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PREVALENCE AND ANTIBIOTIC RESISTANCE PROFILE OF EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING UROPATHOGENIC ENTEROBACTERIACEAE ISOLATED AT THE BACTERIOLOGY-VIROLOGY LABORATORY OF CHNU DE FANN, DAKAR

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ABSTRACT: *Introduction: Urinary tract infections caused by Enterobacteriaceae producing extended- spectrum β-lactamases represent a growing infectious risk, and in many cases may even lead to therapeutic impasses due to their multi-resistance to antibiotics. The aim of this study was to determine the antibiotic susceptibility profile of extended-spectrum betalactamase-secreting uropathogenic enterobacteriaceae isolated at the CHNU de Fann, Dakar .Material and Methods: This was a retrospective study lasting six months (from January 1 to June 30, 2018) concerning all uropathogenic E-BLSE strains isolated at the Bacteriology-Virology laboratory of the CHNU de Fann (Dakar). Results: This study revealed a high prevalence of E-BLSE isolation (41.8%), particularly in outpatients (65.67%). The most represented age group was between 60 and 80 years, with a percentage of 48.11%. E. coli was the most isolated germ (51.49%), followed by Klebsiella pneumoniae (26.87%). A study of the susceptibility profile of EBLSE to other antibiotic molecules revealed high levels of resistance, reaching 100% for sulfamethoxazole trimethoprim and fosfomycin, and 91.3% for fluoroquinolones. For aminoglycosides, high co-resistance was observed with gentamicin (85.7%), while it was low with amikacin (3.84%). Our results also showed 100% sensitivity to imipenem. Conclusion: The emergence of extended-spectrum ß-lactamase-producing urinary tract infections is a major public health problem. Faced with this alarming and worrying situation, and in order to limit the emergence of healthcare-associated infections, it has become imperative to improve hospital hygiene.*

KEYWORDS: Urinary tract infections, Enterobacteria, ESBL, CHNU de Fann.

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INTRODUCTION

Throughout the world, urinary tract infections (UTIs) are one of the main reasons for consultations, microbiological investigations and the intensive use of antibiotics, with the latter having consequences in terms of healthcare costs and the selection of multi-resistant strains in both hospital and community settings [**1**]. Enterobacterial resistance has been strongly reinforced by the acquisition of genes encoding extended-spectrum beta-lactamases (ESBLs). These enzymes (*TEM, SHV, CTX-M* and derivatives) confer resistance to all beta- lactam antibiotics except cephamycins and carbapenems, in addition to associated resistance to other families of antibiotics [**2**].

The mainly plasmid transmission of ESBL-encoding genes is responsible for their rapid dissemination, and thus for the increasing prevalence of ESBL-producing bacteria worldwide [**3**]. In our country, although controlling the spread of these multi-resistant bacteria is a priority, there is little up-to-date data to define the extent of this phenomenon.

It is in this context that we have undertaken this work, the general aim of which is to determine the antibiotic susceptibility profile of uropathogenic enterobacteria secreting extended-spectrum betalactamases. The following specific objectives guide the study, which are:

- To determine the prevalence of EBLSE in urinary tract infections;
- To determine the bacterial etiologies of UTIs;
- To describe the epidemiological characteristics of UTIs; and
- To determine the sensitivity profile of isolated EBLSE to other classes of antibiotics tested.

MATERIALS AND METHODS

This is a retrospective descriptive study from January 1, 2018 to June 30, 2018, conducted at the Bacteriology-Virology Laboratory (LBV) of the Centre Hospitalier National Universitaire de Fann (Dakar). Data were collected from laboratory registers and antibiogram reading sheets. They were entered and analyzed using Excel software, version 2013. Data collected included

- For each patient: gender, age, hospitalization status, department of origin
- For each bacterial strain: bacterial species identified and antibiogram results.

The technique used for antibiotic susceptibility testing was agar diffusion or Kirby-Bauer. Antibiotic-impregnated discs are applied to the agar using a sterile dispenser or forceps. Antibiotic disks are selected according to the recommendations of the French Microbiology Society's Antibiogram Committee (CA-SFM Year 2017).

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RESULTS

During the study period, 70 out of 126 urine samples came from male patients (55.55%), with a sex ratio of 1.25 (**Table I**).

Table I: Distribution of Patients by Sex

Gender	Workforce	%
Men	70	55.55
Woman	56	44.45
Total	126	100

Urine samples were obtained from patients with an average age of 51 years, ranging from 0 to 90 years. The most represented age group was 60 to 80 (**Table II)**.

