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Epidemiological Profile of Urinary Tract Infections Observed at the Institut Pasteur in Bangui, Central African Republic

Alain Farra[1, *], Sylvanus Mogalama[2], Christian Diamant Mossoro-Kpinde[2], Gilles Ngaya[1], Jean Robert Mbecko[1], Hugues Sanke-Waïgana[1], Alexandre Manirakiza[3]

[1]Medical Laboratory, Institut Pasteur in Bangui, Bangui, Central African Republic

[2]Faculty of Health Sciences, University of Bangui, Bangui, Central African Republic

[3]Department of Epidemiology, Institut Pasteur in Bangui, Bangui, Central African Republic

Email address:

alain.farra@pasteur-bangui.cf (A. Farra), sylvanus.mogalama@yahoo.fr (S. Mogalama), mossoro_kpinde@yahoo.fr (C. D. Mossoro-Kpinde), gilles.ngaya@pasteur-bangui.cf (G. Ngaya), mbecko2003@yahoo.fr (J. R. Mbecko), hugues.sanke@gmail.com (H. Sanke-Waïgana), alexandre.manirakiza@pasteur-bangui.cf (A. Manirakiza)

[*]Corresponding author

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Abstract: The urinary tract is the second most common site of bacterial infection after the respiratory tract. Enterobacteria remain the first cause of urinary tract infections (UTIs), followed by staphylococci and non-fermenter bacteria. Furthermore, bacteria producing extended spectrum beta-lactamases (ESBL) have become more frequent, exposing African patients to therapeutic dead ends. The aim of this study was to determine the epidemiological profile of UTIs diagnosed at the Institut Pasteur in Bangui (IPB), Central African Republic (CAR), a research center that carries out antibiotic sensitivity testing according to international standards. For that, the collected demographic, clinical and biological data come from patients calling at the IPB for a urinalysis and who gave their consent for their data to be included and analyzed in this six-month cross-sectional study (January-June 2019). A total of 412 patients were enrolled in this study. The mean age was 35.2 years [1-80], females made up 55.8% of the study population and the sex ratio was 0.79:1 (M: F). Overall, 117 UTIs were detected, giving a prevalence rate of 28.4%. Of the bacterial isolates, 89.8% (105/117) were enterobacteria, of which 52.4% (55/105) were ESBL-producers. *Escherichia coli* accounted for more than half of the isolates 55.5% (65/117) and the ESBL-producers 58.2% (32/55). The 0–15-year age group showed the highest incidence of UTIs, but this rate was not significantly different from the other age groups (P = 0.665). Antecedent UTI was not a significant factor in the observed infections. However, female gender, fever, painful urination, acquisition in a healthcare setting and samples collected outside the laboratory were all significantly associated with UTI cases (P<0.005). The high proportion of ESBL-producing bacteria found during this study poses a real potential threat for public health in the CAR. Controlling antibiotic use should thus be a priority for the Ministry of Health.

Keywords: UTI, Epidemiology, ESBL, Bangui

1. Introduction

Urinary tract infections (UTIs) are frequently encountered in healthcare and community settings and several microorganisms can be responsible for UTIs, particularly enterobacteria [1]. Increasingly, in both healthcare- and community-acquired UTIs, *Escherichia coli* is the main isolated enterobacteria species, and more and more strains produce extended-spectrum beta lactamases (ESBL), exposing patients in Africa to therapeutic dead ends [2-5]. UTIs are known to occur more frequently in women than in

men, due to differences in anatomy and pregnancy [6]. However, in children, UTIs are associated with functional or anatomical abnormalities of the urinary tract, of which the most frequent is vesicoureteral reflux [7]. The urinary tract is second only to the respiratory tract as a site of infection and 80% of UTI cases occur in hospital patients is with an indwelling catheter [8].

In the Central African Republic (CAR), very few studies have been carried out on the etiology and the resistance profiles of bacteria responsible for UTIs. In 2006, a non-published study carried out as part of medical thesis on community-acquired UTIs in adults found a predominance of staphylococci, in contrast to reports in the literature. Here, the aim of this study was to determine the epidemiological profile of UTIs diagnosed at the Institut Pasteur in Bangui, CAR, a research center that carries out antibiotic sensitivity testing according to international standards.

2. Materials and Methods

2.1. Type, Study Population and Sampling

2.1.1. Type of Study

We used a six-month cross-sectional study from January 2019 to June 2019 on patients who were referred or spontaneously came to the Institut Pasteur in Bangui (IPB) for urinalysis.

