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**Diminution de la sensibilité aux antibiotiques des entérobactéries responsables
d'infections urinaires communautaires en Amazonie française**

**Decreased antibiotic susceptibility of Enterobacteriaceae causing community-acquired
urinary tract infections in French Amazonia**

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Declaration of interest

The authors declare no competing interests.

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Mots clés : BLSE ; Guyane française ; infection urinaire

Keywords: ESBL; French Guiana; urinary tract infection

Résumé

Objectifs. Les infections urinaires (IU) sont peu étudiées en Amazonie. Notre objectif était de décrire l'épidémiologie des bactéries responsables d'infections urinaires en Guyane.

Patients et méthodes. Étude monocentrique rétrospective réalisée chez les adultes ayant consulté aux Urgences du Centre Hospitalier de Cayenne en 2014 avec un diagnostic d'IU. La répartition des espèces bactériennes et les profils de sensibilité ont été décrits.

Résultats. Deux-cent-quatre-vingt-neuf patients avec IU ont été inclus, dont 82 (28,4 %) cystites, 166 (57,4 %) pyélonéphrites et 41 (14,2 %) IU masculines. *E. coli* était majoritaire (74,1 %), et avait une sensibilité diminuée à l'ampicilline, amoxicilline-acide clavulanique, fluoroquinolones, co-trimoxazole et furanes par rapport aux données de France métropolitaine. Les BLSE ont été isolées chez 3,1 % d'*E. coli* et 31,6 % de *K. pneumoniae*.

Conclusions. La sensibilité aux antibiotiques dans les IU est moindre que celle rapportée en métropole sans évidence d'une surconsommation antibiotique.

ABSTRACT

Objectives. Urinary tract infections (UTIs) have rarely been studied in the Amazon region.

We aimed to describe the epidemiology of bacteria causing UTIs in French Guiana.

Patients and methods. We performed a monocenter retrospective study of adults consulting at the emergency department of Cayenne Hospital in 2014 with a diagnosis of UTI. The bacterial species and resistance profile were described.

Results. Two-hundred-and-eighty-nine patients presenting with UTI were included: 82 (28.4%) presented with cystitis, 166 (57.4%) with pyelonephritis, and 41 (14.2%) with male UTI. *E. coli* was predominant (74.1%), and had decreased susceptibility to ampicillin, amoxicillin-clavulanic acid, fluoroquinolones, co-trimoxazole, and furans compared with data from metropolitan France. Extended-spectrum beta-lactamases (ESBL) was isolated in 3.1% of *E. coli* and 31.6% of *K. pneumoniae*.

Conclusions. Antibiotic susceptibility in UTI is lower than reported in metropolitan France without evidence for an excessive consumption of antibiotics.

INTRODUCTION

In France urinary tract infections (UTIs) are the second site of bacterial infection after bronchopulmonary infections [1]. In French Guiana, one of the French overseas territories of America located on the Guiana Shield, an Amazon region, data on the bacterial ecology of UTIs is almost non-existent. However, extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae have been extensively studied in the isolated Amerindian community of Trois-Sauts, in the extreme south-east of French Guiana [2-4].

We aimed to describe the epidemiology of bacterial species involved in UTIs in French Guiana to gain insight into local specificities to improve professional practices regarding antibiotic prescribing.

METHODS

Study design and population

We performed a monocenter observational retrospective study. We included patients aged over 15 years who consulted at the emergency department of Andrée Rosemon Hospital in Cayenne, French Guiana, between January 1 and December 31, 2014.

