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Original Research Paper

Phenotypic Characterization of *Enterobacteriaceae* and *Pseudomonas aeruginosa* Isolates Producing Extended-spectrum Beta-lactamase and carbapenemase recovered across five hospitals in Yaoundé, Cameroon

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ABSTRACT:

Enterobacteriaceae and *Pseudomonas aeruginosa* are implicated in severe nosocomial and healthcare-acquired infections. The emergence of strains producing Extended-spectrum β- lactamases (ESBL) and carbapenemases reduces the efficacy of lastline antibiotics, making these infections more difficult to treat. The aim of this study was to characterize phenotypically *Enterobacteriaceae* and *Pseudomonas aeruginosa* isolates producing Extended-spectrum β- lactamases and carbapenemases recovered across five hospitals in Yaoundé. A cross-sectional study was conducted from November 2023 to August 2024. Isolates obtained from various clinical samples were identified using API 20 E and API 20NE Galleries. Antibiotic susceptibility testing was performed according to CASFM/ EUCAST recommendations. Extended-spectrum β- lactamases and carbapenemases production were evidenced by the double disc synergy tests. A total of 280 isolates of *Enterobacteriaceae* were isolated from stool samples, with *Escherichia coli* being the frequently isolated specie 74.29 % (208/280). A high rate of resistance was observed in *Klebsiella pneumoniae*, with 100 % resistance to Ceftazidime and 90 % to Cefotaxime. Similarly, resistance to Carbapenems revealed high rates of resistance in *Escherichia coli* (59.13 % resistance to Imipenem and 33.17 % to Meropenem). Of the 280 enterobacterial isolates, 20.35 % (57/280) were ESBL producers, while 10.71% produced carbapenemases, and 3.57 % of (10/280) showed co-expression of ESBL and carbapenemases. *Pseudomonas aeruginosa* isolates showed a high rate of resistance to β-lactam antibiotics, particularly Ceftazidime (79.09 %) and Ticarcillin (69.09%). ESBL production was observed in 13.63 % (15/110) and carbapenemase production in 19.09% (21/110), while co-production of ESBL and carbapenemase was detected in 7.27% (8/110). This study evidences an increased risk of resistance to the most widely available antibiotics in healthcare settings. It remains important to set up therapeutic and resistance monitoring committees.

Keywords: Enterobacteriaceae, Pseudomonas aeruginosa, Extended-spectrum β-lactamases, Carbapenemases.

1. INTRODUCTION:

Enterobacteriaceae are a group of Gram-negative bacteria commonly found in the intestines of humans and animals [1]. They include notable pathogens such *as Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Proteus mirabilis, Citrobacter freundii, Serratia marcescens, Morganella morgani, Providencia stuartii, Shigella dysenteriae* and *Salmonella typhi*, which are responsible for a wide range of nosocomial infections [2]. Infections caused by Enterobacteriaceae include a wide range of pathologies, often serious, particularly in immunocompromised patients. Among the most common are urinary tract infections (UTIs), mainly

caused by *Escherichia coli*, but also *Klebsiella pneumoniae* and *Proteus mirabilis* [3]. Respiratory infections commonly found in mechanically ventilated patients, particularly pneumonia caused by *Klebsiella pneumoniae* and *Enterobacter spp*, which are often severe and associated with high mortality rates [4]. Also, bacteremia and septicaemia occur when these bacteria invade the bloodstream, often from an infected site, and can lead to severe sepsis with multiple organ failure [5]. Intra-abdominal infections, such as peritonitis and abdominal abscesses, common after surgery on the digestive tract, with *Escherichia coli* being the main causative agents [6].

The treatment of infections caused by *Enterobacteriaceae* is a major challenge due to the emergence of antibiotic-resistant strains and the diversity of resistance mechanisms [7]. *Enterobacteriaceae* have developed a range of antibiotic resistance mechanisms that complicate their treatment and contribute to the current therapeutic impasse [7]. Some species naturally produce chromosomal β-lactamases that hydrolyse certain classes of antibiotics [8]. Extented spectrum beta-lactamases, which are enzymes that degrade beta-lactam antibiotics (including Penicillins and Cephalosporins), rendering them inactive. Among the most common types of ESBL are the enzymes TEM(Temoneira), SHV(Sulfhydryl-Variable), CTX-M(Cefotaximase-Munich) [9]. Carbapenemases are often produced by Enterobacteriaceae multi-resistant strains and include enzymes such as KPC (*Klebsiella pneumoniae* carbapenemase), NDM (New Delhi Metallo-beta-lactamase), VIM (Verona integron-encoded metallo-beta-lactamase) and OXA (oxacillinase) [10]. The production of ESBLs and carbapenemases in enterobaceria is a growing problem. In Europe, the prevalence of *E. coli* producing ESBL was 16 %, while the prevalence of *K. pneumoniae* producing ESBL reached 38 % in certain Eastern European countries [11]. Similarly, the prevalence of carbapenem-resistant *K. pneumoniae* was 7.9 % on average, but exceeded 25 % in some countries such as Greece and Italy [11]. In Africa, studies have reported prevalences of 10 % to 30 % for carbapenemases, depending on the hospital and region [12].

Pseudomonas aeruginosa (P. aeruginosa) is a Gram-negative, strictly aerobic, opportunistic bacterium belonging to the *Pseudomonadaceae* family [13]. It is ubiquitous and can be found in a variety of environments, including water, soil and hospital surfaces [14]. It is of particular concern in hospitals because of its ability to colonise immunocompromised patients and cause serious infections [15]. This bacterium has been implicated in a variety of pathologies, including pulmonary infections in cystic fibrosis patients, nosocomial pneumonia, urinary tract infections associated with catheters, bacteraemia, wound infections (particularly in burn victims), malignant otitis externa and keratitis [16]. Its high pathogenicity is based on several virulence factors, including the production of toxins (exotoxin A, elastase, pyocyanin), the formation of biofilms, which enable it to adhere to surfaces and resist treatment, and the presence of type III secretion systems that inject toxins directly into host cells [17].

