

# Temporal trends and risks factors for antimicrobial resistant Enterobacteriaceae urinary isolates from outpatients in Guadeloupe.

Stéphanie Guyomard-Rabenirina, Joyce Malespine, Célia Ducat, Syndia Sadikalay, Mélanie Falord, Dorothée Harrois, Vincent Richard, Charles Dozois, Sébastien Breurec, Antoine Talarmin

#### ▶ To cite this version:

Stéphanie Guyomard-Rabenirina, Joyce Malespine, Célia Ducat, Syndia Sadikalay, Mélanie Falord, et al.. Temporal trends and risks factors for antimicrobial resistant Enterobacteriaceae urinary isolates from outpatients in Guadeloupe. BMC Microbiology, 2016, 16 (1), pp.121. 10.1186/s12866-016-0749-9. pasteur-01351191

## HAL Id: pasteur-01351191 https://riip.hal.science/pasteur-01351191

Submitted on 2 Aug 2016

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



#### **RESEARCH ARTICLE**

**Open Access** 



# Temporal trends and risks factors for antimicrobial resistant *Enterobacteriaceae* urinary isolates from outpatients in Guadeloupe

Stéphanie Guyomard-Rabenirina<sup>1\*</sup>, Joyce Malespine<sup>1</sup>, Célia Ducat<sup>1</sup>, Syndia Sadikalay<sup>1</sup>, Mélanie Falord<sup>1</sup>, Dorothée Harrois<sup>2</sup>, Vincent Richard<sup>5</sup>, Charles Dozois<sup>6</sup>, The Laboratory working group, Sébastien Breurec<sup>1,3,4</sup> and Antoine Talarmin<sup>1</sup>

#### **Abstract**

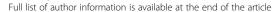
**Background:** Urinary tract infections are bacterial infections most commonly encountered in the community. The resistance rate of uropathogens to commonly prescribed antibiotics has increased worldwide but there are no published data concerning the resistance of strains isolated from community-acquired UTI in Guadeloupe. To assess the susceptibility patterns of *Enterobacteriaceae* strains isolated from outpatients in Guadeloupe we conducted a prospective study from December 2012 to May 2014 among outpatients consulting at private and public laboratories for urine analysis. Risk factors for *E. coli* resistance to amoxicillin, third-generation cephalosporin, and ciprofloxacin were also determined. To study the trends of *E. coli* resistance rates over the past 10 years, data on the susceptibility patterns of *E. coli* from 2003 to 2014 were also collected from three major laboratories for a retrospective study.

**Results:** During the prospective study, we isolated 1293 bacterial strains from the urine of outpatients presenting for urine analysis. The most commonly isolated bacteria were *E. coli* (57 %) and *Klebsiella pneumoniae* (15.5 %). Thirty seven per cent of the *E. coli* strains were resistant to amoxicillin. Resistance rates to third generation cephalosporin were low for *E. coli* and other *Enterobacteriaceae* (3.1 and 12.2 % respectively) and mostly due to the presence of an Extended Spectrum Beta-lactamase. Resistance to cotrimoxazole and ciprofloxacin was moderate (17.8 and 15.6 % respectively). However, the resistance rate of *E. coli* to ciprofloxacin has significantly increased during the last 10 years. Risk factors were consistent with previously reported data, especially for the increasing ciprofloxacin resistance with age.

**Conclusion:** General practitioners in Guadeloupe need to be better informed to favor the prescription of fosfomycin-trometamol to reduce the risk of resistance to fluoroguinolones.

Keywords: Urinary tract infections, Enterobacteriaceae, Antibiotic resistance

<sup>&</sup>lt;sup>1</sup>Unité Environnement Santé, Institut Pasteur de Guadeloupe, Les Abymes, Guadeloupe, France





<sup>\*</sup> Correspondence: sguyomard@pasteur-guadeloupe.fr

#### **Background**

Urinary tract infections (UTI) are bacterial infections most commonly encountered in the community, regardless of age. UTIs are usually benign and the infection (cystitis, prostatitis, urethritis) is limited to the lower urinary tract requires a simple antibiotic treatment. However, recurrences are common and may evolve into an upper UTI (pyelonephritis) requiring a heavier antibiotic treatment and more extensive management [1].

Enterobacteriaceae, especially Escherichia coli, are the most prevalent uropathogens in patients with UTI, both in the community and hospitals [2]. In most cases, the treatment of uncomplicated UTIs is empirical. The French Language Infectious Disease Society (SPFIL) recommends using a single dose of fosfomycin-trometamol in combination for the first line treatment of UTI and pivmecillinam for second line therapy. Beta-lactams, quinolones or cotrimoxazole should be administered after susceptibility testing since strains resistant to these antibiotics are frequently isolated. Indeed, multi drug resistant strains are emerging, especially strains harboring Extended Spectrum Betalactamases (ESBL). ESBL enzymes can hydrolyze almost all beta-lactams (except for carbapenems and cephamycins) and their genes are often closely linked to other genes that confer resistance to several other classes of antibiotics. During the past decade, CTX-M enzymes have gradually replaced the classical TEM and SHV-type ESBLs in many countries. The rapid international spread of CTX-M-15 has been associated with the global dissemination of particular E. coli clones, such as sequence type 131 [3].