2.1.2. Study Population

The study population was made up of males and females of all ages who had come to the IPB laboratory for urinalysis.

2.1.3. Sampling

Sampling was exhaustive, and included all urinalyses performed at the IPB during the study period.

2.1.4. Inclusion and Exclusion Criteria

All patients who were asymptomatic or who showed signs of UTI were included in the study. Patients with sexually transmitted infections and non-consenting patients were excluded from the study.

2.1.5. Study Protocol

Data were collected in sampling rooms. When the sample was submitted, consenting patients filled out an information sheet providing their age, gender, profession, symptoms, antecedents and listing any antibiotics currently or previously taken. The second part of the information sheet was filled out after the urinalysis, giving the results of the microscopic (cytological) exam, the presence or absence of bacteria and, if indicated, antibiotic sensitivity testing.

2.2. Urinalysis at the Laboratory

Analyses were carried out following the procedures in effect at the IPB.

2.2.1. Urine Samples

Urine samples were taken in the morning, at least 3-4 h after the last miction, in a sterile container and after carefully cleaning the genitals with soap and rinsing with an antiseptic (Dakin's solution). Then, mid-stream urine was collected, avoiding the initial stream of urine. After collecting the urine sample, the container was closed securely, labeled and rapidly transported to the laboratory. If the patient had a catheter, the sample was taken using a syringe and a sterile needle directly from the sampling port of the catheter collection bag after it had been disinfected. The sample was then poured into a container and labeled with the indication that it was a catheter sample.

For infants, a single-use urine sample bag was placed on the genital area, which had been carefully disinfected, and left in place for 1 h maximum. Collected urine was poured into a sterile container and labeled as an infant bag sample. It was also possible to collect mid-stream urine during diaper changing.

2.2.2. Sample Storage

Urine samples were stored for up to 1 h at room temperature and 12 h at +4°C in a refrigerator.

2.2.3. Laboratory Urine Analysis

Examination under the microscope was used to score urine samples as clear, pale yellow, dark yellow, brown, cloudy or revealing the presence of blood. Cell counts were then carried out to quantify white blood cells and red blood cells on a Kova slide (with a quantitative grid), as well as to detect crystals, casts or epithelial cells. The sample was cultured on bromocresol purple agar using a 10 µL inoculation loop and incubated at 37°C for 18 to 24 h. The inoculum was spread on the agar plates using the surface streak method, from top to bottom, so as to obtain well-separated individual colonies, regardless of the bacterial load. Bacteria were identified using oxidase tests, catalase tests and the analytical profile index (API) systems 20E, 20NE, API-Staph, API-Strep according to the protocol used at the laboratory (Figure 1). The antibiotic sensitivity test was based on the agar diffusion assay according to the recommendations of the Antimicrobial Sensitivity Testing Committee of the French Society for Microbiology (CA-SFM). The identified bacteria were stored at –80°C in heart-brain infusion broth supplemented with 30% glycerol.

2.3. Data Analysis

Data were recorded in a Epi-info database and analyzed using Strata software and an Excel spreadsheet to make the figures and graphs.