The treatment of infections caused by *P. aeruginosa* is becoming increasingly complex due to the emergence of antibiotic-resistant strains, particularly cephalosporins, which are commonly used to treat many infections, and carbapenems, which are considered drugs of last resort for treating these infections [18]. In fact, this bacterium has a particularly robust natural resistance mechanism based on several host strategies [19]. Firstly, its impermeable membrane limits the entry of antibiotics, due to the low porosity of its porins. Secondly, it expresses efflux pumps such as MexAB-OprM and MexXY-OprM, which actively expel many antibiotics from the cell. In addition, it naturally produces β-lactamases such as AmpC, giving it intrinsic resistance to first-generation penicillins and cephalosporins [20]. However, the emergence of acquired resistant strains has added another layer of difficulty, with the production of extended-spectrum beta-lactamases (ESBLs) such as: SHV, CTX-M, TEM, PER, GES, and carbapenemases such as: VIM, IMP, NDM, KPC and OXA-48 which hydrolyse carbapenems and other beta-lactams, rendering these treatments ineffective [21]. ESBL and carbapenemase-producing strains of *P. aeruginosa* have been reported worldwide, particularly in Asia, Europe, North America and Africa. According to a study conducted in France, 23.1 % of *P. aeruginosa* strains isolated in hospitals were ESBL-producing and 12.5 % were carbapenemase-producing [22]. In Africa, the incidence of carbapenemase-producing *P. aeruginosa* in nosocomial infections has increased over the last 40 years [23]. A study conducted in South Africa revealed that 30.4 % of *P. aeruginosa* strains were ESBL producers, while 15.6 % produced carbapenemases [24]. Similarly, a study conducted in Cameroon revealed that 42.1% *of P. aeruginosa* strains were ESBL producers, while 21.4 % produced carbapenemases [25].

The emergence of strains producing extended-spectrum β-lactamases (ESBLs) and carbapenemases in *Enterobacteriaceae* and *P. aeruginosa* represents a major therapeutic challenge [26]. In this context, it is essential to gain a better understanding of their resistance mechanisms. Thus, the aim of this study was to characterize ESBL and carbapenemase resistance phenotypes in Enterobacteriaceae and *P. aeruginosa* isolated across five hospitals in Yaoundé, Cameroon.

2. **METHODS**:

2.1. Type, Site, and Duration of Study:

A cross-sectional and analytical study was conducted over a 10 months period, from November

2023 to August 2024. Isolates were collected from four public hospitals and one private hospital in Yaoundé, all of which have a high daily patient output: the Yaoundé University Hospital, the Yaoundé Central Hospital, the Yaoundé Military Hospital, the Yaoundé General Hospital and the Saint Matin de Porres Dominican Hospital. Re-identification of isolates and analyses were carried out at the Bacteriology Laboratory of the Centre for the Study and Control of Communicable Diseases.

2.2. Sampling Method and Selection Criteria:

During the study period, all *Enterobacteriaceae* isolated from faeces and *P. aeruginosa* isolates, recovered from pathological samples (pus, urine, wounds, blood, bedsores, catheter, effusion fluid and swabs) at each participating hospital, were systematically collected and included in the study for re-identification and subsequent analyses. Unconfirmed cases of *Enterobacteriaceae* and *P. aeruginosa*, after re-identification and isolates lacking useful clinical information were excluded from the study.

2.3. Re-identification and subculture of collected isolates:

The isolates collected were cultured on selective media: Cetrimide Agar for *P. aeruginosa*, and Mac Conkey for *Enterobacteriaceae* using the streak method. After inoculation, the plates were incubated at 37 °C aerobically for 24 hours. Each pure colony was then transferred to Nutritive Agar and incubated at 37 °C aerobically for 24 hours. The colonies obtained were first examined macroscopically (description of the size, color and appearance) and microscopically (Gram staining), followed by biochemical tests: oxidase, API 20E gallery and API 20NE gallery (BioMerieux, Lyon).

2.4 Antimicrobial Susceptibility Testing (AST):

Antibiotic susceptibility testing was carried out using the Kirby-Bauer Agar diffusion method in accordance with the recommendations of the Antibiogram Committee of the French Society of Microbiology (CA-SFM2021v.1.0). [27]. A total of 17 antibiotic discs from various classes (BIORAD, Marnes-la-coquette, France) at various concentrations: Penicillins (Amoxicillin + Clavulanic Acid (20-10µg), Tircacillin (75µg)); Cephalosporins (Cefepime (30 µg), Cefotaxime (5µg), Cefoxitin (30 µg), Ceftazidime (10 µg)); Carbapenems (Imipenem (10 µg), Meropenem (10 µg)), Monobactams (Aztreonam (30 µg)); Fluoroquinolones (Nalidixic acid (30 µg), Ciprofloxacin (5 µg)); Aminosides (Amikacin (30 µg), Gentamicin (10 µg) Tobramycin (10 µg)); Fosfomycin (200 µg), Chloramphenicol (30 µg), Trimethoprim (5 µg). A pure bacterial suspension adjusted to 0.5 Mc Farland was swabbed onto Mueller-Hinton Agar and antibiotic discs were then placed 25 to 30 mm apart. The plates were incubated at 37 °C for 24 h. Diameters of inhibitions were interpreted according to the European committee on antimicrobial susceptibility testing [27] recommendations as follows: Susceptible (S), Resistant (R), or Intermediate (I).

2.5. Detection of Extended-spectrum β-lactamase (ESBL):

Double disc synergy was used to screen all isolates for ESBL production as recommended by the Clinical and Laboratory Standards Institute (CLSI) [28]. Antibiotic discs of Ceftazidime (30 µg), Cefotaxime (30 µg), and Cefepime (30 µg), were placed 30 mm around the Amoxicillin + Clavulanic acid disc in pre-inoculated Mueller Hinton Agar. The plates were then incubated aerobically at 37 °C for 18-24h. Appearance of a champagne cork indicated positive results for ESBL production.

