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AZEEZ, Mufutau Mosunmade, OGUNDELE, Daniel Feranmi, ALADE, Wakeel Adekunle, AKINLABI, Akinwale Majid, OLANIYAN, Mathew Folaranmi. Carbapenemase-Producing Bacteria from Urinary Tract Infection (UTI) Cases at University College Hospital, Ibadan, Nigeria.Carbapenemase-Producing Bacteria from Urinary Tract Infection (UTI) Cases at University College Hospital, Ibadan, Nigeria

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Abstract

Urinary Tract Infections (UTIs) caused by Carbapenemase-producing bacteria (CPB) have become a substantial public health concern due to their increasing prevalence and resistance to antibiotics leading to challenges in treatment. The increase in the number of antibiotics that these bacteria are resistant to limits the options available to achieve effective therapy for these infections. The aim of this study was to assess the occurrence of Carbapenemase production among bacterial isolates from UTI cases, analyze antibiotic susceptibility profiles, and investigate the prevalence and diversity of bacterial pathogens in UTI cases at University College Hospital, Ibadan. A total of 126 participants, comprising of 68 females (54%) and 58 males (46%) with age range of 18 – 85 years, were enrolled in the study. About 20 mls of mid-stream urine sample collected into sterile plastic universal bottles was received from each of the consenting participants and processed for microscopy, culture, isolates identification, antibiogram testing and carbapenemase production using standard procedures. The prevalence of Carbapenemase-producing bacterial isolates among the study participants was found to be 9.2%. Notably, the prevalence of Carbapenemase production was observed to be higher among males with UTI, accounting for 62.5% of the cases compared to 37.5% in females. Comparative analysis between non-Carbapenemase-producing and Carbapenemase-producing bacterial isolates revealed significant impact of socio-demographic factors such as age and gender. Significant difference in prevalence was observed, particularly within the 30-45 and 45-60 age groups, signifying notable variations between the two age groups ($P<0.05$). However, gender distribution did not show statistically significant differences overall ($p>0.05$). The predominant bacterial uropathogens isolated from UTI cases included *Escherichia coli* (47%), *Klebsiella pneumoniae* (26%), and *Pseudomonas aeruginosa* (16%). Among Carbapenemase-producing bacterial isolates, *Klebsiella pneumoniae* showed the highest prevalence (37.5%), followed *by Escherichia coli* and *Pseudomonas aeruginosa*, each at 25%. The findings revealed a significant occurrence of Carbapenemase in the uropathogens frequently involved in UTI. The implications of these findings underscore the critical role of carbapenems as last-resort antibiotics and highlight the urgency in controlling the spread of Carbapenemase-producing organisms within the community. The observed rates of carbapenemase-producing bacteria (CPB) among UTI patients echo similar trends reported in studies from other regions, emphasizing the global significance of this issue and the need for robust strategies to mitigate the dissemination of multidrug-resistant bacteria in healthcare settings. This study serves as a crucial indicator of the prevalence of Carbapenemase-producing bacteria in UTI cases at University College Hospital, Ibadan, and emphasizes the imperative for concerted efforts in infection control measures and antibiotic stewardship to combat the rising threat of antimicrobial resistance.

Keywords: Carbapenemase-producing bacteria, Urinary Tract Infections, *Escherichia coli*

Introduction

Urinary tract infection (UTI) is an infection of any region of the urinary tract, from the pelvic calyces to the urethra. *Escherichia coli* and *Klebsiella spp,* two gram-negative *Enterobacteriaceae* bacilli, are frequently recovered from urine cultures of UTI patients (Nicolle, 2015). The different forms or types of UTIs are urethritis (affecting the urethra), cystitis (affecting the bladder) and pyelonephritis (affecting the kidneys). Cystitis, otherwise called bladder infection is the most common type of UTI while pyelonephritis (kidney infection) is less common but usually more serious than cystitis, when it occurs (CDC, 2021). Antibiotics drug resistance is often observed in bacterial isolates involved in urinary tract infections, usually attributed to their intrinsic ability to produce beta lactamases, which makes them to be resistant to the beta lactam group of antibiotics. Since beta lactamases cannot inactivate carbapenems, they are typically employed to treat infections caused by these drug-resistant types of bacteria (Nicolle, 2015). Carbapenemase-producing Enterobacteriaceae (CPE) are an important and increasing threat to global health as the development of Carbapenemase enzymes is the most significant mechanism of carbapenem resistance, which is regrettably on the rise in *Enterobacteriaceae* (van Duin and Doi, 2016).

