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Prevalence of Carbapenems Resistant Bacteria: Case of Three Health Facilities in Lomé, Togo

S. Dossim[1,2,3*], M. Salou[2,3,4], A. Azimti[1], B. Bidjada[5], A. M. Godonou[3], E. Aoussi[5], A. Kere-Banla[5], M. Prince-David[2,3] and A. Y. Dagnra[2,3,4]

[1]Laboratoire de Bactériologie, CHU Campus, 03BP 30284, Lomé, Togo.
[2]Département des Sciences, Fondamentales et de Santé Publique, BP 1515, Lomé, Togo.
[3]Centre de Recherche de Biologie Moléculaire et d'immunologie, FSS-U, BP1515 Lomé Togo.
[4]Laboratoire de Microbiologie, CHU Sylvanus Olympio, BP57 Lomé, Togo.
[5]Institut National d'Hygiène, BP1396 Lomé, Togo.

Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The purpose of this study was to determine the prevalence of bacteria resistant to carbapenems within three reference health facilities in Lomé, Togo.
Methods: It was a cross sectional study carried out between April and August 2016 within three medical bacteriology laboratories: Institut National d'Hygiène (INH), Sylvanus Olympio and Campus Teaching Hospitals. Samples of various origins were processed according to national standard procedures. Identification of bacteria was carried out according to the Biomérieux API® technique, antibiotics susceptibility test done according to the 2015 recommendations of the Comité de l'antibiogramme de la Société Française de Microbiologie (CA-SFM). Thus, enterobacteria with a decreased susceptibility to ertapenem and *Pseudomonas aeruginosa*, *Acinetobacter baumannii* resistant to imipenem were included.

**Corresponding author: E-mail: sikorlaure@gmail.com;*

Results: During the study, 306 strains were isolated at Sylvanus Olympio Teaching Hospital, 77 at Campus Teaching Hospital, and 520 at INH. The prevalence was 7.19% (n=22) for Sylvanus Olympio, 2.59% (n=2) for Campus, and 0.77% (n=4) for INH. Among these 28 strains from different origins, 57.14% (n=16) were isolated from hospitalized patients. Most of the strains, 64.29% (n=18) were isolated from urines, 32.14% from pus (n=9), and 3.57% from CSF (n=1). It was 14 strains of *Acinetobacter baumannii,* 11 strains of *Enterobacter cloacae,* 1 strain of *Pseudomonas aeruginosa*, 1 strain of *Klebsiella pneumoniae,* and 1 strain of *Escherichia coli.* Two strains of *E. cloacae* and the strain of *P. aeruginosa* were resistant to colistin.
Conclusion: Cases of strains with decreased susceptibility to carbapenems are isolated within hospitals in Lomé, so a molecular characterization as well as an epidemiological surveillance is needed.

Keywords: Acinetobacter baumannii; carbapenems resistance; Enterobacteria; Pseudomonas aeruginosa; Lomé.

1. INTRODUCTION

Gram-negative bacteria are the major isolated in human pathology. Over the years, their susceptibility to the different antibiotics became very limited, decreasing the therapeutic options. Indeed, we noticed the development of resistance especially to the main class of antibiotics used for their treatment: the beta-lactams.

The detection of the first extended spectrum beta-lactamase SHV-2 encoded by a strain of *K. pneumoniae* isolated in Germany in 1985 [1] announced the era of these enzymes which represent nowadays a real public health issue. β-lactamases are enzymes which inactivate the molecules belonging to the class of β-lactams. They are numerous and from different types depending on their targeted antibiotic. Some are present naturally within some bacteria such as the Acinetobacter's natural cephalosporinase [2]. However, the acquisition of the so-called extended spectrum β-lactamases from the fact that they inactivate all the β-lactams antibiotics with the exception of the carbapenems makes difficult the treatment of some infections. To these enzymes, carbapenemases will appear and target carbapenems, last resort of this family. This resistance was first detected in London in 1982 [3] and since then many reports took place in various regions of the world [4]. Their spread represents a significant threat to public health.

Africa is not spared, in fact singular cases of sporadic outbreaks are noticed in all parts of the continent in humans [5–9], in animals [10] and in the environment [11]. With this in mind, we then wanted to carry out a study on the prevalence of the resistance to carbapenems within the city of Lomé.