2.6. Detection of Specific Carbapenemases:

The combine disc test was used for the detection of specific carbapenemases. A suspension of morphologically similar *P. aeruginosa* colonies was prepared to match the 0.5 McFarland turbidity standard. The inoculum was streaked onto Mueller-Hilton Agar plates, and the following cartridges were applied; Meropenem/Imipenem 10 µg, Meropenem/Imipenem combined with Dipicolinic Acid, Meropenem/Imipenem combined with EDTA (ethylene diamine tetra-acetic acid), Meropenem/Imipenem comnined with Boronic Acid. Plates were incubated at 37 °C for 18 - 24 hours , and the results were read after incubation [28].

2.7. Statistical analysis:

The results obtained were recorded in Excel 2016 and analysed using R statistical software. Fischer's exact test was used to compare ESBL and carbapenemase rates between healthcare units and a p-value < 0.05 was considered statistically significant.

2.8. Ethical considerations:

This study received ethical approval from the Ethical Committee of the Delegation of Public Health for the Centre Region Cameroon, under approval number 00755/ CRESHC/2023. A research authorization was also obtained from the directors of each participating hospital. Anonymity of participants and confidentiality of results were scrupulously respected.

3. RESULTS:

3.1- Socio-demographic characteristics of *Pseudomonas aeruginosa* isolates:

Of the 160 isolates collected, 110 (68.75 %) were confirmed as *P. aeruginosa* after re-identification (Table 1). The majority of isolates originated from Yaoundé University Hospital, 34.54 % (38/110), from male patients, 63.63 % (70/110). Approximately 70.90

% (78/110) of patients were hospitalised and 59.09 % (65/110) were under antibiotic treatment.

Table I: Socio-demographic distribution of *Pseudomonas aeruginosa* isolates

Characteristics	**Number (n)**	**Percentage (%)**
Collection sites		
Yaoundé University Hospital	38	34.54
Yaoundé Military Hospital	27	24.54
Yaoundé Central Hospital	21	19.09
Yaoundé General Hospital	16	14.54
Saint Martin Porres Dominican Hospital	8	7.27
Sex		
Male	70	63.63
Female	40	36.36
Sex ratio	1.75	
Age (in years**)**		
Mean ± standard deviation	48.5 ± 20.3	
Hospitalisation		
Yes	78	70.90
No	32	29.09
Antibiotic treatment		
Yes	65	59.09
No	45	40.90

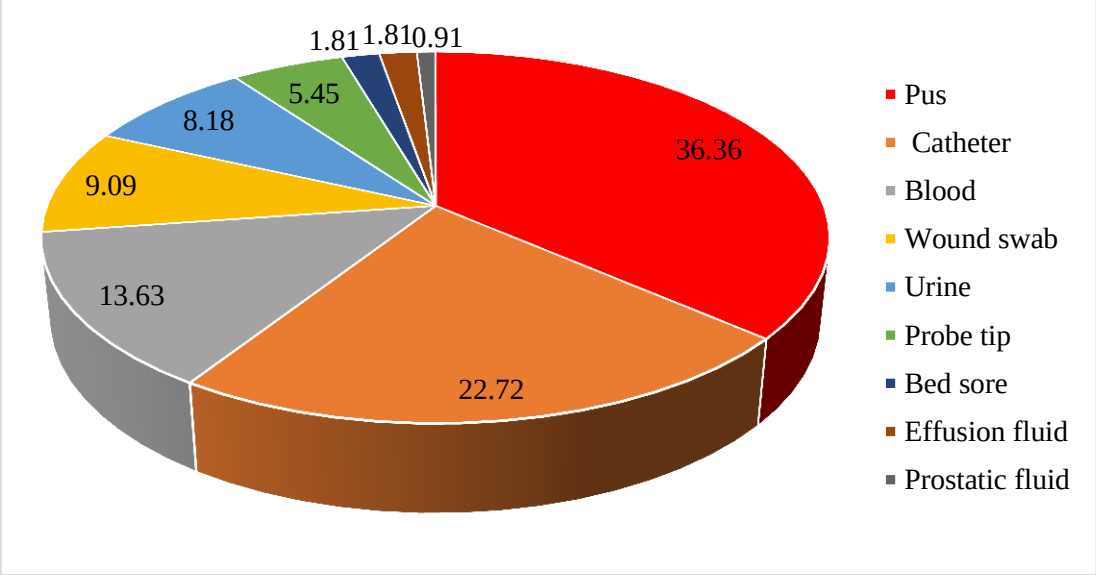

Figure 1: Distribution (%) of *P. aeruginosa* isolates according to sample type

The distribution of *Pseudomonas aeruginosa* isolates according to sample type shows a predominance of isolates from pus (36.36 %), followed by catheters (22.72 %) and blood (13.63 %).

