

# Current State of Resistance to Antibiotics in Enterobacterial Isolates at the National Hospital Center of Nouakchott-Mauritania

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**Received date:** June 15, 2022; **Accepted date:** June 28, 2022; **Published date:** July 22, 2022

**Citation:** Mohamed Lemine Ould Salem, Fatimettou Abdellahi, Mohamed Ahmed MM Sidiya, Sidi Mohamed Ghaber, Sidi El Wafi Ould Baba. (2022) Current state of resistance to antibiotics in enterobacteriales isolates at the National Hospital Center of Nouakchott-Mauritania. *Clinical Research and Clinical Trials*. 6(3); DOI: [10.31579/2693-4779/105](https://doi.org/10.31579/2693-4779/105)

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## Abstract

**Introduction:** Enterobacteriaceae are Gram-negative bacteria, facultative aero-anaerobes found everywhere. They include a very large number of genera and species. Their abundance in the intestine, their mobility, the rapidity of their multiplication, the frequent acquisition of mechanisms of resistance to antibiotics.

**Objective:** The objective of this study was to investigate the antibiotic susceptibility of Enterobacteriaceae strains isolated from various infectious sites in outpatients and hospitalized patients.

**Material and method:** This is a prospective study carried out in the central laboratory of the Nouakchott Hospital Center and involving 300 strains of enterobacteriaceae isolated from various samples taken from different departments or external consultations. The study was conducted from November 1, 2020 to July 30, 2021

**Results:** In our study *E. coli* represents (66.6%), followed by *K. pneumoniae* (27%), *E. cloacae* (2.3%). The study of the resistance of these strains to antibiotics revealed resistance rate: Amoxicicillin (93%), Amoxicicillin-clavulanic acid (77.6%), Gentamicin (16%) and (9.4%) Fosfomycin.

**Conclusion:** The significant increase in the frequency of enterobacteriaceae has become worrying in both hospital and community settings. However, implementation requires collective awareness through in-depth training of healthcare teams. Currently, the reference treatment for infections due to multiresistant enterobacteria is essentially based on the use of carbapenems. It is nevertheless fundamental to obey a rational prescription of these antibiotics to limit the emergence of carbapenemase-producing strains. Controlling the spread of enterobacteriaceae requires strict compliance with simple hospital hygiene measures.

**Keywords:** enterobacteriaceae; *E. coli*; antibiogram; nouakchott; Mauritania

## I-Introduction

Enterobacteriaceae are Gram-negative bacteria, aero-facultative anaerobes found everywhere in soil, in water and especially in the intestine of humans and animals. They include a very large number of genera and species. Their abundance in the intestine, their mobility, the speed of their multiplication, the frequent acquisition of antibiotic resistance mechanisms explain why they are the bacteria most involved in human infectious pathology, especially in the hospital environment [1].

The majority of urinary tract infections have a bacterial origin, and the most frequently encountered pathogens are enterobacteriaceae [2]. *Escherichia coli* is the most incriminated germ; it is responsible in 85% of cases, *Klebsiella pneumoniae* comes in second position with 10% of cases, *Proteus mirabilis* comes in third position with 4% of cases, other Gram-negative bacilli (*Pseudomonas aeruginosa*) or Gram-positive Cocci (*Staphylococcus saprophyticus*, *Staphylococcus aureus*, *Enterococcus sp*) may less often be the cause [3]. Literature data show that *Escherichia coli*

is the predominant bacterium in UTI [4]. About 150 million cases of urinary tract infections per year in the world, they constitute as such a public health concern [5]. Enterobacteriaceae are implicated in pneumonia, mainly in a nosocomial context of ventilator-acquired pneumonia and aspiration pneumonia [6]. Escherichia coli was the leading cause of bacteremia in France, ahead of Staphylococcus aureus [7] The Global Antimicrobial Resistance Surveillance System (known as GLASS) reveals that antibiotic resistance is a widespread problem affecting 500,000 people with suspected bacterial infections in 22 countries. It is also reported that the most frequently reported resistant bacteria include Escherichia coli; Klebsiella pneumoniae; Salmonella spp [8]. In Europe, the European Center for Disease Control (ECDC) has estimated the number of deaths resulting from antibiotic resistance at 25,000 per year [9]. Around 700,000 people worldwide die each year from drug-resistant infections and, if left unchecked, these infections are estimated to cause 10 million people to die annually by 2050. The situation is alarming in countries with limited resources where infectious diseases, poverty and malnutrition are endemic. The emergence of antibiotic resistance is a complex process often involving host, pathogen and environmental factors. In recent years, an increase in the incidence of resistance to antibiotics of germs responsible for urinary tract infections has been observed. The outbreak of Extended Spectrum Beta-lactamase (ESBL)-secreting Enterobacteriaceae is increasingly prevalent [10]. In West Africa, as throughout the world, antibiotic resistance mainly concerns bacteria producing ESBL [11]. The causes of the emergence and dissemination of this resistance are multiple, but the excessive and/or inappropriate use of these antibiotics is, without a doubt, the main reason for this evolution. This evolution of resistance is unpredictable and should prompt regular monitoring of the sensitivity of the predominant bacterial species to the various antibiotics used [12]. It is in this context that our study was carried out with the aim of:

