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Original Article

Resistance Phenotype and Epidemiological Profile of Enterobacteriaceae Responsible for Urinary Tract Infections at the National Reference University Hospital Center in N'Djamena, Chad

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Abstract *- The geographical spread of highly resistant bacteria is a global public health problem. The aim of this study was to determine the resistance phenotypes and the epidemiological profile of Enterobacteriaceae responsible for urinary tract infections at the* National Reference University Hospital Center *(CHU-RN) in N'Djamena.*

This was a one-year cross-sectional study running from October 2021 to October 2022. Standard bacteriological techniques identified Enterobacteriaceae. The diffusion technique of antibiotic disks in agar medium was used to identify highly resistant Enterobacteriaceae, and that of double disk made it possible to detect Enterobacteriaceae producing ESBL. The data was collected via a face-to-face verbal interview with the patients based on the questionnaires on a survey sheet. Chi-square tests were calculated to compare qualitative variables, and a value of $p < 0.05$ *was considered statistically significant.*

Of the 357 patients surveyed, we determined a prevalence rate of Enterobacteriaceae urinary tract infections of 72.55%. Significant differences were observed between the proportions of men and women surveyed and urinary infection of male and female genders with probabilities of 0.001 and 0.02, respectively. The most frequently identified Enterobacteriaceae were Escherichia coli, Klebsiella pneumoniae and Proteus mirabilis, with proportions of 76.45%, 12.74% and 5.79% respectively. The resistance phenotypes detected were ESBL, XDR, MDR and PDR, with proportions of 58.42%, 23.59%, 15.73% and 2.24%, respectively.

This study made it possible to determine high rates of resistance phenotypes of Enterobacteriaceae responsible for urinary tract infections in the departments of the CHU-RN. The results of this study raise the need for the application of recommendations for the proper use of antibiotics and to establish treatment guided by laboratory results.

Keywords *- Enterobacteriaceae, Urinary tract infection, Resistance phenotypes, Epidemiological profile, Antibiotic, Chad.*

1. Background

Urinary Tract Infections (UTI) are among the most common infections in hospitals. The most incriminated bacteria are Enterobacteriaceae, with antibiotic resistance rates exceeding 25% in countries with limited resources [1]. The growth of bacterial antibiotic resistance constitutes today one of the most important problems of anti-infectious therapies in the world, particularly in Chad, where most of the population most often resorts to drugs sold on the roadsides to heal [2]. The evolution of resistance of Enterobacteriaceae to antibiotics has been linked to the misuse and prescription of antibiotics without laboratory evidence by health professionals, which has contributed enormously to the selection of multi-resistant strains which have appeared according to certain resistance mechanisms such as the production of extended-spectrum beta-lactamases (ESBL), the hyperproduction of penicillinases, cephalosporinases or the production of TEM (Temoniera) and SHV (Sulfhydrile-Variable) type beta-lactamases [3, 4]. Enterobacteriaceae (Gram-negative bacilli) responsible for UTI are also becoming increasingly highly resistant, including XDR (bacterial isolates that remain sensitive to antibiotics in only one or two categories), MDR (bacterial isolates that remain resistant to at least three or more classes of antibiotics) and PDR (bacterial isolates remain resistant to all classes of antibiotics) in hospital settings [5, 6, 7]. These phenomena make therapeutic treatment of patients infected with such bacteria very difficult, particularly in low-income countries where the most recent and only effective molecules are not always available or are too expensive [8, 9, 10]. The incidence of ESBL-producing Enterobacteriaceae (ESBL-E) is quite high in hospitals. Thus, Lagha in 2015 at the Laghouat Hospital in Algeria found 7.4% of cases of E-ESBL or 20% of *Enterobacter cloacae* [11]. In Morocco, the overall incidence of ESBLs was 3.8% in 2005 and 7.5% in 2009, with common resistance to fluoroquinolones (ciprofloxacin: 88% to 71%); however, they remain sensitive to Imipenem (100%). [12]. In Ethiopia, Mulatu Gashaw et al. (2018) identified 38 (30.2%) as MDR, 52 (41.3%) as XDR and 24 (19%) were PDR [13].

