# High prevalence of multidrug resistant and extended-spectrum β-lactamase-producing Escherichia coli and Klebsiella pneumoniae isolated from urinary tract infections in West region, Cameroon.

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Research Article

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# Abstract

## Background

Antimicrobial resistance remains a worldwide health problem with serious societal and economical repercussions. Multidrug resistant and Extended-Spectrum β-Lactamase producing-*Enterobacterales* (ESBL-E) are pathogens of critical public health priority that urgently require the research and development of new drugs. This study aims to determine the prevalence and assess the genes conferring resistance to β-lactams among *Escherichia coli* and *Klebsiella pneumoniae* isolated from patients with urinary tract infections (UTIs) in the West region, Cameroon.

## Methods

A cross-sectional study was conducted among two healthcare facilities during a four-month period from February to May, 2023. All mid-stream urine samples were collected from UTIs patients. The *Escherichia coli* and *K. pneumoniae* strains were identified using Enterosystem 18R kit following the manufacturer instructions. The antimicrobial susceptibility test (AST) was performed using the Kirby-Bauer disk diffusion method. The screening of ESBL production was done using ESBL ChromAgar medium combined with the double-disk synergy test (DDT). Antimicrobial resistance genes were detected using polymerase chain methods. The data analysis was performed using Excel 2016 and IBM SPSS version 20.

## Results

A total of 215 urine samples were collected and analyzed during the study period. A 31.62% (68/215) prevalence of *Enterobacterales* was detected with prevalence of 79.41% (54/68) and 14.70% (10/68) for *Escherichia coli* and *Klebsiella pneumoniae* respectively. The overall prevalence of ESBL-*Enterobacterales* was 64.70% (44/68). About 82% (36/44) of isolates were MDR and high antimicrobial resistance was observed for amoxicillin + clavulanic acid and ceftazidime. The resistance genes detected were $bla_{CTX-M}$, $bla_{TEM}$, *tet*(B) and *tet*(A), respectively.

## Conclusion

The findings of this study highlight the high burden of MDR and ESBL-*E. coli* and *K. pneumoniae* isolates from UTIs. The study emphasizes the necessity of routine screening and monitoring of antimicrobial resistance in healthcare facilities and community settings. It is critical to implement antimicrobial stewardship programs in the country and infection prevention and control (IPC) measures in hospital settings.

# Introduction

Hospital- and community-acquired urinary tract infections (UTIs) are amongst the most common infections caused by *Enterobacterales* affecting especially pediatric patients and women in low-and-

middle income countries (LMICs) [1, 2]. High prevalence of uropathogens have been reported in sub-Saharan Africa (sSA) with 89.17% in Nigeria, 39.13% in Uganda, 10.1% in Ghana and 21.2% among children in Gambia [3]. These reports shown that most species belonged to *Enterobacterales* including *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa* and were associated with numerous risk factors such as age, poor economic status, poor hygiene, hospitalization, catheterization, sexual activities, pregnancy and diabetes mellitus [3–5].

Emergence and escalation of extended-spectrum β-lactamase-producing *E. coli* and *K. pneumoniae* is aggravating the global concern of urinary tract infections. They are commonly associated with increased length of hospital stay, use of last-resort and often expensive drug and increase mortality [6]. Numerous studies reported high prevalence of UTI caused by ESBL-*E. coli* and *K pneumoniae* [2, 7–9].

Extended-spectrum β-lactamase (ESBL) enzymes are capable of hydrolyzing penicillin, broad-spectrum cephalosporins and monobactams leading to use carbapenems and quinolone as a last resort treatment option [10]. Its emergence generally derived from $bla_{CTX-M}$, $bla_{SHV}$ and $bla_{TEM}$ expression [10]. It is well known that $bla_{CTX-M}$ among *Enterobacterales* disseminate worldwide including in sub-Saharan Africa. However, here is still a paucity of data regarding the prevalence of β-lactams encoding genes among *E. coli* and *K. pneumoniae* in UTI patients in Cameroon and particularly in the Western region. This study aims at determining the prevalence, phenotypic and genotypic characteristics of ESBL-producing *E. coli* and *K. pneumoniae* isolated from urine of hospitalized and community patients at Bafoussam Regional Hospital and Dschang Regional Annex Hospital in West region, Cameroon.