- Epidemiological study of the prevalence of enterobacteriaceae isolated from various infectious sites in out patients and hospitalized patients.
- Prevalence of resistance of Enterobacteriaceae to antibiotics.

## II. Material and methods

**II.1. Place of study:** Our study was conducted in the central laboratory of the National Hospital Center of Nouakchott (CHN).

### II.2. Study period:

Our study was spread over a period of nine months from November 1, 2020 to July 30, 2021.

### II.3. Type of study:

It's about an observational descriptive study. Data collection was done using a survey form.

### II.4. Nature of samples studied:

The strains were isolated from different samples: Urine (ECBU), Pus, blood cultures, genital samples

### II.5. Inclusion criteria:

The study covers all bacteriological samples for diagnostic purposes received at the Central Laboratory of the National Hospital of Nouakchott (CHN) from hospitalized patients or outpatients.

### II.6. Exclusion criteria:

Duplicate strains: strains isolated from the same patient, at the same anatomical site.

### II.7. Services originating from strains:

The samples were sent by the various departments of the hospital and the consultations on an outpatient basis.

### II.8. Identification of bacteria:

The identification was made either by the PLC system (Biomérieux®) or automatically on the Vitek-2 automaton (Biomérieux®)

### II.9. Antibiotic sensitivity study:

The antibiogram is carried out by the agar diffusion method (disc method) or automatic method on Vitek-2 (Biomérieux®), according to the press release from the antibiogram committee of the French microbiology society (EUCAST CA-SFM) [13].

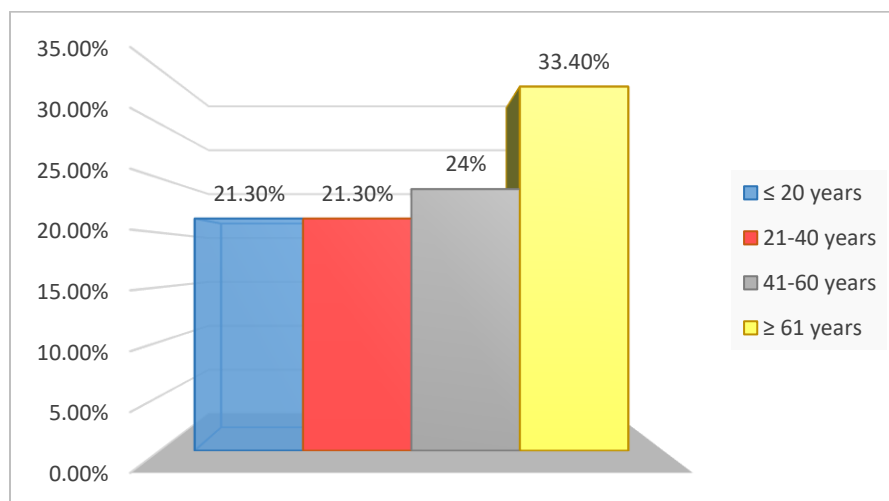
## III-Results

### III-1 Epidemiological Data

#### III-1-1 Age

The average age was 41.8 years with extremes of 1 and 83 years.

Figure 1 shows the distribution of patients by age group.



**Figure1:** distribution of patients according to age group

### III-1-2 Sex

The sex ratio was 0.34 in favor of women

Figure 2 shows the distribution of patients by sex

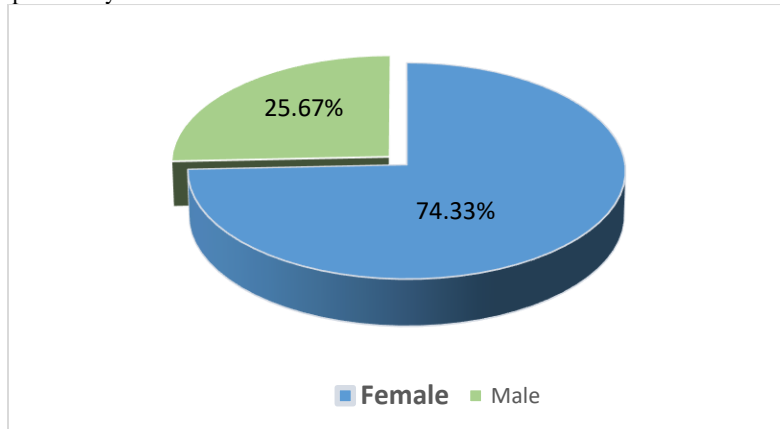


Figure 2: Distribution of patients by sex

### III-1-3 Origin of provenance

Figure 3 shows the distribution of patients according to their origin of provenance

