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Antimicrobial Susceptibility Patterns of *Escherichia Coli*, *Klebsiella Pneumoniae* and *Candida Spp.* in Patients with Clinical Presentation of a Urinary Tract Infection in Yaounde, Cameroon

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Abstract **Background:** Urinary tract infections (UTIs), which are most often caused by *Escherichia coli* (E. coli), *Klebsiella pneumoniae* (*K. pneumoniae*) and Candida species (*Candida spp.*), have until now been a health problem throughout the world, particularly in developing countries. Moreover, with the growing increase in antibiotic resistance in recent years, the treatment of these infections is becoming increasingly difficult. The aim of this study was to present the prevalence of *E. coli*, *K. pneumoniae* and *Candida spp*. in UTIs, investigate the association between the previous species responsible for these infections with age and sex, to present the patterns of antimicrobial resistance and the evolution of these resistances during the study period. **Methods:** This was a retrospective study that was conducted from January 04, 2010 to November 27, 2019 in Yaounde, capital of the Central region in the Centre Pasteur of Cameroon. Following collection of urine samples, the laboratory analyses included macroscopic examination, culture on cystine lactose electrolyte deficient (CLED) medium using the semi-quantitative technique, incubation in an oven at 37°C between 18 and 24 hours and antimicrobial sensitivity testing using the diffusion method and the Vitek 2-Compact device. **Results:** During the study period, 23,507 urine samples were analysed. The prevalence of infection caused by *E. coli*, *K. pneumoniae* and *Candida spp*. was 46.2%. The female sex was the most represented (25.1%) against 21% for the male sex. The mean age of participants with a clinical picture of a UTI was 35.5 years ± 29.2 SD with patients under 20 years of age being the most represented. The prevalence of infection caused by *E. coli* was 32.1% ; that of *K. pneumoniae* was 12.1% and the prevalence of Candida species was 1.9% with *Candida albicans* being more represented. In this study, a statistically significant association was found between the above germs with age group ($p<0.001$) and sex ($p<0.001$). Antimicrobial susceptibility testing showed that *E. coli* and *K. pneumoniae* were particularly resistant to antibiotics of the penicillin family, the cephalosporin family, the sulfamide family and the quinolone family. Candida species were highly sensitive to most of the antifungal agents tested. The profiles of the evolution of antibiotic sensitivity according to the study period showed that, from one family of drugs to another, resistance was generally greater than sensitivity, with lower rates in recent years (2017-2019). **Conclusion:** The treatment of UTIs caused by *E. coli* and *K. pneumoniae* remains a challenge due to the frequent use of highly resistant antibiotics. Continuous monitoring of multidrug resistance by the organisms concerned remains necessary in order to prevent situations of therapeutic failure and to find appropriate treatments for UTIs in our context.

Keywords: *Urinary tract infections, Escherichia coli, Klebsiella pneumoniae, Candida spp., antimicrobial resistance, continuous monitoring*

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1. Introduction

Urinary tract infections (UTIs) are all major infections characterised by an inflammatory response in the epithelium of the urinary tract [1]. UTIs are the second major cause of bacterial infections affecting approximately 150 million people per year [2,3] with an estimated annual global incidence of 250 million in developing countries [4]. The population at risk of these infections is made up of newborns, preschool children, sexually active women and the elderly of both sexes [2]. Other risk factors include: poor perineal hygiene, diabetes mellitus, anatomical and functional abnormalities of the urinary tract and increased frequency of sexual activity [5,6]. But, in general, UTIs affect both men and women at any age, with women probably being the most affected because of anatomical differences, hormonal effects and behavior [1]. UTIs are clinically classified into uncomplicated (simple) and complicated. Uncomplicated urinary tract infections (uUTIs) affect healthy individuals without structural and neurological abnormalities of the urinary tract ; they are generally known as cystitis (affecting the lower urinary tract) or pyelonephritis (affecting the upper urinary tract) and are usually acquired in the community. Complicated urinary tract infections are generally associated with factors related to urinary tract dysfunction (urinary obstruction, urinary retention, renal failure), host defense (immunosuppression, renal transplantation and pregnancy), and foreign bodies (catheters or other drainage devices) [2]. Other previous studies, notably that of Alanazi *et al* [7], consider that UTIs can be classified into two types: hospital-acquired urinary tract infections (HAUTIs) and community acquired urinary tract infections (CAUTIs) with women constituting the predominant group associated with the second type.

The majority of urinary tract infections are caused by *Escherichia coli* (*E. coli*) followed by *Klebsiella pneumoniae* (*K. pneumoniae*), Enterobacter, Citrobacter, *Proteus mirabilis* (*P. mirabilis*) and *Pseudomonas aeruginosa* (*P. aeruginosa*) [6]. Other species include: *Proteus spp*., *Staphylococcus epidermidis* (*S. epidermidis*), *Staphylococcus saprophyticus* (*S. saprophyticus*), *Staphylococcus aureus* (*S. aureus*), *Klebsiella spp*. and several other species of the Enterobacteriaceae family [4,6-10], for a proportion of approximately 90% to 95% of cases of infection caused by Gram negative bacteria (GNB) and 10% for Gram positive bacteria (GPB) [11]. Other authors, notably Koksal et al. [12], state that *E. coli* and *Klebsiella* species are the most incriminated agents in CAUTIs with frequent resistance to antimicrobial agents recommended for the treatment of these infections. However, according to most articles, the bacterial species that predominates 70-90% in UTIs is uropathogenic *E. coli* (UPEC), one of the pathotypes of extraintestinal pathogenic *E. coli* (ExPEC) [3,13-15]. The UPEC strain is implicated in 90% of CAUTIs and 50% of nosocomial UTIs [13]. ExPEC strains are responsible for approximately 40,000 deaths and at least $2.6 billion in healthcare treatment in the United States alone [3]. Moreover, the cost of treating UTIs amounts to about 6 billion dollars per year in health services worldwide [16]. In addition to the bacterial species that are predominantly involved in UTIs, a wide variety of fungi are present in UTIs [17]. The most common Candida species are: *Candida albicans* (*C. albicans*), *Candida krusei* (*C. krusei*), *Candida parapsilosis* (*C. parapsilosis*), *Candida tropicalis* (C. tropicalis), *Candida glabrata* (C. glabrata), *Candida spp*. but, *Cryptococcus* and *Aspergillus spp*. are also represented. Candida species represent approximately 10-15% of nosocomial UTIs [17-22]. The presence of these in the urine (candiduria) is asymptomatic and generally rare in healthy patients. However, the presence of Candida species in urine is more frequent in hospitalized patients and more specifically in those in intensive care with a higher risk of mortality in patients in the critical phase of the disease [21,23].

Antibiotic resistance is a real problem in infections in general and UTIs in particular, making treatment difficult in infected patients [6]. These resistances are further increased by the spread of antibiotic resistant strains of the β-lactam class (i.e., penicillins, cephalosporins and aztreonam) which are commonly used in the treatment of UTIs caused by GNB [24]. The best known resistance mechanism in this context is the production of extended spectrum beta-lactamases (ESBLs), one of the main epidemiological problems in infections caused by organisms of the *Enterobacteriaceae* family [25], more specifically by *E. coli* and *K. pneumoniae* [12]. These ESBLs belong to a group of enzymes which are responsible for the development of resistance by hydrolyzing 4 atoms (β-lactam) present in β-lactam class drugs, thus making them ineffective [12]. The mechanisms of production of ESBLs are very complex. However, phylogenetic research has led to the understanding, for example, that the most beta-lactamases encountered in strains of *E. coli* are TEM, VHS and CTX-M [24-27]. In addition, it has been revealed that the isolated production of ESBLs confers co-resistance to aminoglycosides, quinolones, tetracyclines, nitrofurantoin and trimethoprim-sulfamethoxazole (cotrimoxazole) and that the multidrug resistance (MDR) phenotype is due to the presence of large plasmids that carry the resistance genes of the β-lactams, quinolones, aminoglycosides and cotrimoxazole [26]. Urinary tract infections (UTIs) caused by *Candida* species have increased rapidly in recent years and the frequent use of prophylactic antifungal agents has contributed to the increase in resistance in non-*albicans Candida* species [17]. Surveillance of *Candida* species resistance to antifungal agents is therefore necessary to determine the incidence of *Candida* species that cause UTIs, as well as the incidence of resistance to antifungal agents [28].

In order the implementation of antimicrobial resistance surveillance and control strategies in UTIs to be effective in our context, the aim of this retrospective study was to: determine the prevalence of *E. coli*, *K. pneumoniae* and *Candida* species isolated from urine samples between 2010 to 2019; find out if gender and age are risk factors for infection ; present the susceptibility patterns to the antimicrobials agents tested and the evolution of susceptibility according to the years of study.

2. Materials and Methods

2.1. Place and Period Study

We have carried out a retrospective study over a period of 10 years (from January 04, 2010 to November 27, 2019) in Yaounde, capital of the Central region, at the Centre Pasteur of Cameroon (CPC), a reference and public health laboratory, technical body of the Ministry of Public Health of Cameroon and Member of the International Network of Pasteur Institutes.