# Methods
# 1. Study settings and design

This cross-sectional analysis study was conducted over a four-month period from February to May 2023 in two biggest public hospitals in the Western region of Cameroon. All urine samples from patients presenting signs and symptoms of hospital acquired infections (HA-UTI) and/or community acquired infection (CA-UTI) were collected at the medical laboratory of the Dschang Regional Annex Hospital and Bafoussam Regional Hospital. Demographic data were recorded using a case report form and questionnaire.

# 2. Culture and Identification

Clean catch mid-stream urines were cultured on Cysteine Lactose Electrolytes Deficient (CLED) agar using a calibrated loop 0.001 ml, and incubated in presence of oxygen at 37°C for 24 hours. All growing colonies were counted and leukocytes were enumerated with a Malassez cell. UTI was defined based on pyuria ($\geq 10^4$ leukocyte/mL of urine) and positive culture ($\geq 10^5$ colony-forming units) diffusion method.

Only bacteria that grew at a significant rate (Kass criteria) were identified by their morphological, metabolic and biochemical characters using Enterosystem 18R according to the manufacturer's instructions.

# 3. Antibiotic Susceptibility Testing (AST) and ESBL screening methods

Antimicrobial Susceptibility Testing (AST) was performed using Kirby-Bauer disc diffusion method on muller Hinton agar according to the Antibiogram Committee of the French Society of Microbiology (CA-SFM) guidelines. A panel of 12 antibiotics belonging to six different families were tested including: amoxicillin + clavulanic acid (AMC; 10 µg), cefoxitin (CFX; 30 µg), ceftazidime (CAZ; 30 µg), ceftriaxone (CRO; 30 µg), cefotaxime (CTX; 30 µg), imipenem (IMP; 30 µg), aztreonam (AZT; 30 µg), gentamicin (CN; 30 µg), amikacin (AN; 30 µg), ciprofloxacin (CIP; 5 µg), fosfomycin (FOS; 30 µg), nitrofurantoin (NIT; 30 µg). The production of ESBL was detected using through culture on medium CHROMagar™ ESBL (CHROMagar, Paris - France). The samples were then stored at -20°C in cryotubes containing trypticase soya broth supplemented with 20% glycerol for future uses. *Escherichia coli* ATCC25922 and *K. pneumoniae* ATCC700603 were used to assess the quality of the media and antibiotic discs. The inhibition zone diameters were measured and interpreted according to the criteria defined by CA-SFM 2022. The isolates being resistant to at least one antibiotic of three or more families of antibiotics tested were considered as multi-drug resistant bacteria (MDR).

# 4. Conventional and Multiplex polymerase chain reaction (PCR)

Genomic DNA was extracted from all ESBL-*E. coli* and *K. pneumoniae* isolates by boiling method as previously described [11]. Detection of $bla_{CTX-M}$, $bla_{TEM}$ and $bla_{OXA-48}$ genes was carried out by multiplex-PCR method using a BIO-RAD thermal cycler (Bio-Rad Laboratories, Mames-la coquette, France). The reaction was carried out in a 10 µL reaction mixture consisting of 5 µL of Dream Taq green Polymerase Master Mix 2x (New England Biolabs, Ipswich, MA, USA); 2.6 µL of nuclease-free water, 0.1 µL of each forward and reverse primers (10 µM) and 2 µL of DNA. Thermal cycler program was included initial denaturation (95°C for 3min), 30 cycles of denaturation at 95°C for 4s, annealing at 46.9°C for 40s, elongation at 72°C for 50s and final elongation at 72°C for 5 min. In addition, amplification of $bla_{SHV}$, *tet*(A) and *tet*(B) genes occurs in a 10 µL reaction mixture consisting of 5 µL Dream Taq Green Polymerase Master Mix 2x (ThermoFisher Scientic, Vilnius, Lithuania), 2.8 µL nuclease-free water, 0.1 µL each primer direct and reverse [10 µM] and 2 µl of DNA with approximately the same condition.