2. MATERIALS AND METHODS

It was a cross sectional study between April and August 2016 within three medical bacteriology laboratories in Lomé: The laboratories of the Sylvanus Olympio and Campus Teaching Hospitals and that of Institut National d'Hygiène (INH). These three facilities belong to the Togolese public sector and are those offering medical bacteriology services. In this study, we have included all the Gram-negative bacilli (GNB) which are resistant to carbapenems after a susceptibility testing.

The treatment of samples is done within different laboratories according to the national standardized procedures in order to isolate the bacteria. The identification of the bacteria was done through the traditional approach (Gram coloration, oxidase and biochemical test) or analytical profil index (API®) by Bomérieux depending on the cases. The susceptibility to antibiotics was done through antibiotics disks diffusion method on agar medium in accordance with the standards of the national standardized procedures. For the study of susceptibility to carbapenems, disks of ertapenem and imipenem at 10 µg were used. It was about testing as a marker ertapenem for enterobacteria and imipenem for Pseudomonas and Acinetobacter strains. The third generation cephalosporins tested were: Ceftriaxone, cefsulodine, ceftazidime, cefotaxime, cefpodoxime, cefixime, cefotetan, cefepime, cefpirome, cefotiam depending on their availability. The identification of resistant bacteria was done through the phenotypic method. The interpretations were done according to the 2015 recommendations of the Comité de l'antibiogramme de la Société Française de Microbiologie (CA-SFM) [12]. Pseudomonas and Acinetobacter were resistants if Imipenem inhibition diameter was <17 mm and

susceptibles if the diameter was ≥20mm for Pseudomonas and ≥22mm for Acinetobacter. Enterobacteria were considered as susceptibles if ertapenem inhibition diameter was ≥25mm and resistants if the diameter was < 22mm.

3. RESULTS

In our study, 306 bacterial strains were isolated at Sylvanus Olympio Teaching Hospital, 77 at Campus Teaching Hospital, and 520 at INH. Strains resistant to third-generation cephalosporins were isolated, it was about 19.28% (n=59); 14.28% (n=11); and 18.07% (n=94) respectively for Sylvanus Olympio Teaching Hospital, Campus Teaching Hospital, and INH (Table 1). The proportion of bacteria resistant to carbapenems was 7.19% (n=22) for Sylvanus Olympio, 2.59% (n=2) for Campus, and 0.77% (n=4) for INH, representing a total of 28 strains. Among these strains, more than half representing 57.14% (n=16) were isolated in hospitalized patients. Most of the strains, 64.29% (n=18) were isolated from urines, 32.14% from pus (n=9), and 3.57% from CSF (n=1).

At Sylvanus Olympio Teaching Hospital and INH, all the strains resistant to imipenem were strains of *A. baumannii*; at Campus, it was one strain of *A. baumannii* and one strain of *P. aeruginosa*. The strains resistant to ertapenem were exclusively represented by *Enterobacter cloacae* at INH (2), and at Sylvanus Olympio Teaching Hospital it was seven (7) strains of *E. cloacae* and one (1) strain of *Escherichia coli*. No information about patients' recent trips or history of hospitalization was mentioned.

Strains producing extended spectrum beta lactamases were isolated during this period. We noticed 19.28% (n=59) at Sylvanus Olympio, 14.28% (n=11) at Campus and 18.07% (n=94) at INH. All strains resistant to carbapenems were susceptible to colistin except two strains of *E. cloacae* isolated at Sylvanus Olympio and one strain of *P. aeruginosa* at Campus. Various resistances associated were noticed in particular to ciprofloxacin and to aminoglycosides (gentamicin, amikacin, tobramicin) Indeed, most of these strains were ciprofloxacin (n=26) and gentamicin (n=25) resistant (Table 2).

