old were the most



	CAZ	TR	CTR	FO	CZ	AMC	CAC	TE	IPM	CIP	AMP	NIT
1-6	21.21212121	33.33333333	30.3030303	0	36.36363636	63.63636364	9.090909091	27.27272727	12.12121212	9.090909091	54.54545455	0
1-6	55.55555556	29.62962963	62.96296296	0	70.37037037	77.77777778	14.81481481	40.74074074	33.33333333	22.22222222	77.77777778	3.703703704
7-12	21.05263158	26.31578947	21.05263158	0	21.05263158	73.68421053	5.263157895	26.31578947	10.52631579	10.52631579	47.36842105	5.263157895
7-12	0	50	12.5	0	12.5	62.5	0	25	12.5	0	62.5	0
13-18	33.33333333	60	26.66666667	0	40	53.33333333	0	40	33.33333333	26.66666667	46.66666667	20
13-18	0	25	0	0	0	75	0	25	25	0	75	25

Figure-3: Prevalence of the resistance of uropathogenic *Escherichia coli* to antibiotics depending on the age and sex of the children from whom the bacteria were isolated. R=Resistant, I=Intermediate, S=Sensitive, AMC=Amoxycillin, AMP=Ampicillin, CZ=Cefazolin, CAC=Cefazolin/clavulanic acid, CAZ=Ceftazidime, CTR=Ceftriaxone, CIP=Ciprofloxacin, FO=Fosfomycin, IMP=Imipenem, NIT=Nitrofurantoin, TE=Tetracycline, TR=Trimethoprim.

Table 2: Spearman rank correlation test between the susceptibility to antibiotics of the uropathogenic *Escherichia coli* isolated. Statistical significance was considered at $P<0.05$.

	CAZ	TR	CTR	FO	CZ	AMC	CAC	TE	IPM	CIP	AMP
TR											
Spearman coef	0.106										
p-value	0.024										
CTR											
Spearman coef	0.852	0.180									
p-value	0.000	0.065									
FO											
Spearman coef	0.015	0.156	0.013								
p-value	0.881	0.110	0.897								
CZ											
Spearman coef	0.772	0.205	0.794	0.075							
p-value	0.000	0.035	0.000	0.442							
AMC											
Spearman coef	0.399	0.341	0.436	0.029	0.674						
p-value	0.000	0.000	0.000	0.765	0.000						
CAC											
Spearman coef	0.822	0.137	0.764	-0.021	0.730	0.393					
p-value	0.000	0.162	0.000	0.831	0.000	0.000					
TE											
Spearman coef	0.265	0.456	0.267	0.101	0.382	0.403	0.232				
p-value	0.006	0.000	0.006	0.304	0.000	0.000	0.017				
IPM											
Spearman coef	0.435	0.419	0.463	0.008	0.524	0.444	0.493	0.297			
p-value	0.000	0.000	0.000	0.939	0.000	0.000	0.000	0.002			
CIP											
Spearman coef	0.393	0.453	0.414	-0.001	0.450	0.337	0.424	0.307	0.917		
p-value	0.000	0.000	0.000	0.991	0.000	0.000	0.000	0.001	0.000		
AMP											
Spearman coef	0.492	0.345	0.507	0.045	0.733	0.808	0.458	0.373	0.469	0.414	
p-value	0.000	0.000	0.000	0.649	0.000	0.000	0.000	0.000	0.000	0.000	
NIT											
Spearman coef	0.190	0.299	0.241	0.005	0.178	0.096	0.268	0.251	0.399	0.369	0.067
p-value	0.051	0.002	0.013	0.956	0.068	0.326	0.006	0.009	0.000	0.000	0.494

AMC=Amoxycillin, AM=Ampicillin, CZ=Cefazolin, CAC=Cefazolin/clavulanic acid, CAZ=Ceftazidime, CTR=Ceftriaxone, CIP=Ciprofloxacin, FO=Fosfomycin, IMP=Imipenem, NIT=Nitrofurantoin, TE=Tetracyclin, TR=Trimethoprim