# 5. Agarose electrophoresis and gel visualization

PCR products were subjected to electrophoresis analysis performed on an agarose gel of 1.5% (w/v) that was run at 90 V for 45 min along with a 100 bp molecular ladder (New England Biolabs, MA, USA). After electrophoresis, the gel was stained in an ethidium bromide solution (0.5 µg/mL) for 15 min and briefly unstained with water. PCR products were then visualized under UV light using a gel documentation

system G-BOX Chemi-XL (Syngene, Cambridge, UK). An internal quality control for *bla* genes was assessed using a *K. pneumoniae* ATCC700603, then *tet*(A) and *tet*(B) have been done using previously whole genome sequenced isolates serving as internal quality controls (Unpublished result).

# 6. Statistical analysis

Data analysis was performed using Excel 2016 and IBM SPSS Statistics 20. Proportions were compared using the Fischer exact test and chi-square test as appropriate. A participant was considered positive to ESBL-E when at least one ESBL colony was detected. A participant was considered multi-drug resistant when an *Enterobacterales* isolates showed resistance to at least three different antibiotics belonging to three or more families with or without the presence of an ESBL phenotype. A p-value < 0.05 was considered statistically significant.

# Results

# 1. Demographic characteristics

A total of 215 urine samples were collected from Dschang Annex Regional Hospital (n = 107) and Bafoussam Regional Hospital laboratories (n = 108), with 68 (31.63%) of these being positives with at least one *Enterobacterales* (Fig. 1). Women were more infected than men (65.11%, 140/215 vs 34.88%, 75/215). The age of participants varies between 1 year and 49 years with a median age of 25 years (Table 1). Patients aged between 20 to 29 years constitute the most common age group (30.7%) of the population infected by *Enterobacterales*. In addition, female participants was the most infected (139/215; 64,7%) than male (75/215; 35,3%).

Table 1
Distribution of *Enterobacterales* isolated from urinary infections according to sex

| Variables | Isolates n (%) | | | | Total |
|---|---|---|---|---|---|
| | *E. coli* | *K. pneumoniae* | *P. mirabilis* | *C. freundi* | |
| **Sex** | | | | | |
| Female | 44 (81.48) | 8 (80.0) | 2 (66,66) | 1 (100) | 140 (65.11) |
| Male | 10 (18.51) | 2 (20.0) | 1 (33,33) | 0 (0) | 75 (34.88) |
| **MDR** | | | | | |
| MDR Positive | 42 (84) | 8 (16) | 0 | 0 | 50 |
| MDR Negative | 13 (72.22) | 2 (11.11) | 2 (11.11) | 1 (5.56) | 18 |
| **ESBL** | | | | | |
| ESBL Positive | 37 (84.09) | 7 (15.91) | 0 | 0 | 44 (100) |
| ESBL Negative | 18 (75) | 3 (12.50) | 2 (8.33%) | 1 (4.17) | 20 (100) |
| **Resistance genes** | | | | | |
| $bla_{CTX-M}$ | 35 (94.89) | 7 (71.42) | 0 | 0 | 42 (95.5) |
| $bla_{TEM}$ | 18 (48.64) | 2 (28.57) | 0 | 0 | 24 (54.5) |
| $bla_{SHV}$ | 1 (2.70) | 1 (14.28) | 0 | 0 | 2 (4.5) |
| *tet*(A) | 7 (18.92) | 1 (14.28) | 0 | 0 | 8 (18.2) |
| *tet*(B) | 8 (21.62) | 0 | 0 | 0 | 7 (15.9) |
| $bla_{OXA-48}$ | 2 (5.40) | 0 | 0 | 0 | 2 (4.5) |

## 2. Prevalence of ESBL-producing E. coli and K. pneumoniae

Out of the 68 *Enterobacterales* isolated, the most represented species were *E. coli* (54/68; 79.41%) and *K. pneumoniae* (10/68; 14.70%). The overall prevalence of ESBL- producing *Enterobacterales* was (n = 44; 64.70%) with ESBL-*E. coli* (n = 37/44; 84.09%) and ESBL-*K. pneumoniae* (n = 7/44; 15.91%) (Table 1).