Carbapenems, a class of broad-spectrum antibiotics, have traditionally been considered the last line of defense against multidrug-resistant bacteria, including those causing severe UTIs. However, the rise of Carbapenemase-producing bacteria, which produce enzymes capable of degrading carbapenem antibiotics, poses a serious threat to effective treatment (Nordmann *et al.,* 2011).

These bacteria exhibit resistance not only to carbapenems but often to multiple classes of antibiotics, severely limiting the available treatment options and increasing the risk of treatment failure, morbidity, and mortality. The prevalence and impact of Carbapenemase-producing bacteria in UTIs vary across different geographic regions, healthcare settings, and patient populations. Studies have reported varying rates of carbapenem resistance in UTI isolates, highlighting the need for local surveillance and research to understand the specific challenges and risks in each context (Akova *et al.*, 2012).

Because there are few effective treatments available, treating these carbapenem-resistant *Enterobacteriaceae* (CRE) infections is extremely difficult. The fatality rates of CRE infections, which range from 18-48% in patients on various treatment regimens, reflect this fact. Understanding the local epidemiology is essential for the execution of infection control strategies, hence it is important to characterize CRE with regard to their resistance mechanisms (Akova *et al.*, 2012).

Currently, CRE resistance to frequently tested newer medicines is of utmost concern and finding the best therapeutic interventions is urgently required. The best approach, according to several experts, is to maximize the use of older medications like colistin, Fosfomycin, and Nitrofurantoin. This idea of "reviving older antibiotics" is crucial in a nation like ours where the majority of newer medications have failed due to bacterial resistance mechanisms (Cassir *et al.,* 2014).

In a prospective study at UCH, where the frequency of Carbapenemase-producing organism in UTI patients was assessed, a subset of the carbapenemase-resistant organism (CRO) isolates was characterized using phenotypic techniques (Modified Carbapenem Inactivation Method). This involved using the most recent recommended susceptibility testing techniques, to evaluate the in-vitro activity of older drugs including Colistin, Fosfomycin, and Nitrofurantoin. The resistant isolates among them were then searched for plasmid-borne genes that conferred resistance to these three drugs (Cassir *et al.,* 2014).

Materials and Methods

Study area and Sampling: The study was carried out at the Medical Microbiology Department of University College Hospital (UCH), Ibadan. UCH is a renowned tertiary healthcare facility and teaching hospital that serves a diverse population from Ibadan and its surrounding regions. UCH was established by an Act Parliament in August, 1952 in response to the need for medical personnel

and other healthcare professionals in the country and the West African Sub-Region. The University College Hospital is strategically located in Ibadan, the largest city in West Africa. The Hospital's physical development began in 1953 on its current site and was formally commissioned on November 20, 1957, after completion. The Hospital has a large patient attendance.

Study Design: The study is a cross-sectional study across different age groups and gender among patients with UTI cases at UCH, Ibadan.

Study Population: Consenting participants who were UTI patients attending UCH, Ibadan, comprising of 58 males and 68 females were recruited to take part in the study. Participants were consecutively recruited into the study as they come. Participants were just enrolled once, and a single urine sample was collected from the participants.

Inclusion criteria: i. Suspected UTIs patients (males or females) in UCH, Ibadan who consented willingly were recruited for the study. ii. Patients with previous history of UTI infections were recruited for the study. iii. Patients that complained of painful urination were recruited for the study. iv. Patients with a previous history of sexually transmitted infections (STI) were recruited for the study.

Exclusion criteria: i Patients without any symptom of Urinary tract infections and those who refused to consent were excluded from the study. ii. Critically ill patients were excluded from the study. iii. Patients on antibiotics were excluded from the study.

Ethical Consideration: Ethical clearance for this study was obtained from University College Hospital, Ibadan before the commencement of the project with reference number UI/EC/23/0511 (Appendix I). Also, individual consent was obtained from each participant with assurance of anonymity and confidentiality. All protocols were translated to the local language they understand for participants who could not read or write. The study was voluntary to all UTI patients and non-maleficence or harmful to participants.

Study period: This study was carried out between July and November, 2023.

Sample Size: The sample size of 126 was obtained using Cochran's formular and prevalence value of 8% from a previous study (Manenzhe *et al.,* 2015). In addition to an attrition rate of 10%

Sample collection: Mid-stream clean catch urine samples (about 20 mls each) were collected from all the 126 participants in sterile, dry, wide mouthed, leak proof screw cap universal containers. Instructions on the procedure for collection were earlier given to the participants

Sample Processing: The samples were examined macroscopically, microscopically and culturally as earlier described by Ochei and Kolhatkar (2000).