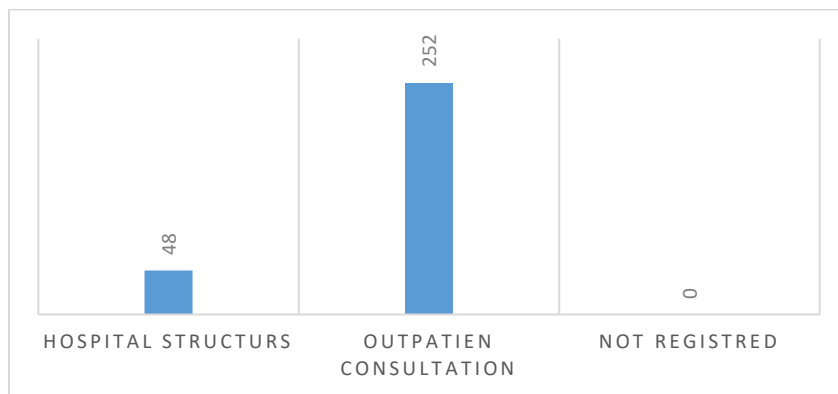


Figure 3: the distribution of patients according to their origin of provenance

### III-1-4 Patient hospitalization services

Figure 4 shows the distribution of patients according to reception services

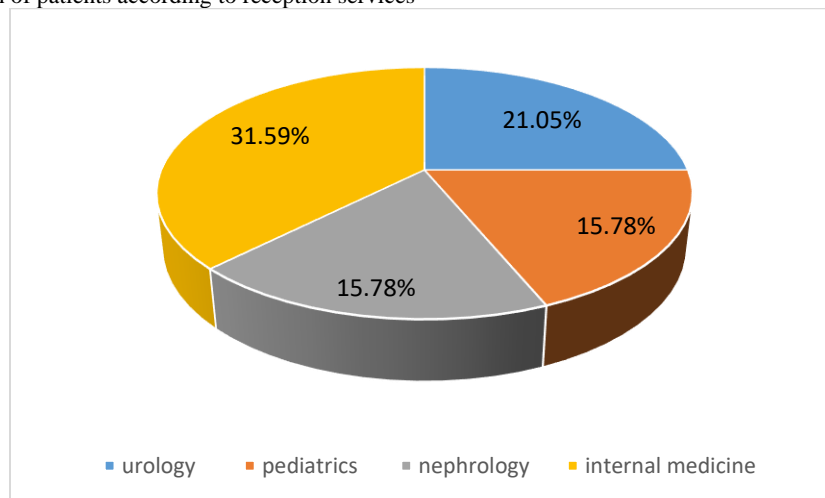


Figure 4: distribution of patients by department

### III-1-5 Types of samples

Table I shows the distribution of patients according to the type of sample

Type of sample	Number (N)	Percentage (%)
ECBU	292	97,33 %
Pus	6	2 %
blood culture	1	0,33 %
PV	1	0,33 %
<b>Total</b>	<b>300</b>	<b>100 %</b>

**Table I:** distribution of patients according to the type of sample

### III-1-6 Risk factors:

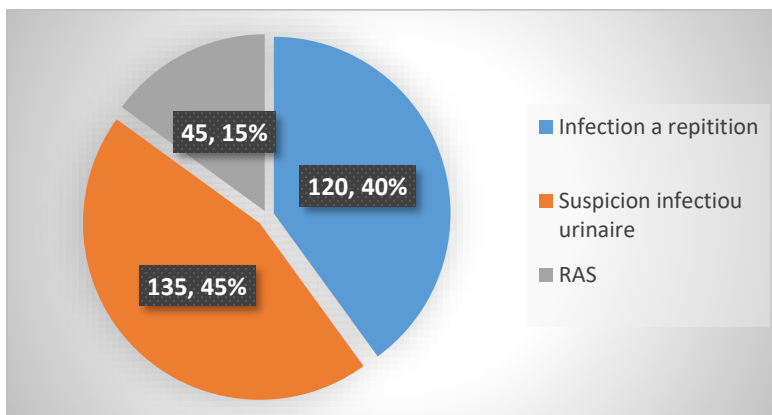
Table II shows the distribution of patients according to risk factors