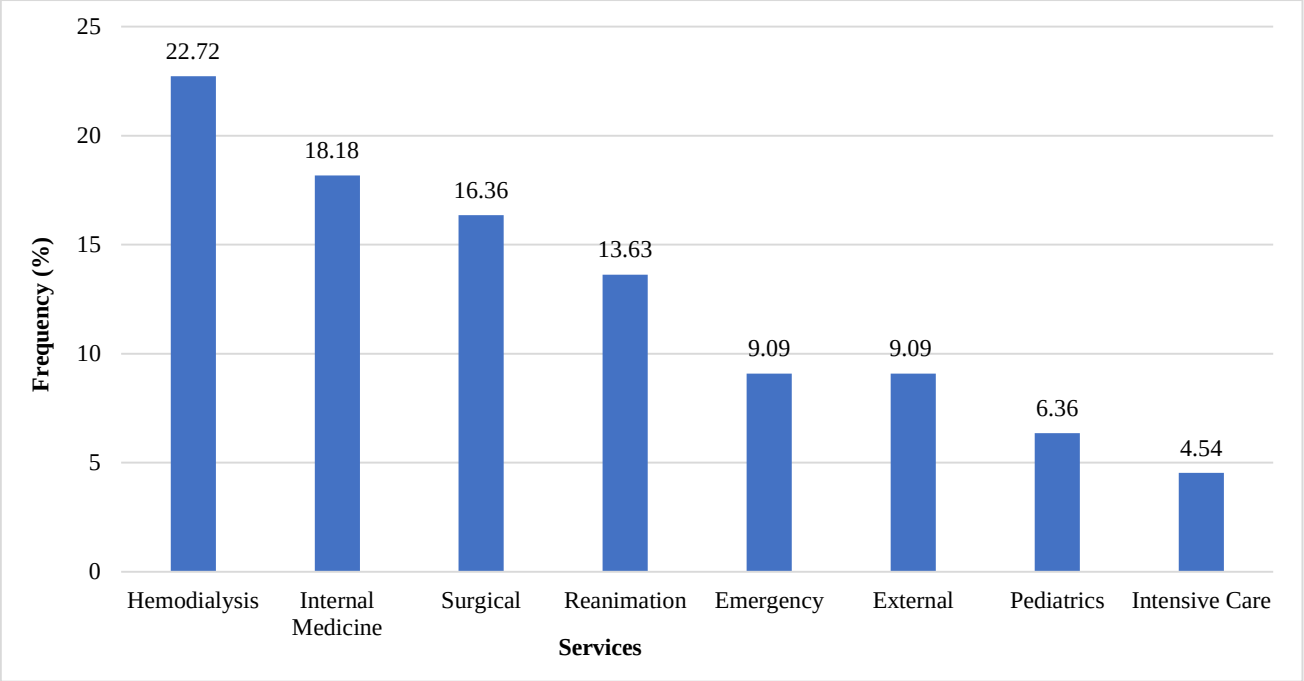

Figure 2: Distribution (%) of *Pseudomonas aeruginosa* isolates according to healthcare units

The hemodialysis (27.72 %), internal medicine (18.18 %) and surgery (16.36 %) units accounted for the highest proportions of *Pseudomonas aeruginosa* isolates.

3.2- Antimicrobial susceptibility profile of *Pseudomonas aeruginosa* Isolates:

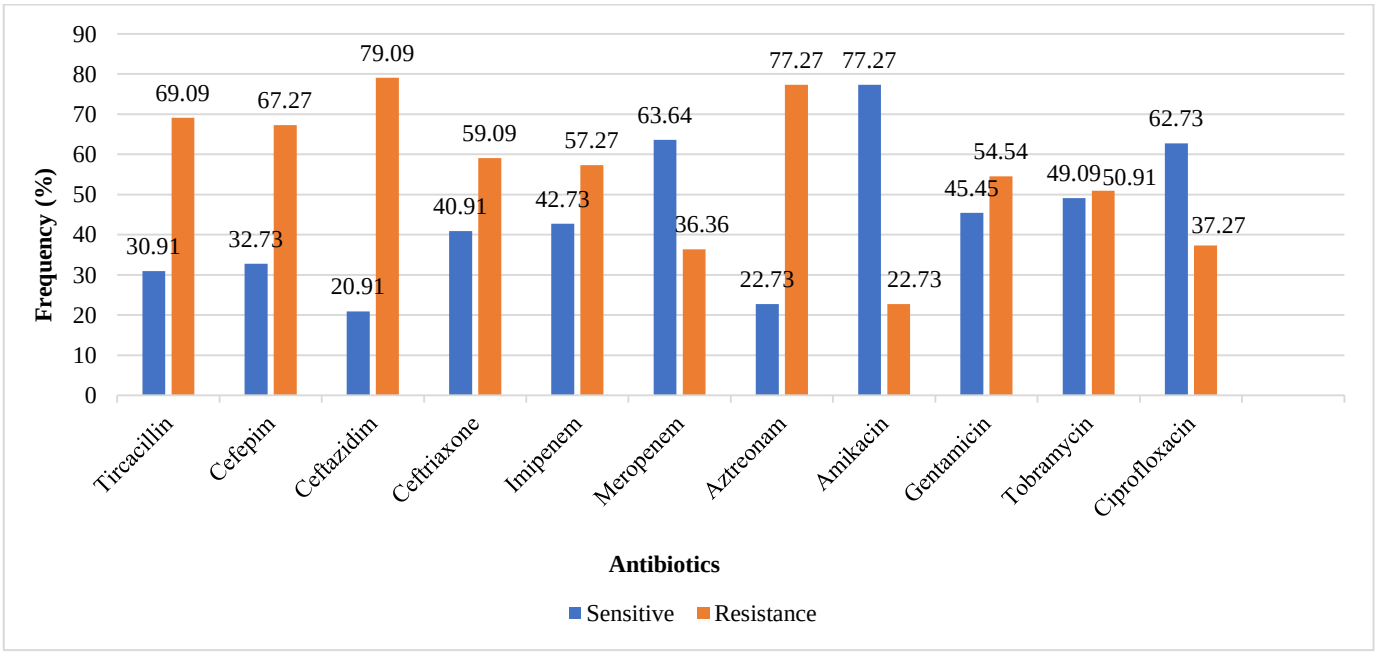

Figure 3 : Antimicrobial susceptibility profile of *Pseudomonas aeruginosa*

The antimicrobial susceptibility profile of the 110 *Pseudomonas aeruginosa* isolates is shown below (Figure 3). *Pseudomonas aeruginosa* isolates showed a high rate of resistance to β-lactam antibiotics, particularly Ceftazidime (79.09 %), Aztreonam (77.27 %) and Ticarcillin (69.09 %). Similarly, resistance was observed to aminoglycosides, in particular Gentamicin (54.54 %), Amikacin (22.73 %) and fluoroquinolones (Tobramycin (50.91 %) and Ciprofloxacin (37.27 %)). In contrast, *Pseudomonas aeruginosa* showed high sensitivity to Amikacin (77. 27 %) and Meropenem (63.64 %).

3.3- Resistance phenotypes of *P. aeruginosa* isolates:

This study shows a high prevalence of *P. aeruginosa*-producing carbapenemase and ESBL.