The resistance rate of uropathogens to commonly prescribed antibiotics has increased worldwide: resistance to quinolones and trimethoprim increased in Europe between the ECO-SENS I (1999–2000) and ECO-SENS II (2007–2008) studies and in Africa (Senegal, Central African Republic) between 2003 and 2006, reducing therapeutic options [4–7].

Guadeloupe, a French overseas territory located in the Caribbean, is a very high resource country according to the Human Development Index in 2013. There are no published data concerning the resistance of strains isolated from community-onset UTI in Guadeloupe and data from the Caribbean more generally are rare. We, therefore, conducted a prospective study, from December 2012 to May 2014, to assess the susceptibility patterns of Enterobacteriaceae strains isolated from outpatients and to determine the risk factors for UTIs due to Enterobacteriaceae resistant to commonly used antimicrobial agents. We also studied the genetic basis for the antibiotic resistance of ESBL-producing Enterobacteriaceae. Finally, to determine the recent trends of resistance to antibiotics, we conducted a retrospective study on the antibiotic resistance of *E. coli* isolated from outpatients during the last 10 years.

#### **Methods**

#### **Patients**

We collected 1293 bacterial strains isolated from the urine of outpatients presenting for a urine analysis from 13 of the 23 private Guadeloupian laboratories and the laboratory of the Hospital of Basse-Terre between December 2012 and May 2014. All strains responsible for lower and upper UTI and bacteriuria according to SPFIL criteria (pyuria ≥10<sup>4</sup> leucocyte/mL and bacteriuria  $\ge 10^3$  for *E. coli* or *S. saprophyticus* and  $\ge 10^4$  for other species) [8] were included in the study. Only one specimen was collected from each patient. The leucocyte count, isolation, identification and antibiotic susceptibility testing of bacteria were conducted by all laboratories according to their routine diagnostic procedures. All Enterobacteriaceae strains were sent to the Pasteur Institute of Guadeloupe for complete antibiotic susceptibility testing.

The study protocols were approved by the French Advisory Committee on Information Processing in Material Research in the Field of Health (CCTIRS 12–220). Written informed consent to participate in the study was obtained from all patients.

# Antibiotic susceptibility testing of Enterobacteriaceae at the Pasteur Institute of Guadeloupe

We assessed the susceptibility to the following antibiotics by the disk diffusion technique on Mueller-Hinton agar (MH) as recommended by the Antibiogram Committee of the French Microbiology Society (ACFMS) [9]: amoxicillin (10 µg), amoxicillin-clavulanic acid (20 µg/ 10 μg), ticarcillin (75 μg), cephalothin (30 μg), cefotaxime (30 μg), ceftazidime (30 μg), cefoxitin (30 μg), aztreonam (30 μg), imipenem (10 μg) gentamicin (15 μg), amikacin (30 µg), trimethoprim/sulfamethoxazole (1,25/ 23,75 µg), nalidixic acid (30 µg), ciprofloxacin (5 µg), fosfomycin (50 µg), nitrofurantoin (300 µg) and tetracycline (30 UI).. Inhibition growth diameters were measured using the Adagio automated system (Bio-Rad, France). Intermediate and resistant strains were grouped together and classified as resistant strains. Extended spectrum beta-lactamases were detected for strains with reduced inhibition growth diameters around cefotaxime, ceftazidime or aztreonam by the combined disk method with the following combinations: cefotaxime (30 µg) and ceftazidime (30 µg); cefotaxime (30 µg) and clavulanate (10  $\mu$ g); and ceftazidime (30  $\mu$ g) and clavulanate (10  $\mu$ g).

The minimum inhibitory concentration (MIC) for cefotaxime and ceftazidime were determined using the agar-dilution method as recommended by the ACFMS for ESBL-carrying strains [9]. The cut-off values used for

classification were: susceptible strains were defined as those having a MIC <8 mg/L for cefotaxime, and a MIC  $\leq$ 4 mg/L for ceftazidime; and resistant strains as those having a MIC  $\geq$ 32 mg/L for cefotaxime and a MIC  $\geq$ 8 mg/L for ceftazidime. *E. coli* ATCC 25922 was used as a control stain.

#### Molecular characterization of ESBL-producing strains

DNA was extracted using the Nucleospin tissue kit (Macherey Nagel, Hoerdt, France). Previously described polymerase chain reaction (PCR) methods were used to screen for plasmid-encoded  $bla_{CTX-M}$ ,  $bla_{\rm tem}$  and  $bla_{\rm SHV}$  genes [10–12]. Both  $bla_{\rm CTX-M}$ ,  $bla_{\rm SHV}$  and  $bla_{\rm TEM}$  were then characterized by Direct DNA sequencing of the PCR products.

The nucleotide and deduced amino acid sequences were analyzed and compared with sequences available through the Internet on the National Center for Bio-technology Information web site (http://www.ncbi.nlm.nih.gov).