Risk factors	Number	Percentages (%)
Urinary catheter	253	84,3 %
Diabetes	14	4,7 %
IRC	9	3 %
Urinary tract surgery	8	2,7 %
Repeated hospitalization	5	1,7 %
Renal lithiasis	4	1,3 %
Pregnancy	4	1,4 %
Urinary retention	2	0,6 %
Cancer	1	0,3 %
Total	300	100 %

**Table II:** Distribution of patients according to risk factors

### III-1-7 Breakdown of patients according to ECBU indication

Figure 5 shows the distribution of ECBU according to indication



**Figure 5:** shows the distribution of ECBU according to indication

### III-2 Bacteriological data

#### III-2-1 Overall distribution of enterobacteriaceae isolated according to bacterial species

Table III shows the distribution of Enterobacteriaceae according to bacterial species

Entérobactériaceae	Number	Percentage
Escherichia. coli	200	66,6 %
Klebsiella pneumoniae	81	27%
Enterobacter cloacae	7	2,3%
Proteus mirabilis	5	1,7%
Salmonella	2	0,7%
Proteus penneri	1	0,3%
Enterobacter aerogenes	1	0,3%
Serratia marcescens	1	0,3%
Shigella sonnei	1	0,3%
Enterobacter spp	1	0,3%
Total	<b>300</b>	<b>100</b>

**Table III:** distribution of enterobacteriaceae according to bacterial species

#### III-2-2 The distribution of bacterial species according to sex

Table IV shows the distribution of bacterial species according to sex

Species	Male	Female	Total
<i>E.coli</i>	43	157	200
<i>Klebsiella pneumoniae</i>	26	55	81
<i>Enterobacter cloacae</i>	3	4	7
<i>Proteus mirabilis</i>	2	3	5
<i>Salmonella</i>	1	1	2
<i>Klebsiella aerogenes</i>	0	1	1
<i>Enterobacter spp</i>	1	0	1
<i>Proteus penneri</i>	0	1	1
<i>Serratia marcescens</i>	1	0	1
<i>Shigella sonnei</i>	0	1	1
<b>Total</b>	<b>77</b>	<b>223</b>	<b>300</b>

**Table IV:** Distribution of bacterial species according to sex

#### III-2-3 The distribution of bacterial species according to age

Table V shows the distribution of bacterial species according to age

Species	≤ 20 years	21-40 years	41-60 years	≥ 61 years	Total
E.coli	40	48	49	63	200
Klebsiella pneumonia	20	11	18	32	81
Enterobacter cloacae	1	2	2	2	7
Proteus mirabilis	2	2	1	0	5
Salmonella	0	0	1	1	2
Klebsiella aerogenes	0	0	1	0	1
Enterobacter spp	0	0	0	1	1
Proteus penneri	1	0	0	0	1
Serratia marcescens	0	1	0	0	1
Shigella sonnei	0	0	0	1	1
Total	<b>64</b>	<b>64</b>	<b>72</b>	<b>100</b>	<b>300</b>

**Table V:** Distribution of bacterial species according to age

### III-2-4 Beta-lactam resistance profile of E. coli

Table VI shows the resistance of E. coli to beta-lactams

Antibiotics	Resistance Percentage
Amoxicillin	93 %
Ampicillin	93 %
Amoxicillin-clavulanic acid	77,6 %
Ticarcillin	82 %
Piperacillin	82 %
Temocillin	9,6 %
Mecillinam	7,6 %
Cefalotin	58,7 %
Ceftriaxone	18 %
Cefotaxim	18 %
Cefoxitin	17 %
Cefixime	18 %

Ceftazidim	18 %
Cefuroxime	39 %
Ertapenem	8 %
Imipenem	0,8 %

**Table VI:** Beta-lactam resistance profile of *E. coli*

### III-2-5 Resistance of *E. coli* to aminoglycosides

Table VII shows the resistance of *E. coli* to aminoglycosides

Antibiotics	Resistance Percentage
Gentamicin	16 %
Amikacin	4,7 %
Tobramycin	5 %
Netimmycin	3,7 %

**Table VII:** Resistance of *E. coli* to aminoglycosides

### III-2-5 Resistance of *E. coli* to quinolones:

Table VIII shows the resistance of *E. coli* to quinolones

Antibiotics	Resistance percentage
Nalidixic acid	34,4 %
Ofloxacin	31 ,03 %
Ciprofloxacin	19,4 %
pipemidic acid	34 ,4 %
Pefloxacin	31,03 %