Macroscopic Examination. This involved the visual examination of urine samples for their colour (yellow to amber) and clarity (clear or cloudy) and observations recorded.

Microscopic Examination. After culture, about 10 to 15 ml of well-mixed urine was poured into a test tube and centrifuged at 3000rpm for 5 minutes, with the supernatant discarded and the deposit mixed and examined microscopically using X10 and X40 objectives. Results were recorded accordingly.

Culture. The urine samples were cultured, using standard wire loop (semi-quantitative method) on the following agar plates: Cystine Lactose Electrolyte Deficient (CLED) agar and blood agar (BA) plates and incubated at 37^{o}C, aerobically and checked for growth after 18-24 hours of incubation as earlier described by Ochei and Kolhatkar (2000). Briefly, it was performed as follows:

i. A well flamed standard wire loop of 0.001ml (approx.1.5mm internal diameter) was dipped into a well-mixed un-centrifuged urine and inoculated on Cystine lactose electrolyte-deficient (CLED) agar and blood agar plates.
ii. The plates were then incubated aerobically at 35- 37^{o}C for 18 to 24 hours.
iii. The plates were then examined for significant bacteriuria,

The number of colonies observed on the each plate was recorded and $\geq 10^5$ organism /ml (100 colonies or more) were considered significant.

Identification of Bacteria isolates: The bacteria isolates growing on all cultured plates were identified and characterized using colonial morphology, Gram staining and biochemical reactions- lactose fermentation, indole, citrate utilization, urease and oxidase, carried out according to standard procedures as earlier described by Karah *et al.* (2020).

Antimicrobial Susceptibility Testing: All isolates obtained after 18 – 24 hours incubation were tested for antimicrobial susceptibility to carbapenem agents- imipenem, meropenem and ertapenem and other routinely tested antibiotics by Kirby- Bauer disc diffusion method following CLSI guidelines (Patel, 2017). Briefly, i for each isolate, 8-10 well isolated morphologically similar looking colonies were marked and inoculated into sterile nutrient broth. The broth was then incubated at 37°C for 2 hours. ii. The broth was then adjusted using 0.5 MacFarland's standard. A lawn culture was streaked onto Mueller Hinton agar plate using this adjusted broth within 15 minutes of adjustment. iii. The antibiotic discs were then placed onto the lawn cultures within 15 minutes of streaking and the plate incubated overnight at 37°C.

Detection of Carbapenemase production: The Modified carbapenemase inactivation method, a recent phenotypic method which has been published by the Clinical and Laboratory Standards Institute (CLSI) for the detection of Carbapenemase production by an organism was used, as earlier described by Pierce *et al.* (2017). Briefly.

i. A 1 ul loopful of test organism from an overnight agar plate was transferred to a tube containing 2ml of trypticase soy broth (TSB) and the suspension was vortexed.
ii. A standard 10-ug meropenem disc was added to the suspension and fully immersed.
iii. The TSB-disc suspension was incubated for 4 hours at 35°c in ambient air.
iv. Just prior to the completion of the 4-hours incubation cycle, a 0.5 McFarland suspension of *E. coli* ATCC 25922 was prepared and inoculated onto a Mueller Hinton agar plate following the routine disc diffusion procedure.
v. The meropenem disc was removed from the TSB suspension using a 10ul loop, taking care to remove excess liquid from the disc.
vi. The meropenem disc was immediately placed on the Mueller Hinton agar plate that has been inoculated with *E. coli* ATCC 25922.
vii. Both positive and negative controls were set up using the same procedure as above.
viii. The plate was incubated for 18-24 hours at 35°c in ambient air.
ix. Following overnight incubation, the zone of inhibition around the meropenem disc was measured. (CLSI, 2017).

Interpretation of Results: After incubation, plates were examined for inhibition zone of the antimicrobial susceptibility disk.

Positive Result: Carbapenemase positive – Zone of inhibition of 6-15mm diameter indicated production of Carbapenemase enzyme.

Negative Result: Carbapenemase negative – Zone of inhibition of $\geq$19mm diameter indicated absence of Carbapenemase production.