## 3. Antibiotic resistance profile of ESBL -E. coli and K. pneumonaie

All ESBL-*E. coli* isolates tested displayed a high level of resistance to amoxicillin -clavulanic acid (30/37; 81.1%), ceftriaxone (28/37; 67.56%), ceftazidime (30/37; 67.56%), gentamicin (23/37; 62.16%), fosfomycin (31/37; 83.8%) and ciprofloxacin (29/37; 78.4%). In addition, ESBL-*K. pneumoniae* have shown a high-level resistance to nitrofurantoin (5/7; 71.43%), amoxicillin clavulanic acid (5/7; 71.43%),

aztreonam (4/7; 57.14%) and gentamicin (5/7; 71.43%) (Fig. 2). However, imipenem, amikacin displayed high susceptibility for both ESBL-*E. coli* and ESBL-*K. pneumoniae*.

## 4. Multidrug resistance of ESBL-producing E. coli and K. pneumoniae

Majority of ESBL-producing *Enterobacterales* were multi-drug resistant (42/44; 95.45%) with ESBL-*E. coli* as 85.71% (n = 36/42) and ESBL-*K. pneumoniae* as 14.26% (n = 6/42) isolates. The most prevalent phenotypic profile was **AMC-CRO-CTX-CAZ-F-ATM-AK-FOS-CIP-CN (**3/42; 7,14**%)** including 10 antibiotics from 5 different family (Table 2).

Table 2
Resistant patterns of ESBL-*E. coli* and *K. pneumoniae*

| Phenotypic profiles | Number of antibiotics | Number of antibiotic families | Frequency of isolates (%) |
|---|---|---|---|
| AMC-CRO-CTX-CAZ | 4 | 1 | 2(5.55) |
| AMC-ATM-FOS | 3 | | 2(5.55) |
| AMC-CN | 2 | 3 | 1(2.77) |
| AMC-CRO-CTX-CAZ-FOS | 5 | | 1(2.77) |
| AMC-CRO-CTX-FOX-AK-FOS-CN-IPM | 8 | | 2(5.55) |
| AMC-CRO-CTX-CAZ-F-ATM-CIP | 7 | | 2(5.55) |
| AMC-CRO-AK-FOS | 4 | 3 | 1(2.77) |
| AMC-CRO-CAZ-FOX-F-AK-CN | 7 | | 1(2.77) |
| AMC-CRO-CTX-CAZ-FOX-F-AK | 7 | | 1(2.77) |
| AMC-CRO-CAZ-F-FOS-CIP | 6 | | 1(2.77) |
| AMC-CRO-CTX-CAZ-FOS-CIP-CN | 7 | | 2(5.55) |
| AMC-CRO-FOX-F-FOS-CN | 6 | | 2(5.55) |
| AMC-CRO-CTX-FOX-F-FOS-CIP-PM | 8 | | 1(2.77) |
| AMC-CRO-CAZ-FOX-F-ATM-AK-FOS | 8 | | 2(5.55) |
| AMC-CRO-CAZ-ATM-AK-FOS-CIP-CN | 8 | 4 | 2(5.55) |
| AMC-CAZ-F-AK-FOS-CN | 6 | | 1(2.77) |
| AMC-CRO-CTX-CAZ-ATM-FOS-CIP-CN | 8 | | 1(2.77) |
| AMC-CRO-ATM-AK-FOS-CIP | 6 | | 1(2.77) |
| AMC-CRO-CTX-CAZ-F-ATM-AK-FOS-IPM | 9 | | 2(5.55) |
| AMC-CRO-ATM-AK-FOS-CIP-CN | 7 | | 1(2.77) |
| **AMC-CRO-CTX-CAZ-F-ATM-AK-FOS-CIP-CN** | **10** | | **3(8.33)** |
| AMC-CRO-CTX-F-AK-FOS-CIP-CN | 8 | | 2(5.55) |

| Phenotypic profiles | Number of antibiotics | Number of antibiotic families | Frequency of isolates (%) |
|---|---|---|---|
| AMC-CRO-CAZ-F-ATM-AK-FOS-CN | 8 | | 2(5.55) |
| AMC-F-ATM-AK-FOS-CIP-CN | 7 | | 1(2.77) |
| AMC-CAZ-FOX-F-AK-FOS-CIP | 7 | 5 | 1(2.77) |
| AMC-CRO-CAZ-FOX-F-FOS-CIP-CN | 8 | | 2(5.55) |
| AMC-CRO-CTX-F-ATM-AK-FOS-CIP-CN | 9 | | 1(2.77) |
| AMC-CRO-CTX-CAZ-F-ATM-FOS-CIP-CN | 9 | | 1(2.77) |