In Chad, a study carried out by Fissou et al. (2019) showed a high prevalence of resistance of Enterobacteriaceae and other bacteria responsible for various infections to antibiotics.

This study aimed to identify the different resistance phenotypes of Enterobacteriaceae in patients hospitalized due to UTI in the urology and infectious diseases departments at the National Reference University Hospital Center (CHU-RN) of N' Djamena.

The results of this study could serve as an awareness tool for the fight against self-medication and abusive prescriptions of antibiotics without laboratory evidence in Chad.

2. Material and Methods

2.1. Setting, Period and Type of Study

This cross-sectional study and etiological diagnosis were conducted on Enterobacteriaceae, responsible for one-year urinary tract infections from October 2021 to October 2022. It was conducted at the laboratory bacteriology unit of the National Reference University Hospital Center (CHURN) of N'Djamena and the Bacteriology Unit of the Laboratory for Research, Diagnosis and Scientific Expertise (Lab-ReDES) of the Faculty of Human Health Sciences (FSSH) of the University of N'Djamena. Urine samples were taken in the CHU-RN's infectious diseases (SMI) and urology department.

2.2. Eligibility Criteria

Any patient hospitalized in the Urology or Infectious Diseases department with symptoms suggestive of a lower urinary tract infection was included. However, patients on antibiotics two weeks before sample collection and those on catheters or whose poor health prevented sample collection were excluded from sampling.

2.3. Sampling

Sampling for convenience about the duration of the study.

2.4. Method and Condition of Urine Collection

In cooperative adults, urine was collected using the so-called "midstream" technique and according to strict rules that condition the quality of the cytobacteriological examination of urine (ECBU). The urine is preferably collected in the morning after carefully washing the external genitalia with an antiseptic solution or mild soap and careful rinsing with water.

In a woman who presents losses, even minimal, the installation of vaginal protection is essential. The first part of the urination is rejected, making it possible to eliminate all or part of the commensal flora of the lower urethra, and only the middle of the stream is collected in a sterile bottle. The sample is accompanied by a laboratory examination report in less than 2 hours.

2.5. Bacteriological Analysis

The realization of a cytobacteriological examination of urine (ECBU) involves different steps:

2.6. Macroscopic Urine Examination

Note the appearance of the urine: clear, turbid, purulent, hemorrhagic (hematic, hematuria), port wine.

2.7. Microscopic Examination

On a urinary pellet obtained after centrifugation of 10 mL of urine at 2000 rpm for 10 min, note the presence of crystals, cylinders, cells and microorganisms (parasites) by direct examination and by examination of the smear made from the pellet of centrifugation and Gram stain. The presence of epithelial cells of vaginal origin indicates contamination.

2.8. Isolation of Enterobacteriaceae in Culture Medium

Inoculate 10 µL of homogenized urine (calibrated loop) on CLED agars and incubate at 37 o C for 18 to 24 hours in a bacteriological incubator. After 24 hours of incubation, cultures positive on CLED agar (Cystine lactose electrolyte deficient) were sub-cultured on Mueller-Hinton (MH) agar for biochemical identifications and antibiogram.

2.9. Biochemical Identification of Enterobacteriaceae

McFarland's homogeneous bacterial suspension with an opacity of 0.5 was prepared from a 24-hour fresh colony in a 5 mL bottle of medium water to inoculate the biochemical identification galleries (API 20 E, BioMérieux).

The API20E gallery is a system for identifying Enterobacteriaceae and other Gram-negative bacilli using 20 standardized and miniaturized biochemical tests in microtubules in dehydrated form. The principle is based on the inoculum of microtubules with a bacterial suspension, which rehydrates the media. Incubation is carried out at 37°C for 24 hours, during which biochemical reactions take place (decarboxylation, fermentation, deamination.), which result in spontaneous colored products revealed by the addition of the reagents. The identification of bacteria is obtained using the API20E catalog. The catalog provides the identification of a large number of profiles obtained on API20E, which gives great reliability to the interpretation of the results.

2.10. Study of the Sensitivity of Enterobacteriaceae to Antibiotics

Choice of antibiotics: The antibiotics were chosen according to their prescription for the treatment of urinary tract infections in the urology and infectious diseases departments of the CHURN.