#### Epidemiological data

A standardized specific questionnaire was completed to collect demographic data. Risk factors for *E. coli* resistance to amoxicillin, third-generation cephalosporin (3GC) and ciprofloxacin were assessed from questions about: age, gender, chronic illness, hospitalization during the last year, UTI during the previous last 3 months, urinary catheterization during the previous year, antibiotic exposure during the last month, and hospital or family hospital occupation.

#### Evolution of antibiotic resistance in E. coli from 2003

To analyze the trends of resistance to antibiotics during the last 10 years, data were collected on the resistance of *E. coli* strains isolated from community-acquired UTIs in outpatients presenting at the emergency units of the hospitals of Basse-Terre and Pointe à Pitre and at the Pasteur Institute of Guadeloupe between 2003 and 2014. These data were added to that collected during the prospective study for 2013 and 2014.

#### Data analysis

Statistical analysis was performed using R software (reference: R Development Core Team. R: A Language and Environment for Statistical Computing [Internet]. Vienna, Austria: R Foundation for Statistical Computing; 2010. Available: http://www.R-project.org/).

We used logistic regression to estimate the relation between resistance to each antibiotic and the various covariates (age, gender, clinical symptoms). All covariates with a p value lower than 0.20 were included in the multivariable model. Multivariable, backward, step-bystep binomial negative regressions were used to take into account confounders, bias, and interactions linked to the dependent variable.

To compare annual resistance rates, we performed Poisson regression and chi2 tests. Statistical differences were considered significant for *p*-values <0.05.

#### **Results**

#### **Patients**

We collected a total of 1293 strains during the study period. Most (73.5 %) were isolated from women (sex ratio 0.34). The median age of patients was 57.4 years (range 0 to 95 years). Sixteen patients carried significant numbers of two different strains. We obtained epidemiological data for 340 patients; pregnant women accounted for 10.6 % of women interviewed, and 69 % of patients had UTI symptoms.

#### Bacterial strains and antibiotic susceptibility

More than 86 % of the isolates were Enterobacteriaceae: 736 E. coli (57.0 %), 202 Klebsiella pneumoniae (15.5 %), 56 Proteus mirabilis (4.3 %), 54 Enterobacter spp. (4.2 %), 38 Citrobacter koseri (2.9 %), and 35 other Enterobacteriaceae (2.7 %). Other Gram-negative bacteria (Pseudomonas spp. and Acinetobacter spp.) accounted for 0.6 % of the isolates. Among the isolates, 170 were Gram-positive bacteria (13.1 %): Streptococcus agalactiae (4.3 %), Enterococcus faecalis (4.2 %), and Staphylococcus saprophyticus (2.3 %).

Many of the *E. coli* isolates were susceptible to numerous drugs, but 42.1 % of the strains were resistant to amoxicillin and ticarcillin.

A small proportion of strains were not susceptible to 3GC (3.1 % *E. coli* and 12.2 % other *Enterobacteriaceae*; Table 1). Most 3GC-resistant strains had a MIC greater than 64 mg/L for cefotaxim and ceftazidime (85 and 67.5 %, respectively). This resistance was mostly due to the presence of an ESBL (n = 39, 85 %):  $24 \, K$ . pneumoniae,  $11 \, E$ . coli,  $3 \, Enterobacter \, spp$ . and one M. morganii.

Resistance to cotrimoxazole and ciprofloxacin was 17.8 and 15.6 %, respectively.

Resistance rates to fosfomycin and nitrofurantoin were low among *E. coli* strains (1.6 and 1.2 % respectively). These rates were higher for other *Enterobacteriaceae*: 17.9 % for fosfomycin and 32.6 % for nitrofurantoin.

Only a small proportion of *Enterobacteriaceae* strains were resistant to gentamicin (6.4 %) and amikacin (0.5 %) (Table 1). Only one strain (*Morganella morganii*) was resistant to imipenem.

Most 3GC-resistant strains had at least one co-acquired resistance: 85 % were resistant to ciprofloxacin, 67.5 % to cotrimoxazole and 52.5 % to gentamicin (Table 2).

**Table 1** Susceptibility of outpatients *Enterobacteriaceae* urinary isolates to various antimicrobial agents

	Number of isolates resistant to antibiotics (%)								
	E. coli (n =733)	Other Enterobacteriaceae (n =376)	All Enterobacteriacea (n =1109)						
Amoxicillin	42.1	88	57.6						
Co-amoxiclav	18.6	32.7	23.4						
Ticarcillin	38.9	75.8	51.4						
Cefalothin	16.7	30	21.2						
Cefoxitin	2.7	23.1	4.5						
Cefotaxim	3.1	12.2	6.2						
Ceftazidim	2.3	12.8	5.7						
Aztreonam	1.9	11.7	7						
Imipenem	_	6.7	2.3						
Cotrimoxazole	18.6	16	17.8						
Amikacin	0.4	0.5	0.5						
Gentamicin	5.4	8.2	6.4						
Nalidixic acid	19.7	21.3	20.2						
Ciprofloxacin	13.8	19.4	15.6						
Fosfomycin	1.6	17.9	7.1						
Nitrofurantoin	1.2	32.6	13.7						
Tetracyclin	25	32.7	27.6						

#### Determinants of antibiotic resistance in 3GC-R Enterobacteriaceae strains

The 39 ESBL producing strains are described in Table 2. Among them 38 expressed a CTX-M enzyme including 29 CTX-M15 and 7 CTX-M1. Additional  $\beta$  lactamases were found in most of strains (87.5 %).