# 5. Characterization of resistance determinants

The overall prevalence of genes was $bla_{CTX-M}$ (42/44; 95.5%), $bla_{TEM}$ (24/44; 54.5%), $tet$(A)(8/44; 18.2%), $tet$(B)(7/44; 15.9%), $bla_{SHV}$ (2/44; 4.5%) and $bla_{OXA48}$ (2/44; 4.5%). A high prevalence of $bla_{CTX-M}$ was observed among ESBL-$E. coli$ (34/37; 91.89%) and ESBL-$K. pneumoniae$ (5/7; 71.42%). Also, a high prevalence of $bla_{TEM}$ was observed among ESBL-$E. coli$ compare to ESBL-$K. pneumoniae$ with 48.64% (18/37) and 28.57% (2/7), respectively. The prevalence of $tet$(A) and $tet$(B) genes detected among ESBL-$E. coli$ was 18.92% (7/37) and 21.62% (8/37) respectively. Each $tet$(A) genes was detected among ESBL-$K. pneumoniae$ (Table 1).

# Discussion

Urinary tract infections caused by ESBL-producing $E. coli$ and $K. pneumoniae$ have been widely reported worldwide and represent a critical public health challenge. The alarming resistance rates observed in sub-Saharan Africa by Murray et al. (2022) urge the importance of surveillance and monitoring efforts for better prevention and containment measures as well as evidence-based decision [12]. This study aimed to determine the prevalence and characterize phenotypically and genotypically the ESBL-$E. coli$ and ESBL-$K. pneumoniae$ in the West region of Cameroon.

The findings showed that $E. coli$ and $K. pneumoniae$ were the major $Enterobacterales$ species involved in urinary tract infections in the West region of Cameroon. The overall prevalence of $Enterobacterales$ species was 31.62%. This result is higher than those obtained in Madagascar (12,9%), Gambia (12.8%) and Ghana (10%) [3, 13, 14]. However, it is lower than those reported Cameroon (59.6%) by Nzalie et $al.$ (2016) in 2016 where the authors investigated UTIs among the two biggest hospital settings in Yaoundé and shown that $E. coli$ (50,9%) and $K. pneumoniae$ (16.4%) were the most important bacteria involved in UTI [15, 16]. This result showed that UTI prevalence's depend on the geographical location in Africa. The result is also lower than that reported in Tanzania (41%) in 2022 [15].

Our findings revealed that *E. coli* and *K. pneumoniae* were the most common *Enterobacterales* species implicated in UTI which affected predominantly women. This could be explained by the pathophysiology of urinary tract of women which is generally ascending and colonize by *Enterobacterales* especially *E. coli* coming from intestinal tract origin. This is in agreement with numerous African studies including Tanzania, Nigeria, Republic of Djibouti investigated *E. coli* (40%, 31.7%, 82.39%) and *K. pneumoniae* (28%, 17.5%, 9.86%) among Hospital and community acquired urinary tract infections [17].

The elevated prevalence of ESBL-*E. coli* in our study is alarming but similar to those obtained in India in 2023 (82.5%). However, this finding is higher than the results obtained in Iraq (71.7%), Iran (52%), Republic of Djibouti (41%), Algerie (37.1%), Tunisie (30.8%), Northern Ethiopia (27.8%) and Morocco (12.2%) [1, 18–20]. In addition, the prevalence of ESBL-*K. pneumoniae* is lower than those reported in India (74.3%) and Ethiopia (33.8%) [20] but higher than that obtained in the Republic of Djibouti (7%) [17–18]. The discrepancies observed could be explained by the fact that we have analyzed numerous isolates compare to those reported in these studies.