2.11. Antibiogram

The antibiogram was carried out by the technique of Kirby and Bauer, which is the method by diffusion of discs impregnated with antibiotics in MH agar medium flooded with the bacterial inoculum in suspension. The identification of ultra-resistant bacteria was carried out following the recommendations of the Antibiogram Committee of the French Society of Microbiology, the European Committee on Antimicrobial Susceptibility Tests (CA-SFM, EUCAST; 2016-2020), of the Clinical Laboratory Standards Institute (CLSI) and the United States Food and Drug Administration (FDA) [14-15].

2.12. Detection of Extended-Spectrum Beta-Lactamase (ESBL) Production

The demonstration of the ESBL was made on Muller-Hinton agar by the double disc synergy test method according to the procedure of Jarlier et al. (1988). Discs of cefotaxim (30 µg), ceftazidim (30 µg), cefepim (30 µg), and aztreonam (30 µg) were placed 30 mm (center to center) from an amoxicillin/acid disc clavulanic (20/10 µg) then incubated at 35 – 37°C (Figure 1). After 18 to 24 hours of incubation, ESBL production by the test organism was based on partially inhibiting ESBL by clavulanic acid. A champagne cork-shaped image characterizes the existence of even weak synergy between cefotaxim, ceftazidim, cefepim, aztreonam, and clavulanic acid.

2.12.1. Reading

Double Disc Method

- C3G-AMC-C3G, 25mm distance
- If the formation of a champagne cork image, BLES+

Combine Disc Method

- C3G-CLAV-CG3, distance 30 mm

Calculation of the difference of 2 diameters

- If < 5 mm ESBL-
- If > 5 mm ESBL+

2.13. Data Collection and Processing

Information on socio-demographic variables (age, sex, profession, origin, etc.) was collected from each participant during a face-to-face verbal interview using structured questionnaires. Clinical data related to hospitalization history for surgery and antibiotic use were collected by reviewing patient medical records in consultation with respective physicians at the CHU-RN's Urology and Infectious Diseases Departments.

Data were entered and analyzed using Microsoft Word and Excel. The chi-square test (χ^2) was used to compare qualitative variables with a significance level set at 5%.

2.14. Ethics Statement

The advisory and research ethics committees of the Faculty of Human Health Sciences (FSSH) of the University of N'Djamena and the National Reference University Hospital Center (CHU-R N) of N'Djamena accepted and approved this study.

Table 1: Antibiotics selected for susceptibility testing

Category	Family	Antibiotic/dose	Diameter (mm)		
			Sensible	intermediate	Resistant
Antibiotic (Bio-Rad)	Aminosides	Gentamicin (10 µg)	>16	14-16	<14
	B-Lactams	Ampicillin (10 µg)	>14	12-14	<12
		Amoxicillin (25 µg)	>23	19-23	<19
		AMC (20-10 µg)	>24	18-24	<18
		Aztreonam (30 µg)	>24	19-25	<19
		Cefotaxim (30 µg)	>31	25-31	<25
		Ceftazidim (CAZ)	>33	25-33	<25
		Cefipim (30 µg)	>22	19-22	<19
		Imipenem (10µg)	>32	17-24	<17
	Cyclins	Tetracyclin (30 µg)	>20	17-20	<17
	Fluoroquinolones	Ciprofloxacin (5µg)	>22	19-22	<19
	Quinolones	NAL (30 µg)	>22	19-22	<19
	Sulfa drugs	SXT (1,25 /23,75 µg)	>22	19-22	<19
	6 Families	13 antibiotics			

Nalidixic acid (NAL); Trimethoprim-sulfamethoxazole (SXT).

