Carbapenem resistance associated with coliuria among outpatient and hospitalised urology patients

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Abstract

The World Health Organization in 2017 listed carbapenem resistant Enterobacteriaceae (CRE) with critical priority for research. A research to assess carbapenem resistant Escherichia coli (CREc) in coliuria among the outpatients and inpatients of a tertiary health institution was carried out using conventional methods, polymerase chain reaction, Sanger sequencing, and bioinformatics. There were 39 positive coliuria cases from the urine samples collected from a total of 126 patients with various genitourinary diseases. The E. coli enumeration (log10 CFU/mL) revealed that 82.1% (n = 32) of the samples showed significant coliuria, 12.8% (n = 5) showed non-significant coliuria while 5.1% (n = 2) showed indeterminate coliuria even when repeated. Significantly higher numbers (p > 0.05) of the sampled inpatients yielded positive coliuria (57.9%) than the outpatients. Though there were significantly more (P > 0.05) urology female patients (n = 77) than male (n = 49), coliuria was more prevalent in sampled male patients (34.9%) than female (28.6%). Highest prevalence of coliuria was observed among the age range (18–30) years. Selected CREc that was sequenced and the sequences submitted to GenBank of National Center for Biotechnological Information (NCBI) were Escherichia coli AYO-WINI111 and Escherichia coli AYO-WINI112 with accession number MT735391 and MT735392, respectively. High resistance was observed against ertapenem (53%), imipenem (62%), meropenem (48%), and doripenem (47%), while 7%–22% of the isolates showed phenotypic intermediate carbapenem resistance. Critically dangerous CREc are harboured by large number urology patients in the study area, depicting the need for more attention in the management of the condition, as CREc are close to achieving totally antibiotic resistance.

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Introduction

The “Medical Dictionary for Regulatory Activities” Terminology (MedDRA) classified coliuria as Escherichia urinary tract infection (UTI). Since the count of bacteria is vital in bacteriuria including the coliuria, their counts can be significant, insignificant [1], and immediately significant. Coliuria with count ≥5 log CFU/ml lacking clinical symptoms are referred to significant asymptomatic coliuria. Due to lack of symptoms, they are left untreated in large percentage of individuals, especially women [2]. Pathogens from coliuria contribute extensively to bacterial loads in municipal wastewater treatment plants [3,4], septic systems [5] as well as cesspits and soakpits [6]. Coliuria belongs to the most prevalent groups of bacterial infections in humans [7]. Some estimations placed the prevalence of minimum coliuria per gender at 10.3 for women to men, with those women who experienced recurrence with indices that ranged from 0.27 to 0.48 [8,9].
Coliuria constitutes a little less than half of nosocomial infections and half of bacterial infections that contribute to longer period of hospitalisation [10], with attendant economic loss [11,12] and high mortality [13]. Different types of symptomatic coliuria may include, but not limited to pyelonephritis and cystitis [11]. Some not directly classified during laboratory culture requisitions may simply be classified as UTI. The symptomatic coliuria or UTIs may be subsequent to complication like Benign Prostatic Hyperplasia (BPH) which is a form obstruction of lower urinary tract prevalent in adult male patients [14]. BPH usually progresses to bladder outlet obstruction (BOO) that precedes UTIs [14].

The bacterium E. coli in coliuria is recognised as the most versatile and ubiquitous microbe [15]. The bacterium is acknowledged as gut commensal as well as pathogens, which may be either diarrhoeagenic E. coli [16,17] or extraintestinal pathogenic E. coli [15]. The bacteria have been pathotyped by various researchers [18,19]. UTIs have been prominent among the infections for which E. coli is an aetiological agent [20–22]. Uropathogenic E. coli is the most prevalent extraintestinal pathogen and it is the primary cause of UTIs all over the world [21,23].

Potential predisposing factors for coliuria include poor toilet habit and personal hygiene, multiple sex partners, anal sex, immunosuppression, use of indwelling catheters, among others [24,25]. Badran et al. [24] identified hygiene and sexual behaviours as potential factors responsible for coliuria. In the Amiri et al. [24] studies, those not practicing postcoital washing had odd ratio (OR) of 2.89 and those accustomed to washing their genital frontward from anus, with potential to bring E. coli to the genitalia had OR of 2.96. HIV/AIDS related immunosuppression has long been established as a predisposing factor to coliuria and indeed all kinds of bacteriuria [25]. Prolonged catheterisation predisposes to coliuria and urinary tract infection [26].