Zone 23mm = Negative
Figure 1: Modified Carbapenemase Inactivation method (mCIM) Negative control

Zone 6mm = Positive
Figure 2: Modified Carbapenemase Inactivation method (mCIM) Positive control

Statistical analysis: The data obtained from the study were collated and the values were imputed for statistical analysis using the Statistical Package for Social Science (SPSS) software version 23. The results from this study were presented in frequencies and mean. Association between variables was done using Chi-square. The level of significance was determined at 95% CI (i.e., a=0.05). P<0.05 is significant while P>0.05 is not significant.

Results

One hundred twenty-six subjects were enrolled in this study, with urine samples obtained from them. Table 1 shows the demographic (age and gender) characteristics of the studied samples. The age distribution revealed a majority falling within the 45–60 years and 60–85 years categories, constituting 30% and 36% of the sample, respectively. Additionally, individuals aged 18–30 years and 30-45 years accounted for 17% each. Also, the study population consisted of 46% males and 54% females. The mean age of the studied samples was calculated to be 54.27 years, with a standard deviation of 18.81 years.

Table 1: **Demographic Characteristics of the study participants**

Characteristics	Frequency	Percent (%)
Age(years)		
18-30	22	17
30-45	21	17
45-60	38	30
60-85	45	36
Gender		
Male	58	46
Female	68	54

The overall prevalence of urinary tract infection (UTI) in the study area was found to be 69% (Figure 3) which is noteworthy.

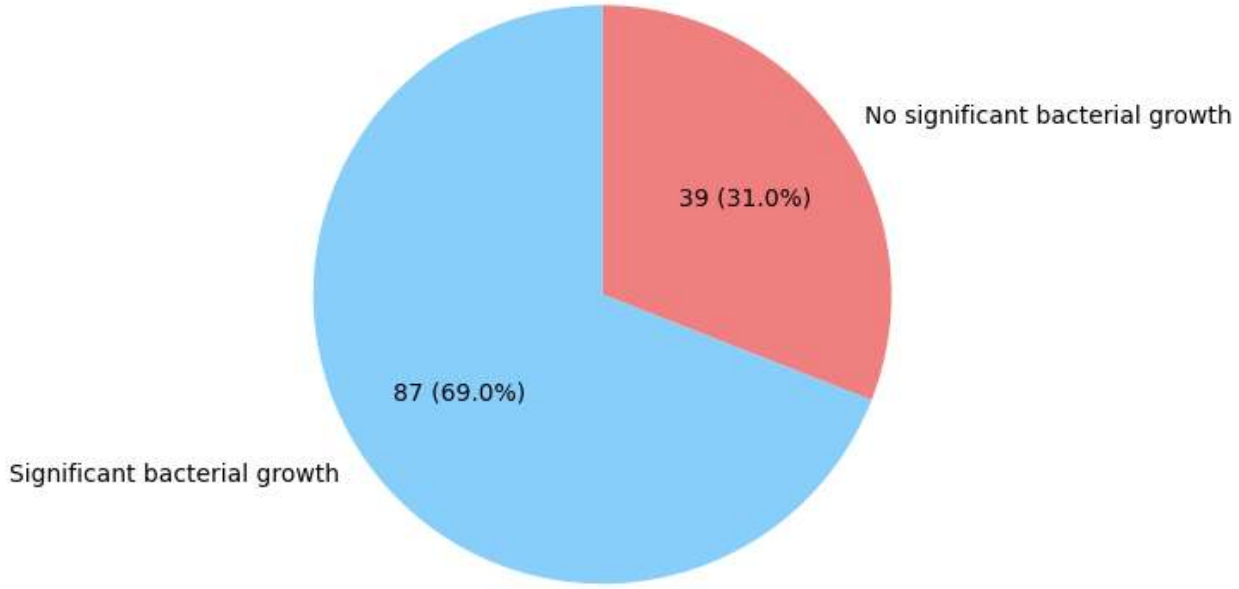

Figure 3: **Overall prevalence of UTI among the study participants.**

Table 2 captures the breakdown of isolated uropathogens. It presents the prevalence of various isolated bacterial species, including *Escherichia coli*, *Proteus vulgaris*, *Klebsiella oxytoca*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, and *Klebsiella pneumoniae*. *Escherichia coli* was the most prevalent among the isolated uropathogens, constituting 47% of the cases. This was followed by *Klebsiella* species, which collectively make up 29% of the cases, with *Klebsiella pneumonia* being more prevalent (26%) than oxytoca (3%). Then, *Pseudomonas aeruginosa*, represents 16% of the cases. The *proteus* genus was the least isolated, with *Proteus mirabilis* accounting for 6% of the cases, and *Proteus vulgaris* was identified in 1% of the cases.