In this study, amoxicillin + clavulanic acid (81.1%), ceftazidime (67.56%), gentamicin (62,16%), fosfomycin (62.16%), aztreonam (59.45%) were the most resistant antibiotics against ESBL-*E. coli* [3, 15, 21]. In addition, ESBL-*Kp* were more resistant to amoxicillin + clavulanic acid (71.42%), aztreonam (71.42%), gentamicin (71.42%), ceftazidime (57.14%) and fosfomycin (57.14%). A moderate susceptibility to quinolone and β-lactams families have been observed, despite the broadly prescriptions of theses antibiotics commonly recommended by the physicians to threat UTIs caused by ESBL-*Ec* and ESBL-*Kp* in our context, as described by [3, 15, 21]. In contrast, the relative good sensitivity of nitrofurantoin, imipenem and amikacin against ESBL-*K pneumoniae* and ESBL-*E coli*. These findings are consistent with report suggesting that ESBL-*Ec* and ESBL-*Kp* are susceptible to the antibiotics [15]. Our findings corroborate with a Cameroonian study carried out in Garoua and where amikacin and imipenem had highest sensitivity on ESBL-*Enterobacterales* [19]. We could be explained by the fact that Imipenem is not the first line antibiotics recommended in the treatment of UTIs in our context leading to the best therapeutic option. This could further be explained by the non-existence of antimicrobial stewardship program in the country, self-medication and over-the-counter supply of antibiotics, over-reliance on antibiotics from physicians, sub-optimal diagnostic and antimicrobial susceptibility testing prior prescription that all contribute to the selective pressure on the microbiome and increasing antimicrobial resistance [22]. The lack of infection prevention and control measures and programs contribute to the fluidity of resistant bacteria between patients in hospitals and communities. The overall prevalence of MDR-*E coli* and MDR-*K pneumoniae* was observed which agreed with the results already reported [23]. This high level of MDR-*E coli* and MDR-*K pneumoniae* reported could be explained by the excessive and inappropriate use of antibiotics in West region in Cameroon, where antibiotics are easily accessible over the counter without a prescription.

Among the different ESBLs genes tested, $bla_{CTX-M}$ and $bla_{TEM}$ genes were the most frequently detected. This is an agreement with previous studies which showed that $bla_{CTX-M}$ was the most common ESBLs gene carried among *Enterobacterales* responsible for UTIs [17]. These findings disagree with the results

of Zemtsa et al (2022) where the high prevalence of $bla_{TEM}$ and $bla_{CTX-M}$ among HIV patients in Yaoundé in 2022 was 72% and 48%, respectively [24]. This result can be explained by the systematic prescription of third generation cephalosporins which promote the selection of resistant mutants.

## Conclusion

High prevalence of MDR and ESBL-producing *E. coli* and *K. pneumoniae* among patients suffering from UTIs in West Cameroon were reported. This study shown the high prevalence of community acquired urinary tract infections, intimating the need to understand the source of this infection. It revealed that imipenem and amikacin remain a antibiotics with a good activities against ESBL-*E. coli* and *K. pneumoniae.* This study highlights the imperative of antimicrobial stewardship implementation across the country. It emphazises the urgent need for antimicrobial stewardship, to fight against antimicrobial resistance through the implementation of national action plan at the regional and local levels.

## Abbreviations

MDR
Multidrug resistance
UTI
Urinary Tract Infection
CAUTI
Community Acquired Urinary Tract Infections
HAUTI
Hospital Acquired Urinary Tract Infections
ESBL-E
Extended Spectrum β-lactamase producing-*Enterobacterales*

## Declarations

### Ethics approval and consent to participate

This research was approved by the Regional Ethics Committee for Research in Human Health, West, Cameroon N°393/31/05/2023/CE/CRERSH-OU/VP. In addition, it was approved by the Research institute of the Centre of Expertise and Biological Diagnostic of Cameroon (CEDBCAM-RI) under the number (N° 002/02/22/LA/CEDBCAM-RI/DG). Written informed consent to participate in this study was provided by the participants or the  legal guardian/nearest relative for minor. The study was conducted in accordance with the declaration of Helsinki. In addition, the research authorizations of the various healthcare structures have been granted. All methods and protocols used were approved by the CEDBCAM-RI in accordance with the relevant national and international guidelines and regulations for research laboratory ethics.