#### Risk factors for E. coli resistance to amoxicillin, third-generation cephalosporin and ciprofloxacin

Strains isolated from male patients had a significantly higher amoxicillin resistance rate than those isolated from female patients (p = 0.04). The ciprofloxacin resistance rate tended to increase with increasing age (p < 0.01) (Table 3).

Among 286 patients with an *Enterobacteriaceae*, 68 (23.7 %) declared to have received antibiotic treatment during the previous month and 72 (25.2 %) to have had a UTI during the three previous months. More *Enterobacteriaceae* strains isolated from patients who declared a UTI during the three previous months were resistant to amoxicillin (p = 0.02) and ciprofloxacin (p < 0.01) than those isolated from patients without a UTI during the three previous months. Moreover, urinary catheterization was associated with higher resistance rates for amoxicillin and cotrimoxazole (p < 0.01) (Table 3).

#### Evolution of antibiotic resistance in E. coli from 2003

Resistance rates for amoxicillin, cotrimoxazole and amikacin have been stable during the last 10 years. On the contrary, we found a significant (p < 0.01) increase in the

**Table 2** Characteristics of the ESBLE<sup>a</sup>

Species and	Additionnal β lactar	nase	Acquired co-resistance <sup>b</sup>					
ESBL type	non ESBL SHV	TEM1-like	OXA-1 like	SXT	GM	CIP	TE	
K. pneumoniae (24)								
CTX M-15 (21)	16	11	11	14	11	21	11	
CTX M-1 (2)	1	1	1	1	2	2	2	
SHV-12 (1)	-	-	-	1	-	2	-	
E. coli (11)								
CTX M-15 (5)	-	2	-	3	2	3	3	
CTX M-1 (4)	-	3	-	4	2	1	3	
CTX M-14 (1)	-	1	-	-	1	1	1	
CTX M-27 (1)	-	1	1	1	-	1	1	
E. cloacae (2)								
CTX M-15 (2)	-	2	2	2	1	2	1	
E. aerogenes								
CTX M-1	-	-	-	-	-	-	-	
M. morganii								
CTX M-15	-	-	-	1	1	1	1	

<sup>&</sup>lt;sup>a</sup>Number of strains is indicated in parentheses when >1

<sup>&</sup>lt;sup>b</sup>SXT cotrimoxazole, GM gentamicin, CIP ciprofloxacin, TE tetracyclin

 Table 3 Analysis of independent risk factors for E. coli resistance to amoxicillin, trimethoprim/sulfamethoxazole and ciprofloxacin

Risk factor	Number	%	AMX				SXT				CIP			
			Crude OR [95 %]	P value	Ajusted OR [95 %]	P value	OR [95 %]	P value	Ajusted OR [950%]	P value	OR [95 %]	P value	Ajusted OR [95 %]	P value
Sex - Male	124	19.9	1.5 [1.1–2.3]	0.04			1.4 [0.8–2.2]	0.21			1.6 [0.9–2.7]	0.09		
Age category														
less than 40 years	168	26.9	Ref				Ref				Ref			
40–59 years	141	23.7	0.9 [0.5–1.4]	0.55			1.1 [0.6–2.0]	0.81			2.7 [1.1–6.9]	0.03		
60–69 years	115	21.2	1.1 [0.7–1.8]	0.66			1.9 [1.1–3.4]	0.03			4.5 [1.9–10.9]	< 0.01		
70 year and more	176	28.2	1.2 [0.7–1.8]	0.45			1.9 [1.1–3.3]	0.03			4.8 [2.1–11.3]	< 0.01		
Presence of clinical signs	147	73.5	0.6 [0.4–1]	0.07	0.5 [0.2–0.9]	0.03	0.9 [0.3–3.1]	0.87			1.2 [0.6–2.6]	0.59		
Chronic illness	56	26.7	1.1 [0.7–1.9]	0.64			1.1 [0.3–3.7]	0.91			1.4 [0.7–2.7]	0.41		
Prior (3 months) UTI	52	24.8	1.8 [1-3.2]	0.04	2.3 [1.1-4.9]	0.02	3.1 [1-10.1]	0.05			5.4 [2.7–11]	< 0.01	5.1 [2.5–10.3]	< 0.01
Prior (12 months) hospitalization	32	15.2	2.2 [1.2–4.4]	0.02			5.1 [1.6–16.5]	<0.01			1.7 [0.8–3.7]	0.2		
Prior (6 months) urinary catheter	14	7	11.6 [2.7–50.6]	<0.01	8.8 [1.9–40.8]	<0.01	10.1 [2.5–40.4]	<0.01	11.1 [2.4–51.6]	<0.01	2.1 [0.7–5.7]	0.16		
Prior (6 months) antibiotic exposure	14	21.4	1.4 [0.8–2.4]	0.26			3.8 [1.1–12.9]	0.03	4 [0.9–18.9]	0.07	2.4 [1.2–4.9]	0.02		