Case definition and inclusion criteria

The 10th International Classification of Diseases (ICD-10) was used to identify cases of UTI. The diagnosis was based on a clinical presentation compatible with UTI associated with a positive cyto-bacteriological examination of urine. The diagnosis of cystitis and pyelonephritis was restricted to female patients. The diagnosis of cystitis was based on the presence of symptoms of lower UTI (dysuria, urgency, frequency, or suprapubic tenderness). The

diagnosis of acute pyelonephritis was considered in the presence of fever and/or back pain associated with a cytobacteriological examination of urine with leukocyte count $>10^4$ /ml and bacteriuria $>10^3$ CFU/ml for *E. coli* and $>10^4$ CFU/ml for other Enterobacteriaceae [1]. The diagnosis of male UTI was based on the association of urinary signs (pollakiuria, dysuria, urinary burns) to which could be added pelvic pain (spontaneous or caused by rectal examination), acute retention of urine, and fever, associated with a positive cytobacteriological examination of urine with a leukocyte count $>10^4$ /ml and a bacteriuria threshold of 10^3 CFU/ml.

Patients with a negative urine culture were also included in the study if the diagnosis had been made by a specialist during the post-emergency consultation or hospitalization despite a negative cytobacteriological examination of urine, particularly in case of antibiotic treatment prior to microbiological sampling and/or positive blood culture with compatible clinical signs and bacteria.

Microbiological methodology

Bacterial inoculation was performed on Uriselect[®] media (Biorad, Marnes-la-Coquette, France) at 35-37°C for 18-24 hours and in an aerobic medium. The bacterial identification was based on conventional biochemical techniques with manual methods by gallery API 20E and API 20 NE for Enterobacteriaceae and gallery API Staph for staphylococci (BioMérieux, Marcy l'Étoile, France) and methods automated by VITEK2[®] (BioMérieux, Marcy l'Étoile, France). The antimicrobial susceptibility tests were performed by diffusion method in Mueller-Hinton medium (BioMérieux, Marcy l'Étoile, France). The susceptibility of antibiotics was estimated as per the 2013 guidelines of the Antibiogram Committee of the French Society for Microbiology (French acronym CA-SFM) [5]. The identification of ESBL-producing

Enterobacteriaceae was performed on an ESBL medium (BioMérieux, Marcy l'Étoile, France), and was then confirmed by disc diffusion method to detect synergy [6].

Data collection and analysis

Data was collected from the computerized records of patients (DMU[®] and CORA[®]) and biological results (AGFA SRI[®]) and were then anonymized. They included demographic, clinical, and microbiological data with results from urine and blood cultures and bacterial identification data, susceptibility testing, and production of ESBL.

Ethical consideration

The retrospective analysis of medical records in a single-center study is authorized by the French Data Protection Authority (French acronym CNIL) for the evaluation of professional practices (declaration of the database no. 2145898).

RESULTS

In 2014 a total of 47,251 visits to the emergency department of the Hospital of Cayenne were recorded, including 34,000 for patients aged over 15 years (Figure 1). After deletion of duplicates and exclusion criteria, 289 patients presenting with confirmed UTI were included: 82 (28.4%) had cystitis, 166 (57.4%) pyelonephritis, and 41 (14.2%) male UTI. The sex ratio was 0.17 (1 man for 6 women). The mean age was 39.0 ± 19.6 years (men: 57.4 ± 20.0 ; women: 36.5 ± 18.9 years; $P < 0.001$). A total of 261 (90.7%) urine cultures performed in the 289 patients presenting with UTI resulted in bacterial identification (Table I). The distribution of bacterial species showed a strong predominance of *Escherichia coli* (74.1%), followed by *Klebsiella pneumoniae* (7.3%)

and coagulase-negative staphylococci (CNS) (6.2%) including *Staphylococcus saprophyticus*, *S. warneri*, and *S. hominis*. The most common bacteria observed in women (N=224) were *E. coli* (74.3%), *K. pneumoniae* (6.7%), and CNS (7.2%). The most common bacteria observed in men (N=37) were *E. coli* (73%) and *K. pneumoniae* (10.8%). *E. coli* was predominant, especially in pyelonephritis and male UTIs (85.9% and 73.0%, respectively). *E. coli* accounted for only 54.9% of the bacteria responsible for cystitis, followed by CNS (14.6%; mainly *S. saprophyticus*).