## Data availability

The data are available upon request in accordance with confidentiality and privacy regulations from the corresponding author.

## Consent for publication

Not applicable

## Competing of interest

The authors declare no conflict of interest.

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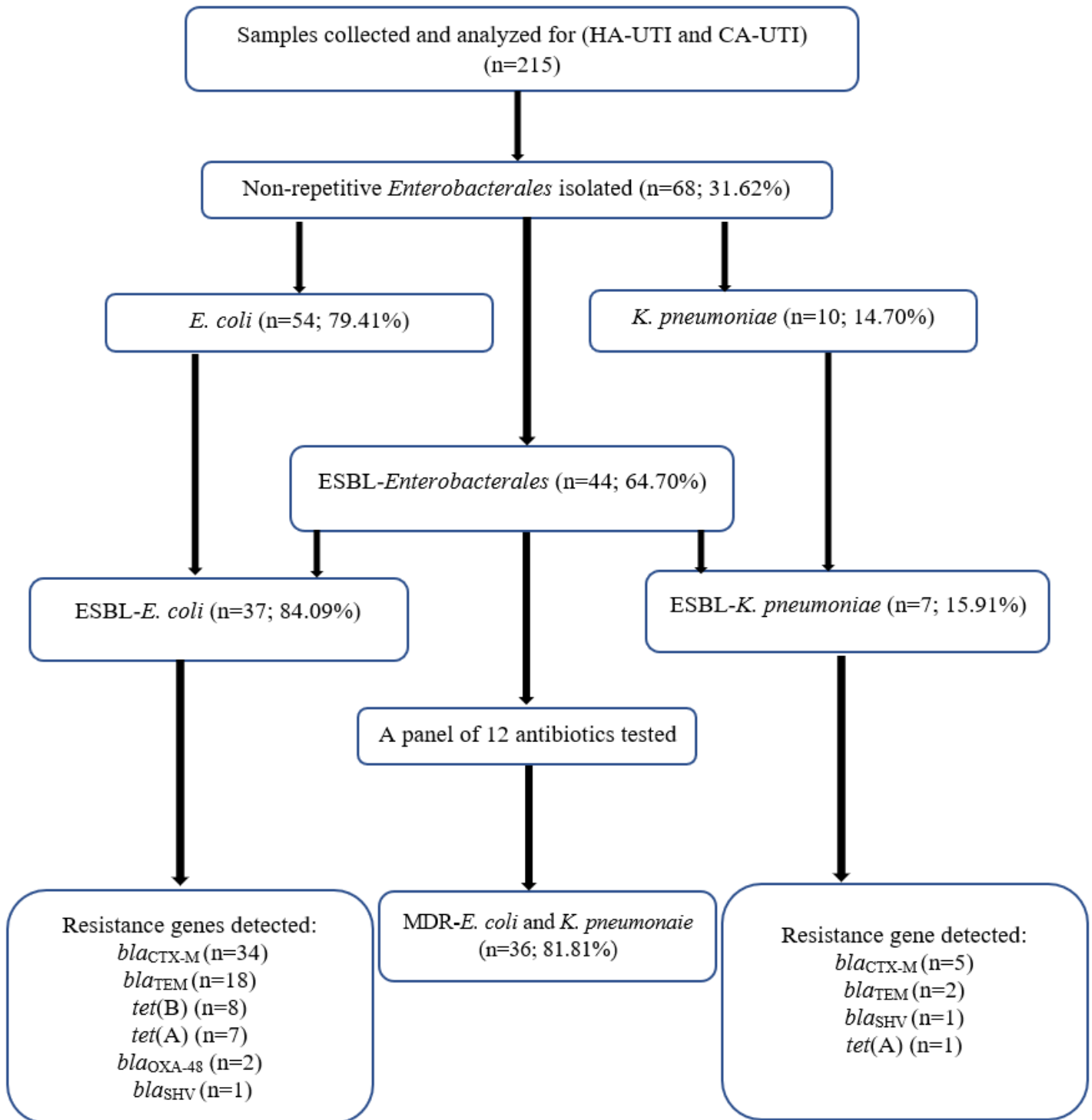
# Figures