2.2. Urine Collection

In order to avoid errors in the collection of urine samples, the control measures for aseptic conditions were monitored by the staff in charge of sample collection. A sterile vial was used for the collection of urine samples from a midstream urine. Other sources of urine samples were obtained by suprapubic puncture, urinary catheter, etc. Once the samples were collected, they were carefully identified and carried to the Bacteriology laboratory for analysis.

2.3. Biological Analysis of Urine Samples

At the laboratory, the urine samples were analysed within ≤ 1 hour. The processing of the urine samples started with a macroscopic examination (color of the urine, turbidity etc.) and then a cytological examination (cell count, search for epithelial cells, cylinders, crystals etc.). The search for *E. coli* and *K. pneumoniae* species was carried out on a cystine lactose electrolyte deficient (CLED) medium using the semi-quantitative technique. Once inoculated, the culture media were incubated in an oven at 37°C between 18h and 24h. Other identification tests including Gram staining [29], study of biochemical characteristics (production of indole, urea, hydrogen sulphide, citrate, tryptophan deaminase, etc.) were carried out using API 20E [30] galleries.

The diffusion method was used for carrying out the antimicrobial susceptibility tests. Its implementation on Muller-Hinton medium (MH) was in conformity with the indications of the Committee on Antibiogram of the French Society of Microbiology/European Committee on Antimicrobial Susceptibility Testing (CA-SFM/EUCAST) [31]. The different antibiotic discs tested in this research were : AMP: ampicillin (10 µg); AMO: amoxicillin (20 µg); AMC: amoxicillin + clavulanic acid (20 µg/10 µg); TIC: ticarcillin (75 µg); TCC: ticarcillin + clavulanic acid (75 µg/10 µg); PIC/PIP : piperacillin (30 µg); TZP: piperacillin + tazobactam (30 µg/6 µg); MEC: mecillinam (10 µg); ICM/IMI: imipenem (10 µg); meropenem (10 µg); CFT: cephalotin (10 µg); CXM : cefuroxime (30 µg); CXT: cefoxitin (30 µg); CTX: cefotaxime (5 µg); CAZ: ceftazidime (10 µg); CFM: cefixime (5 µg); FEP: cefepime (30 µg); GEN: gentamicin (10 µg); TOB : tobramycin (10 µg); AKN: amikacin (30 µg); NET: netilmicin (10 µg); CMP: chloramphenicol (30 µg); TET: tetracycline (30 µg); COL: colistin (10 µg); SXT/TSU: trimethoprim + sulfamethoxazole (1.25 µg/23.75 µg); FUR: nitrofurantoin (100 µg); NAL: nalidixic acid (30 µg); OFL: ofloxacin (5 µg); NOR: norfloxacin (10 µg); CIP: ciprofloxacin (5 µg); LEV: levofloxacin (5 µg); FOS: fosfomycin (200 µg). The interpretation of the results for antibiotic sensitivity or resistance was in accordance with the instructions of the Clinical and Laboratory Standards Institute (CLSI) [32,33]. Quality control was performed with the reference strain *E. coli* (ATCC 25922). In addition to the diffusion method, the Vitek-2 Compact (bioMérieux, France) was also used for antimicrobial susceptibility testing.

For the detection of fungi in urine samples, the observation of yeast elements under the microscope with 10X and 40X objectives followed by Gram staining were previously performed. The culture was then carried out on Sabouraud + Chloramphenicol medium for the identification of fungal species using API 20C galleries and the Vitek 2-compact device for the study of morphological and biochemical characteristics [34,35]. The antimicrobial susceptibility test was carried out on Sabouraud medium using the diffusion method to determine the susceptibility to the antifungal agents tested. The families of antifungal agents represented were azoles with miconazole, econazole, ketoconazole, fluconazole, voriconazole and clotrimazole and polyenes with amphotericin B and nystatin. The loading of the antifungal discs, the use of quality controls and the interpretation of the results were in accordance with the CLSI guidelines [36,37]. The reference strain *Candida albicans* ATCC 90028 was used as a control for the detection of sensitivity to antifungal agents.

2.4. Data Collection and Statistical Analysis

The data were retrieved from the GLIMS software (data management system of CPC). The database contained the variables date of collection, gender, origin of the urine sample, identified germs, patient age (years) and the antibiotics and antifungals tested (represented by their 3 letter codes). After extraction of the data from GLIMS, the database was cleaned with Microsoft Office Excel 2019 and statistical analyses were performed using R language version 3.6.1 (2019-07-05) [38]. The finalfit package was used to create the tables [39] and the ggplot 2 package was used to create the graphs [40]. The statistical tests used in this research were: The Pearson and Fischer exact Chi-square tests for the comparison of proportions and associations between qualitative variables; the non-parametric Kruskal-Wallis test for the comparison of patient age means by age group and gender. The logistic regression model was used to evaluate the association between the identified germs and sex with the Odds-ratio (OR) values that were determined to see if sex is a risk factor for infection. The significance level was set at $p<0.05$.

3. Results

3.1. Characteristics of Study Population

During the study period, 23,507 urine samples were analysed with a prevalence of infection caused by *E. coli*, *K. pneumoniae* and *Candida* species of 46.2% (10,860 samples positive for the presence of the species mentioned above). Mid-stream urine was the most represented

method of urine collection (58.3%), followed by urine samples from pocket urine (36.4%). The female sex was the most represented with 5901 (54.3%) samples compared to 4943 (45.5%) samples for the male sex. This difference in sample gender distribution was statistically significant (p<0.0001). The mean age of participants was 35.5 years ± 29.2 standard deviation (SD). The distribution of the age variable into groups showed that patients under 20 years of age (<20 years) were the most represented (42.6%) with a mean age of 6.3 years ± 3.4 SD in this group. The difference in age group distribution of participants was statistically significant (p<0.0001). The year 2012 was the most represented in terms of contaminated samples for a significant difference in the distribution of samples across study years (p<0.0001). The rest of the information concerning the socio-demographic characteristics can be found in Table 1.

3.2. Prevalence of *Escherichia Coli, Klebsiella pneumoniae* and *Candida spp*. Isolated from Urine Samples

Of the 23,507 urine samples analysed, *E. coli* was isolated in 7549 samples, for a prevalence of infection of 32.1%. As for *K. pneumoniae*, it was present in 2837 samples, for a prevalence of 12.1%. Regarding fungal species, *C. albicans* followed by *Candida sp.* were the most represented with respective prevalence of 1.4% and 0.5%. The distribution of other *Candida* species is shown in Table 2.

Table 1. Presentation of socio-demographic characteristics

Variables	Age groups (years)					Total	p-value	Sex		Total	p-value
	<20 (n=10224) No. (%)	20-39 (n=4125) No. (%)	40-59 (n=2745) No. (%)	60-79 (n=4680) No. (%)	≥80 (n=1585) No. (%)	(n=23507) No. (%)		Men (n=11375) No. (%)	Women (n=12102) No. (%)	(n=23507) No. (%)	
Age											
mean (SD)	6.3 (3.4)	31.3 (4.9)	49.7 (6.0)	69.6 (5.7)	84.8 (4.4)	35.5 (29.2)	**<0.0001***	38.4 (32.0)	33.1 (26.5)	35.5 (29.2)	**<0.0001***
Origin											
Mid-stream	618 (6.0)	1484 (36.0)	1396 (50.9)	2099 (44.9)	681 (43.0)	6278 (26.7)	**<0.0001**	2476 (21.8)	3851 (31.8)	6327 (26.9)	**<0.0001**
Pocket urine	3930 (38.4)	4 (0.1)	4 (0.1)	4 (0.1)	2 (0.1)	3944 (16.8)		1977 (17.4)	1963 (16.2)	3940 (16.8)	
Suprapubic	14 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	14 (0.1)		7 (0.1)	7 (0.1)	14 (0.1)	
Catheter	8 (0.1)	32 (0.8)	49 (1.8)	269 (5.7)	124 (7.8)	482 (2.1)		447 (3.9)	34 (0.3)	481 (2.0)	
Other	57 (0.5)	7 (0.2)	6 (0.2)	8 (0.2)	4 (0.2)	82 (0.3)		36 (0.3)	46 (0.4)	82 (0.3)	
Years											
2010	516 (5.0)	152 (3.7)	171 (6.2)	168 (3.6)	84 (5.3)	1091 (4.6)	**<0.0001**	451 (4.0)	641 (5.3)	1092 (4.6)	**<0.0001**
2011	454 (4.4)	167 (4.0)	159 (5.8)	228 (4.9)	118 (7.4)	1126 (4.8)		520 (4.6)	616 (5.1)	1136 (4.8)	
2012	599 (5.9)	159 (3.9)	156 (5.7)	220 (4.7)	121 (7.6)	1255 (5.3)		555 (4.9)	703 (5.8)	1258 (5.4)	
2013	601 (5.9)	167 (4.0)	135 (4.9)	209 (4.5)	118 (7.4)	1230 (5.2)		489 (4.3)	746 (6.2)	1235 (5.3)	
2014	492 (4.8)	143 (3.5)	137 (5.0)	244 (5.2)	78 (4.9)	1094 (4.7)		535 (4.7)	565 (4.7)	1100 (4.7)	
2015	453 (4.4)	176 (4.3)	142 (5.2)	308 (6.6)	81 (5.1)	1160 (4.9)		587 (5.2)	572 (4.7)	1159 (4.9)	
2016	434 (4.2)	174 (4.2)	169 (6.2)	282 (6.0)	73 (4.6)	1132 (4.8)		552 (4.9)	587 (4.9)	1139 (4.8)	
2017	409 (4.0)	137 (3.3)	127 (4.6)	237 (5.1)	53 (3.3)	963 (4.1)		459 (4.0)	508 (4.2)	967 (4.1)	
2018	323 (3.1)	119 (2.9)	129 (4.7)	265 (5.7)	48 (3.0)	884 (3.8)		426 (3.7)	461 (3.8)	887 (3.7)	
2019	346 (3.4)	133 (3.2)	130 (4.7)	219 (4.7)	37 (2.3)	865 (3.7)		369 (3.2)	502 (4.1)	871 (3.7)	
Overall prevalence	4627 (45.2)	1527 (37.0)	1455 (53.0)	2380 (50.8)	811 (51.2)	10860 (46.2)	**<0.0001**	4943 (43.5)	5901 (48.8)	10860 (46.2)	**<0.0001**