Table 2: **Distribution of isolated bacterial uropathogens**

Organism	No	Percentage (%)
Escherichia coli	41	47
Proteus vulgaris	1	1
Klebsiella oxytoca	3	3
Pseudomonas aeruginosa	14	16
Proteus mirabilis	5	6
Klebsiella pneumonia	23	26

Figure 4 illustrates the prevalence of Carbapenemase-producing bacteria in isolates, revealing that 9.2% of the isolates are associated with Carbapenemase production, while 90.8% are not Carbapenemase-producing.

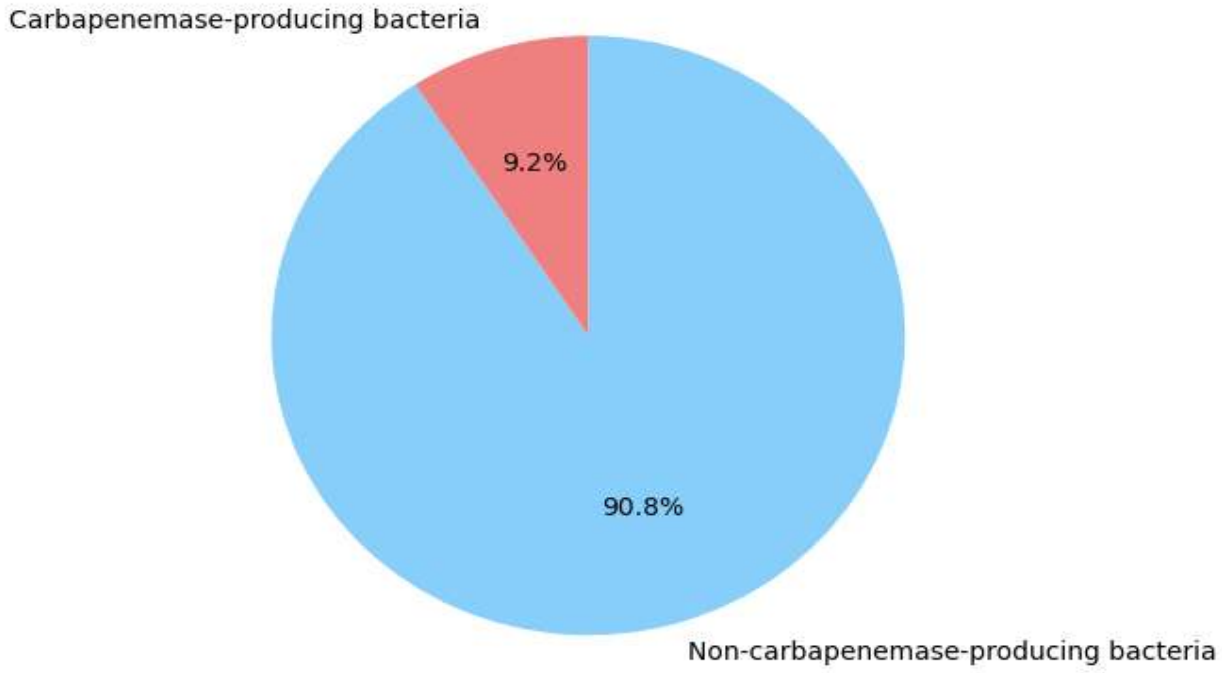

Figure 4: **Prevalence of Carbapenemase-production among bacterial isolates.**

The distribution of Carbapenemase-producing bacterial isolates was shown in table 3. Notably, *Klebsiella pneumoniae* has the highest percentage among the identified species, accounting for 37.5% of the Carbapenemase-producing isolates. *Escherichia coli* and *Pseudomonas aeruginosa* both follows with 25%, *Klebsiella oxytoca* was the least 12. 5%.

Table 3: **Distribution of Carbapenemase-producing bacterial isolates**

Organism	Count	Percentage (%)
Klebsiella oxytoca	1	12. 5
Escherichia coli	2	25.0
Pseudomonas aeruginosa	2	25.0
Klebsiella pneumoniae	3	37. 5

Figure 5 illustrates the distribution of Carbapenemase-producing bacterial isolates. Notably, *Klebsiella pneumoniae* has the highest percentage among the identified species, accounting for 37.5% of the Carbapenemase-producing isolates. *Escherichia coli* and *Pseudomonas aeruginosa* both follows with 25%, *Klebsiella oxytoca* was the least 12. 5%.