Table II: Patient Distribution by Age Group

Age range (years)	Workforce	Percentage (%)
< 20	10	9,43
[20-40]	23	21,70
[40-60]	13	12,26
[60-80]	51	48,11
≥ 80	09	8,50

The distribution of ESBL-producing strains by patient origin showed that 44 (32.83%) came from inpatients, compared with 88 (65.67%) from outpatients (**Figure 1**).

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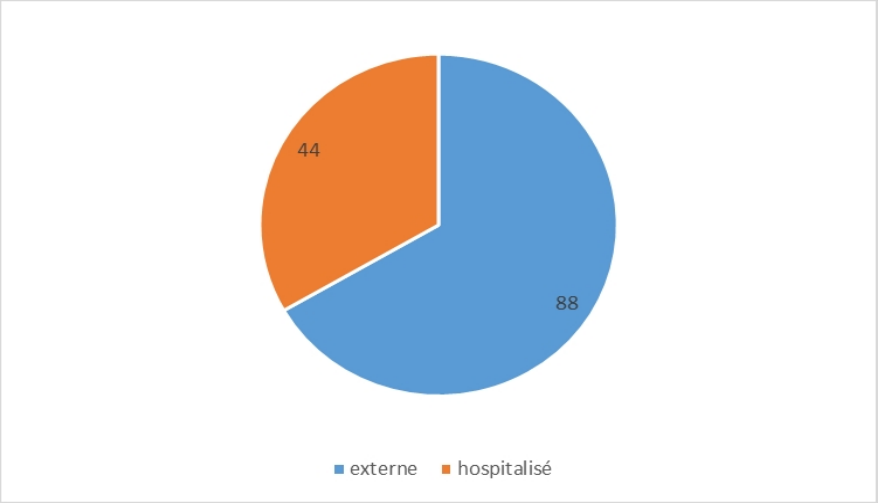

Figure 1: Distribution of patients by status

Of the 2081 urine samples collected, 408 were positive, representing a positivity rate of 19.6%. Among the 408 positive samples, 320 strains of Enterobacteriaceae were isolated, including 134 secretors of extended-spectrum betalactamase, i.e. 41.8%. Of the 134 ESBL-producing Enterobacteriaceae strains isolated from urine, *Escherichia coli* ranked first with 51.49% of strains, followed by *Klebsiella pneumoniae* (26.87%) and *Enterobacter spp* (13.43%) (**Table III**).

Table III: Distribution of species isolated

Species	**Workforce**	**Percentage (%)**
Escherichia coli	69	51,49
Klebsiella pneumoniae	36	26 ,87
Enterobacter spp.	18	13 ,43
Citrobacter spp.	7	5,22
Klebsiella oxytoca	3	2,25
Proteus mirabilis	1	0,74
Total	**134**	**100**

For ESBL+ *Escherichia coli* strains, the highest levels of resistance were observed with fosfomycin (100%), nalidixic acid (94.2%) and ciprofloxacin (91.3%) (**Figure 2).**

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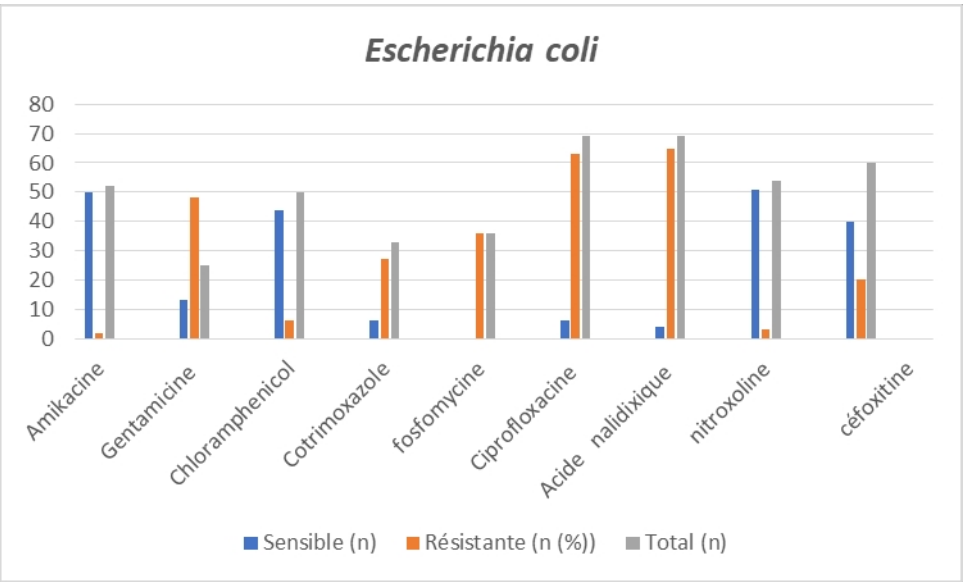

Figure 2: *Escherichia coli* resistance profile to other antibiotic molecules tested

Klebsiella pneumoniae ESBL+ strains were all susceptible to amikacin. We achieved 100% resistance to fosfomycin and 90.4% resistance to cotrimoxazole. Quinolones were 50% sensitive to ciprofloxacin and 65% to nalidixic acid (Figure 3).