p-value: p-value of Pearson's Chi-squared test ; *: p-value of Kruskal-Wallis rank sum test

3.3. Association Between Isolated Germs and Age Groups

Evaluation of the association between age groups and identified germs showed that age can be considered a risk factor for infection due to *E. coli*, *K. pneumoniae* and *Candida* species. The p-value of the Pearson's Chi-2 test was indeed significant (p<0.001). Regarding the germ specific p-value, it was significant for *E. coli* (p<0.0001), *K. pneumoniae* (p<0.0001) and *Candida albicans* (p<0.001) with a predominance of these germs in the younger age group (<20 years). As for the distribution of *Candida glabrata*, the p-value of the exact Fisher's test was significant (p = 0.044) in favor of patients of 20-39 years old. For information showing the distribution of the other species according to age groups refer to Table 3.

3.4. Association between isolated Germs and Sex

The results in Table 4 show that in this study gender was also associated with infection. The p-value of the Pearson's Chi-squared test was significant (p<0.001). More specifically, gender was found to be a protective factor against urinary tract infection caused by *E. coli* (OR = 0.53; CI = 0.48-0.57) for a significant difference in the distribution of *E. coli* by gender (p<0.0001).

For *K. pneumoniae*, gender was a risk factor for infection (OR = 1.83; CI = 1.68-2.00) with male patients 1.8 times more likely to have *K. pneumoniae* infection in their urine than female patients. The difference in *K. pneumoniae* distribution by sex was also statistically significant (p<0.0001). For fungal species, gender was a risk factor only for C. albicans (OR = 1.74; CI = 1.39-2.19) with the risk of infection occurring 1.7 times greater for males than females. The difference in distribution of *C. albicans* by sex was statistically significant (p<0.0001).

Table 2. Prevalence of *E. coli*, *K. pneumonia* and *Candida spp.* from urine samples

Ranking	Organism	No. of isolates	% of total
	Bacteria		
1	*Escherichia coli*	7549	32.1
2	*Klebsiella pneumoniae*	2837	12.1
	Fungi		
3	*Candida albicans*	337	1.4
4	*Candida sp.*	127	0.5
5	*Candida tropicalis*	5	0.0
6	*Candida glabrata*	2	0.0
7	*Candida parapsilosis*	2	0.0
8	*Candida dubliniensis*	1	0.0
	Total	10860	46.2

Table 3. Distribution of *Escherichia coli, Klebsiella pneumoniae* and *Candida spp.* according to age group

	Age groups (years)						
Isolated organism	<20 (n=10224) No. (%)	20-39 (n=4125) No. (%)	40-59 (n=2745) No. (%)	60-79 (n=4680) No. (%)	≥80 (n=1585) No. (%)	Total (n=23507) No. (%)	p-value
Bacteria							
Escherichia coli	3004 (29.4)	1170 (28.4)	1088 (39.6)	1690 (36.1)	560 (35.3)	7512 (32.0)	**<0.0001**
Klebsiella pneumoniae	1380 (13.5)	298 (7.2)	323 (11.8)	605 (12.9)	209 (13.2)	2815 (12.0)	**<0.0001**
Fungi							
Candida albicans	180 (1.8)	38 (0.9)	35 (1.3)	55 (1.2)	28 (1.8)	336 (1.4)	**<0.001**
Candida sp.	58 (0.6)	18 (0.4)	8 (0.3)	29 (0.6)	14 (0.9)	127 (0.5)	0.1209
Candida tropicalis	3 (0.0)	0 (0.0)	1 (0.0)	1 (0.0)	0 (0.0)	5 (0.0)	0.951*
Candida glabrata	0 (0.0)	2 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.0)	**0.04375***
Candida parapsilosis	2 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.0)	0.8112*
Candida dubliniensis	0 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	0.3512*
Overall prevalence	4627 (45.2)	1527 (37.0)	1455 (53.0)	2380 (50.8)	811 (51.2)	10800 (45.9)	**<0.001**

p-value: p-value of Pearson's Chi-squared test ; *: p-value of Fisher's exact test

Table 4. Distribution of Escherichia coli, Klebsiella pneumoniae and Candida spp. according to sex

	Sex				
Isolated organism	Men (n=11375) No. (%)	Women (n=12102) No. (%)	Total (n=23507) No. (%)	OR (95%-CI)	P-value
Bacteria					
Escherichia coli	3073 (27.0)	4469 (36.9)	7542 (32.1)	0.53 (0.48-0.57)	**<0.0001**
Klebsiella pneumoniae	1604 (14.1)	1225 (10.1)	2829 (12.0)	1.83 (1.68-2.00)	**<0.0001**
Fungi					
Candida albicans	198 (1.7)	138 (1.1)	336 (1.4)	1.74 (1.39-2.19)	**<0.0001**
Candida sp.	64 (0.6)	63 (0.5)	127 (0.5)	1.21 (0.84-1.75)	0.2735
Candida tropicalis	3 (0.0)	2 (0.0)	5 (0.0)	1.79 (0.21-21.45)	0.6651*
Candida glabrata	0 (0.0)	2 (0.0)	2 (0.0)	0.00 (0.00-6.35)	0.5039*
Candida parapsilosis	1 (0.0)	1 (0.0)	2 (0.0)	1.19 (0.02-93.66)	1.000*
Candida dubliniensis	0 (0.0)	1 (0.0)	1 (0.0)	0.00 (0.00-46.53)	1.000*
Overall prevalence	4943 (43.5)	5901 (48.8)	10844 (46.1)		**<0.001**

p-value: p-value of Pearson's Chi-squared test ; *: p-value of Fisher's exact test ; OR: Odd ratio ; CI: Confidence interval

Table 5. Sensitivity and resistance profile of *Escherichia coli* and *Klebsiella pneumoniae* to the antibiotics tested

Antibiotics	*Escherichia coli* (n=7549)	*Klebsiella pneumoniae* (n=2837)
	%I/%R/%S	
Penicillins		
AMP	0.0/30.6/3.2	0.0/31.4/0.0
AMO	0.1/58.2/7.6	0.0/67.2/0.6
AMC	6.0/56.0/37.2	5.4/59.0/34.7
TIC	0.0/86.1/12.7	0.1/98.0/0.6
TCC	0.0/1.1/1.0	0.0/0.8/0.5
PIC/PIP	0.0/31.8/5.0	0.1/35.8/1.3
TZP/PIT	6.5/3.7/23.1	7.8/5.9/19.6
MEC	0.0/0.1/0.0	0.0/0.0/0.0
Carbapenems		
ICM/IMI	0.2/0.2/24.8	0.1/0.2/24.5
MER	0.0/0.0/2.1	0.0/0.0/2.0
Cephalosporins		
CFT	12.3/59.1/26.7	2.7/65.2/30.2
CXM	0.0/0.2/0.3	0.0/0.5/0.4
CXT	2.1/6.7/49.6	0.4/8.2/49.3
CTX	0.3/29.7/69.4	1.4/56.5/41.3
CAZ	3.8/26.0/69.2	10.4/47.3/40.9
CFM	0.2/17.0/33.9	0.5/32.2/21.0
FEP	0.9/0.4/0.9	0.8/0.5/0.8
Aminosides		
GEN	0.4/32.6/66.7	0.1/58.6/40.7
TOB	0.1/35.2/61.0	0.2/48.8/47.7
AKN	4.5/7.1/88.0	3.4/4.4/91.5
NET	0.1/3.6/11.0	0.2/5.2/9.2
Phenicoles		
CMP	0.0/0.0/0.1	0.0/0.0/0.1
Tetracyclines		
TET	0.0/0.6/0.1	0.0/0.6/0.4
Polypeptides		
COL	0.0/0.0/0.0	0.0/0.0/0.0
Sulfamides		
SXT/TSU	0.1/79.5/16.5	0.1/75.0/23.0
Nitrofurans		
FUR	0.5/2.7/90.5	8.1/20.9/61.2
Quinolones		
NAL	0.1/42.1/25.6	0.4/28.9/37.5
OFL	1.3/51.4/44.2	0.7/39.3/56.8
NOR	0.2/39.5/36.6	0.1/30.5/46.7
CIP	1.8/42.3/55.3	3.3/31.9/63.7
LEV	0.0/0.0/0.0	0.0/0.0/0.2
Fosfomycine		
FOS	0.1/1.2/92.6	0.2/8.6/86.2