**Figure 1**

Flowchart of participants isolates. MDR-*E. coli* and *K. pneumoniae* = Multidrug Resistance *E. coli* and *K. pneumoniae*, ESBL-E= Extended Spectrum β-lactamases producing-*Enterobacterales*, n=number.
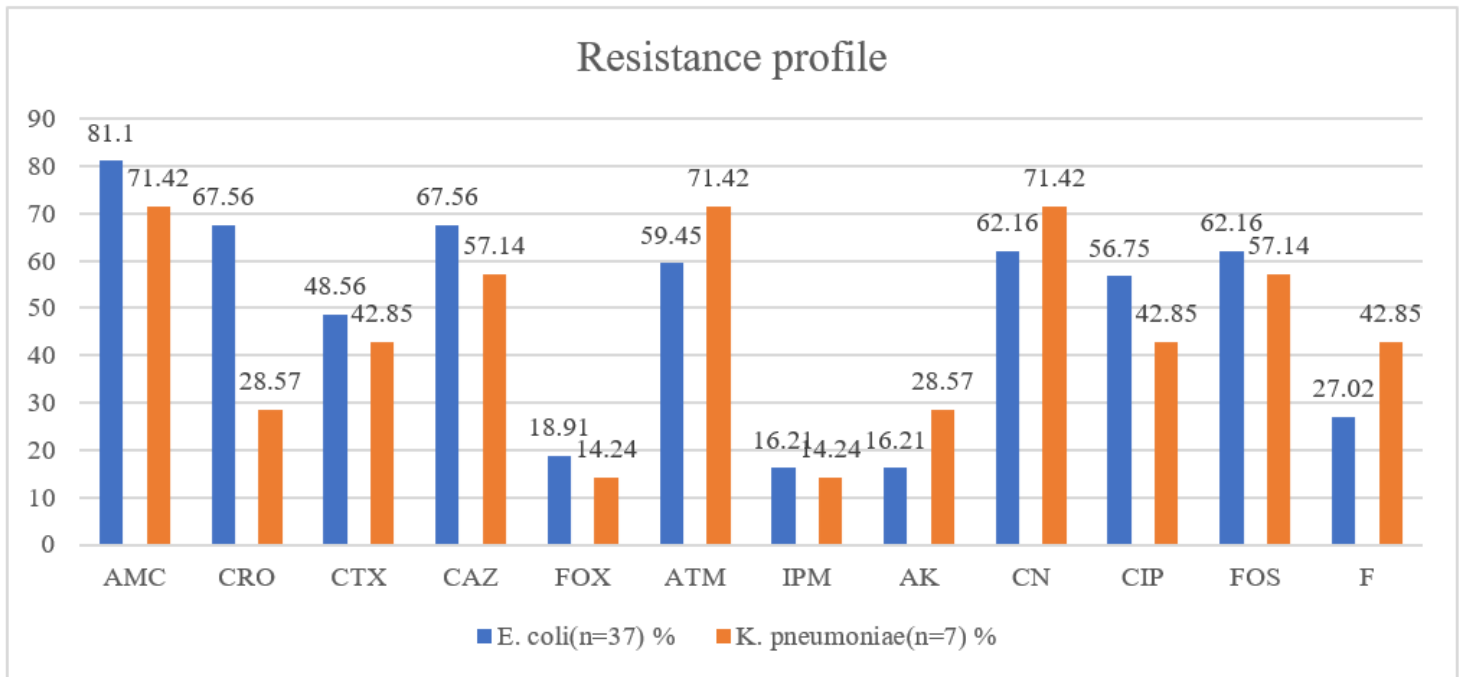
**Figure 2**

Resistance levels of ESBL-*E. coli* and *K. pneumoniae*. **AMC:** Amoxicillin + Clavulanic acid, **FOX:** Cefoxitin, **CAZ:** Ceftazidime, **CRO:** Ceftriaxone, **CTX:** Cefotaxime, **IPM:** Imipenem, **ATM:** Aztreonam, **CN:** Gentamicin, **AK:** Amikacin, **CIP:** Ciprofloxacin, **FOS:** Fosfomycin, **F:** Nitrofurantoin.

# Supplementary Files

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