A total of 253 (97.7%) antimicrobial susceptibility tests were performed on the 259 isolated microorganisms; 233 were performed on Enterobacteriaceae strains (Table II). Overall, 32.6% of the strains were susceptible to ampicillin, 95.1% to cefotaxime, 100% to imipenem, 62.4% to co-trimoxazole, 99.1% to amikacin, 94.3% to gentamicin, and 81.6% to nalidixic acid. *K. pneumoniae* showed a more resistant profile than *E. coli*. Of the 233 Enterobacteriaceae identified, 12 (5.1%) were ESBL-producing strains (Table II). The proportion of ESBL-producing *K. pneumoniae* strains (6/19 or 31.6%) was higher than that of ESBL-producing *E. coli* strains (6/192 or 3.1%) ($P<0.01$).

DISCUSSION

To our knowledge no study has been performed on UTIs in neighboring countries of French Guiana such as Guyana and Suriname. Although many articles on that subject are available in the Brazilian literature, no study has to our knowledge been performed in the Amazonian states near French Guiana [7-11].

The most common bacteria observed in our study were *E. coli* (74.3%), *K. pneumoniae* (7.3%), CNS (6.1%), and *Proteus mirabilis* (4.2%). These findings were similar to those

observed in the French literature [12-14]. In contrast, staphylococci were overrepresented in the bacterial ecology of cystitis (14.6%), including *S. saprophyticus* (12.2%) and *S. aureus* (3.7%). *S. saprophyticus* is usually observed in 7% of lower UTIs in Europe [1, 12, 15].

The antibiotic susceptibility of *E. coli* was usually lower than that reported in metropolitan France [1]. Susceptibility to ampicillin, amoxicillin-clavulanic acid, trimethoprim-sulfamethoxazole, fluoroquinolones, and furans were therefore significantly lower than that reported in metropolitan France (Table II). Susceptibility to cephalosporins and aminoglycosides was similar to that reported in metropolitan France, and no resistance to carbapenems was observed in our study. The authors of a 2017 article on antibiotic consumption in French Guiana reported a significantly different antibiotic consumption in French Guiana compared to that of metropolitan France [16]. Cyclin consumption was for instance higher in French Guiana, amoxicillin – with or without clavulanic acid – and sulfonamide consumption was comparable or higher, while consumptions of third-generation cephalosporins, carbapenems, and fluoroquinolones were lower than in metropolitan France. Discrepancies between the estimate of antibiotic consumption in French Guiana and the lower susceptibility of these strains can therefore be observed. It is unclear whether this greater proportion of antibiotic resistance is part of a broader regional pattern as no data is available in surrounding countries.

Of the Enterobacteriaceae observed in our study, 5.1% were ESBL-producing Enterobacteriaceae, exclusively *E. coli* and *K. pneumoniae* (3.1% and 31.6%, respectively). This prevalence of ESBLs among *E. coli* is similar to literature data [17-19]. The proportion of ESBL-producing Enterobacteriaceae was therefore 3.3% and 6.6% among 51,643 urine specimens positive for *E. coli* and *K. pneumoniae* in France [17-19]. In neighboring Brazil, ESBL-producing Enterobacteriaceae accounted for 7.1% of 324 *E. coli* strains isolated from patients presenting with lower urinary tract infections in Brasilia and for 3.0% of 5,722

Enterobacteriaceae isolated from patients presenting with UTIs in São Paulo [7, 9]. The epidemiological situation of French Guiana in terms of bacterial resistance differed from that of metropolitan France [16]. A lower frequency of resistance for *S. aureus*, *E. coli*, and *P. aeruginosa* but a higher frequency for *K. pneumoniae* were indeed reported. The main limitation of the study is its retrospective nature with missing data. No genotypic characterization of ESBL-producing Enterobacteriaceae was performed during the study period.