Carbapenems which are antibiotics in the last line of defense are importantly prescribed against some critical pathogens and before now, almost all Enterobacteriaceae were treatable with excellent therapeutic success [27]. The antibiotic group which includes imipenem, meropenem, ertapenem and doripenem is lethal to bacteria that produce various types of beta lactamase enzymes [28,29], being a broad-spectrum antimicrobial with protected β-lactam ring [30].

As resistance of carbapenem is being reported, Enterobacteriaceae reported with such attributes show worrisome trend of failure to other antibiotics [29]. A report on Statnews.com as reviewed by Adegoke et al. [29] showed how a Nevada woman died in the United States from carbapenem-resistant Enterobacteriaceae (CRE) infection that resisted 26 different antibiotics [31]. So, the WHO [32] classified CRE with critical criteria for research as the threat it poses is critical.

The performance of each of the antibiotics within the carbapenem groups is reportedly not the same [33], thus, supporting the need for periodic surveillance. For a long time now, imipenem has been generally accepted to possess better therapeutic outcomes against Gram-positive cocci, unlike its derivative, meropenem, which is more effective against Gram-negative bacilli [33]. Since strains within bacteria do not respond exactly the same way, it is imperative to intermittently assess their performance to these antibiotics. Joly-Guillou et al. [34] reported total E. coli susceptibility to meropenem and imipenem, but that 99% and 98% of other Enterobacteriaceae were susceptible to meropenem and imipenem respectively.

Since this was a long time ago, there is need to assess the varying antibiotic profile of the carbapenem antibiotics till date. This is because the prescription of carbapenem have increased extensively till date [30,35,36].

Carbapenem resistance is also linked to many factors including indwelling devices that allow biofilm formation and development of resistance [37], previous treatment for more severe illness that necessitated the use of antibiotic in the last line of defense [38], nosocomial origin [39], prior antibiotic administrations [40] and bacterial intrinsic factors. Bacterial intrinsic factor may include production carbapenemase, mutation or efflux mechanisms [41]. This article assessed the carbapenem resistance associated with coliuria among outpatients and hospitalised patients in a tertiary hospital.

Materials and methods

Sampling area, experimental design and sample collection

The samples used in this study were majorly collected from University of Uyo Teaching Hospitals (UUTH). The hospital serves as referral center for over 5 million population. The research was a response to the classification of carbapenem resistance Enterobacteriaceae with critical criteria (Priority 1) for research. It was a cross-sectional study which determined the prevalence of carbapenem resistant E. coli in cases of significant coliuria among urology patients. One hundred and twenty-six (126) mid-stream urine samples were collected from the patients using sterile screw cap universal sterile container while the information about the clinical conditions, age, sex, marital status was documented. The patients were guided to clean their external genitalia with a sterile wipe before urinating and the samples were then taken to the microbiology laboratory under ice for analysis.
**Microbiological analysis of urine samples**

**Estimation of microbial loads.** Bacterial enumeration through pour plate methods was used [41,42]. Ten-fold serial dilution was adopted on each urine sample using 1 mL inoculum to achieve the dilutions $10^{-4}$, $10^{-5}$ and $10^{-6}$ which were aseptically pipetted into sterile Petri dishes in triplicates. Fifteen (15) mL of prepared eosin methylene blue (EMB) agar was poured on the sample bearing the inoculum in the Petri dishes. The plates were incubated at 37°C for 18–24 h. A presumptive *E. coli* counts ≥ $10^5$ CFU/mL of urine was taken as significant coluria; < $10^4$ CFU/mL was taken as not significant while counts between $10^4$ and $10^5$ CFU/mL were considered indeterminate. The experiments that gave intermediate results were repeated.

**Isolation and purification of *E. coli*.** Isolates showing green metallic sheen on EMB agar plate were subcultured for purification and incubated at 37°C for 18–24 h. Pure colonies were stocks in nutrient agar slant in McCartney bottles.

**Morphological and biochemical characterisation of microbial isolates.** The characterisation of bacterial isolates was based on their cultural, morphological and biochemical characteristics as described by Cheesebrough [41] and Collins and Lyne [42]. Selected biochemical characterisation including Gram’s staining, catalase test, oxidase test, methyl red-Voges-Proskauer (MR-VP) test [43–45], triple iron sugar agar test [43] and indole test were carried out.