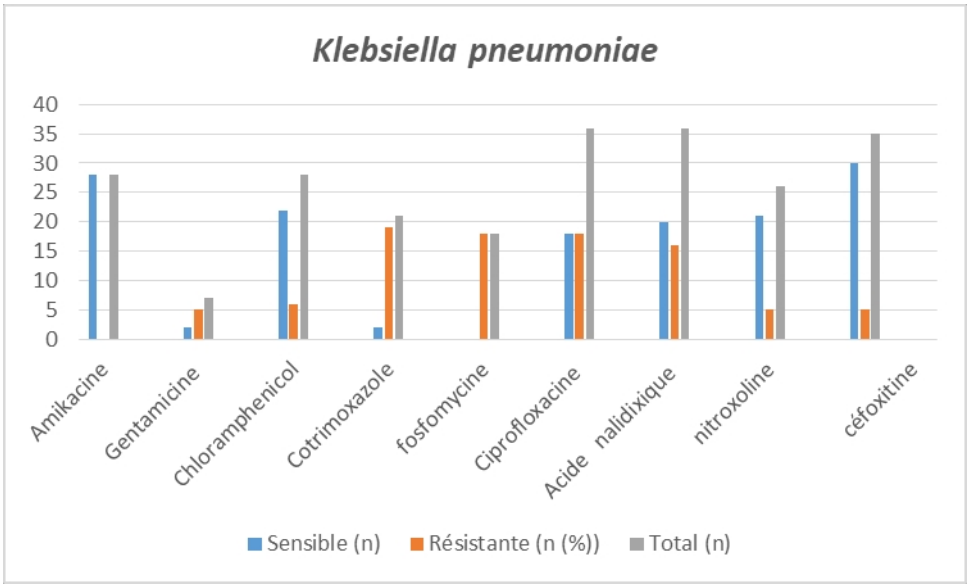

Figure 3: Susceptibility profile of isolated *Klebsiella pneumoniae* to the main antibiotics

Enterobacter spp. ESBL+ strains were all susceptible t o amikacin and all resistant to fosfomycin. Gentamicin resistance was 85.7% and ciprofloxacin 66.6% (Figure 4).

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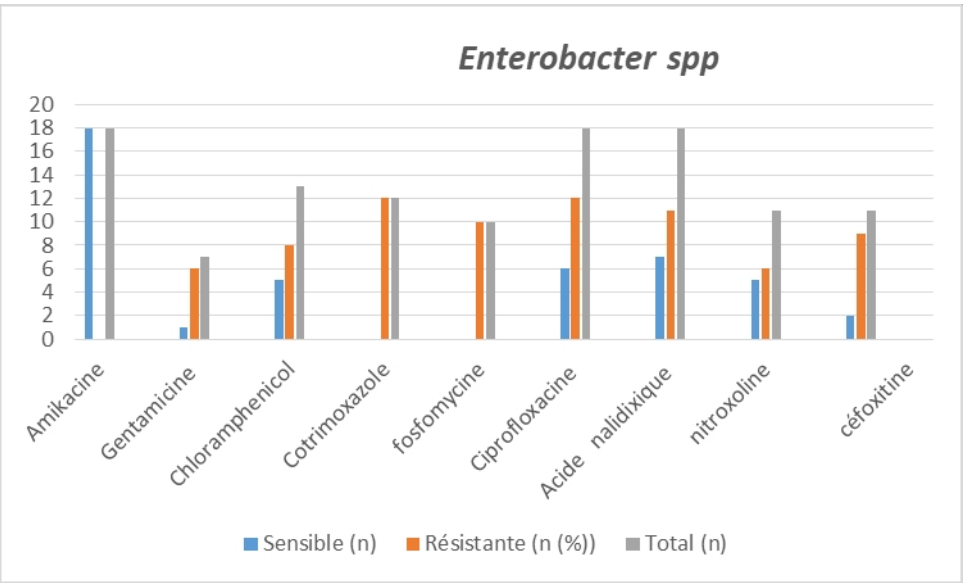