Table II: Distribution of *P. aeruginosa* isolates according to resistance phenotypes

Type of phenotype	Number (n)	Percentage (%)
ESBL only	15	13.63
Carbapenemases only	21	19.09
ESBL+ Carbapenemases	8	7.27

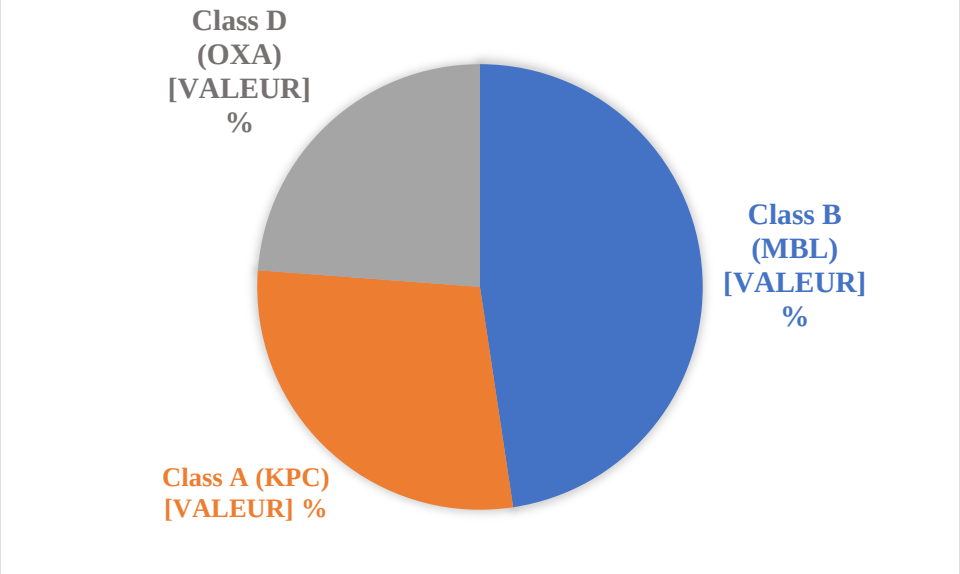

Figure 4 : Carbapenemase classes of *P. aeruginosa* isolates

Of the 110 *P. aeruginosa* isolates, 13.63 % (15/110) produced extended-spectrum β- lactamases and 19.09 % (21/110) produced carbapenemases, with 47.61% class B, 28.57 % (10/21) class A (6/21) and 23.8 % (5/21) class D (Figure 4). In addition, 7.27 % (8/110) of isolates showed co-expression of ESBL and Carbapenemases.

Extended-spectrum β-lactamases-producing *P. aeruginosa* isolates showed a statistically significant association with Yaoundé University Hospital (p = 0.011), the Hemodialysis unit (p = 0.041), inpatients (p = 0.001), as well as pus (p = 0.004) and catheter samples (p = 0.002) (Table III).

Table III: Distribution of *P. aeruginosa* isolates producing extended-spectrum beta-lactamases according to collection site, type of sample and department.

Variables	Total (n)	Production of ESBL n (%)	IC to 95 %	p-value
Collection sites				
Yaoundé University Hospital	38	7(16.66)	0.114-0.319	0.011
Yaoundé Military Hospital	27	4(14.81)	0.064-0.291	0.073
Yaoundé Central Hospital	21	2(9.52)	0.035-0.243	0.245
Yaoundé General Hospital	16	2(12.5)	0.060-0.394	0.49
Healthcare unit				
Hemodialysis	25	5 (20)	0.089-0.375	0.041
Internal Medicine	20	3 (15)	0.061-0.271	0.243
Surgical	18	2 (11.1)	0.032-0.226	0.495
Reanimation	15	1(6.7)	0.006-0.171	0.541
Emergency	10	2(20)	0.061-0.376	0.234
External	10	2(20)	0.061-0.376	0.234
Sample type				
Pus	25	5(20)	0.089-0.391	0.004

Catheter	15	3(20)	0.070-0.452	0.002
Blood	10	3(30)	0.108-0.603	0.179
Wound	9	2(22.22)	0.063-0.547	0.0567
Urine	6	2(33.33)	0.097-0.700	0.567
Hospitalisation				
Yes	78	10(12.82)	0.528-0.839	0.001
No	32	5(15.62)		
Antibiotic treatment				
Yes	65	9(13.84)	0.074-0.242	0.837
No	45	6(13.33)		

Carbapenemase-producing *P. aeruginosa* isolates showed a statistically significant association with Yaoundé University Hospital (p = 0.003), hemodialysis (p = 0.021) and intensive care units (p = 0.0021), inpatients (p = 0.019), as well as pus (p = 0.0033), catheter (p = 0.010) and wound (p = 0.005) samples (Table IV).

Table IV: Distribution of carbapenemase-producing *P. aeruginosa* isolates according to collection site, sample type and healthcare unit

Variables	**Total (n)**	**Production of Carbapenemase n (%)**	**IC to 95 %**	**P-Value**
Collection sites				
Yaoundé University Hospital	38	10 (26.31)	0.194-0.363	0.003
Yaoundé Military Hospital	27	5(18.51)	0.139-0.359	0.054
Yaoundé Central Hospital	21	3(14.28)	0.099-0.397	0.424
Yaoundé General Hospital	16	2(12.5)	0.072-0.423	0.552
Saint Martin Porres Dominican Hospital	8	1(12.5)	0.106-0.754	0.557
Healthcare unit				
Hemodialysis	25	5 (20)	0.089-0.342	0.021
Internal Medicine	20	3 (15)	0.112-0.493	0.046
Surgical	18	2 (11.11)	0.071-0.453	0.084
Reanimation	15	1(6.66)	0.027-0.372	0.315
Emergency	10	2(20)	0.099-0.746	0.146
External	10	2(20)	0.099-0.746	0.146
Pediatrics	7	1(14.28)	0.039-0.759	0.368
Intensive Care	5	5(100)	0.089-0.342	0.0021
Sample type				
Pus	25	5(20)	0.135-0.351	0.033
Catheter	15	6(40)	0.186-0.524	0.010
Blood	10	3(30)	0.029-0.349	0.075
Wound	9	5(55.55)	0.146-0.664	0.005
Urine	6	2(33.33)	0.047-0.561	0.358
Hospitalisation				
Yes	78	13(16.66)	0.101-0.299	0.019
No	32	8(25)		
Antibiotic treatment				
Yes	65	9(13.84)	0.074-0.225	0.223
No	45	12(26.66)		

3.4- Occurrence of Multiple antibiotic resistance indexes (MAR):

The multidrug resistance index (MAR) of *P. aeruginosa* isolates is shown in Table V. The MAR index of the isolates ranged from 0.27 to 0.72. The majority of isolates (23.33 %) had a MAR between 0.54 and 0.45, indicating resistance to more than half of the antibiotics tested.