Conclusion

To our knowledge this is the first study assessing the susceptibility profile of bacteria responsible for UTI in French Guiana. Few articles have been published on the subject in the Amazon region. In this Amazon and French medical environment, coagulase-negative staphylococci seem to be more common and ESBL production more common for *K. pneumoniae*, but similar to metropolitan France for *E. coli*. The antibiotic susceptibility of *E. coli* in UTIs is lower than that reported in metropolitan France for antibiotics of daily use.

Contribution of authors

CB, SOE, and LE designed the study protocol and set up the study.

CB and LE wrote the article.

LE performed the statistical analysis.

BM performed the microbiological analyses and drafted the microbiological method.

GW, EM, and FD reviewed the article.

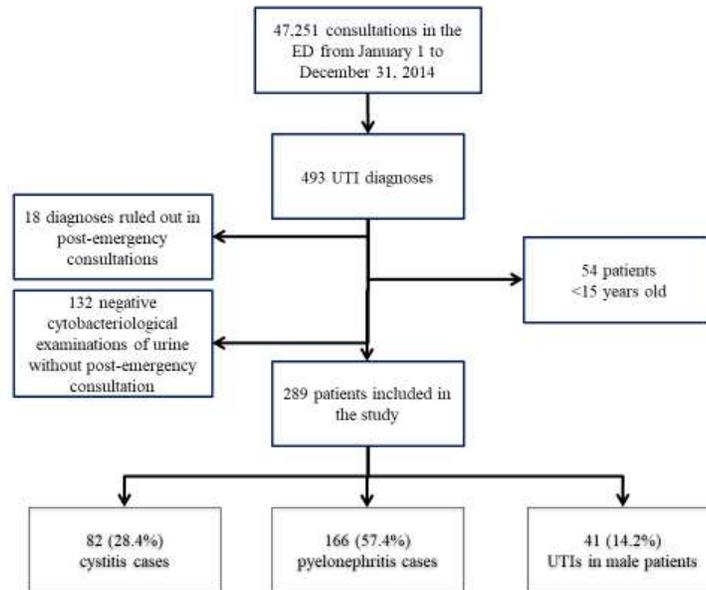
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Figure I. Flow chart of the study

Figure I. Diagramme de flux de l'étude



UTI = urinary tract infection; ED = Emergency department

Table I. Distribution of bacterial species according to the type of urinary tract infection

Tableau I. Répartition des espèces bactériennes selon le type d'infection urinaire

Bacteria	Female		Male	
	Cystitis N (%) N=82	Pyelonephritis N (%) N=142	Upper UTI N (%) N=37	Total N (%) N=261
<i>Escherichia coli</i>	45 (54.9)	122 (85.9)	27 (73)	194 (74.3)
<i>Klebsiella pneumoniae</i>	6 (7.3)	9 (6.3)	4 (10.8)	19 (7.3)
<i>Staphylococcus saprophyticus</i>	10 (12.2)	4 (2.8)	0 (0)	14 (5.3)
<i>Proteus mirabilis</i>	6 (7.3)	2 (1.4)	2 (5.4)	10 (3.8)
<i>Streptococcus agalactiae</i>	4 (4.9)	2 (1.4)	0 (0)	6 (2.3)
<i>Enterobacter cloacae</i>	3 (3.7)	1 (0.7)	1 (2.7)	5 (1.9)
Other Enterobacteriaceae*	1 (1.2)	2 (1.4)	1 (2.7)	4 (1.5)
<i>Enterobacter aerogenes</i>	2 (2.4)	0 (0)	2 (5.4)	4 (1.5)
<i>Staphylococcus aureus</i>	3 (3.7)	0 (0)	0 (0)	3 (1.1)
Other coagulase negative staphylococci*	2 (2.4)	0 (0)	0 (0)	2 (0.8)
No bacterium identified	0/82 (0)	24/166 (14.5)	4/41 (9.8)	28/289 (9.7)
Total	82	166	41	289

UTI = urinary tract infection; ED = Emergency department; Other Enterobacteriaceae: *Salmonella* sp. (n=1), *Citrobacter koseri* (n=1), *Acinetobacter baumannii* (n=1), *Pantoea* sp. (n=1) ; other coagulase negative staphylococci: *S. warneri* (n=1) et *S. hominis* (n=1).