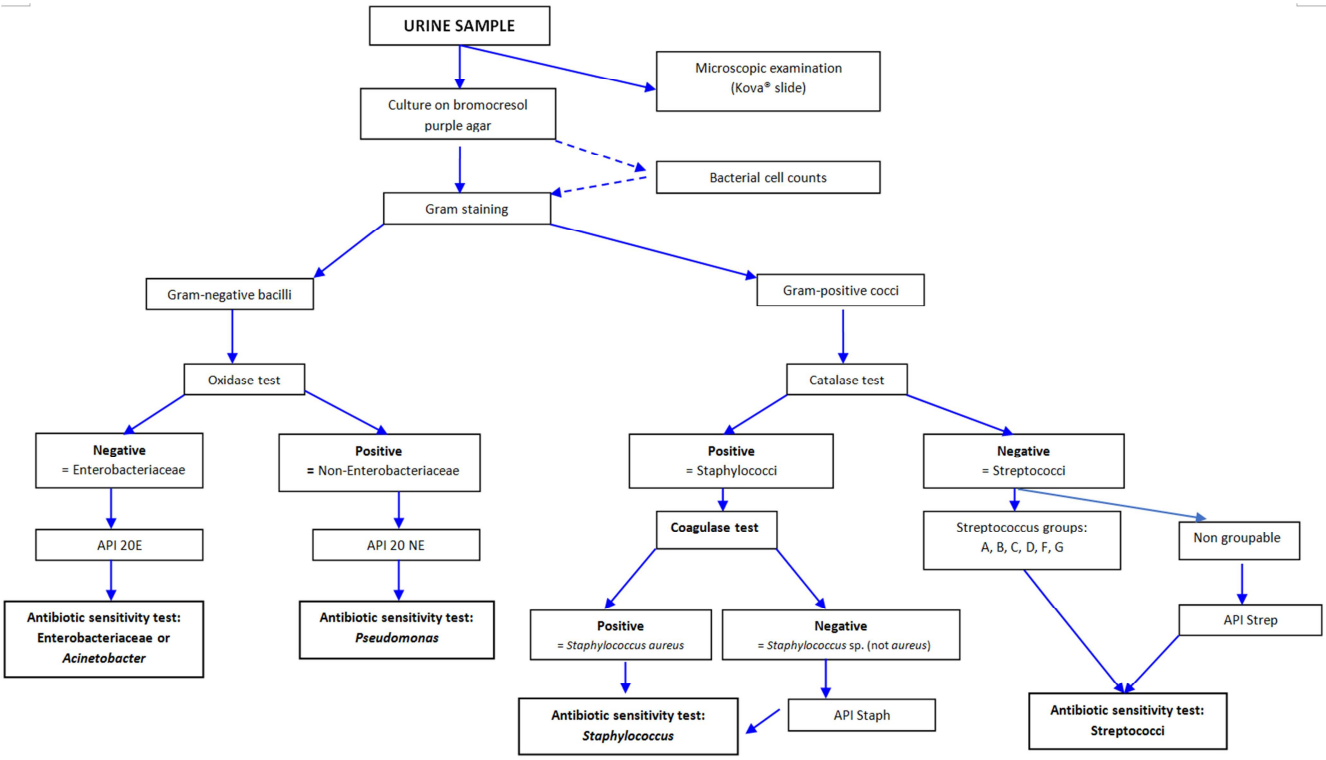

Figure 1. *Urinalysis diagnosis procedure followed at the Institut Pasteur in Bangui.*

3. Results

3.1. Characteristics of the Study Population

A total of 412 patients were enrolled in this study. The average age of the included patients was 35.2 years, ranging from 1 to 80 years. The majority of patients were in the 31 to 45 years age range (30.6%). More than half the population was female (55.8%), giving a male-female sex ratio of 0.79:1; 77.8% of the patients were salaried workers.

3.2. Prevalence of Observed UTIs

During the study period, 117 UTIs were detected in the 412 enrolled patients, giving a prevalence of 28.4%.

3.3. Epidemiological Profile of the UTIs Observed During the Study

Patients between 0 and 15 years of age showed the highest incidence of UTIs (32.9%), but the difference compared with the other age groups was not significant (P = 0.665).

Previous UTI episodes were not a significant factor in the observed cases of infection. However, female gender, indwelling catheter use, hospital acquisition and samples collected outside the laboratory were significantly associated with UTI patients (P<0.005; Table 1).

Table 1. *Epidemiological profile of the urine samples analyzed during the study.*

	Results of the urine culture				
	Positive	**Negative**	**OR**	**CI_{95}**	**P**
Age group (years)					
0–15	23 (32.9)	47 (67.1)			0.665
16–30	34 (31.8)	73 (68.2)			
31–45	31 (24.8)	94 (75.2)			
46–60	17 (25.4)	50 (74.6)			
>60	12 (27.9)	31 (72.1)			
Gender					
Female	80 (34.8)	150 (65.2)	2	[1.2-2.4]	0.0006
Male	37 (20.3)	145 (79.7)			
Previous UTIs					
No	109 (29.1)	266 (70.9)			
Yes	8 (21.6)	29 (78.4)			0.174
Indwelling catheter					
Yes	11 (100.0)	0 (0.0)	4	[3.2-4.5]	0.0000034
No	106 (26.4)	295 (73.6)			
Origin of acquisition					

	Results of the urine culture				
	Positive	**Negative**	**OR**	**CI_{95}**	**P**
Community	106 (26.6)	292 (73.4)			
Hospital	11 (78.6)	3 (21.4)	0.3	[0.2-0.4]	0.00005
Sample collection site					
Laboratory	78 (23.5)	254 (76.5)			
Outside of the laboratory	39 (48.8)	41 (51.2)	0.5	[0.4-0.6]	0.000008

OR, odds ratio; CI_{95}, 95% confidence interval; P, probability.