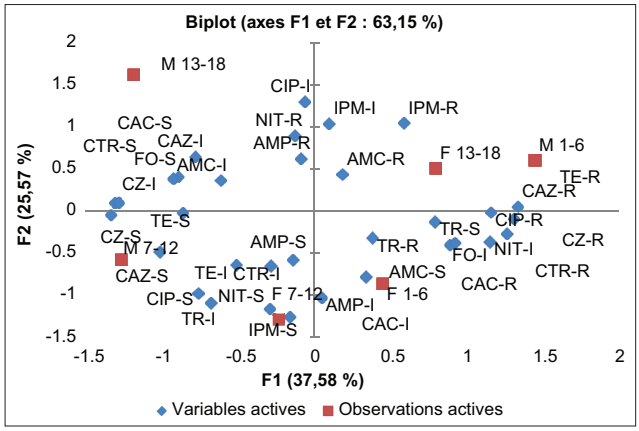


Figure-4: Principal component analysis of age, sex (F=female; M=male) and susceptibility (R=Resistant; I=Intermediate; S=Sensitive) to AMC=Amoxycillin, AMP=Ampicillin, CZ=Cefazolin, CAC=Cefazolin/clavulanic acid, CAZ=Ceftazidime, CTR=Ceftriaxone, CIP=Ciprofloxacin, FO=Fosfomycin, IMP=Imipenem, NIT=Nitrofurantoin, TE=Tetracycline, TR=Trimethoprim.

R to TR. Trimethoprim-sulfamethoxazole is one of the most recommended antibiotics for treating acute uncomplicated UTIs [28,29], but resistance to this antibiotic is increasing in the management of UTIs and was also reported elsewhere [30]. Eliopoulos and Huovinen [31] reported that bacterial resistance to TMP is mediated by the following five main mechanisms: (1) The permeability barrier and/or efflux pumps, (2) naturally insensitive target enzymes, (3) regulatory changes in the target enzymes, (4) mutational or recombinational changes in the target enzymes, and (5) the acquisition of resistance by drug-R target enzymes. In UPEC, the adaptation resulting from recurrent exposure to the antimicrobial is usually one of the most evoked ways of explaining this growth in resistance. Nevertheless, studies have reported that resistance alleles such as *sul1*, *sul2*, *sul3*, and *dfr* along with Type 1 and Type 2 integrons were actively involved in the horizontal transmission of TR resistance [32]. In a study conducted by Blahna *et al*. [32] to describe the distribution of TR-S resistance genes and the role of horizontal gene transfer and clonal expansion in recent increases of antibiotic resistance rates among UPEC in Europe and Canada, the authors found that *dfrA1* was the most common in Europe. However, unfortunately in our study, no analysis was performed on the genetic features associated with resistance.

Interestingly, all of our isolates were susceptible to FO, another antibiotic frequently recommended for

Table 3: MDR index and resistance pattern of the isolated UPEC.