Only significant adjusted OR are presented *OR* odds ratio, *UTI* urinary tract infection \*Significant difference (*P* < 0.05)

reported resistance to nalidixic acid, ciprofloxacin, cefalotin, and gentamycin (Table 4). The increase in the 3GC resistance rate was not significant as assessed by the Poisson regression test but was significant as evaluated by the Chi2 test. Until 2008, fewer than 1.0 % of *E. coli* strains were resistant to 3GC, but this proportion increased significantly between 2008 and 2009 (p < 0.01) and has been stable during the last 5 years (Table 4).

#### Discussion

As expected, E. coli was the most frequent strain isolated from urines in Guadeloupe (57.0 % of isolates), but nevertheless less frequent than in Europe and Canada (range from 61.0 to 87.5 %) [13-18]. K. pneumoniae was the second most frequent pathogen (15.5 %), even in pre-menopausal women, with a rate similar to those reported in Africa and Asia (ranging from 13.8 to 25.5 %) [6, 19-22]. S. agalactiae was the most frequent Grampositive bacteria (4.3 %), whereas generally reported rates are less than 3 %. The differences in relative prevalence may be due to environmental and/or host genetic factors, or the virulence of the bacterial pathogens. Of note, the prevalence of diabetes is high (8.2 %) in Guadeloupe [23] and UTIs due to K. pneumoniae and S. agalactiae have been reported to be two to three times more frequent among patients with diabetes than those without [24].

As previously described, *S. saprophyticus* was isolated more frequently from women under 35 years of age than men or older women [25].

Overall, resistance rates were similar to those observed in developed countries including mainland France. Indeed, we found an amoxicillin-resistance rate of 42.1 % for *E. coli*, similar to the rate of 43.4 % reported for North America [26] and slightly lower than the rate of 48.3 % reported for Europe [27] . This contrasts with the reported situation in African and developing Asian countries where resistance rates may be as high as 80 % [6, 7, 28, 29].

Moreover, resistance to 3GC was low, and although this rate increased significantly between 2008 and 2009, it remains below 4 % for E. coli strains and 7 % for all Enterobacteriaceae. Guadeloupe should be considered to be a low prevalence ESBL-producing Enterobacteriaceae territory as are the European and North American countries [5, 15, 27, 30]. In our study, bla<sub>CTX-M15</sub> was detected in most of the ESBL-producing strains (74.3 %), highlighting the shift during the 2000s from ESBL bla<sub>TEM</sub>/bla<sub>SHV</sub> to ESBL group 1 bla<sub>CTX-M</sub>, and in particular to bla<sub>CTX-M15</sub>. This is in accordance with other epidemiological studies of ESBL-producing Enterobacteriaceae [31]. Most ESBL-producing strains (97.5 %) were resistant to other antibiotics in keeping with the ARESC and ECO-SENS II studies [5, 27]. Surprisingly, most ESBL-producing strains isolated in our study were K. pneumoniae, whereas in the community, E. coli strains with CTX-M enzymes usually predominate [32] because of the spread of clonal multidrug-resistant E. coli strains such as clone O25b-ST131 [33]. The prevalence of K. pneumoniae in our study can be explained not only by the high proportion of K. pneumoniae strains among uropathogens, but also by the spread of successful clones as described in Africa and Asia [34].

We did not isolate any carbapenemase-producing strains, although these strains have been observed in the community, even in low prevalence countries such as England [15] where their presence is often related to travel in Asia where these strains are endemic [35]. In Guadeloupe, *Enterobacteriaceae* carbapenemase-producing strains have just begun to emerge in hospital settings with the first description of an NDM-1-producing *K. pneumoniae* in 2014 [36], and more recently, of an OXA-48-producing *E. coli* [37].

Ciprofloxacin resistance remains moderate (15.6 %) compared to rates observed in Asia which can be as high as 75 % [19]. Nevertheless, we found that this rate has increased significantly during the last 10 years as described for other countries [6, 15, 26, 38]. Although

**Table 4** Trends of resistance rates to various antimicrobial agents of *E. coli* between 2003 and 2014

	01 100.00	arree race	.5 .6 .6	, 05 0110111		90	_,,		00 01.101 2	•			
Year	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	P value
n E.coli	198	300	338	437	384	399	606	763	854	766	1019	950	
Amoxicillin	43	46.6	43	42.3	43.2	44.1	39.7	37.7	45	44.2	41.4	42.9	NS
Cefalotin	8	6.3	7.8	7.3	5.5	6.2	15	14	16.6	17.6	17	20.4	<0.01*
Cefotaxime	0	0.7	0.3	0	0.9	0.2	1.8	2.5	2.7	3	2.6	2.3	<0.01**
Amikacin	0.5	0.0	0.0	0.5	0.6	0.2	0.2	1	0.7	0.3	0.3	0.3	NS
Gentamicin	1	3.3	4.4	2.3	2.6	4.2	3.6	3.9	5.6	5.2	3.4	4.6	<0.01*
Nalidixic acid	5.5	11	UD	UD	UD	13.4	15	13.1	13.7	17.2	16.2	20.8	<0.01*
Ciprofloxacin	4	5.3	6.8	8.5	9.6	8.5	11.4	8.2	10.9	9.9	9.9	12.3	<0.01*
Cotrimoxazole	18.7	23	21.6	22.4	23.2	23.3	20.9	19	20.5	19.4	18.6	18	NS