3.4. Clinical Aspects of the Diagnosed UTIs

Symptoms such as burning sensations during miction, pollakiuria, hematuria, lower back pain and pelvic pain were not significantly associated with the diagnosed UTIs (P > 0.005). However, fever and dysuria were significantly linked to UTI diagnosis in this study (Table 2).

Table 2. *Symptoms associated with the urine samples tested for urinary tract infection.*

	Results of the urine culture				
	Positive	**Negative**	**OR**	**CI_{95}**	**P**
Fever					
Yes	38 (38.8)	60 (61.2)	1.5	[1.1-2.1]	0.005
No	79 (25.2)	235 (74.8)			
Burning sensation when urinating					
Yes	14 (36.8)	24 (63.2)			0.118
No	103 (27.5)	271 (72.5)			
Pollakiuria					
Yes	5 (25.0)	15 (75.0)			0.730
No	112 (28.6)	280 (71.4)			
Dysuria (pain)					
Yes	8 (53.3)	7 (46.7)	0.5	[0.3-0.8]	0.000004
No	109 (36.7)	288 (63.3)			
Hematuria					
Yes	2 (66.7)	1 (33.3)			0.108
No	115 (28.1)	294 (71.9)			
Pelvic pain					
Yes	29 (24.4)	90 (75.6)			0.248
No	88 (30.0)	205 (70.0)			
Lower back pain					
Yes	16 (26.2)	45 (73.8)			0.384
No	101 (28.8)	250 (71.2)			

OR, odds ratio; CI_{95}, 95% confidence interval; P, probability.

3.5. Biological Profile of the Observed UTIs

3.5.1. Cytological Profile

Cloudy urine and the presence of white blood cells (WBCs) were significantly associated with diagnosed UTIs (P=0.0000; Table 3).

Table 3. *Visual examination of the urine samples and detection of white blood cells.*

	Results of the urine culture				
	Positive	**Negative**	**OR**	**CI_{95}**	**P**
Visual examination					
Clear	4 (16.7%)	20 (83.3%)			
Pale yellow	60 (19.1%)	254 (80.9%)			
Cloudy	51 (72.3%)	20 (27.7%)	0.3	[0.2-0.3]	0.0000
Presence of blood	2 (66.7%)	1 (33.3%)			
Presence of WBCs					
Yes	58	37	6.8	4.1-11.3	0.0001
No	59	258			

OR, odds ratio; CI_{95}, 95% confidence interval; P, probability.

3.5.2. Bacteriological Profile

Enterobacteria represented 89.8% (105/117) of isolates, followed by non-fermenters and staphylococci, each isolated in 5.1% (6/117) of the UTIs. *E. coli* accounted for

more than half of the isolates 55.5% (65/117), of which 61.8% were of community origin, followed by *Klebsiella pneumoniae*. Among the non-fermenters, *Pseudomonas aeruginosa* was observed only in healthcare-origin samples, whereas *Acinetobacter baumannii* was exclusively detected in community-origin cases. *Staphylococcus aureus* was exclusively found in cases from non-healthcare settings, whereas coagulase-negative staphylococci were found in both healthcare- and community-acquired cases (Table 4).

Table 4. *Bacterial species isolated from the observed urinary tract infections and the setting in which they were acquired.*

Isolated species	Origin of acquisition		
	Community (%)	Hospital (%)	Total (%)
Escherichia coli	63 (61.8)	2 (13.3)	65 (55.5)
Klebsiella pneumoniae	20 (19.6)	3 (20.0)	23 (19.6)
Klebsiella oxytoca	5 (4.9)	1 (6.7)	6 (5.1)
Enterobacter cloacae	4 (3.9)	2 (13.3)	6 (5.1)
Citrobacter freundii	0 (0.0)	2 (13.3)	2 (1.7)
Citrobacter youngae	1 (0.9)	0 (0.0)	1 (0.8)
Morganella morganii	1 (0.9)	0 (0.0)	1 (0.8)
Serratia odorifera	0 (0.0)	1 (6.7)	1 (0.8)
Pseudomonas sp.	0 (0.0)	3 (20.0)	3 (2.6)
Acinetobacter baumannii	3 (2.9)	0 (0.0)	3 (2.6)
Staphylococcus aureus	3 (2.9)	0 (0.0)	3 (2.6)
Coagulase-negative staphylococci	2 (1.9)	1 (6.7)	1 (0.8)
Total	102 (87.2)	15 (12.8)	117 (100)