Table V: Multidrug resistance index of *P. aeruginosa* isolates

MAR index	**0.72**	**0.63**	**0.54**	**0.45**	**0.36**	**0.27**	Total
Number of *P. aeruginosa* isolates	6	8	14	14	6	12	60
Percentage (%)	10	13.33	23.33	23.33	10	20	100

In order to compare the levels of multidrug resistance (MDR) between ESBL-producing and carbapenemase-producing isolates of *P. aeruginosa*, a Mann-Whitney U test was performed (Table VI). The results show that the mean MARs are significantly higher for ESBL isolates (mean = 0.70; standard deviation = 0.26) than for carbapenemase isolates (mean = 0.40; standard deviation = 0.375), with a p-value = 0.015. This result indicates a significant difference in resistance levels between the two phenotypes. The Chi² test revealed a highly significant association between MAR level and ESBL/carbapenemase phenotype (Chi² = 18.51; p = 0.00098).

Tableau VI : Association between multiresistance index and resistance phenotypes of *P. aeruginosa* isolates

Type of phenotype	**Mean**	**Std. Deviation**	**Std. Error Mean**	**P-value Test of Mann-Whitney U**	**P-value test chi²**	**IC à 95 %**
ESBL	0.70	0.26	0.067	0.015	<0.001	[0.56-0.84]
Carbapenemase	0.40	0.375	0.082			[0.23-0.58]

3.5- Distribution of species of *Enterobacteriaceae* isolated:

Table VII shows the distribution of *Enterobacteriaceae* species isolated by hospital. A total of 280 strains of *Enterobacteriaceae* were isolated in this study. The majority were from male patients, representing 64.64 % (181/280). *Escherichia coli* was the most frequently isolated species, accounting for 74.29 % (208/280). *Klebsiella pneumoniae* was the second most isolated species with 10.71 % (30/280), followed by *Enterobacter cloacae* with 5.36 % (15/280).

Table VII: Number and percentage of *Enterobacteriaceae* species isolated

Characteristics	**Number (n)**	**Percentage (%)**
Age (in years)		
Mean ± standard deviation	42.09 ± 24.01	
Sex		
Male	181	64.64
Female	99	35.35
Sex ratio	1.83	
Species		
Escherichia coli	208	74.29
Klebsiella pneumoniae	30	10.71
Enterobacter cloacae	15	5.36
Proteus mirabilis	10	3.57
Citrobacter freundii	8	2.86
Serratia marcescens	5	1.79
Morganella morgani	3	1.07
Providencia stuartii	1	0.36

3.6- Antibiotic resistance profile of *Enterobacteriaceae* species:

Table VIII illustrates the resistance profile of the most common species of *Enterobacteriaceae*. All species were highly resistant, up to 100 %, to penicillins and Cephalosporins. The highest rates of resistance to Carbapenems were observed in *E. coli*, (with 59.13 % resistance to Imipenem and 33.17 % to Meropenem) and in *K. pneumoniae* (with 16.66 % resistance to Imipenem and 20 % to Meropenem).

Table VIII: Proportion of antibiotic resistance in the most isolated species of *Enterobacteriaceae*

	E. coli **N=208**	***K. pneumoniae*** **N=30**	***E. cloacae*** **N=15**	***P. mirabilis*** **N=10**	***C. freundii*** **N=8**
Penicillins					
Amoxicillin+ Clavulanic	62.5	66.66	70	70	75
Cephalosporins					
Cefepime	66.34	90	66.66	60	87.5
Cefotaxime	61.5	90	66.66	80	75
Ceftazidime	80.76	100	86.66	100	37.5
Carbapenems					
Imipenem	59.13	16.66	13.33	10	0
Meropenem	33.17	20	20	20	0
Monobactams					
Aztreonam	53.84	50	40	60	12.5
Aminosides					
Amikacin	36.05	30	13.33	20	12.5
Gentamicin	72.59	70	66.66	50	62.5
Fluoroquinolones					
Ciprofloxacin	26.92	20	73.33	70	25
Nalidixic Acid	62.5	70	73.33	70	75
Ofloxacin	64.90	66.66	60	60	50

3.7- Resistance phenotype of *Enterobacteriaceae* species:

Table IX describes the distribution of ESBL and carbapenemase-producing strains according to collection site and *Enterobacteriaceae* species. Of the 280 isolates, 20.35 % (57/280) were ESBL producers, while 10.71 % produced carbapenemases. *E. coli* was the most represented species, with ESBL and carbapenemase production rates of 18.75 % and 10.57 % respectively. In addition, 3.57 % of isolates (10/280) expressed both types of enzymatic resistance simultaneously. *Enterobacteriaceae* producing ESBL and carbapenemase showed a statistically significant association with Yaoundé University Hospital ($p = 0.043$ and $p = 0.021$ respectively) and Yaoundé General Hospital ($p = 0.035$ and $p = 0.041$ respectively). The production of these enzymes was also significantly associated with certain bacterial species, notably *E. coli* ($p = 0.0001$ for ESBLs; $p = 0.0051$ for carbapenemases) and *K. pneumoniae* ($p = 0.0411$ for ESBLs; $p = 0.0455$ for carbapenemases). In contrast, *E. cloacae* was only significantly associated with ESBL production ($p = 0.0125$)

Table IX: Distribution of ESBL and carbapenemase-producing strains according to collection site and *Enterobacteriaceae* species.