**Molecular identification of selected *E. coli***

**Extraction of DNA.** Bacterial DNA was isolated from the selected presumptive *E. coli* using boiling method as described by Salehi et al. [44] with slight modifications. The isolates were cultivated overnight in Luria-Bertani (LB) broth and transferred to 2 mL Eppendorf tube and centrifuged at 14,000 rpm for 2 min. The supernatant was discarded. The cells were resuspended phosphate buffer saline, spun at 14,000 rpm for 2 min and the supernatant was discarded. The cells were resuspended in 200 μL distilled water and vortexed properly to achieve a thoroughly mixed isolates in water. This resulting mixture was boiled at 95°C for 15 min and then centrifuged at 15,000 rpm; 4°C for 15 min. The supernatant was removed and the DNA concentration was measured on Nanodrop 2000 spectrophotometer (Thermo Fisher Scientific, United States) at 260nm and 280 nm to ascertain the genomic purity while the remaining supernatant was stored at -20°C for further analysis.

**DNA electrophoresis.** Agarose gel electrophoresis was also utilised to ascertain the integrity of the DNA by size fractionation on 1.0% agarose gels. Agarose gels were prepared by dissolving and boiling 1.0 g agarose in 100 mL 0.5X TBE buffer solution. The gels were allowed to cool down to about 45°C and 10 μL of 5 mg/mL ethidium bromide was added, mixed together before pouring it into an electrophoresis chamber set with the combs inserted. After the gel has solidified, 3 mL of the DNA with 5 μL sterile distilled water and 2 μL of 6x loading dye was mixed together and loaded in the well created. Electrophoresis was done at 80 V for 2 h. The integrity of the DNA was visualised and photographed on UV light source.

**PCR detection and gel electrophoresis of the *E. coli*.** PCR based detection of *E. coli* was performed with primers (Inqaba Biotechnical Industries, South Africa) for a conserved region of *E. coli* alanine racemase (atr) gene using the forward primer CTGGAAGAGGCTAGCCTGGAGAG and reverse primer AAAATCGGCACCCTGGAGGC GATC at the amplicon size of 366 bp. The reaction mixture contained 12.5 μL of one taq quick load 2x master mix with standard buffer (Inqaba Biotechnical Industries, South Africa), 20 μM each of the forward and reverse primers, water and 3 μL of DNA template suspension in a final volume of 25 μL. The PCR condition contained an initial 6 min enzyme activation and denaturation step at 95°C. This was followed by 35 cycles having denaturation at 95°C for 20 s, primer annealing/extension at 72°C for 1 min 30 s, and a final extension for 5 min at 72°C. *E. coli* ATCC 8739 was used as a positive control.

Agarose gel electrophoresis was performed at 100 V for 35 min in 1.5% agarose gel in Tris Borate-EDTA (TBE) buffer, stained with ethidium bromide gel stain (ThermoFisher Scientific, South Africa).

**Purification of PCR products.** The amplicon was purified in preparation for sequencing using 2 M sodium acetate wash techniques. A measure of 1 μL 2M NaAct pH 5.2 was added to 10 μL of the PCR product. Further 20 μL 100% Ethanol was added and the solution kept at -20°C for 1 h. Centrifuged at 10,000 rpm for 10 min. After the centrifugation, the precipitate was washed with 70% ethanol, allowed to dry in air and resuspended in 5 μL sterile distilled water and kept at 4°C for sequencing.

**Preparation of sample for gene sequencer (ABI 3130 xl machine) sequencing and analyses of sequenced data.** The cocktail mix was a combination of 9 μL of Hi di formamide with 1 μL of purified sequence forming a total of 10 μL. The samples were loaded on the gene sequencer (ABI 3130 x 1 genetic analyser, Applied Biosystems). Sequencing analysis was done following the protocols of Tamura and Nei [38]. The resulting chromatograph was viewed and edited with Finch TV (Version 14.0; www.geospiza.com/finchtv). The identities of generated DNA sequences were through Basic Local Alignment Search Tool (BLAST) program alignment tool from GenBank on the National Center for Biotechnology Information (NCBI), USA.
Following successful base calling, the sequences were subjected to multiple alignments with NCBI isolates as references using Bioedit (Version 7.0.5.3). The phylogenetic tree depicting the ancestry and relatedness was computed and developed using Maximum Likelihood method in MEGA 7 (Version 7.0.26).

De-novo sequences were submitted to GenBank of the NCBI with their unique identifiers and accession numbers as stated in result section.

Carbapenem susceptibility testing
The identified isolates were tested against four conventional carbapenem antibiotics (Oxoid, UK) consisting of imipenem (10 μg), meropenem (10 μg), doripenem (10 μg), and ertapenem (10 μg). Inoculum standardisation was carried out as previously described by Komolafe and Adegoke [46] and CLSI [47] to achieve 0.5 MacFarland standard. About 100 μL of the dilution was inoculated on the Mueller-Hinton agar plates. Each of the carbapenem antibiotic discs was aseptically placed at equidistance, on the surface of the agar, with the aid of sterile forceps. The culture plates were then subjected to 24 h incubation at 37°C.