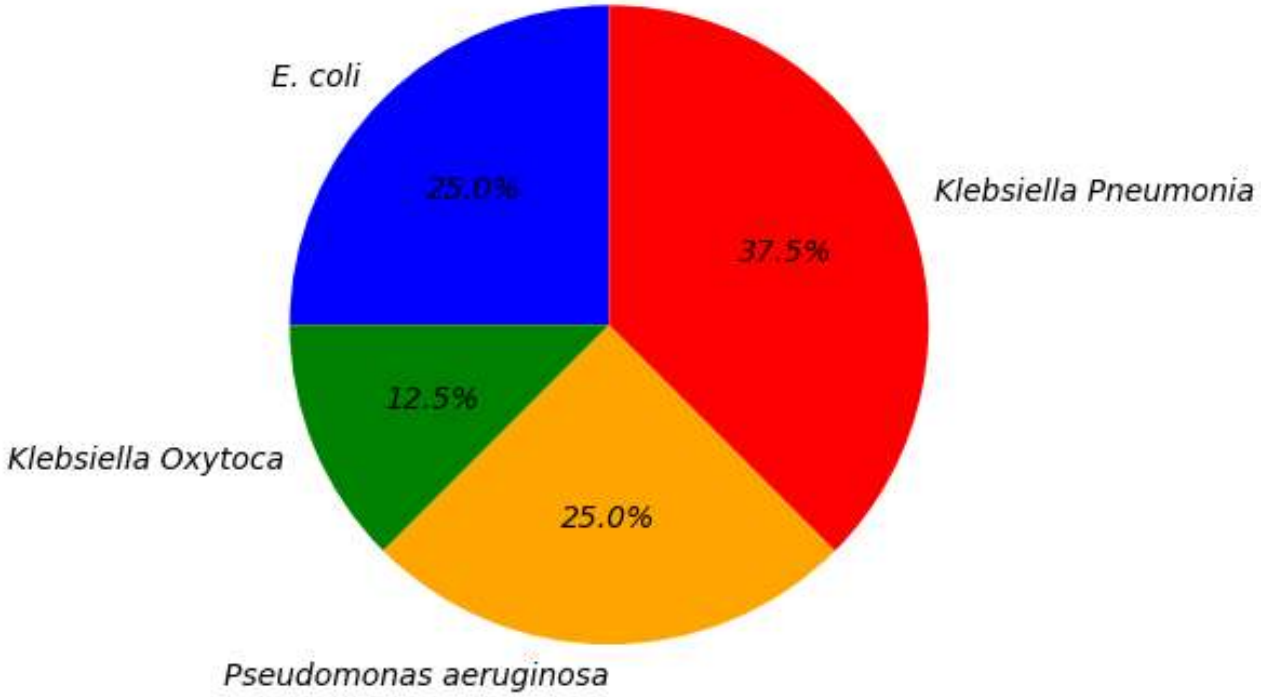

Figure 5: Distribution of Carbapenemase-producing bacterial isolates

A detailed comparison of demographic and clinical parameters between non-Carbapenemase-producing bacterial isolates (N=79) and Carbapenemase-producing bacterial isolates (N=8) in UTI samples was shown in table 4. The examination of age distribution unveiled noteworthy variations, particularly in the 30-45 and 45-60 age groups, where the number of cases differed significantly between the two bacterial types. The Chi-square (X^2) test yielded a statistically insignificant X^2 value of 3.57, resulting in a p-value of 0.31. Regarding gender distribution, differences were observed between males and females. However, the overall comparison indicated a non-significant X^2 of 3.82 with a p-value of 0.57. Analysis of WBC counts across different categories revealed indicates a significant association between white blood cell counts and the different categories, as evidenced by the Chi-square (X^2) test statistic of 7.60 and a corresponding p-value of 0.05.