UD unavailable data, NS non significant

we were not able to obtain retrospective data on fluoroquinolone consumption in Guadeloupe, increasing rates of ciprofloxacin-resistant strains suggest the inappropriate use of fluroquinolones in outpatients. Among the 48 patients reporting antibiotic consumption during the month prior to the infection, 15 had consumed a fluoroquinolone and among 24 patients that also reported a previous UTI, 12 received a fluoroguinolones whereas only one was given fosfomycin. Indeed, ciprofloxacin resistance in E. coli has been linked with ciprofloxacin consumption in the same month as the infection and the month before [39]. The rate of ciprofloxacin resistance tended to increase with age as has been described for mainland France and Canada [16, 40] Antimicrobial susceptibility testing of uropathogens is known to overestimate rates of resistance because antibiograms are performed mostly if empirical treatment fails, or if patients have underlying factors [41]. Nevertheless, the trends remain valid.

Consistent with previous reports [28, 42] we observed that prior UTI (likely to be associated with prior antibiotic treatment) was associated with higher amoxicillin and ciprofloxacin resistance rates. This suggests the abusive use of these antibiotics for the treatment of community acquired infections. Surprisingly, a previous antibiotic treatment was not associated with such a risk. Since the use of antibiotics for which the resistance rate exceeds 10–20 % is associated with an increased risk of treatment failure and the selection of resistant strains [43], ciprofloxacin should be administered only if compatible with the antimicrobial resistance pattern of the strain.

#### **Conclusions**

Although a few patients may have been infected by hospital-acquired strains, this is the first description of susceptibility patterns of urinary bacterial strains isolated from outpatients in Guadeloupe.

The antibiotic resistance rates among urinary bacteria isolates from outpatients in Guadeloupe are similar to those of North America and Europe. Nevertheless, this study highlights the need for general practitioners in Guadeloupe to be better informed so that they are encouraged to prescribe fosfomycin-trometamol for the treatment of UTI to reduce the risk of increasing resistance rates to fluoroquinolones.

#### Abbreviations

UTI, urinary tract infection; SPFIL, The French Language Infectious Disease Society; ESBL, Extended Spectrum beta lactamase; MIC, minimum inhibitory concentration; PCR, polymerase chain reaction; 3GC, third generation cephalosporin

#### Acknowledgements

We thank all study participants.

The laboratory working group includes: Clément Bourgoin<sup>1</sup>, Farid Saheb<sup>1</sup>, Guy-Joseph Theodore<sup>1</sup>, Emmanuelle Bourgoin<sup>1</sup>, Frédéric Leroy<sup>1</sup>, William Laurent<sup>1</sup>, Arnaud Lethuillier<sup>1</sup>, Patricia Tamby<sup>1</sup>, Petra Kassab<sup>1</sup>, Anne-Christine Becker<sup>1</sup>, Pierre Marie<sup>1</sup>, Sandrine Hippomène<sup>2</sup>, Olivier Menuteau<sup>2</sup>, Marie-Line Péan<sup>2</sup>, Sylvaine Bastian<sup>3</sup>, Edith Malpote<sup>3</sup>, Didier Mattera<sup>4</sup>

<sup>1</sup>Laboratoire Biopole Antilles

<sup>2</sup>Laboratoire Synergibio

<sup>3</sup>Laboratoire de Microbiologie, Centre Hospitalo-Universitaire, Les Abymes <sup>4</sup>Laboratoire de Biologie Clinique, Centre Hospitalier de Basse-Terre, Basse-Terre, Guadeloupe

#### **Funding**

This work was financed by grants from the Institut Pasteur International Network, ACIP A13\_2011 and by grant FEDER FED-1-1.4 32932 from the European Union.

#### Availability of data and materials

Data supporting the findings is contained within the manuscript.

#### Author's contributions

SG designed the study, analyzed data and wrote the manuscript, JM, CD and SS collected bacterial strains and epidemiological data, performed antimicrobial susceptibility testing and molecular characterization of ESBL-producing strains, MF performed molecular characterization of ESBL-producing strains, DH collected bacterial strains, epidemiological data and retrospective data on the resistance of *E. coli* strains and critically revised the manuscript, VR performed data analysis and critically revised the manuscript, ChD designed the study and critically revised the manuscript, SB collected retrospective data on the resistance of *E. coli* strains and critically revised the manuscript, AT designed the study and critically revised the manuscript. All authors read and approved the final manuscript.

#### Competing interests

The authors declare that they have no competing interests.