**Table VIII:** Resistance rate of *E. coli* to Quinolones

### III-2-5 Resistance of *E. Coli* to other antibiotics:

Table IX shows resistance to other antibiotics

Antibiotics	Resistance Percentage
Fosfomycin	9,4 %
Cotrimoxazole	68,42 %
Colistin	0 %
Chloramphenicol	24,4 %
Nitrofurantoin	16,17 %

**Table IX:** Resistance rate of *E. coli* to other antibiotics

### III-2-6 Resistance of *Klebsiella pneumoniae* to beta-lactams:

Table X shows the resistance of *Klebsiella pneumoniae* to beta-lactams

Antibiotiques	Pourcentage de résistance
Amoxicilline	100 % RN
Ampicilline	100 % RN
Amoxicilline-acide clavulanique	69 %
Ticarilline	100 % RN
Pipéracilline	100 % RN
Témocilline	22,22 %
Mecillinam	4%
Céfalotine	54 %
Ceftriaxone	33,33%
Cefotaxime	33,33%
Céfoxitine	30,3 %
Cefixime	33,33 %
Ceftazidime	33,33%
Céfuroxime	40 %
Ertapénème	2 %
Imipénème	0 %

**Table X:** rate of resistance of *Klebsiella pneumonia* to beta-lactams

### III-2-7 Resistance of *Klebsiella pneumonia* to aminoglycosides, quinolones and other antibiotics:

Tables XI, XII and XIII show the resistance of *Klebsiella pneumonia* to aminoglycosides, quinolones and other antibiotics.

Antibiotics	Resistance Percentage
Gentamicin	16,4 %
Amikacin	4,6 %
Tobramycin	5,66 %
Netilmycin	4 %

**Table XI:** Resistance of *Klebsiella pneumoniae* to aminoglycosides

Antibiotiques	Resistance Percentage
Acide nalidixique	40,27 %
Ofloxacin	37 ,33 %



Ciprofloxacin	30,18 %
Acide pipemidique	40,27 %
Pefloxacin	37,33 %

**Table XII:** Resistance of *Klebsiella pneumoniae* to quinolones

Antibiotics	Resistance Percentage
Fosfomicin	70,58 %
Cotrimoxazole	100 %
Colistin	0 %
Phenicol (chloraphenicol)	28,57 %
Nitrofurantoin	39,53 %

**Table XIII:** Resistance of *Klebsiella pneumoniae* to other antibiotics**III-2-8 Resistance of *Enterobacter cloacae*, *Proteus mirabilis* to beta-lactams and aminoglycosides:**

	Enterobacter cloacae		Proteus mirabilis	
	Resistance Percentage		Resistance Percentage	
Amoxicillin		100%		60%
Amoxicillin-clavulanic acid		100%		80%
Ticarcillin		80%		50%
Piperacillin		80%		40%
Cefalotin		100%		75%
Cefixime		20%		0%

**Table XIV:** Resistance of *Enterobacter cloacae*, *Proteus mirabilis* to beta-lactams

	Enterobacter cloacae		Proteus mirabilis	
	Resistance Percentage		Resistance Percentage	
Gentamicin		28%		20%
Amikacin		33%		0%
Tobramycin		0%		0%
Netilmicin		0%		0%
Nalidixic acid		57%		33%
Ofloxacin		40%		25%

Ciprofloxacin		0%		0%
pipemidic acid		100%		0%

**Table XV:** Resistance of *Enterobacter cloacae* and *Proteus mirabilis* with aminoglycosides

### Resistance of other Enterobacteriaceae:

In our series we have 2 strains of salmonella which were resistant to amoxicillin, Ticarcillin, Piperacillin, no resistance to aminoglycosides or quinolones.

We have a single strain of *Proteus penneri* which was resistant, in addition to its natural resistance (to amoxicillin, C1G, cefuroxime) to Ticarcillin, amoxicillin+clavulanic acid, and to C2G while it was sensitive to C3G and all aminoglycosides and quinolones.

Our series contains a single strain of *Klebsiella aerogenes* that was resistant to C3G susceptible to aminoglycosides and quinolones.

For *Serratia marsescens* we have a single strain which was resistant to the betalactamines tested (except carbapenems) while it was sensitive to aminoglycosides and quinolones.

## IV-Discussion

### IV-1 Epidemiological data:

#### IV-1-1 Age:

In our study the average age was 41.8 years with extremes of 1 and 83 years. The most affected age was over 61 with a percentage of 33.4%.