AMP: Ampicillin ; AMO: Amoxicillin ; AMC: Amoxicillin + Clavulanic Acid ; TIC: Ticarcillin; TCC: Ticarcillin + Clavulanic Acid; PIC/PIP: Piperacillin; TZP/PIT: Piperacillin + Tazobactam ; MEC: Mecillinam ; ICM/IMI: Imipenem ; MER: Meropenem ; CFT: Cephalotin ; CXM : Cefuroxime ; CXT: Cefoxitin ; CTX: Cefotaxime ; CAZ: Ceftazidime ; CFM: Cefixime ; FEP: Cefepime ; GEN: Gentamicin ; TOB: Tobramycin ; AKN: Amikacin ; NET: Netilmicin ; CMP: Chloramphenicol ; TET: Tetracycline ; COL: Colistin ; SXT/TSU: Trimethoprim + Sulfamethoxazole (Cotrimoxazole) ; FUR: Nitrofurantoin ; NAL: Nalidixic Acid ; OFL: Ofloxacin ; NOR: Norfloxacin ; CIP: Ciprofloxacin ; LEV: Levofloxacin ; FOS: Fosfomycin ; I: Intermediate ; R: Resistance ; S: Susceptibility

Table 6. Sensitivity and resistance profile of *Candida* species to antifungal agents tested

Isolated organism (No.)	%I/%R/%S							
	MIC	ECO	KET	FLU	AMB	NYS	VRC	CLO
Fungi								
Candida albicans (337)	2.8/0.0/90.5	1.8/0.0/89.6	0.6/0.3/84.3	0.0/0.0/2.1	0.6/11.0/80.4	0.3/3.6/85.5	0.0/0.0/1.8	3.0/0.9/85.2
Candida sp. (127)	3.1/0.0/85.0	1.6/0.0/82.7	2.4/0.0/84.3	0.0/0.0/2.4	1.6/15.0/70.9	0.8/7.9/78.7	0.0/0.8/0.8	12.3/3.9/71.7
Candida tropicalis (5)	0.0/0.0/100.0	0.0/0.0/100.0	0.0/0.0/100.0	0.0/0.0/0.0	0.0/0.0/100.0	0.0/0.0/80.0	0.0/0.0/0.0	0.0/0.0/100.0
Candida glabrata (2)	0.0/0.0/100.0	0.0/0.0/100.0	0.0/0.0/100.0	0.0/0.0/0.0	0.0/100.0/0.0	0.0/50.0/50.0	0.0/0.0/0.0	0.0/50.0/50.0

Isolated organism (No.)	%I/%R/%S							
	MIC	ECO	KET	FLU	AMB	NYS	VRC	CLO
Candida parapsilosis (2)	0.0/0.0/100.0	0.0/0.0/100.0	0.0/0.0/100.0	0.0/0.0/0.0	0.0/50.0/50.0	0.0/0.0/100.0	0.0/0.0/0.0	0.0/0.0/100.0
Candida dubliniensis (1)	0.0/0.0/100.0	0.0/0.0/100.0	0.0/0.0/100.0	0.0/0.0/0.0	0.0/100.0/0.0	0.0/0.0/100.0	0.0/0.0/0.0	0.0/0.0/100.0

MIC: Miconazole ; ECO: Econazole ; KET: Ketoconazole ; FLU: Fluconazole ; AMB: Amphotericin B ; NYS: Nystatin ; VRC: Voriconazole ; CLO: Clotrimazole ; I: Intermediate ; R: Resistance ; S: Susceptibility

3.5. Antimicrobial Susceptibility Patterns of Escherichia coli, Klebsiella pneumoniae and Candida spp

Table 5 shows the susceptibility and resistance profiles of *E. coli* and *K. pneumoniae* to different families of antibiotics tested. For the antibiotics of the penicillin family, the highest resistance was in favor of ticarcillin with 86.1% and 98.0% for *E. coli* and *K. pneumoniae* respectively followed by amoxicillin with 58.2% resistance for *E. coli* and 67.2% resistance for *K pneumoniae* and in order to amoxicillin + clavulanic acid with 59% resistance for *K. pneumoniae* and 56% resistance for *E. coli*. Overall, *K. pneumoniae* had higher rates of resistance to antibiotics of the penicillin family than *E. coli*. In the cephalosporin family, the highest percentages of resistance were in favor of cephalotin with 59.1% resistance for *E. coli* and 65.2% resistance for *K. pneumoniae* followed by cefotaxime for which the resistance rates were 56.5% for *K. pneumoniae* and 29.7% for *E. coli* and finally ceftazidime whose resistance rates were respectively 47.3% for *K. pneumoniae* and 26% for *E. coli*. In terms of sensitivity, *E. coli* was more susceptible to the antibiotics cefotaxime (69.4%) and ceftazidime (69.2%) compared to *K. pneumoniae* for which the susceptibility was lower (41.3% and 40.9% respectively for cefotaxime and ceftazidime). In the aminoglycoside family, *K. pneumoniae* was also more resistant than *E. coli* to gentamicin and tobramycin (see Table 5). Amikacin was very effective against both species with 88% susceptibility to *E. coli* and 91.5% susceptibility to *K. pneumoniae*. In the sulfamide family, both species were very resistant to trimethoprim + sulfamethoxazole (cotrimoxazole) with respectively 79.5% resistance for *E. coli* and 75.0% resistance for *K. pneumoniae*. *E. coli* was more sensitive to nitrofurantoin (90.5%) than *K. pneumoniae* (61.2%). In the quinolone family, the resistance of *E. coli* to ofloxacin was higher than that of *K. pneumoniae* and conversely, *K. pneumoniae* was more sensitive to ofloxacin and ciprofloxacin than *E. coli* (Table 5). Finally, fosfomycin like amikacin and nitrofurantoin was very effective against both species with 92.6% sensitivity for *E. coli* and 86.2% sensitivity for *K. pneumoniae*.

For fungi, the data in Table 6 showed that fungi were mostly sensitive to the majority of antifungal agents tested.

3.6. Evolution of Resistance and Sensitivity of *Escherichia coli* and *Klebsiella pneumoniae* to the Antibiotics Tested during the Study Period

Figure 1 shows the evolution of susceptibility and resistance of *E. coli* and *K. pneumoniae* to antibiotics of the penicillin family. Overall, resistance levels were relatively high around 2012-2013 for both species except for amoxicillin for which the number of resistant samples was declining during this period. For this family of antibiotics, 2019 was the year with the least resistance.

In the cephalosporin family, *E. coli* and *K. pneumoniae* showed almost identical profiles in terms of sensitivity and resistance to cefoxitin with the year 2014 marked by a significant decrease in the sensitivity of both species to this antibiotic (Figure 2). Overall, *K. pneumoniae* was more resistant to the antibiotics of this family than *E. coli*.

4. Discussion

This study showed that the overall prevalence of urinary tract infections caused by *E. coli*, *K. pneumoniae* and *Candida spp.* was 46.2%. The mean age of the participants was 35.5 years ± 29.2 SD with the under 20-year-old group (42.6%) being the most represented and female patients (54.3%) the most concerned by UTI caused by these germs. These results are close to those of Ganesh *et al.* [1], who worked on the epidemiology of UTIs and antimicrobial resistance in children in hospitals in Nepal. Indeed, in their study, although the prevalence of UTIs was only 12.3%, females were the most infected (60.9%) compared to 39.1% for male children. In the study by Garrido *et al.* [16], the prevalence of infection was also higher among female children in hospital (79.41%) and outpatient (92%) than male children (20.59% in hospital and 8% outpatient). In yet another study, that of Nikolić *et al.* [24], the prevalence of UTI caused by *E. coli* was higher in adult women (66%) compared to adult men (34%) for an average age of infected patients of 61 ± 0.1 years. In Ethiopia, Seifu and Gebissa [11] in their study also found a higher prevalence of UTI caused by *E. coli* in females than in males. The fact that urinary tract infection (UTI) is higher in women than in men could be explained by anatomical differences, hormonal effects and behaviour as stated by Ganesh et *al.* [1] or by recurrent UTIs, sexual history and sexual relations with new partners [11,41]. Furthermore, as stated by Nikolić *et al.* [24], most epidemiological studies of UTIs have identified *E. coli* as the most common pathogen in the female population at all ages.