Quality control was performed using reference strains *Escherichia. coli* ATCC 25922; *Pseudomonas aeruginosa* ATCC 27853; *Klebsiella pneumoniae* ATCC 700603 (CA-SFM/EUCAST, 2016-2020; CLSI, 2020)

3. Results

3.1. Overall Prevalence of Enterobacteriaceae Responsible for Urinary Tract Infection

A total of 357 patients were included in this study. There were 255 (71.43%) men and 102 (28.57%) women (Ch2 = 16.261>Ch20>3.84, ρ = 0.001, df =1: there is a significant difference in participation in the survey in favor of men with a sex ratio of 2.5. The average age was 50 years, with the extremes of 15 and 85 years. After urine culture, the results showed that of the 357 patients sampled, 259 (72.55%) cultures were positive for Enterobacteriaceae and 98 (27.45%) cultures were negative.

3.2. Distribution of Enterobacteriaceae Infection by sex (Table 2.1)

Of the 259 positive cases, 72.97% (n=189) were male, and 27.03% (n=70) were female (Ch2=28.269>Ch20>3.84, ρ=0.02, dof=1: a significant difference in high rate of male-dominated Enterobacteriaceae urinary tract infection).

3.3. Distribution of Enterobacteriaceae Infection by age group (Table 2.2)

The most represented age group was that of 40 to 64 years with 105/259 (41%) cases, followed by 65 to 85 years 83/259 (32%) and 71/259 (27%) for that of 15 to 39 years (Table 2.2).

3.4. Distribution of Enterobacteriaceae Infection by Occupations (Table 2.3)

Pensioners and homemakers were the most represented, with 35.13% and 21.62% respectively.

3.5. Distribution of Enterobacteriaceae Infection according to the Notion of Self-Medication (Table 2.4)

Among the 259 infected patients, 185 (71.43%) claimed to practice self-medication, 52 (20.07%) claimed to be in the habit of using antibiotics with a medical prescription and 22 (8.50%) ignored (Table 2.4).

Table 2. Epidemiological profiles of patients and Enterobacteriaceae isolated from urine

Parameter	**Distribution of Enterobacteriaceae infection by patient category**						
1. Distribution of infection by sex				**2. Distribution of infection by age groups**			
Sex		Culture				Culture	
	Number	Positive (%)	Negative (%)	Age group (an)	Number	Positive (%)	Negative (%)
Male	255	189	66	15-39	119	71 (60)	48 (40.33)
Female	102	70	32	40-64	132	105 (79.54)	27 (20.45)
Total	**357**	**259**	**98**	65-85	106	83 (78.30))	23 (22)
				Total	**357**	**259 (72.54)**	**98 (27.45)**
3. Distribution of infection by profession				**4. Distribution of patients according to self-medication**			
		Culture				Culture	
	Number	Positive (%)	Negative (%)	Response	Number	Positive (%)	Negative (%)
Pupil/Student	36	14 (39)	22 (61.11)	Yes	217	185 5(85.25)	32 (15)
Civil servant	53	39 (73.58)	14 (26.41)	No	61	52 (85.24)	9 (15)
homemaker	71	56 (79)	15 (21.12)	Ignored	79	22 (28)	57 (72.15)
Trader	66	52 (79)	14 (21.21)	**Total**	**357**	**259 (72.54)**	**98 (27.45)**
retiree	104	91(87.5)	13 (12.5)	**5. Frequency of isolated Enterobacteriaceae in urine**			
Other	27	7 (4)	20 (74.07)	Bacteria species		Number	Percentage
Total	**357**	**259 (72.54)**	**98 (27.45)**	*Escherichia coli*		198	76.4
				Klebsiella pneumoniae		33	12.7
				Proteus mirabilis		15	5.8
				Pseudomonas aeruginosa		11	4.2
				Enterobacter cloacae		2	0.8
				Total		**259**	**100**
6. Distribution of Enterobacteriaceae isolated by departments							
		Service					
Bacteria species		Urology	MI	**Total**			
Escherichia coli		103	95	198			
Klebsiella pneumoniae		14	19	33			
Proteus mirabilis		9	6	15			
Pseudomonas aeruginosa		8	3	11			
Enterobacter cloacae		2	0	2			
Total		**136 (52.51)**	**123 (47.49)**	**259 (100)**			
Legend: % = Percentage; MI= Infectious diseases; Other = (Dressmaker/Tailor, Bricklayer, Cultivator, Breeder.							