Variables	**Total (n)**	**Production of ESBL n (%)**	**P-Value**	**Production de carbapenemase n (%)**	**P-Value**
Collection sites					
Yaoundé University Hospital	68	18(26.47)	0.043	10(14.70)	0.021
Yaoundé Military Hospital	75	13(17.33)	0.211	8(10.66)	0.341
Yaoundé Central Hospital	51	8(15.68)	0.451	6(11.76)	0.541
Yaoundé General Hospital	51	6(11.76)	0.035	5(9.80)	0.041
Saint Matin de Porres Dominican Hospital	35	3(0.85)	0.243	1(2.85)	0.1422
Species					
E. coli	208	39 (18.75)	0.0001	22 (10.57)	0.0051
K. pneumoniae	30	9 (30)	0.0411	4 (13.33)	0.0455

E. cloacae	15	6 (40)	0.0125	2 (13.33)	0.1573
P. mirabilis	10	2 (20)	0.1573	2 (20)	0.1573
C. freundii	8	1 (12.5)	0.3174	0	-
S. marcescens	5	0	-	0	-
M.morgani	3	0	-	0	-
P. stuartii	1	0	-	0	-

3.8 Occurrence of Multiple antibiotic resistance indexes (MAR)

The multidrug resistance (MDR) index of enterobacterial species is shown in Table X. The isolates presented a MAR index ranging from 0.25 to 0.66. Analysis of the MAR indices reveals a high proportion of multidrug-resistant strains among *E. coli, K. pneumoniae* and *E. cloacae,* with a majority of isolates presenting MAR indices ≥ 0.41.

Table X: Multidrug resistance index for *Enterobacteriaceae* species

species	**0.66**	**0.58**	**0.5**	**0.41**	**0.33**	**0.25**	Total
E. *coli*	5 (5 %)	20 (20 %)	18 (18 %)	23 (23 %)	18 (18 %)	16 (16 %)	100
K. pneumoniae	3 (10 %)	5 (16.6 %)	10 (33.3 %)	6 (20 %)	3 (16.6%)	3 (16.6%)	30
E. cloacae	-	3 (20 %)	2 (13.3 %)	7 (46.6%)	1 (6.6%)	2 (13.3 %)	15
P. mirabilis	-	-	1 (10 %)	1 (10 %)	2 (20 %)	6 (60 %)	10

In order to compare multidrug resistance (MDR) levels between ESBL-producing and carbapenemase-producing *Enterobacteriaceae* species, Chi^2 test was performed (Table XI). The results showed a highly significant association between the MAR level of the different species and the ESBL/carbapenemase phenotype ($Chi^2 = 23.41$; $p = 0.001$).

Table XI: Association between the multidrug resistance index and the resistance phenotypes of enterobacterial species

Type of phenotypes	**Species**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**IC to 95 %**	**P-value Chi ^{2}**
ESBL	E. *coli*	0.74	0.29	0.05	[0.63- 0.85]	0.001
	K. pneumoniae	0.55	0.34	0.08	[0.36-0.74]	
	E. cloacae	0.66	0.29	0.12	[0.42-0.90]	
	P. mirabilis	0.78	0.33	0.19	[0.43-1.13]	
Carbapenemase	E. *coli*	0.82	0.25	0.06	[0.71-0.93]	
	K. pneumoniae	0.55	0.34	0.11	[0.36-0.74]	
	E. cloacae	0.33	0.29	0.16	[0.11-0.55]	
	P. mirabilis	0.25	0.25	0.22	[0.06-0.44]	

4. DISCUSSION:

Infections caused *Enterobacteriaceae* and *Pseudomonas aeruginosa* represent a major challenge in healthcare settings due to their ability to develop resistance to antibiotics. This study determined the ESBL and Carbapenemase resistance phenotypes in E*nterobacteriaceae* and *Pseudomonas aeruginosa* recovered across five hospitals in Yaoundé. Of the 160 isolates collected, 68.75 % were confirmed as *P. aeruginosa*. The majority of isolates (34.54 %) came from Yaoundé University Hospital. The high patient volume at this hospital may be a contributing factor to this phenomenon. Pus (36.36 %) had the highest proportion of *Pseudomonas aeruginosa*, followed by catheters (22.72 %). A study conducted by Kameni *et al.,* 2025 in Yaoundé, Cameroon showed that 38.40 % of the samples were pus *P. aeruginosa*, a result similar to the trends observed in this study [29]. Similarly, kollef *et al*., 2019 reported that *P. aeruginosa* is among the most frequently isolated bacteria from venous catheter-related infections (40 %) [30]. The predominance of *P. aeruginosa* in catheters could be explained by its ability to colonise damaged tissue and form biofilms on the surfaces of medical devices [31]. The hemodialysis unit (27.72 %) recorded the highest percentage of *P. aeruginosa* isolates. Our results are in agreement with those of Gomez *et al*., 2018 who observed that 30 % of vascular access(venous and

arterial catheters) infections in hemodialysis were caused by *P. aeruginosa* [32]. Hemodialysis patients are particularly vulnerable to nosocomial infections due to the repeated use of vascular catheters. *P. aeruginosa*, capable of forming biofilms on catheters and medical equipment, is a major agent of bacteraemia and infections associated with medical devices [33].

Pseudomonas aeruginosa isolates showed a high rate of resistance to β-lactam antibiotics, particularly Ceftazidime (79.09 %), Aztreonam (77.27 %) and Ticarcillin (69.09 %). Similarly, a high resistance rate to aminoglycosides was observed, notably Gentamicin (54.54 %), Amikacin (22.73 %) and Fluoroquinolones (Tobramycin (50.91 %) and Ciprofloxacin (37.27 %)). These results are in line with those reported by Napa *et al.*, 2021 in Cameroon who also observed strong resistance to beta-lactam, particulary Tircacillin (86.66%) and Ceftazidime (40%), as well as resistance to aminosides (Tobramycin (60%)) and Fluoroquinolones, attributed to Ciprofloxacin (40%) [34]. *Pseudomonas aeruginosa* naturally produces a β- lactamase (Ampc) which gives it intrinsic resistance to Penicillins and certain Cephalosporins. Additionally, also possesses efflux pumps (MexA-MexB-OprM and MexX-MexY-OprM) that actively expel several classes of antibiotics (β-lactams, Aminoglycosides, Fluoroquinolones, Tetracyclines, Sulphonamides and Macrolides) [33].