Table II. Susceptibility to various antibiotic classes of ESBL and non-ESBL Enterobacteriaceae and comparison with metropolitan France data according to the SPILF 2015 update.

Tableau II. Sensibilité aux différentes familles d'antibiotiques des entérobactéries BLSE et non BLSE et comparaison aux données de métropole selon la mise au point de la SPILF 2015.

	Total Enterobacteri aceae	Non-ESBL- producing Enterobacteri aceae	ESBL- producing Enterobacteri aceae	<i>K. pneumon iae</i>	<i>E. coli</i>	Susceptibi lity to <i>E. coli</i> according to SPILF
	N (%)	N (%)	N (%)	N (%)	N (%)	(%)
amoxicilli n- clavulani c acid	126 (55.2)	123/217 (56.7)	3/11 (27.3)	12/18 (66.7)	104/1 89 (55.0)	67.4-71.1
ampicillin	74/227 (32.6)	72/216 (33.3)	2/11 (18.2)	1/18 (5.6)	67/18 8 (35.6)	54.8-56.1
ticarcillin	89/228 (39.0)	87/218 (39.9)	2/10 (20.0)	1/17 (5.9)	72/18 9 (38.1)	-
piperacilli/ tazobacta m	175/189 (92.6)	170/180 (94.4)	5/9 (55.6)	11/16 (68.8)	147/1 56 (94.2)	-
cefalotin	136/225 (60.4)	134/214 (62.6)	2/11 (18.2)	13/18 (72.2)	112/1 87 (59.9)	-
cefotaxim e	214/225 (95.1)	211/217 (97.2)	3/11 (27.3)	13/18 (72.2)	181/1 89 (95.8)	96.5
ceftazidi me	217/229 (94.8)	214/218 (98.2)	3/11 (27.3)	13/18 (72.2)	183/1 89 (96.8)	-
cefoxitin	211/217 (97.2)	205/227 (94.5)	6/11 (54.5)	14/18 (77.8)	185/1 89 (97.9)	-
imipenem	227/227 (100)	216/216 (100)	11/11 (100)	18/18 (100)	189/1 89 (100)	-
ertapene m	228/228 (100)	217/217 (100)	11/11 (100)	18/18 (100)	189/1 89 (100)	-
tobramyc in	178/191 (93.2)	175/182 (96.2)	3/9 (33.3)	12/16 (75)	148/1 57	-

amikacin	226/228 (99.1)	217/218 (99.5)	9/10 (90)	16/17 (94.1)	(94.3) 188/1 89	97
gentamicin	216/229 (94.3)	212/218 (97.2)	4/11 (36.4)	13/18 (72.2)	181/1 89	-
nalidixic acid	186/228 (81.6)	183/217 (84.3)	3/11 (27.3)	11/18 (61.1)	154/1 89	77-84
ofloxacin	154/185 (83.2)	152/179 (86.9)	2/8 (25.0)	127/156 (81.4)	11/13 (84.6)	-
ciprofloxacin	204/223 (91.5)	200/212 (94.3)	4/11 (36.4)	171/184 (92.9)	12/18 (66.7)	85-90.4
TMP/SMX	143/229 (62.4)	141/218 (64.7)	2/11 (18.2)	114/189 (60.3)	11/18 (61.1)	76.5-87
furans	207/1/20	197/217 (90.8)	10/11 (90.9)	188/189 (99.5)	13/18 (72.2)	98.2-98.7

ESBL: extended-spectrum beta-lactamase ; TMP/SMX: trimethoprim/sulfamethoxazole