3.5.3. Resistance Profiles

Among the enterobacteria, more than half 52.4% (55/105) were ESBL enterobacteria (Table 5). Among the isolated staphylococcus strains, two of the three *S. aureus* strains were methicillin-resistant (MRSA).

Table 5. *Extended-spectrum beta lactamase (ESBL)-producing enterobacteria found in the observed urinary tract infections.*

	ESBL-producing strain		
	YES (%)	NO (%)	Total
Enterobacter cloacae	1 (17.0)	5 (83.0)	6
Escherichia coli	32 (49.0)	33 (51.0)	65
Klebsiella pneumoniae	16 (73.0)	7 (27.0)	23
Klebsiella oxytoca	3 (50.0)	3 (50.0)	6
Citrobacter youngae	0 (0.0)	1 (100.0)	1
Citrobacter freundii	2 (100.0)	0 (0.0)	2
Morganella morgani	(0.0)	1 (100.0)	1
Serratia oderifera	1 (100.0)	0 (0.0)	1
Total	55 (52.4)	50 (47.6)	105

4. Discussion

This study involved 412 patients enrolled for urinalysis at the IPB from January to June 2019. Among the enrolled patients, those 15 years and younger showed the highest proportion of UTI cases, but this proportion was not significantly greater than in the other age groups. Most published studies on UTIs cover either only children or only adults, and very few involve the general population. In studies carried out in Africa, Europe or America, UTIs generally do not appear to be influenced by age [5, 9]. However, the female gender has been frequently statistically linked to UTI incidence, due to the female anatomy [6].

In this study, cloudy urine was significantly associated with UTI cases, but some studies have shown that urine from UTI patients is not always cloudy [10, 11]. Visual examination of urine should not influence the decision to culture the sample, despite the practices encountered in some makeshift laboratories in developing countries. Culturing the urine sample is the only way to confirm or rule out a UTI.

White blood cells accompanied by a high bacteria count in a urine sample is a well known and documented sign of UTI. However, some UTIs are not associated with the presence of white blood cells [6, 10].

This study confirmed the predominance of enterobacteria in UTIs, with *E. coli* being the leading species and found primarily in community-acquired cases, as reported previously in the CAR and other studies [12, 13]. *P. aeruginosa* was isolated only from samples from healthcare-acquired cases and *S. aureus* in non-healthcare-origin samples. However, *K. pneumoniae* was detected in samples from both origins of acquisition [14]. ESBL-producing enterobacteria, which accounted for 3.7% of enterobacteria in 2004 and 19.6% in 2006, reached 52.4% (54/105) in this study [13]. This alarming proportion is clearly greater than those reported from other African countries, such as Gabon (12.8%) or Mauritania (15.4%) [15, 16]. This situation likely stems from the fact that the CAR Ministry of Health does not regulate the medical drug sector, and antibiotics such as ciprofloxacin or ceftriaxone are sold on the street and used as self-medication. In addition, many non-qualified persons prescribe antibiotics, often in a probabilistic manner, without relying on any laboratory tests. This massive increase in the spread of ESBL enterobacteria is a cause of concern and constitutes a real threat for public health in the CAR. Studies carried out in the CAR have already shown a worrisome increase in ESBL enterobacteria, whether in surgical site infections or from carriage, with a rate of 59% [17, 18]. The prevalence of ESBL enterobacteria could worsen in the coming decade if drastic measures are not taken at the institutional level to control their spread.

5. Conclusion

This study showed that enterobacteria remain the primary cause of UTIs, with *E. coli* being the leading species. The constant increase in the proportion of ESBL-producing enterobacteria poses a real threat for public health in the CAR. At the institutional level, broad – or even drastic – measures need to be taken to control the use of antibiotics in the CAR to avoid running the risk of therapeutic dead ends for treating UTIs or other types of infections. In addition, monitoring this already alarming epidemiological situation calls for a national-level surveillance scheme to limit the propagation of antimicrobial resistance in the CAR.

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