Table 4: **Comparison of demographic and clinical parameters between Carbapenemase-producing non-Carbapenemase bacteria isolates from UTI cases at UCH, Ibadan**

	Non-Carbapenemase-producing bacteria (N=79)	Carbapenemase-producing bacteria (N=8)		
Age group(years)			X^2	**P-value**
18-29	14	0	3.57	0.31
30-44	11	0		
45-59	19	3		
60-85	35	5		
Gender			3.82	0.57
Male	42	5		
Female	37	3		
WBC (P/HPF)			7.60	0.05
0-5	3	0		
5-10	16	5		
10-20	13	0		
Numerous	47	3		

Table 5 provides a comprehensive overview of the antimicrobial susceptibility pattern of carbapenemase-producing bacteria. Notably, *Escherichia coli* exhibits susceptibility to antibiotics such as AK (60%), CT (100%), and MEM (100%), but resistance to CT (0%) and CIP (100%). *Klebsiella oxytoca* displays susceptibility to AK (100%) and CT (100%) but exhibits resistance to CAZ (100%) and ETP (100%). Similarly, *Klebsiella pneumonia* shows susceptibility to AK (67%) and CT (100%), with resistance observed for CRO (100%) and CAZ (100%). *Pseudomonas aeruginosa* demonstrates susceptibility to AK (25%) and CT (100%) but resistance to CXM (100%) and ETP (100%). These findings underscore the varying responses of carbapenemase-producing bacterial strains to different antibiotics, crucial information for guiding effective treatment strategies.

Table 5: Antimicrobial susceptibility patterns of Carbapenemase-producing bacteria

Bacteria	Pattern	AK (%)	CT (%)	CXM (%)	CRO (%)	CAZ (%)	MEM (%)	TZP (%)	CIP (%)	AUG (%)	CN (%)	CO (%)	FOX (%)	ETP (%)	NIT ()	GM ()	AMC ()	ETP ()
E. coli	S	3(60)	3(100)	0(0)	0(0)	0(0)	0(0)	1(33)	0(0)	0(0)	0(0)	2(100)	0(0)	0(0)	0	0	-	-
	R	2(40)	0(0)	4(100)	5(100)	5(100)	4(100)	2(67)	2(100)	1(100)	1(100)	0(0)	1(100)	0(0)	100	100	-	-
Kleb Oxytoca	S	2(100)	2(100)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	-	0(0)	-	-	-	0	-	-
	R	0(0)	0(0)	1(100)	1(100)	2(100)	2(100)	1(100)	1(100)	(100)	-	1(100)	-	-	-	100	-	-
Kleb. Pneumoniae	S	2(67)	1(100)	0(0)	0(0)	0(0)	0(0)	-	0(0)	-	-	1(100)	0(0)	0(0)	0			
	R	1(33)	0(0)	1(100)	3(100)	3(100)	2(100)	-	3(100)	-	-	0(0)	1(100)	1(100)	100	-	100	100
P aeruginosa	S	1(25)	1(100)	-	0(0)	0(0)	0(0)	0(0)	0(0)	-	-	100	-	0(0)	-	-	-	0
	R	3(75)	0(0)	-	1(100)	5(100)	2(100)	5(100)	5(100)	-	-	0(0)	-	2(100)	-	-	-	100

AK (Amikacin), CT (Cefotetan), CXM (Cefuroxime), CRO (Ceftriaxone), CAZ (Ceftazidime), MEM (Meropenem), CIP (Ciprofloxacin), AUG (Amoxicillin/Clavulanate), CN (Gentamicin).ETP (Ertapenem), TZP (Piperacillin/Tazobactam), FOX (Cefoxitin), CO (Collistin)

Discussion

Urinary tract infections (UTIs) are a prevalent public health issue and rank second among infectious diseases in medical practice. Effective therapy of these infections caused by Gram-negative bacteria (Bonkat *et al*., 2017), becomes a challenge due to Carbapenemase-producing *Enterobacteriaceae* (CPE). These bacteria, capable of breaking down crucial antibiotics like penicillins, cephalosporins, and carbapenems (Begum *et al*., 2016), complicate the treatment of UTIs, especially with last-resort antibiotics such as carbapenems. The World Health Organization categorized Carbapenemase-producing *Escherichia coli* and *Klebsiella pneumoniae* as "critical" and "high priority" pathogens in 2017 (Nomeh *et al*., 2022).

The *Enterobacteriaceae* family, common culprits behind hospital and community UTIs, are increasingly resistant to primary and secondary-line antibiotics. The escalating global rise in carbapenem resistance due to Carbapenemase-producing *Enterobacteriaceae* (CPE) has led to a severe public health crisis, endangering healthcare delivery and patient safety (Van *et al*., 2016).