#### Consent for publication

Not applicable.

#### Ethics approval and consent to participate

The study protocols were approved by the French Advisory Committee on Information Processing in Material Research in the Field of Health (CCTIRS 12–220). Written informed consent to participate in the study was obtained from all patients.

#### **Author details**

<sup>1</sup>Unité Environnement Santé, Institut Pasteur de Guadeloupe, Les Abymes, Guadeloupe, France. <sup>2</sup>Laboratoire de Biologie Clinique, Centre Hospitalier de Basse-Terre, Basse-Terre, Guadeloupe, France. <sup>3</sup>Faculté de Médecine, Université des Antilles, Pointe-à-Pitre, Guadeloupe, France. <sup>4</sup>Laboratoire de Microbiologie Clinique et Environnementale, Centre Hospitalo-Universitaire de Pointe-à-Pitre/Abymes, Pointe-à-Pitre, Guadeloupe, France. <sup>5</sup>Institut Pasteur de Nouvelle-Calédonie, Nouméa, Nouvelle-Calédonie, France. <sup>6</sup>Institut Armand Frappier, Laval, Canada.

### Received: 5 January 2016 Accepted: 15 June 2016 Published online: 24 June 2016

#### References

- Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol. 2015;13:269–84.
- Bishop MC. Uncomplicated Urinary Tract Infection. EAU Updat Ser. 2004;2:143–50.
- Rogers BA, Sidjabat HE, Paterson DL. Escherichia coli O25b-ST131: a pandemic, multiresistant, community-associated strain. J Antimicrob Chemother. 2011;66:1–14.
- Kahlmeter G, Menday P. Cross-resistance and associated resistance in 2478
   Escherichia coli isolates from the Pan-European ECO.SENS Project surveying
   the antimicrobial susceptibility of pathogens from uncomplicated urinary
   tract infections. J Antimicrob Chemother. 2003;52:128–31.

- Kahlmeter G, Poulsen HO. Antimicrobial susceptibility of Escherichia coli from community-acquired urinary tract infections in Europe: The ECO SENS study revisited. Int J Antimicrob Agents. 2012;39:45–51.
- Bercion R, Mossoro-Kpinde D, Manirakiza A, Le Faou A. Increasing prevalence of antimicrobial resistance among Enterobacteriaceae uropathogens in Bangui, Central African Republic. J Infect Dev Ctries. 2009;3:187–90.
- Sire JM, et al. Antimicrobial resistance in outpatient Escherichia coli urinary isolates in Dakar, Senegal. J Infect Dev Ctries. 2007;1:263–8.
- SPILF 2014 Mise au point Diagnostic et Antibiothérapie des infections Urinaires Bactériennes Communautaires de l'Adulte. Splif. 2014. http://www.infectiologie.com/UserFiles/File/medias/Recos/2014-infections\_urinaires-long.pdf.
- CA-SFM. Comite de l'Antibiogramme de la Societe Francaise de Microbiologie: Recommandations. 2013. Edition de janvier 2013.
- Saladin M, et al. Diversity of CTX-M beta-lactamases and their promoter regions from Enterobacteriaceae isolated in three Parisian hospitals. FEMS Microbiol Lett. 2002;209:161–8.
- Arlet G. Rouveau, M. & Philippon, a. Substitution of alanine for aspartate at position 179 in the SHV-6 extended-spectrum beta-lactamase. FEMS Microbiol Lett. 1997;152:163–7.
- Eckert C, et al. Dissemination of CTX-M-Type β -Lactamases among Clinical Isolates of Enterobacteriaceae in Paris, France. Antimicrob Agents Chemother. 2004;48:1249–55.
- Hryniewicz K, et al. Antibiotic susceptibility of bacterial strains isolated from urinary tract infections in Poland. J Antimicrob Chemother. 2001;47:773–80.
- Bruyère F, Vidoni M, Péan Y, Ruimy JA, Elfassi R. Analyse microbiologique de plus de 600 infections urinaires fébriles prises en charge dans un réseau de soin. Progrès en Urol. 2013;23:890–8.
- Ironmonger D, et al. Surveillance of antibiotic susceptibility of urinary tract pathogens for a population of 5.6 million over 4 years. J Antimicrob Chemother. 2015;70:1744–50.
- Laupland KB, Ross T, Pitout JDD, Church DL, Gregson DB. Community-onset urinary tract infections: A population-based assessment. Infection. 2007;35:150–3
- Magliano E, et al. Gender and age-dependent etiology of community-acquired urinary tract infections. ScientificWorldJournal. 2012;2012;349597.
- Maraki S, Mantadakis E, Michailidis L, Samonis G. Changing antibiotic susceptibilities of community-acquired uropathogens in Greece, 2005–2010.
   J Microbiol Immunol Infect. 2013;46:202–9.
- Lu PL, et al. Epidemiology and antimicrobial susceptibility profiles of Gramnegative bacteria causing urinary tract infections in the Asia-Pacific region: 2009–2010 results from the Study for Monitoring Antimicrobial Resistance Trends (SMART). Int J Antimicrob Agents. 2012;40:S37–43.
- Hanley J, Branford I, Gugnan HC, Wilkinson C. U. T. urinary bacterial pathognes in St. Kitts.pdf. West Indies Med J. 2009;58:670.
- Kothari A, Sagar V. Antibiotic resistance in pathogens causing communityacquired urinary tract infections in India: a multicenter study. J Infect Dev Ctries. 2008;2:354–8.
- Akoachere J-FTK, Yvonne S, Akum NH, Seraphine EN. Etiologic profile and antimicrobial susceptibility of community-acquired urinary tract infection in two Cameroonian towns. BMC Res Notes. 2012;5:219.
- 23. Fosse-Edorh S. Journée modiale du diabète. Beh. 2014;30-31:491-529.
- Ronald A. The etiology of urinary tract infection: Traditional and emerging pathogens. Dis Mon. 2003;49:71–82.
- 25. Raz R, Colodner R, Kunin CM. Who are you Staphylococcus saprophyticus? Clin Infect Dis. 2005;40:896–8.
- Sanchez GV, Master RN, Karlowsky JA, Bordon JM. In vitro antimicrobial resistance of urinary Escherichia coli isolates among U.S. outpatients from 2000 to 2010. Antimicrob Agents Chemother. 2012;56:2181–3.
- Schito GC, et al. The ARESC study: an international survey on the antimicrobial resistance of pathogens involved in uncomplicated urinary tract infections. Int J Antimicrob Agents. 2009;34:407–13.
- Randrianirina F, et al. Antimicrobial resistance among uropathogens that cause community-acquired urinary tract infections in Antananarivo, Madagascar. J Antimicrob Chemother. 2007;59:309–12.
- Ma KL, Wang CX. Analysis of the spectrum and antibiotic resistance of uropathogens in vitro: Results based on a retrospective study from a tertiary hospital. Am J Infect Control. 2013;41:601–6.
- Laupland KB, Church DL, Vidakovich J, Mucenski M, Pitout JDD. Communityonset extended-spectrum beta-lactamase (ESBL) producing Escherichia coli: importance of international travel. J Infect. 2008;57:441–8.