Our study showed that the prevalence of UTI caused by *E. coli* was 32.1%, a result close to that of Galindo-Méndez [27], where the prevalence of CAUTIs caused by *E. coli* strains in the population of ESBL producers was 31.3%. As for *K. pneumoniae*, the second most represented Gram-negative bacterium, its prevalence in urine samples was 12.1%. This result is close to that of Ganesh *et al.* [1], who found a prevalence of *E. coli* (58.7%) and *K. pneumoniae* (22.5%) in urine samples from children. Albu *et al.* [9], who worked in chronic patients with indwelling urinary catheter, also obtained similar results to

those of the present study with *E. coli* isolated in 41.2% of patients followed by *K. pneumoniae* isolated in 24.7% of patients. Apart from these two *Enterobacteriaceae*, the fungi most represented in this study were *C. albicans isolated in* 337 (1.4%) samples and *Candida sp.* isolated in 127 (0.5%) samples. Other *Candida* species less represented were: *Candida tropicalis* (*C. tropicalis*), *Candida glabrata* (*C. glabrata*), *Candida parapsilosis* (*C. parapsilosis*) and *Candida dubliniensis* (*C. dubliniensis*). These results are close to those obtained in most of the studies [17,18,28,42] where *C. albicans* was the most abundant species in urine samples followed by other non-*albicans Candida* species. Indeed, Lima *et al.* [18] found that intensive care units (ICU) patients exposed to different antibiotics had about a 35% risk of developing candidemia and that if *Candida* was isolated from another site such as urine, the risk could increase to 80%. Furthermore, although the etiology of candidiasis varies according to geographical region, period of study or type of hospital, *C. albicans* is the fungal species most involved in cases of candidiasis with an actual presence of other non-*albicans* species. Another study carried out over 10 years (2008-2017) by Gajdács *et al.* [43], on the epidemiology of candiduria and UTIs caused by *Candida*, also showed that *C. albicans* was the most predominant species in both inpatients and outpatients.

This study showed that age was a risk factor for UTIs caused by *E. coli*, *K. pneumoniae* and *Candida spp.* ($p<0.001$). Differences in distributions were significant for *E. coli* ($p<0.0001$), *K. pneumoniae* ($p<0.0001$), *C. albicans* ($p<0.001$) and *C. glabrata* ($p = 0.043$) with those under 20 years of age (<20 years) being the most infected. Sex was also a risk factor for infection ($p<0.001$). For UTIs caused by *E. coli*, sex was a protective factor (OR: 0.53, 95% CI: 0.48-0.57, $p<0.0001$) while it was a risk factor for infection caused by *K. pneumoniae* (OR: 1.83, 95% CI: 1.68-2.00, $p<0.0001$) with male patients who are 1.8 times more likely to have a UTI caused by *K. pneumoniae* than female patients. These results are close to those of Albu *et al.* [9], where the difference in the distribution of urine samples infected by *E. coli* in patients with a urinary catheter over a long period was significant ($p = .0001$) with the women who were most contaminated (51.3%). As for *K. pneumoniae*, despite a non significant distribution according to sex ($p = .07$), men were at greater risk of infection (28.6%) compared to 20.5% of the infection with this germ in women as in the present study. Our results are also close to those of Lagunas-Rangel [44] who showed that age and sex are the main risk factors for urinary tract infections (UTIs) with women being the most exposed to the infection (RR: 1.705, 95% CI: 1.492-1.948, $p<0.0001$) and patients with an age ≥ 60 years (RR: 1.298, 95% CI: 1.163-1.448, $p<0.0001$). In the study by Pérez Heras *et al.* [45], sex as a risk factor for infection ($p = .001$) was associated with a higher contamination in women (68.2%) compared to men (31.7%) although the production of ESBLs by strains of *E. coli* was more encountered in men (66%) compared to women (33%). In another cohort study, that of Erb *et al.* [46], sex was a risk factor associated with UTI caused by *E. coli* as in the present study with 4197 (80%) women infected against 1049 (20%) men for a significant p-value of the Chi-square test ($p<0.001$). For fungi, this study showed that gender was also a risk factor for *C. albicans* infection (OR: 1.74, 95% CI: 1.39-2.19, $p<0.0001$) with male patients being 1.74 times more exposed than female patients. Age was also associated with UTI caused by *C. albicans* ($p<0.001$) with the youngest (<20 years) being the most contaminated. Concerning the sex variable, these results are close to those of Edward *et al. [47]*, where sex was associated with UTI caused by *C. albicans* with men being more contaminated (61.1%) compared to women (38.9%). However, in their study, the frequency of *C. albicans* and non-*albicans* species was higher among elderly people (61-70 years).

Antibiotic susceptibility patterns have shown that the highest levels of resistance are found in the penicillin family. Within this family, *E. coli* and *K. pneumoniae* were most resistant to ticarcillin with resistance rates of 86.1% and 98.0% respectively, followed by amoxicillin with 58.2% and 67.2% respectively and amoxicillin + clavulanic acid with resistance rates of 56.0% and 59.0% respectively. In addition, for antibiotics of this family, the number of resistance was globally high around the years 2012-2013 for both species except for amoxicillin for which the resistance rates were decreasing during the same period. Still in this family, amoxicillin + clavulanic acid was the only antibiotic for which higher sensitivity rates were recorded (37.2% for *E. coli* and 34.7% for *K. pneumoniae*). These results are close to those obtained in most studies [1,3,10,48,49], where the resistance of *E. coli* and *K. pneumoniae* was higher for antibiotics of the penicillin family. However, in the study by Ganesh *et al.* [1], *E. coli* and *K. pneumoniae* which were most represented in urine samples were more resistant to ampicillin (77.8% and 71.9% respectively) compared to all other antibiotics tested. Similar results were obtained in the study by Ramírez-Castillo *et al.* [3], or Kaduma *et al.* [48]. In the study by Ramírez Castillo *et al.* [3], UPEC was more resistant to ampicillin (70.9%) followed by amoxicillin + clavulanic acid (55.5%) and in the study by Kaduma *et al.* [48], the highest resistance was found for ampicillin in *E. coli* and *Klebsiella spp.* respectively in pregnant women with preeclampsia (group of cases) or not (control group). In the study by Lee *et al.* [50], *E. coli* isolated from urine samples was also more resistant to ampicillin (> 65%) followed by piperacillin (> 58%); in contrast, for *K. pneumoniae* isolated from urine samples, the highest resistance rate was in favor of piperacillin (> 45%). The study by Koksal *et al.* [12], *E. coli* and *Klebsiella spp.* producers of ESBLs were also more resistant to ampicillin (95.5%) compared to other antibiotics of the penicillin family. In the cephalosporin class, this study showed that *E. coli* and *K. pneumoniae* were more resistant to cephalotin (59.1% and 65.2% respectively) followed by cefotaxime (29.7% and 56.5% respectively) and ceftazidime (26.0% and 47.3% respectively). In terms of sensitivity, *E. coli* was more sensitive to cefotaxime (69.4%) and ceftazidime (69.2%) than *K. pneumoniae*, which had respective sensitivities of 41.3% and 40.9% to these two antibiotics. These results are different from those of Seitz *et al.* [41], where the sensitivities of *E. coli* to cefotaxime and ceftazidime in women with acute uncomplicated cystitis (AUC) were high (95.6% for cefotaxime and 95.3% for ceftazidime). In the published article by Albu *et al.* [9], the resistance of