These results could be explained by the fact that these people are more vulnerable to infections because of the fragility of their immune system.

In a study carried out in the bacteriology-virology department of the National Institute of Public Health (INSP) in Bamako, a high frequency of positive ECBU was found in elderly patients (age > 60 years) with 30.4% of case or 183 samples. The average age of this study was 46 years (for the 567 samples whose age was entered) with the extremes ranging from 1 to 96 years [14]. In 2017 a study by SABOR et al. showed that people over 60 were the most represented with a percentage of 25.37% [15]. In 2005 Zhanel et al in North America found a predominance of this same category in their studies with rates of 34.1% [16].

#### IV-1-2) Gender:

In our study, we found a female predominance giving a percentage of 74.3% with a sex ratio of 0.34. A study carried out by KALAMBRY in 2019 in Mali shows a female predominance with 54.2% of positive ECBU among women (326 out of 602 ECBU positives) and 43.0% in men (276 out of 602 ECBU positives) with a sex ratio of 1.18. This same observation has been made by other studies [17]. Another study conducted in Morocco by Lahlou Amine also showed a female predominance with a female/male sex ratio of 1.08 (hospitalized: 0.52 and consultants: 1.48) [18]. A study carried out at the bacteriology-virology department of the National Institute of Public Health (INSP) in Bamako, a female predominance was noted with a sex ratio F/H=1.18[14].

This female predominance is linked to anatomical factors.

#### IV-1-3) Hospitalization structure:

In our study 94 patients from urology and 47 patients from the internal medicine department and 46 patients from the nephrology department.

In the study carried out at the bacteriology-virology department of the National Institute of Public Health (INSP) in Bamako on a sample of 602 cases, 37 patients from the urology department and 3 internal medicine patients and 4 patients from the nephrology [14].

At the CHNU de Fann in Dakar in 2015, which objectified a predominance of the neurology department, i.e. 42%, followed by the infectious and tropical diseases department with 35.68% of cases [19].

This could be explained by the long hospital stay and the use of invasive devices (urinary catheter, etc.), urological procedures and contributing factors such as prostate hypertrophy.

### Breakdown by type of sample and place of origin:

The distribution of the species isolated according to the sampling sites reveals that ECBU are the most encountered, followed by suppuration from blood cultures and vaginal samples with rates of 97.33%, 2% and 0.33% and 0.33% respectively.

*E. coli* is by far the most frequently isolated germ, followed by *Klebsiella pneumoniae*. This is related to the pathophysiology of urinary tract infection which is generally ascending, and there is strong colonization of the perineum by enterobacteria of digestive origin, and in particular *Escherichia coli*. Added to this are specific uropathogenicity factors.

Thus, *Escherichia coli* has adhesins, capable of binding the bacterium to the urinary epithelium and preventing its elimination through bladder emptying. *Klebsiella* secrete a urease which alkalizes the urine, whose naturally acidic pH prevents the proliferation of germs [20].

### IV-2) Bacteriological data:

#### IV-2-1) Frequency of isolated species:

In our series *Escherichia coli* remains the most frequent species with an isolation rate of 66%, followed by *Klebsiella pneumoniae* 27.7%. This predominance is reported in several studies, but with frequencies varying between 46% and 60% for *Escherichia coli*, and between 9 and 28% for *Klebsiella pneumoniae* [2,21]. *Enterobacter cloacae* and *Proteus mirabilis* are less common with isolation rates of 2.3% and 1.7%. The same classification was reported by Nijssen et al but with lower rates of 2.2% and 2.9% respectively [22], while higher frequency rates were reported by Cherkaoui in 2014, 9% and 6% respectively [23]. The same observation is reported by Lagha in Algeria, but with rates of 4% and 9% respectively [2].

In the study carried out at the bacteriology-virology department of the National Institute of Public Health (INSP) in Bamako, *Escherichia coli* was the most isolated enterobacteriaceae (66.6%), probably because of its ability to adhere to cells, followed by *Klebsiella pneumoniae* (17.0%) [14], which is consistent with a study realized at the Hospital of Mali in 2019 [17]. In addition, SABOR in 2017 in DAKAR also found a predominance of these two species of enterobacteriaceae with a rate for *Escherichia coli* of 40.2% and 27.54% for *Klebsiella pneumoniae* [15].

Also, these species are distributed differently according to the sampling sites *Escherichia coli* is considered to be the leader of enterobacterial infections. *Escherichia coli* is the most isolated bacterial species in women with 157 against 43 for men among the 200 species of *Escherichia coli* isolated in our study and affects subjects whose age is over 60 years. This female predominance is explained previously on the basis of the fact that the risk of infections is 50 times more frequent in women, due to the proximity of the urinary meatus and the anus (short perineum) and the shortness of the urethra which is also wide and opens during sexual intercourse [6].