- Arpin C, et al. Nationwide survey of extended-spectrum {beta}-lactamaseproducing Enterobacteriaceae in the French community setting. J Antimicrob Chemother. 2009;63:1205–14.
- Pitout JDD, Laupland KB. Extended-spectrum beta-lactamase-producing Enterobacteriaceae: an emerging public-health concern. Lancet Infect Dis. 2008:8:159–66.
- Smith SP, Manges AR, Riley LW. Temporal changes in the prevalence of community-acquired antimicrobial-resistant urinary tract infection affected by Escherichia coli clonal group composition. Clin Infect Dis. 2008;46:689–95.
- Breurec S, et al. Klebsiella pneumoniae resistant to third-generation cephalosporins in five African and two Vietnamese major towns: Multiclonal population structure with two major international clonal groups, CG15 and CG258. Clin Microbiol Infect. 2013;19:349–55.
- 35. Kumarasamy KK, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: A molecular, biological, and epidemiological study. Lancet Infect Dis. 2010;10:597–602.
- 36. Bastian S, et al. First case of NDM-1 producing Klebsiella pneumoniae in Caribbean islands. Int J Infect Dis. 2015;34:e53–4.
- Breurec S, et al. Emergence of OXA-48-producing Escherichia coli in the Caribbean islands. J Glob Antimicrob Resist. 2015;3:217–8.
- Andrade SS, et al. Increased resistance to first-line agents among bacterial pathogens isolated from urinary tract infections in Latin America: Time for local guidelines? Mem Inst Oswaldo Cruz. 2006;101:741–8.
- Vernaz N, et al. Modelling the impact of antibiotic use on antibiotic-resistant Escherichia coli using population-based data from a large hospital and its surrounding community. J Antimicrob Chemother. 2011;66:928–35.
- Grignon O, et al. Escherichia coli antibiotic resistance in emergency departments. Do local resistance rates matter? Eur J Clin Microbiol Infect Dis. 2014;34:571–7.
- 41. Heginbothom ML, et al. Laboratory testing policies and their effects on routine surveillance of community antimicrobial resistance. J Antimicrob Chemother. 2004;53:1010–7.
- 42. Dromigny JA, Nabeth P, Juergens-Behr A, Perrier-Gros-Claude JD. Risk factors for antibiotic-resistant Escherichia coli isolated from community-acquired urinary tract infections in Dakar, Senegal. J Antimicrob Chemother. 2005;56:236–9.
- 43. Dalhoff A. Global fluoroquinolone resistance epidemiology and implictions for clinical use. Interdiscip Perspect Infect Dis. 2012;2012:976273.

# Submit your next manuscript to BioMed Central and we will help you at every step:

- We accept pre-submission inquiries
- Our selector tool helps you to find the most relevant journal
- We provide round the clock customer support
- Convenient online submission
- Thorough peer review
- Inclusion in PubMed and all major indexing services
- Maximum visibility for your research

Submit your manuscript at www.biomedcentral.com/submit