Table 3. Evaluation of the efficacy of antibiotics against isolated enterobacteriaceae

ATB	Bacteria species									
	Escherichia coli (n = 198)		*Klebsiella pneumoniae* (n = 33)		*Proteus mirabilis* (n = 15)		*Enterobacter cloacae* (n = 2)		*Pseudomonas aeruginosa* (n = 11)	
	S (%)	R+I (%)	S (%)	R+I (%)	S (%)	R+I (%)	S (%)	R+I (%)	S (%)	R+I (%)
GNN	145 (73.2)	53 (26.76)	17 (51.51)	16 (48.48)	11 (73.33)	4 (26.67)	2 (100)	0 (0)	6 (54.54)	5 (45.45)
AMP	21 (10.6))	177 (89.39)	9 (27.27)	24 (72.72)	4 (26.66)	11 (73.33)	1 (50)	1 (50)	0 (0)	11 (100)
AMX	32 (16.16)	166 (83.83)	13 (39. 39)	20 (60.60)	7 (46.66)	8 (53.33)	2 (100)	0 (0)	0 (0)	11 (100)
AMC	97 (48.98))	101 (51.01)	16 (48.48)	17 (51.51)	9 (60)	6 (40)	2 (100)	0 (0)	4 (36.36)	7 (63.63)
ATM	100 (50.50)	98 (49.49)	22 (66.66)	11 (33.33)	10 (66.66)	5 (33.33)	2 (100)	0 (0)	6 (54.54)	4 (45.45)
CTX	81 (41)	121 (61.1)	24 (72.73)	9 (27.27)	3 (20)	15 (80)	2 (100)	0 (00)	8 (72.72)	3 (27.27)
CRO	117 (59.1)	81 (41)	14 (4.42)	19 (57.57)	6 (40)	9 (60)	2 (100)	0 (0)	8 (72.72)	3 (27.27)
CAZ	167 (84.34)	31 (15.65)	23 (69.69)	10 (30.30)	11 (73.33)	4 (26.66)	2 (100)	0 (0)	9 (81.82)	2 (18.18)
FEP	136 (68.68)	62 (31.31)	31 (96.87)	2 (6.06)	14 (93.33)	1 (6.66)	2 (100)	0 (0)	9 (81.82)	2 (18.18)
IMP	180 (90.90)	18 (9.09)	26 (78.78)	7 (21.21)	15 (100)	0 (0)	2 (100)	0 (0)	6 (54.54)	5 (45.45)
TET	21 (10.60)	177 (89.39)	5 (15.15)	28 (84.48)	2 (13.33)	13 (86.66)	1 (50)	1 (50)	2 (18.18)	9 (81.82)
CIP	102 (51.51)	96 (48.48)	6 (18.18)	27 (81.81)	13 (86.67)	2 (13.33)	2 (100)	0 (100)	5 (45.45)	6 (54.55)
NAL	112 (56.56)	86 (43.43)	21 (63.63)	12 (36.36)	10 (66.66)	5 (33.33)	2 (100)	0 (0)	3 (27.27)	8 (72.72)
SXT	55 (27.77)	143 (72.22)	15 (45.45)	17 (51.51)	2 (13.33)	13 (86.66)	1 (50)	1 (50)	2 (18.18)	9 (81.82)

Legend: ATB= antibiotic; n= number; %(R+I) = resistance percentage; S = percentage of sensitivity.
Gentamicin (GNN); Ampicillin (AMP); Amoxicillin (AMX); Aztreonam (ATM); Cefotaxim (CTX); Amoxicillin + clavulanic acid (AMC); Ceftriaxone (CRO); Ceftazidim (CAZ); Cefipim (FEP); Imipenem (IMP); Tetracycline (TET); Ciprofloxacin (CIP); Nalidixic acid (NAL); Trimethoprim-sulfamethoxazole (SXT

Table 4. Resistance phenotype of enterobacteriaceae detected

Bacteria species	**Resistance phenotypes**				
	MDR	XDR	PDR	BLSE	Total
Escherichia coli	9	15	0	41	65
Klebsiella pneumoniae	2	3	1	7	13
Proteus miralis	0	0	0	2	2
Pseudomonas aeruginosa	3	3	1	0	7
Enterobacter cloacae	0	0	0	2	2
Total %	**14 (15.73)**	**21 (23.59)**	**2 (2.24)**	**52 (58.42)**	**89 (100)**

ESBL: Extended Spectrum Beta-Lactamases, XDR: Bacterial isolates remain susceptible to antibiotics in only one or two classes, MDR: Bacterial isolates remain resistant to at least three or more classes of antibiotics, PDR: Bacterial isolates remain resistant to all classes of antibiotics.