4. DISCUSSION

It is the first study carried out on strains' susceptibility to carbapenems in Togo. The prevalence of resistance to carbapenems varies according to the level of importance of each facility. Indeed, Sylvanus Olympio Teaching Hospital is the reference center in Togo, followed by Campus Teaching Hospital in terms of hospitalization and follow-up of patients of the public sector; that justifies the fact that the prevalence is more significant. In fact, the strains resistant to carbapenems are often found in hospitalized patients in intensive care units or in people with history of multiple hospitalizations due to strains' selection under the pressure of different antibiotic treatments [13]. More than half of the strains resistant to carbapenems (57.41%) were isolated in hospitalized patients in our study, what confirms this fact. Regarding INH which mission is to do bio-medical analyses, the low prevalence noticed is understandable.

Table 1. Distribution of bacteria resistant to carbapenems in the three laboratories

	K. pneumoniae	*E. cloacae*	*E. coli*	*A. baumannii*	*P. aeruginosa*	Total
CHU Sylvanus Olympio	1	7	1	13	0	22
CHU Campus	0	0	0	1	1	2
INH	0	2	0	2	0	4
Total	1	9	1	16	1	**28**

Table 2. Proportion of associated resistance to quinolones, aminoglycosides and colistin in each type of bacteria

	Ciprofloxacin	Gentamicin	Tobramycin	Amikacin	Colistin
A. baumannii	15 (93,75%)	16 (100%)	0	8 (50%)	0
P. aeruginosa	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)
E. cloacae	8 (88,88%)	6 (75%%)	6 (75%)	1 (11,11%)	2 (22,22%)
E. coli	1 (100%)	1 (100%)	1 (100%)	0	0
K. pneumoniae	1 (100%)	1 (100%)	1 (100%)	0	0
Total	26	25	9	10	3

Furthermore, the presence of strains resistant to carbapenems within INH could let think of community strains but it should be recalled that INH collects also samples from private clinics of the city, what explains the high number of samples.

Data on the history of patients' hospitalization and trips could not be collected. These information are necessary especially in terms of epidemiology of the antibiotic resistance. This aspect thus needs improvement.

Enterobacteria resistant to carbapenems were dominated by *E. cloacae* (7 at Sylvanus Olympio and 2 at INH); only one strain of *K. pneumoniae* as well as one of *E. coli* were described. Indeed these three bacteria are the most described among those carrying genes encoding a carbapenemase [14]. In Canada, the report of a surveillance of enterobacteria resistant to carbapenems (ERC) in 2014 found the same bacteria with higher rates ; their surveillance was based on 33 hospitals [15]. In the north of our country, in Burkina Faso, it was described a plasmid carrying $bla_{OXA-181}$, a gene encoding a carbapenemase within an *E. coli* [9]. In fact, that country for not having a port, maintains a business relationship in which goods are sent from our port to their country. The plasmid-mediated resistance spreading quickly enough, it is necessary to reinforce the epidemiological surveillance in order to avoid any possible outbreak.

Apart from the ERCs, some non-fermentative bacteria such as *P. aeruginosa* and *A. baumannii* are also incriminated as carrying resistance to carbapenems. These bacteria are generally signs of infections associated with care because these are found in hospital environment [5,16]. Thus it is not surprising that these bacteria are mostly found in the two hospitals in the study. In Africa, strains of *A. baumannii* were described as carrying genes of carbapenemases in clinics in Ethiopia and in Algeria [5,7], and in the environment in Senegal [11]. Strains of *P. aeruginosa* which produce carbapenemase were also described in Nigeria [6]. It is essential to reinforce hygiene practices within our hospitals in order to avoid the spread of these resistant strains.

The bacteria resistant to carbapenems are most often multi-resistant. In our study, most of these strains were resistant to ciprofloxacin and gentamicin so quinolons and aminoglycosides options of threating these infections are down. To treat infections caused by these strains, colistin will be the antibiotic of last resort. However, in our study, 2 strains of *E. cloacae* and one of *P. aeruginosa* were resistant to colistin. To our knowledge, this antibiotic is not yet used in hospitals in our city. Thus, further investigations should be conducted to establish the acquisition mechanisms of this resistance.

5. CONCLUSION

This work has highlighted resistance of bacteria to carbapenems in the city of Lome through its three reference centers in terms of medical bacteriology. Awareness about proper use of antibiotics associated with epidemiological surveillance are essential in order to avoid spread of the resistance to carbapenems. Furthermore, molecular studies should be done on these bacteria in order to identify the genes they carry.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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