K. pneumoniae, producer of ESBLs to ceftazidime was higher (82.1%) than that of *E. coli*, also producer of the same group of enzymes (64.3%). Our study also showed that *E. coli* and *K. pneumoniae* were highly resistant to trimethoprim + sulfamethoxazole (cotrimoxazole) with resistance percentages of 79.5% and 75.0% respectively. The resistance of these two species to this antibiotic was also higher than the sensitivity throughout the study period with a lower rate in 2016 for *E. coli* and lower in 2019 for *K. pneumoniae*. In the quinolone family also the resistance of both species was higher for ofloxacin (51.4% for *E. coli* and 39.3% for *K. pneumoniae*) followed by ciprofloxacin (42.3% for *E. coli* and 31.9% for *K. pneumoniae*). As for norfloxacin and nalidixic acid, resistance was lower than the two antibiotics mentioned above. Depending on the study period, resistance to nalidixic acid was increasing in 2012-2016 as well as sensitivity to this antibiotic. On the other hand, the sensitivity to ofloxacin for both *Enterobacteriaceae* was decreasing from 2012-2018 while the resistance to this antibiotic was increasing. In this study, there was also a decrease in sensitivity to norfloxacin and ciprofloxacin during the study period with varying degrees of resistance. These results are close to those of Pérez Heras *et al.* [45], who also found high levels of resistance for ESBL produced by *E. coli* in children to cephalosporin and quinolone antibiotics. The study by Klingeberg *et al.* [51], also showed high percentages of resistance of *Escherichia coli* between 2013-2016 to trimethoprim, cotrimoxazole, ciprofloxacin and amoxicillin + clavulanic acid by antimicrobial resistance surveillance systems. Yábar *et al.* [52], who worked on MDR and risk factors associated with the presence of ESBLs in *E. coli* strains in children and adults showed that resistance was also higher for trimethoprim + sulfamethoxazole (cotrimoxazole), ampicillin, cefotaxime and ceftazidime. In the work of Kengne *et al.* [4], carried out in Ndjamena, Chad, the resistance of *E. coli* and *K. pneumoniae* isolated from urine samples was high for beta-lactam and quinolone antibiotics. Dehbanipour *et al.* [14], who isolated *E. coli* strains from clinical urine samples, also found high resistance to penicillin (ampicillin), cephalosporin and fluoroquinolone antibiotics. This high resistance to penicillin (including ampicillin), cephalosporin and quinolone antibiotics could be explained by the regular use of these antibiotics in emergency therapy, but also and especially by the presence of genes from ESBLs such as $bla_{CTX\text{-}M}$, bla_{TEM} and bla_{SHV} as shown by the work of Cristea *et al.* [26], Ramírez-Castillo *et al.* [3], Raeispour and Ranjbar [53], Forson *et al.* [54], Dehshiri *et al.* [55] and Ali *et al.* [56]. Regarding antibiotic sensitivity, our study showed that *E. coli* and *K. pneumoniae* were highly sensitive to amikacin (88.0% and 91.5% respectively), nitrofurantoin (90.5% and 61.2% respectively) and fosfomycin (92.6% and 86.2% respectively). In addition, as shown by the evolution curves, sensitivity to these antibiotics was very high throughout the study period. These results are very close to those obtained in other studies [7,13,41,50,56-59] where the sensitivities of *E. coli* and *K. pneumoniae* were very high for amikacin, fosfomycin and nitrofurantoin but also for imipenem, ertapenem and meropenem. Indeed, as suggested by Choi and Yoo [60], the Korean Society of Antimicrobial Therapy, in its 2018 guidelines, strongly recommends the use of fosfomycin and nitrofurantoin in cases of simple cystitis due to the low resistance of *E. coli to* these antibiotics, resulting in therapeutic success in the case of their use. In addition, they show that the use of these antibiotics, which are rarely administered in the case of other pathologies, is important to reduce the use of other broad-spectrum antibiotics such as beta-lactams and quinolones.

On the fungal side, this research showed that *C. albicans*, which was more abundant in the urine samples, was sensitive to most of the antifungals tested. In the azole family, the sensitivity to miconazole was 90.5%, to econazole was 89.6%, to ketoconazole 84.3% and to clotrimazole 85.2%. For the polyene family, sensitivities were also high with 80.4% sensitivity to amphotericin B and 85.5% sensitivity to nystatin. For *Candida sp.* sensitivities to antifungal agents were also high in both the polyene and azole families. For azoles, sensitivities were 85.5% for miconazole, 82.7% for econazole, 84.3% for ketoconazole and 71.7% for clotrimazole. Among polyenes, the sensitivity to amphotericin B was 70.9% and to nystatin 78.7%. For the other non-*albicans Candida* species (*C. tropicalis*, *C. glabrata*, *C. parapsilosis* and *C. dubliniensis*), which were very poorly represented, the percentages of sensitivities were generally high. In this research, fluconazole and voriconazole were tested in very few study participants, hence the very low sensitivity rates obtained. These results are different from those obtained by Edward *et al.* [47], where the sensitivities of *Candida* species (*C. albicans* and *Candida* non-*albicans*) were higher to fluconazole (42.9%) with minimal inhibitory concentrations (MICs) between 128-1024 µg/ml. In the study by Osawa *et al.* [61], *Candida* species (*Candida spp.*) isolated from urine samples were mostly sensitive to azole antifungal agents as in the present study with 100% sensitivity to 5-fluorocytosine during 2009, 2010 and 2011 in both *Candida albicans and* non-*albicans* species; 100% sensitivity to voriconazole during the three years of the study for *C. albicans* and 90.5%, 87.9% and 89.1% sensitivity to voriconazole for the years 2009, 2010 and 2011 respectively. As for the other antifungals tested (fluconazole and itraconazole) during this study [61], the sensitivity rates were also high. Another study, notably that of Onozawa *et al.* [62], showed that *C. albicans* isolated from urine samples was sensitive to all the antifungal agents tested as in the present study. In the other studies [17,18,21,23,28,63-65], sensitivity to antifungal agents was also important for *Candida spp.*. These results underline the importance of azoles, inhibitors of the biosynthesis of 14-α-sterol demethylase, encoded by the *ERG11* gene, an enzyme involved in the synthesis of ergosterol constituting the membrane of fungi [66-68]. In addition, as Behzadi *et al.* [67], antifungal agents of the azole family, in particular fluconazole and polyenes with amphotericin B, are widely indicated in cases of symptomatic and asymptomatic candiduria, with daily doses of up to two weeks.

Based on the results of this study, the use of antibiotics such as amikacin, nitrofurantoin and fosfomycin is essential in the context of UTIs on the one hand, and the use of azoles and polyenes in case of candiduria on the other hand is an effective therapeutic method in our

context. However, molecular investigation methods remain important for the mapping of resistance genes involved in multidrug resistance to antimicrobial agents.

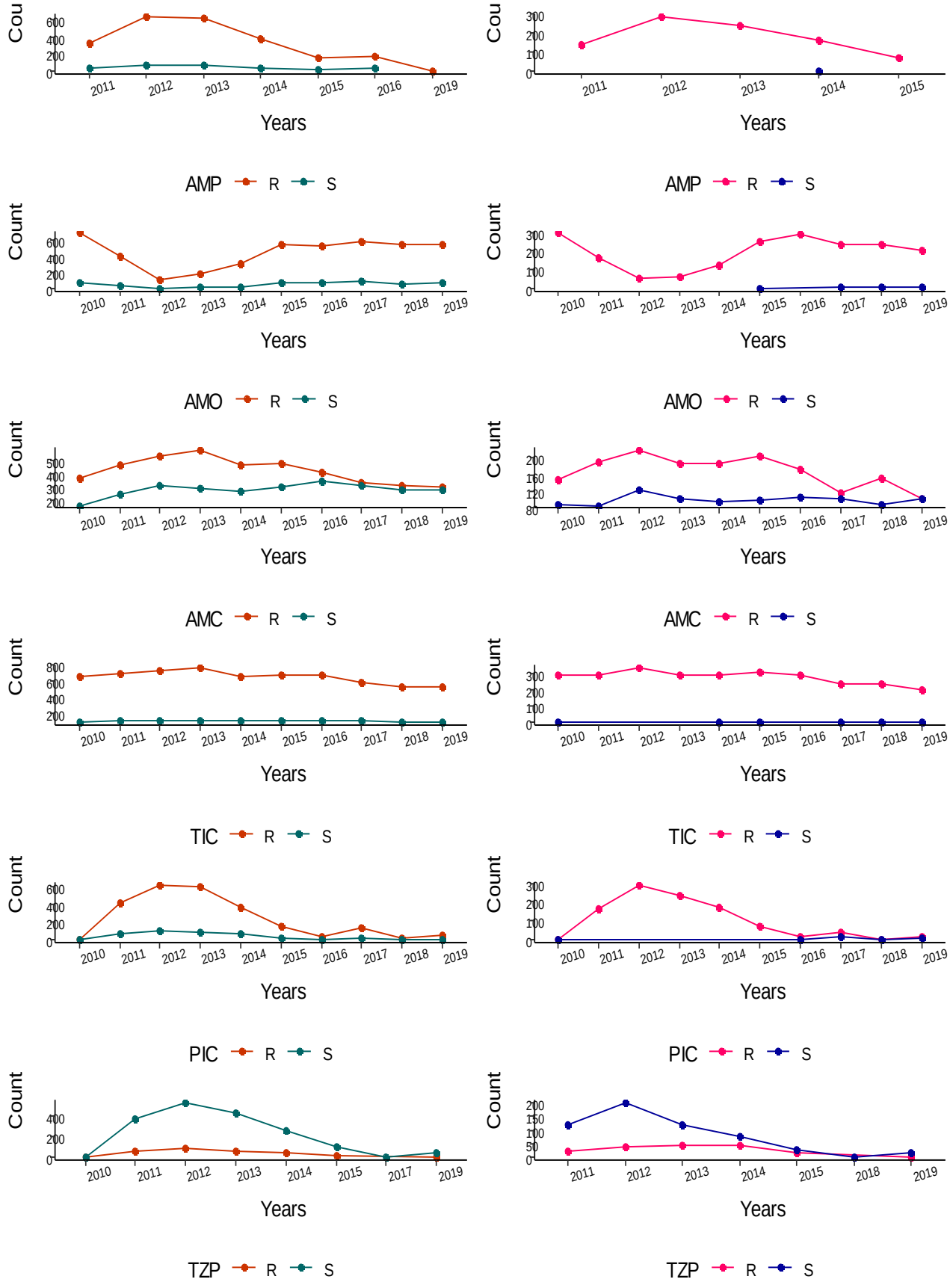

Figure 1. Evolution of resistance and susceptibility of *Escherichia coli* (left) and *Klebsiella pneumoniae* (right) to antibiotics of penicillin family