Number of UPEC		Antibiotic resistance profiles of isolated UPEC strains	MDR index	p-value
N.	a×b			
22	22×0	Not resistant	0.00	0.208
13	7×1	AMC	0.08	0.123
	2×1	AMP		
	1×4	TE NIT TR CZ		
9	5×1	AMC, AMP	0.17	0.085
	1×4	AMC, NIT AMC, CZ AMC, TR TR, TE		
12	5×1	AMC, AMP, TE	0.25	0.113
	2×1	AMC, AMP, TR		
	1×5	AMC, AMP, IPM AMC, AMP, CZ AMP, CIP, NIT AMC, TE , TR TE, TR, IPM		
7	5×1	AMC, AMP, TR, TE	0.33	0.066
	2×1	AMC, AMP, CTR, CZ		
12	4×1	CAZ, CTR, CZ, AMC, AMP	0.42	0.113
	4×1	AMC, AMP, TE, TR, IPM		
	2×1	AMC, AMP, TE, CTR, CZ,		
	2×1	AMC, AMP, IPM, NIT, TR, AMC, AMP, TR, TE, NIT		
7	2×2	CAZ, CTR, CZ, AMC, IPM, AMP TR, CTR, CZ, AMC, TE, AMP	0.50	0.066
	3×1	TR, AMC, TE, IPM, AMP, NIT CAZ, TR, CTR, CZ, AMC, AMP CAZ, CTR, CZ, AMC, CAC, AMP		
15	5×1	CAZ, TR, CTR, CZ, AMC, TE, AMP	0.58	0.142
	2×2	CAZ, CTR, CZ, AMC, CAC, TE, AMP CAZ, CTR, CZ, AMC, IPM, CIP, AMP		
	6×1	CAZ, TR, CTR, AMC, TE, IPM, CIP CAZ, TR, CTR, CZ, AMC, IPM, AMP CAZ, TR, CZ, AMC, CAC, TE, AMP		
		TR, CZ, AMC, TE, IPM, AMP, NIT TR, CZ, AMC, TE, IPM, AMP, NIT TR, CAZ, AMC, TE, IPM, AMP, NIT		
6	3×1	CAZ, TR, CTR, CZ, AMC, IMP, CIP, AMP	0.67	0.057
	3×1	CAZ, CTR, CZ, AMC, TE, IPM, CIP, AMP CAZ, TR, CTR, CZ, AMC, CAC, TE, AMP CAZ, TR, CZ, AMC, TE, IPM, CIP, AMP		
3	2×1	CAZ, TR, CTR, CZ, AMC, TE, IPM, CIP, AMP	0.75	0.028
	1×1	CAZ, TR, CTR, CZ, AMC, CAC, TE, CIP, AMP		

a=Number of UPEC strains. b=Number of resistance phenotypes in each UPEC strain. N=Total number of resistance phenotypes in each group in the studied UPEC strains. *P*=Probability coefficient. R=Resistant; I=Intermediate; S=Sensitive, AMC=Amoxycillin, AMP=Ampicillin, CZ=Cefazolin, CAC=Cefazolin/clavulanic acid, CAZ=Ceftazidime, CTR=Ceftriaxone, CIP=Ciprofloxacin, FO=Fosfomycin, IMP=Imipenem, NIT=Nitrofurantoin, TE=Tetracyclin, TR=Trimethoprim, UPEC=Uropathogenic *Escherichia coli*

the management of UTIs. This finding is in accordance with the study of Hirsch *et al*. [33], in which all UPEC strains investigated were susceptible to FO [33]. Likewise, Kresken *et al*. [34] reported that less than 1.5% of UPEC were R to this antibiotic [28]. This suggests that FO could be considered as a first-line treatment for UTIs; indeed, this antibiotic is currently approved for use in some European countries as a treatment for uncomplicated UTIs caused by *E. coli* [35]. Although FO remains the preferred agent for treating uncomplicated cystitis, its use may be limited in many patients due to low creatinine clearance and concerns about reduced efficacy [30,36,37]. Finally, the correlation observed between the sensitivity of our isolates to antibiotics suggests that antibiotic resistance is a problem that may affect most existing antibacterial, given the overall evolution observed.

Conclusion

Antibiotic resistance should be continuously evaluated in patients of all ages and in all hospitals where possible, so as to monitor the evolution of this major public health issue. In this investigation performed on UPEC strains isolated from urine samples of children diagnosed with UTIs in Russian Children's Clinical Hospital in Moscow, we found that FO was the only antibiotic to which all UPEC were S. The unusual resistance to IMP and more globally to other antibiotics observed in some strains is alarming and suggests the need for more judicious use of these antibiotics. However, our study has several limitations, especially regarding the lack of information on the subjects' medication profile before their UTIs and the lack of

investigation of genetic elements related to the resistance.

Authors' Contributions

SS, BMN, and PIV: Conceptualized and designed the research. SS: Conducted laboratory experiments. MMJA, SS, PIV, VEG, and YNV: Wrote the first manuscript draft, edited and revised the manuscript. All authors critically reviewed and approved the final manuscript.

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Competing Interests

The authors declare that they have no competing interests.

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