#### IV-2-2) Resistance to antibiotics:

During this study, we counted 10 different genera belonging to different families of the order Enterobacterales were tested against 29 molecules of antibiotics including 15 $\beta$ -lactams, 4 aminoglycosides, 5 quinolones, colistin, fosfomicin, chloramphenicol, Nitrofurantoin, and cotrimoxazole.

Enterobacteriaceae are classified into seven groups based on their natural resistance to  $\beta$ -lactams: Group 0 (*Salmonella*; *Proteus mirabilis*), Group 1 (*Escherichia coli*; *Shigella*spp), Group 2 (*Klebsiella*spp; *Citrobacter diversus*), Group 3 (*Enterobacter* spp; *Serratia* spp; *Providencia* spp; *Citrobacter freundii*; *Hafnia alveii*; *Morganella*), Group 4 (*Yersinia*), Group 5 (*Proteus penneri*; *Proteus vulgaris*), Group 6 (*Kluyvera*) [24].

Analysis of the resistance profile of *Escherichia coli* strains in our study shows an increase in resistance rates to  $\beta$ -lactams except carbapenems. Carbapenems and in particular imipenem are molecules of paramount importance which have sometimes become the only effective agents for the treatment of serious infections caused by enterobacteriaceae secreting an extended-spectrum  $\beta$ -lactams (ESBLE), the sensitivity of the latter to imipenem remains high according to several authors [25].

Low resistance rates were obtained for tobramycin 5%, gentamicin 16%, amikacin 4.7%, netilmicin 3.7%. Quinolone resistance has become a concern with a rate of 34.3% for nalidixic acid, 31.8% for ofloxacin, and 19.4% for ciprofloxacin.

While a high resistance rate was obtained for cotrimoxazole 68.42%.

In a study carried out in Bamako over 3 years, more than 72.6% of the group I enterobacteriaceae showed resistance to the combination amoxicillin + clavulanic acid [14]. Our results are similar to those of KALAMBRY, 2019 in Mali, which found 71.0% [17]. But they are lower than those of Kara Terki et al. In Algeria, which found 94.0% [26].

The multicenter study by Bouza et al. [27] reports a resistance rate of *Escherichia coli* of 55% vis-à-vis ampicillin.

A study carried out in the middle urology at the Henri-Mondor hospital, although old (unpublished data), shows that the rates of resistance evolved from 1998 to 2005, going from 65 to 80% for amoxicillin, five to approximately 15% for cefotaxime, 20 to approximately 35% for ciprofloxacin, ten to more than 20% for gentamicin.

A study in Morocco by Lahlou et al shows a very clear statistical relationship between the sensitivity to antibiotics that can be used orally for the treatment of cystitis and the history of antibiotic therapy is observed, especially when taking into account the type of antibiotic received: relationship between taking  $\beta$ -lactams and resistance to amoxicillin - clavulanic acid, the difference in sensitivity being more than 20% between history (41%) and no history (64%); relation between taking quinolone and resistance to ciprofloxacin, the difference in sensitivity being more than 20% between history (78%) and no history (97%) [18].

Other studies [28] go in the same direction and report that in the event of recent intake of quinolones, resistance to nalidixic acid and ciprofloxacin is increased (37% versus 9 to 13% and 22% versus 3 to 6%, respectively) as well as resistance to amoxicillin and amoxicillin + clavulanic acid when taking  $\beta$ -lactams (59% versus 36% and 59% versus 33%). History of recent urinary tract infection (<6 months), *Escherichia coli* resistance rates are higher for nalidixic acid (16 to 20% versus 3 to 10%) and cotrimoxazole (38 to 49% versus 22 to 29%) [28,29].

This acquired resistance would be the consequence of the selection pressure linked to the excessive consumption of these antibiotics. [30]. These high rates of resistance to amoxicillin justify that aminopenicillins are no longer currently recommended for the probabilistic treatment of urinary tract infections. The massive use of ciprofloxacin and norfloxacin

to treat urinary tract infections caused by enterobacteriaceae in community medicine explains the similar rates of resistance obtained for community (36%) and nosocomial (40%) strains. This can be essentially explained first by the massive use of fluoroquinolones to treat urinary tract infections in first intention without prior documentation because of their wide bacterial spectrum and their good urinary diffusion. Acquired resistance to quinolones is classically due to chromosomal mutations by specific modifications of the targets, type II (DNA gyrase) and IV topoisomerases, and its diffusion is limited. Resistance by decreasing the intracellular concentration of these antibiotics by membrane impermeability and/or overexpression of efflux systems is rarer [31]. The only known mechanisms of resistance to quinolones have long been chromosomal support, that is to say stable and not transferable.