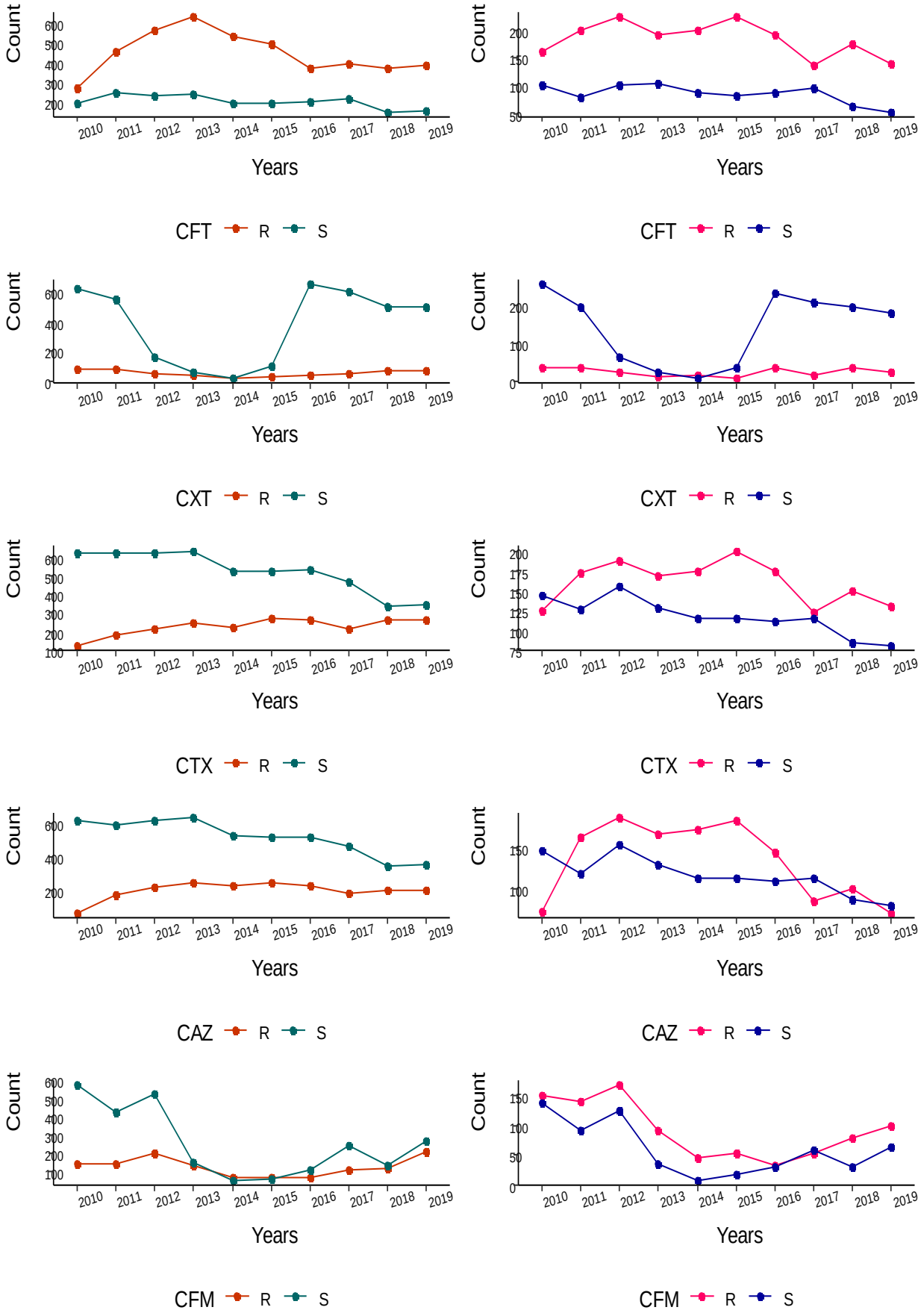

Figure 2. Evolution of resistance and sensitivity of *Escherichia coli* (left) and *Klebsiella pneumoniae* (right) to antibiotics of the cephalosporin family

For aminoglycosides, *E. coli* was more sensitive throughout the study and for *K. pneumoniae*, higher levels of resistance were recorded around the year 2015 for gentamicin and tobramycin (see Figure 3).

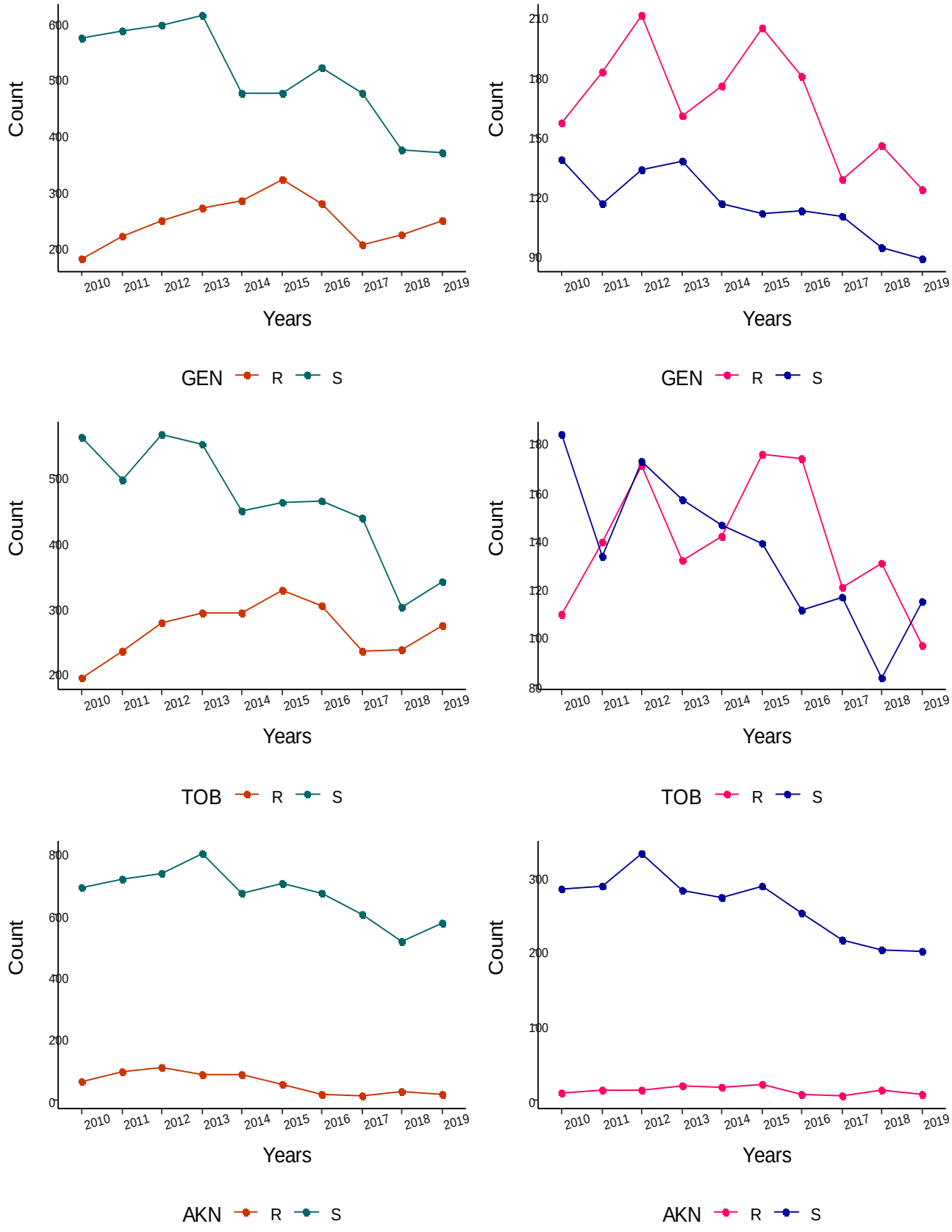

Figure 3. Evolution of resistance and sensitivity of *Escherichia coli* (left) and *Klebsiella pneumoniae* (right) to antibiotics of the aminoglycoside family

There was also a decrease in sensitivity to norfloxacin and ciprofloxacin during the study period for both species with lower levels of resistance to ciprofloxacin throughout the study (Figure 4).