The overall prevalence of 69% was high with the predominant isolate being *Escherichia coli* representing 47% and *Klebsiella pneumoniae* at 26%. The prevalent rate observed in this study aligns with previous research findings by Mlugu et al. (2023) with a reported prevalence of 47% for *Escherichia coli* and Suwaiba *et al*. (2020), whose work also showed *Escherichia coli* as the most prevalent at 28%. However, there is discordance in the prevalence rate of *Klebsiella pneumoniae*, which in this study was 26% as against 13% reported by Suwaiba *et al.* (2020) and 11.4% reported by Mlugu *et al.* (2023). This discrepancy in reported prevalence rates for *K. pneumoniae* emphasizes the need for careful consideration, when evaluating the spectrum and prevalence of bacteria causing urinary tract infections.

The high prevalence of *Escherichia coli* (47%) and *Klebsiella pneumoniae* (26%) in urine samples concurs with the assertion that they are the most common *Enterobacteriaceae* associated with UTIs (May *et al*., 2015). These bacteria pose treatment challenges due to their acquired resistance to multiple antimicrobial agents and intrinsic factors (Sharma *et al*., 2012).

This study found 9.2% of the isolates to be associated with Carbapenemase production, while 90.8% were not Carbapenemase-producing. This high prevalence of Carbapenemase-production among bacterial isolates from the study participants contrasts with the 2.73% reported by Eshetie *et al*. (2015). Disparities in the reported carbapenemase-producing *Enterobacteriaceae* (CPE) prevalence percentages among previous studies may stem from diverse antibiotic usage, trends in carbapenem utilization, cultural factors, patient transfers, population targets, sample sizes, and methodologies impacting CPE epidemiology as earlier posited (Eshetie *et al*., 2015).

The disturbing trend of high resistance of bacterial isolates from clinical specimens is also observed in this study study. *Escherichia coli* isolates displayed considerable resistance to nearly all administered antibiotics, with resistance rates at 75% and sensitivity at 25%. *Klebsiella pneumoniae* isolates showcased high resistance to imipenem, cefuroxime, and ceftriaxone but relatively lower resistance to cefotetan, amikacin, and colistin (Table 5). Colistin, gentamicin, and amikacin play vital roles in treating Carbapenemase-resistant *Enterobacteriaceae* (CRE) UTIs (Aslan *et al*., 2022).

Approximately 50% of the tested strains exhibited sensitivity to gentamicin, whereas ceftazidime, piperacillin-tazobactam, and fluoroquinolones (previously significant options), now face over 80% resistance levels. This echoes Eshetie *et al*. (2015) findings attributing *Enterobacteriaceae's* multidrug resistance to enzymes like carbapenemases, which significantly contribute to drug resistance in this bacterial family. This emergence of *Klebsiella pneumoniae* carbapenemase (KPC) production extends beyond the confines of *Klebsiella pneumoniae* alone, showcasing a worrying trend in *Enterobacteriaceae*. The KPC-producing strains may have different levels of resistance to carbapenems, due to additional mechanisms such as different expression levels

of porins and efflux pumps associated with the production of extended spectrum β-lactamases (Vera-Leiva *et al.,* 2017).

Infections stemming from the production of carbapenemase by *Enterobacteriaceae* have escalated in complexity and pose a significant threat to successful treatment regimens (Vera-Leiva *et al.,* 2017). Studies, such as that conducted by Hussaini *et al*. (2017), highlight this widening spectrum of bacterial resistance mechanisms, emphasizing the expanding prevalence of KPC production among various members of the *Enterobacteriaceae* family.

Carbapenems, a crucial antibiotic against multi-drug resistant (MDR) Gram-negative bacteria, face a global threat due to bacterial production of Carbapenemase enzymes, with multiple risk factors contributing to the acquisition of Carbapenemase-producing bacteria in healthcare settings. Carbapenems are the last line of defence against ever more prevalent MDR Gram-negative bacteria, but their efficacy is threatened worldwide by bacteria that produce Carbapenemase enzymes (Meletis, 2016). Many risk factors may be associated with the acquisition of Carbapenemase-producing bacteria in healthcare settings, which may include, recent antibiotic therapy, prolonged hospital stay, use of invasive devices and immunosuppression.

Conclusion

Carbapenems are considered as last-resort antibiotics for the treatment of infections caused by multidrug-resistant Gram-negative bacteria. The 9.2% prevalent rate of carbapenemase-producing organism (CPO) mostly among *Enterobacteriaceae* in urinary tract infection patients observed in this study is significant in its alignment with reports from previous studies from other parts of the world and therefore emphasizes the urgent need to control CPO spread within the community.

Recommendation: Continuous monitoring and surveillance for CPOs and reducing the usage of antibiotics by observing UTI prevention methods are recommended.

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Conflict of interest

The authors report no conflicts of interest in this work.

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