Figure 4: Susceptibility profile of isolated *Enterobacter spp* to the main antibiotics tested

DISCUSSION

Throughout the world, urinary tract infections (UTIs) are one of the main reasons for consultations, microbiological investigations and the intensive use of antibiotics, with the latter having consequences in terms of healthcare costs and the selection of multi-resistant strains in both hospital and community settings [**1]**. Since their first discovery in 1983, extended-spectrum beta-lactamase-producing Enterobacteriaceae (E-BLSE) have been widely distributed throughout the world, with isolation frequencies varying from one hospital structure to another, and even from one department to another within the same hospital institution. The involvement of E-BLSEs in both community-acquired and healthcare-associated urinary tract infections is a real public health problem **[4].** Knowledge of the epidemiological profile of E-BLSEs, as well as their current level of antibiotic resistance, is needed to adapt the antibiotic therapy protocol for urinary tract infections to epidemiological data. In our study, the incidence of E-BLSE was more marked in males, with a sex ratio of 1.25. Male predominance has been reported in various studies [**5 - 6]**.

The distribution of ESBL-producing strains according to patient origin showed that the majority came from outpatients. For hospitalized patients, most of the ESBL-producing Enterobacteriaceae strains isolated came from the infectious diseases and neurology departments.

Our results revealed a worrying trend in the frequency of isolation of uropathogenic E-ESBs. Indeed, this frequency reached 41.8% of isolated Enterobacteriaceae. This prevalence is well above those found in some studies, in particular the one carried out in Rabat in 2013 (18%) [**5**], and higher than those found in other studies published to date, in particular the one carried out at Marrakech University Hospital in 2017 (10.86%), in France in 2012 (13.6%) [**7,6**], in Belgium (6.6%), and the one carried out in Japan in 2011 (6.4%) [**8,9**]. This prevalence is lower than that reported in Côte d'Ivoire (58.8%) and comparable to that in Algeria (37.1%) [**11,10**].

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Geographical differences reflect differences in the use of antibiotics, particularly broad-spectrum antibiotics for infection control, which vary from country to country and even from region to region [**12**].

According to the results of our study, almost 80% of EBLSEs detected during the study were *K. pneumoniae* and *E. coli* strains. This is in line with the results of several studies which have shown that these two species are the most frequently involved i n EBLSE production [**13,14**]. A study of EBLSE susceptibility to other antibiotic molecules revealed high levels of resistance, reaching 100% for sulfamethoxazole trimethoprim and fosfomycin, and 91.3% for fluoroquinolones. These levels of resistance are all the more worrying as they lead to a reduction in the choice of antibiotic molecules for the adequate management of ITU. This situation is the consequence of selection pressure due to irrational prescribing and the abusive use of broad-spectrum antibiotics in both hospital and community settings (over-the-counter prescriptions, self-medication, free samples, etc.), not to mention the impact of a poorly controlled food supply, where more and more antibiotics are used in agriculture and livestock farming.

We also noted 100% sensitivity to Imipenem. These results are in line with those reported in previous studies carried out at Marrakech University Hospital, Rabat University Hospital and in a 2016 study in Qatar [**1**].

With regard to aminoglycosides, high co-resistance was noted with gentamicin (85.7%), but low co-resistance with amikacin (3.84%). These results are comparable to those obtained in Rabat in 2013 [**5]**, with 76% resistance to gentamicin and 12% to amikacin. These prevalences are also comparable to those reported in Algeria in 2015 (90

% and 15% respectively) [**10**].

Even higher rates of resistance to amikacin, up to 54%, have been reported in several studies carried out in Morocco, Algeria, Tunisia and France [**15, 10, 5, 6, 16**]. These high rates of resistance in enterobacterial strains currently justify amikacin as an effective molecule in the aminoglycoside family for the treatment of urinary tract infections caused by multi-resistant bacteria, particularly those producing extended-spectrum betalactamases.

CONCLUSION

Our results, in line with the literature, showed that E-BLSEs are becoming increasingly important among multi-resistant bacteria, due to their high level of co-resistance to antibiotics, in both hospital and community settings. The emergence of these multi-resistant strains is now an established fact in Senegal and throughout the world. Faced with this alarming and worrying situation, and given the potential risks (therapeutic impasse, increased morbidity and mortality, additional economic costs and emergence of highly resistant bacteria in hospital wards), and in order to limit the emergence of healthcare-associated infections (HAIs), it has become imperative to improve hospital hygiene.

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