Of the 110 *P. aeruginosa* isolates, 13.63 % produced Extended-spectrum β- lactamases and 19.09 % carbapenemases, with 47.61% class B (MBL), 28.57 % class A (KPC) and 23.8 % class D (OXA). In addition, 7.27 % of isolates showed co-expression of ESBLs and Carbapenemases. These results are similar to those of Klang *et al*., 2021 who reported a prevalence of 10-15 % of *P. aeruginosa* ESBL isolates in Asian hospitals [35]. Also, a study reported by Kameni *et al.*, 2025 revealed high rates in Cameroon, with 28.20 % *P. aeruginosa* isolates producing both carbapenemases and ESBL [29]. *P. aeruginosa* has a strong capacity to acquire plasmid resistance genes, which favours the dissemination of ESBLs. The presence of ESBLs *P. aeruginosa* leads to resistance to beta-lactams, particulary penicillins and cephalosporins, while the production of carbapenemases confers resistance to carbapenems, antibiotics often used as a last resort in serious infections. The co-production of these two types of β-lactamases is a cause for concern, as it considerably reduces the available therapeutic options [36].

ESBL and carbapenemase-producing *P. aeruginosa* isolates showed a statistically significant association with hemodialysis and intensive care units, hospitalized patients and pus and catheter samples. Our results are similar to those of Gomez *et al*., 2018 who reported a 25 % rate of ESBL producing *P. aeruginosa* in catheter-related infections at the hemodialysis unit [32] and those of Ramos *et al*., 2020 who found that 30 % of nosocomial infections in the hemodialysis unit were due to carbapenemase-producing strains [37]. The high rate of ESBL and carbapenemase producing isolates in the hemodialysis unit could be explained by the fact that, patients undergoing dialysis are exposed to repeated antibiotic therapy, favouring the selection of resistant strains.

P. aeruginosa isolates showed a MAR index that ranged from 0.27 to 0.72. The majority of isolates (23.33 %) had a MAR between 0.54 and 0.45, indicating resistance to more than half of the antibiotics tested. The Chi^2 test revealed a highly significant association between MAR level and ESBL/carbapenemase phenotypes. These results are similar to those of Sharma *et al*., 2021 in West Africa, who found a MAR ≥ 0.5 in 50 % of *P. aeruginosa* isolates [38]. A high MAR, as observed in our study, suggests high exposure to antibiotics and the bacterium's ability to acquire and maintain a variety of resistance mechanisms.

A total of 280 strains of *Enterobacteriaceae* were isolated in this study. *Escherichia coli* was the most frequently isolated species, accounting for 74.29 %. These results are similar to those reported by Renaud *et al*., (2019) in France, who found that *Escherichia coli* was the most frequently isolated species (67 %) [39]. The predominance of *Escherichia coli* in stool sample could be justified by the fact that, *E. coli* is a natural microbe of the gut microbiota and the digestive tract is its primary habitat [40].

The resistance profile of *Enterobacteriaceae* species shows high levels of resistance of up to 100 % to Penicillins and Cephalosporins. The highest rate of resistance was observed in *K. pneumoniae* species, with 100 % resistance to Ceftazidime, 90 % to Cefotaxime and Cefepime. Resistance to Carbapenems was also observed, with the highest rate of resistance in *E. coli* (59.13 % resistance to Imipenem and 33.17 % to Meropenem). These results are similar to those of Emilia *et al*., 2021 in Cameroun, who reported 78.4 % resistance to Cefotaxime and Ceftazidime, and 76.7 % to cefepime [41]. *Klebsiella pneumoniae* is naturally resistant to β-lactam antibiotics, and naturally possesses a gene encoding a chromosomal penicillinase that confers low-level resistance to penicillins (amino, carboxy- and ureido-penicillins) [8].

Of the 280 isolates, 20.35 % produced ESBLs and 10.71 % produced carbapenemases. *E. coli* was the most represented species, with an ESBL production rate of 18.75% and a carbapenemase production rate of 10.57 %. In addition, 3.57% of isolates expressed both types of enzymatic resistance simultaneously. These results are comparable to those of Djuikwo- Teukeng *et al*, 2021, who reported in Cameroon a prevalence of ESBL of 17.9 % in *Enterobacteriaceae* [42]. However, the prevalence of carbapenemases observed in this study is slightly higher than that reported in Senegal by Seck *et al*., 2020, which was 6.8 % [43]. In

addition, a significantly high proportion of ESBL- and carbapenemase-producing strains were observed at the Yaoundé University Hospital and the Yaoundé General Hospital. The species *E. coli* and *K. pneumoniae* were statistically associated with the production of ESBL and carbapenemases, which is consistent with the results of Murray *et al*. 2022 who identified these two species [44]. These situations may be explained by the frequent self-medication and uncontrolled use of broad-spectrum antibiotics, the overcrowding of public hospitals, increasing the risk of cross-transmission, the lack of strict antibiotic control policies and the lack of microbiological monitoring to guide treatment.

Enterobacteriaceae species showed MAR indices ranging from 0.25 to 0.66, with a high proportion of multidrug-resistant strains in *E. coli*, with the majority of isolates showing MAR indices ≥ 0.41. This trend was also observed by Olowe *et al*, 2019 in Nigeria who reported MAR indices between 0.2 and 0.7 [45]. The Chi^2 test showed a highly significant association between the MAR level of the different species and the ESBL/carbapenemase phenotype. This correlation was also demonstrated by Ahmed *et al*, 2021 in Sudan, where ESBL-producing strains showed significantly higher MAR indices than non-producing strains [46]. The high proportion of multi-resistant strains in our study can be justified by the inappropriate use of antibiotics, often without a medical prescription, the circulation of medicines of dubious quality, and the lack of rigorous control over the use of antimicrobials in public hospitals.

5. CONCLUSION:

These results highlight the emergence and worrying progression of *P. aeruginosa* strains and Enterobacteriaceae producing extended-spectrum β-lactamases (ESBLs) and Carbapenemases in several hospitals in Yaoundé (Cameroon), which could be attributed to several factors, including uncontrolled self-medication, high population density, overcrowded hospitals and poor hygiene in our hospital establishments. Faced with this situation, rigorous microbiological surveillance, better management of antibiotic use and more stringent hygiene measures are essential to limit the spread of these resistant strains and preserve the effectiveness of antimicrobial treatments.

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