In the Bamako study they obtained a very high frequency of resistance to 3rd generation cephalosporins, it varied from 34.9% to 66.1% [14]. These results are close to those obtained by Dembélé et al in Mali between 2016-2018 who found resistance of *Escherichia coli* to C3Gs which varied between 53% and 85% [14]. Furthermore, Moghim et al in 2018 in Iran [32] found resistance from *Escherichia coli* to Ceftazidime in 38.5% of cases and to Cefotaxime in 48.3%. a resistance rate of 71.6% to Cefalotin, 56.1% for Cefixime, 55.8% for Cefotaxime 45% for Ceftazidime [14]. These results are very similar to those obtained in 2018 by Mughim et al in Iran [32] who found 39.1% for Ceftazidime and 47.8% for Ceftriaxone of *Klebsiella pneumoniae*. A higher frequency was obtained in Algeria by Djahida et al. [12] with 80% resistance to Ceftazidime.

*Escherichia coli* is naturally sensitive to all aminopenicillins and cephalosporins but faced with the prevalence of ESBL-producing bacteria whose essential mechanism of acquired resistance to  $\beta$ -lactams is of an enzymatic nature by production of  $\beta$ -lactamases [33]. The study of the resistance of strains of *Klebsiella pneumoniae* reveals high resistance rates for amoxicillin/clavulanic acid (69%), acefalon (54%), cefuroxime (40%), ceftriaxone (33.33%), cefotaxime (33.33%), ceftazidime (33.33%). For aminoglycosides, the highest rate was observed for gentamicin (16.4%), followed by tobramycin (5.66%). With regard to quinolones, the resistance rates were as follows: 40.27% for nalidixic acid and 63.3% for ofloxacin and 30.18% for ciprofloxacin. No resistance was observed for imipenem and colistin with 100% of susceptible strains.

Then a study carried out in Bamako the rate of resistance to C3G varied between 58.2% and 21.4% in *Klebsiella pneumoniae* [14].

In our series, the resistance of *Klebsiella pneumoniae* to C3G varies between 33.5% and 50%. According to the 5th Demographic and Health Survey from Mali (EDSM V 2012-2013), 52.0% of the urban population and 63.0% of the rural population practiced self-medication [17]. Educating the population, banning the sale of antibiotics without a prescription and minimizing probabilistic antibiotic therapy in hospital wards could be solutions to limit antibiotic resistance.

Regarding quinolones, resistance rates in the INSP department in Bamako were 45.5% for ciprofloxacin and 55% for norfloxacin. On the other hand, nalidixic acid is less effective with 71.7% resistance [14]. These results are superior to those of recent studies conducted on the resistance of Enterobacteriaceae in Senegal by SABOR et al who found a resistance of 52.5% to Norfloxacin and 42.1% to Ciprofloxacin [15]. But lower than those found in Mali in 2012 by Minta et al, who found 70% resistance for Ciprofloxacin from *Escherichia coli* [34].

## V. Conclusion

Antibiotic resistance is one of the most serious threats to global health today. It is the cause of prolonged hospitalizations and leads to increased medical expenses and mortality. A better knowledge of the local bacterial ecology makes it possible to establish behaviors based on objective data

After the publication of its first report, in April 2014 on bacterial resistance, the WHO is alarmed by a “serious threat to public health” pointing to the ineffectiveness of antibiotics against certain bacteria.

This study, which falls within the framework of a survey on the state of bacterial resistance to antibiotics, has made it possible to highlight certain epidemiological characteristics.

During the study period, 300 strains of enterobacteriaceae were identified in the medical bacteriology laboratory of the CHN.

The rate of resistance to the usual antibiotics is high, this emergence of resistance would be linked to the importance of the prescription of an antibiotic

It is therefore important then

- ✓ To implement a global management of the use of antibiotics with the aim of reducing and rationalizing their consumption, very early detection of infections with multidrug-resistant germs
- ✓ Manage the risk factors for enterobacteriaceae infections.

Standard measures include hand washing with a hydroalcoholic solution, wearing gloves in the event of contact with biological fluid and wearing an overcoat in the event of contaminating care, regardless of the patient.

Our study is a prospective study which is related to all samples

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DOI: [10.31579/2693-4779/105](https://doi.org/10.31579/2693-4779/105)

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