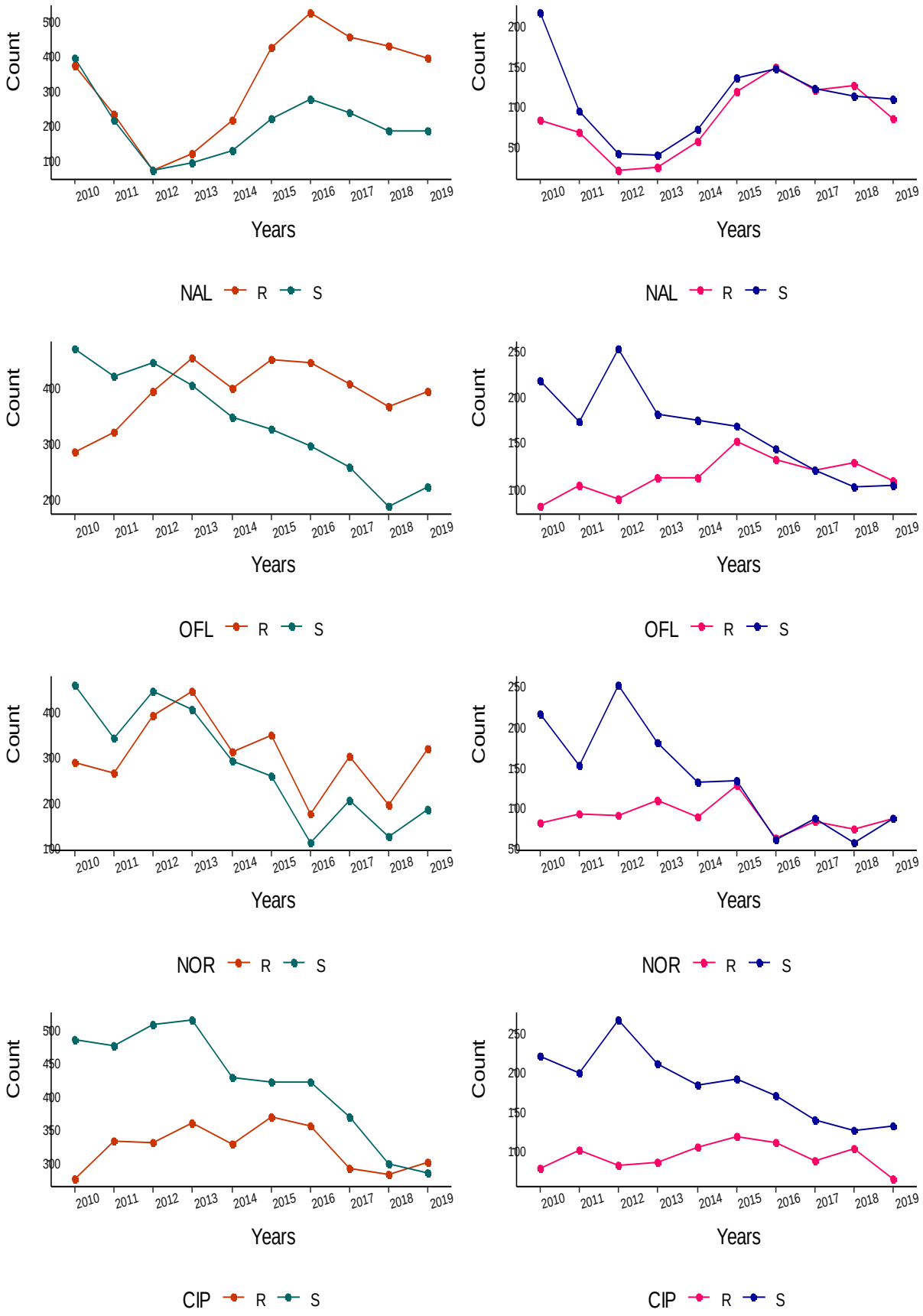

Figure 4. Evolution of resistance and sensitivity of *Escherichia coli* (left) and *Klebsiella pneumoniae* (right) to antibiotics of the fluoroquinolone family

According to Figure 5, both strains were highly resistant throughout the study period to trimethoprim + sulfamethoxazole (cotrimoxazole) with, conversely, very high levels of sensitivity throughout the study of both species to nitrofurantoin and fosfomycin.

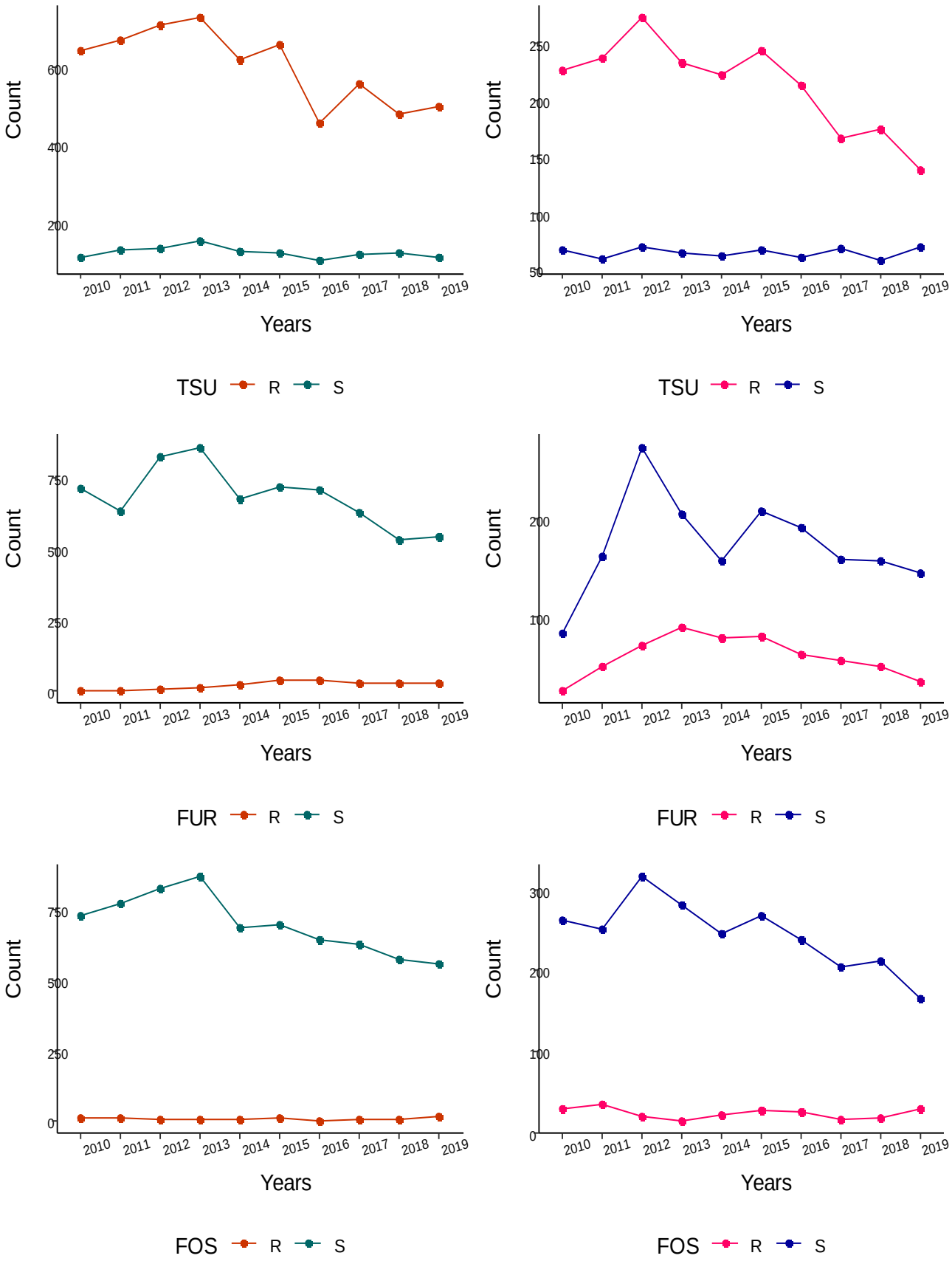

Figure 5. Evolution of resistance and sensitivity of *Escherichia coli* (left) and *Klebsiella pneumoniae* (right) to cotrimoxazole, nitrofurantoin and fosfomycin

5. Conclusion

Urinary tract infections (UTIs) are currently a global public health problem due to the frequent presence of multi-drug resistant bacterial species. The results of this study showed that *Escherichia coli* followed by *Klebsiella pneumoniae* are the most abundant germs in urine samples with women and younger people who are most at risk of infection. Antimicrobial susceptibility testing showed that *Escherichia coli* and *Klebsiella pneumoniae* were multi-resistant germs to most of the antibiotics tested, with the penicillin and sulfamide families which are the most concerned. In light of these results, it is necessary for health authorities to develop antibiotic resistance control programs to minimize the risk of infection and to improve the monitoring and management of inpatients and outpatients. This multidrug resistance control program must also include awareness and using data from antimicrobial susceptibility testing.

List of Abbreviations

AUC	acute uncomplicated cystitis
CA-SFM	Comité de l'antibiogramme de la Société Française de Microbiologie
CAUTIs	community acquired urinary tract infections
CLED	Cystine Lactose Electrolyte Deficient
CLSI	Clinical and Laboratory Standards Institute
CPC	Centre Pasteur of Cameroon
ESBL	extended spectrum beta lactamase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
ExPEC	extraintestinal pathogenic Escherichia coli
GNB	Gram negative bacteria
GPB	Gram positive bacteria
HAUTIs	hospital-acquired urinary tract infections
ICU	intensive care unit
MDR	multidrug-resistant
MH	Muller-Hinton
MIC	minimal inhibitory concentrations
UPEC	uropathogenic Escherichia coli
UTIs	Urinary Tract Infections
uUTIs	uncomplicated Urinary Tract Infections

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Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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