3.6. Frequency of Isolated Enterobacteriaceae in Urine (Table 2.5)

Different species of bacteria from the Enterobacteriaceae family were isolated in the urine during the study period. Escherichia coli (76.4%) were in the lead, followed by Klebsiella pneumoniae (12.7%) (Table 2.5).

3.7. Distribution of Enterobacteriaceae Isolated by Service (table 2.6)

The proportion of infection was higher in the Urology department (52.51%), followed by the infectious diseases department (47.49%).

3.8. Study of the Sensitivity of Isolated Enterobacteriaceae to Antibiotics (Table 3)

Table 3 shows the sensitivity and resistance profiles of the Enterobacteriaceae strains isolated from the urine to the antibiotics tested. In general, the resistance of the isolated strains was more marked with aminopenicillins (ampicillin, amoxicillin, amoxicillin-clavulanic acid) and a third-generation cephalosporin.

Most Enterobacteriaceae strains were more than 80% resistant to sulfonamides (Trimethoprim-sulfamethoxazole) and more than 60% to tetracyclin.

On the other hand, the sensitivity of the isolates was varied too (Aminosides, Macrolides, Fluoroquinolones, Carbapenems (Beta-lactams), Cyclins). We have identified in our series 18 strains of Escherichia coli resistant to imipenem seven (7) Klebsiella pneumoniae carbapenemases (KPC).

We also identified 2 (18.18%) strains of Pseudomonas aeruginosa resistant to fourth-generation cephalosporin (Cefipim) and 5 (45.45%) strains of Pseudomonas aeruginosa carbapenemase (Table 3).

3.9. Enterobacteriaceae Resistance Phenotypes Detected by Double Synergy and Kirby-Bauer Techniques (Table 4)

Of the 259 Enterobacteriaceae strains identified, 89 (34.36%) were highly resistant (MDR, XDR, PDR and ESBL), and 170 (65.63%) were of varying sensitivity and resistance. The prevalence of MDR was 15.73%, XDR (23.59%), PDR (2.24%) and ESBL was 58.42%.

Among the 52 strains of extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, *Proteus mirabilis* (100%) and *Enterobacter cloacae* (100%) were in the lead, followed by *Escherichia coli* (82.69%) and *Klebsiella pneumoniae* (13.46%). Among the highly resistant Enterobacteriaceae strains, *Pseudomonas aeruginosa* (MDR (43%) and XDR (43%)) were in the lead, followed by strains of *Escherichia coli* (MDR (13.43%) and XDR (13.43%)). We detected 2 (2.24) PDRs, including a *Pseudomonas aeruginosa* and a *Klebsiella pneumoniae,* with 14.28% and 8% rates, respectively (Table 4).

4. Discussion

Our research work was focused on the isolation, biochemical identification, and detection of the phenotype of the resistance of Enterobacteriaceae in the urology and infectious diseases departments of the National Reference University Hospital of N'Djamena in Chad.

This study shows a prevalence of 72.55% of Enterobacteriaceae involved in urinary tract infections. This prevalence is higher than that of Niang et al. in Dakar in 2020 and Kajumbula in 2018 in Uganda [16, 17].

Regarding the profession, retirees 35.13% (91/259) and homemakers 21.62% (56/259) were the most represented socio-professional strata. In addition, occupation was a factor favoring urinary tract infections [17]. This could be explained by the fact that retirees are elderly people with limited resources, which does not allow them to cope with their health problems in Chad. The very high rate of urinary infections among homemakers could be linked to the failure to observe basic rules of hygiene crowned with the very low literacy rate of these housewives in Chad,

Concerning the frequency of isolated Enterobacteriaceae, *Escherichia coli* were the most represented (76.45%) in this study, followed by *Klebsiella pneumoniae* (12.74%). Similar results have been reported in Chad and China by several authors [18, 19].

Considering the age of the patients, urinary infections affected the age groups 40 to 64 and 65 to 85 years much more. The results of this study are superimposable to those of Selamyhun (2023), who reported the most affected groups from 29 to 38 years old and 39 to 48 years old, respectively [20].

Indeed, in the elderly, there is a reduction in the immune defenses of the urinary tract due to changes in the urinary tract, particularly the bladder and genital tract.
Regarding patient participation in the survey, men were predominant in our series (71.43%) against (28.57%) women. Our results can be superimposed on those of Selamyhun (2023), who reported a male predominance (54.7%) against (45.3%) of women [20].

With regard to the resistance phenotypes of the Enterobacteriaceae identified, the present study made it possible to detect the resistance phenotypes MDR, XDR, PDR and ESBL with proportions of 15.73%, 23.59), (2.24%) and 58.42% respectively. The results of this study are superimposable to previous work [21].

Several studies have shown that most Gram-negative bacteria become increasingly antibiotic-resistant [22-25].

The present study found a lower rate of XDR (23.59%) and a lower rate of PDR (2.49%). Moreover, the authors have reported a high proportion of PDR and lower XDR [26, 27]. The circulation of highly resistant Enterobacteriaceae in Chad could be explained by the illicit sale of medicines on the side of the streets, the prescription without laboratory evidence by health professionals, the abusive use of medicines, and the lower socio-economic level of Chadians not allowing them to attend health facilities in their country.

The mobility of populations could explain the geographical spread of highly resistant Enterobacteriaceae and the lack of hygiene and sanitation both in hospital and community settings. Considering the sensitivity and resistance of Enterobacteriaceae to antibiotics, this study noted a strong resistance of the strains (*Escherichia coli* and *Klebsiella pneumoniae*) isolated to tetracycline in the order of 89.39% and to amoxicillin clavulanic acid of the order of 51%.

The growing increase in the rate of resistance to antibiotics commonly used in our country by the germ in question would be attributable to self-medication and the increased geographical cross-transmission of drug-resistant drugs.

Moreover, a recent corroborative study in 2016 showed that travelers returning from Hajj had acquired MDR (*Acinetobacter baumannii*) and NDM (*Escherichia coli*) during the Hajj event in Saudi Arabia [28-36].

In addition, this study made it possible to identify 18 strains of *Escherichia* resistant to Imipenem, 7 strains of *Klebsiella pneumoniae* carbapenemases (KPC), 2 strains of *Pseudomonas aeruginosa* resistant to fourth-generation cephalosporin (Cefipim) and 5 strains of *Pseudomonas aeruginosa* carbapenemases [37, 38]. In *E. coli*, the resistance level to Carbapenems remains high in the contiguous areas of North and East Africa [37, 39].

Other authors have shown that the genes (blaOXA-48, blaNDM-1 and blaOXA-181) conferring resistance to Carbapenems were from a wide variety of plasmid transferable resistances, raising concerns about the future reliability of Carbapenems. [39].

Other authors have also noted that XDR bacteria can be present and spread through wastewater, including that from healthcare facilities, agriculture and aquaculture [40, 41].

Regarding the detection of double champagne cork images indicating the production of extended-spectrum beta-lactamases (ESBL), this study noted a rate of 58.42% of ESBL, which is higher than those reported by the previous study in Chad in 2015, which was 33.33%.

5. Conclusion

This study made it possible to determine the epidemiological profile and detect different resistance phenotypes (MDR, XDR, PDR and ESBL) of Enterobacteriaceae responsible for urinary tract infections in the urology and infectious diseases departments of the CHURN of N'Djamena. These results suggest the need to implement management procedures guided by the antibiogram results.

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Author Contributions

Bessimbaye Nadlaou, Abdelsalam Tidjani, and Rimtebaye Kimassoum designed the study, processed the data, wrote the manuscript and researched the literature; Mbaïressem Tamsengar Olivier collected the data. All authors contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

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