Measurement of the diameter/zone of inhibition was appropriately taken in millimetre while interpretation was done using the guidelines of Clinical and Laboratory Standard Institute (CLSI) [40].

Tests for beta lactamase
The intralactam acidimetric detection test strips (Mast Group, UK) were placed on a slide and moistened with distilled water. Growth from an overnight culture of the test isolate on a suitable solid medium was swiped with the edge of the intralactam strips. A change in colour from purple to yellow within 10 min was recorded as positive, while no change was recorded as negative.

Statistical analysis
Descriptive statistics were utilised to analyse the results. Mean value was calculated for enumeration plates performed in triplicates. Differences in carbapenem resistances among the E. coli were determined using chi-square test at p value < 0.05 (significant).

Results

Clinical conditions of the patients
The clinical diagnosis of the patients varied. Though only 39 samples of the total number of patients (N = 126) showed positive coliuria, the remaining 87 (69%) patients might be suffering from other aetiological agents or other causes. The indicated clinical conditions of the patients included cystitis (n = 17; 13.5%), Febrile UTI (n = 48; 36.5%), patients with indwelling catheters (n = 14; 11.1%) etc. Important observation made here was that thirteen of the 14 patients with indwelling catheters showed coliuria. The details of the clinical diagnosis of the sampled patients are tabulated in Table 1.

Significance of the estimated coliuria
Thirty-nine (39) samples showed positive coliuria. The E. coli count (log10 CFU/mL) showed that 82.1% (n = 32) of the samples had significant coliuria, 12.8% (n = 5) showed non-significant coliuria while 5.1% (n = 2) showed indeterminate coliuria even when repeated as shown in Fig. 1.

Demographic variables of the study participants
The treatment mode and demographic variables of the study participant is tabulated in Table 2. More of the sampled inpatients yielded positive coliuria (57.9%) than the outpatients with a significant difference (p > 0.05). Though there were more female patients (n = 77) than male (n = 49), there was higher prevalence of coliuria in sampled male patients (34.9%) than the female (28.6%). This difference is also significant (p > 0.05). Highest prevalence of coliuria was observed among the age range (18–30 years. The difference in prevalence was significant (p > 0.05).

Cultural, morphological and biochemical characterisation of the isolates and their probable identification
Two isolates were selected from each of the positive coliuria plates (n = 39). The results of the cultural, morphological, and biochemical characterisation are represented in the Table 3. All the isolates preliminarily suspected to be E. coli on the primary plates showed positive confirmatory biochemical identity as depicted in Table 3.

Molecular confirmation of the isolates
The results of the gel electrophoresis following the initial PCR done for the two selected isolates for molecular analysis. The two isolates were in line with the positive control (+) E. coli ATCC 8739 at the expected amplicon size of 399 bp showing

| S/N | Clinical diagnosis/complaint | n  | %  |
|-----|-----------------------------|----|----|
| 1.  | Cystitis                     | 17 | 13.5 |
| 2.  | Pyuria/UTI                   | 8  | 6.3 |
| 3.  | Febrile UTI                  | 47 | 36.5 |
| 4.  | Patients with indwelling catheter | 14 | 11.1 |
| 5.  | Pyelonephritis               | 5  | 3.2 |
| 6.  | Vulvovaginal irritation      | 7  | 5.6 |
| 7.  | Benign prostatic hyperplasia (BPH) | 16 | 12.7 |
| 8.  | Bacterial vaginosis/vaginitis | 10 | 7.9 |
| 9.  | Urethritis                   | 2  | 2.4 |
| Total|                             | 126| 100 |

UTI means urinary tract infection.
them to be E. coli. The blast results showed the sequences were E. coli but not with complete identity with any of the strain in the GenBank. The potential de-novo E. coli strains were processed and approved with their unique accession number by NCBI, USA as depicted in Table 4.

Fig. 2 showed the relatedness of the identified strains to other known strains. The two de-novo sequences appeared to be more closely related, though are likely from same ancestral parents as some of the known references.

**Carbapenem-resistant profiles of the isolates**

The results of percentage resistance and intermediately resistant profile were depicted in Fig. 3. Least carbapenem resistance of 47% was observed for doripenem while higher resistance was observed for the other carbapenem antibiotics. Beta lactamase was produced in all the isolates tested.

**Discussion**

Urine is supposed to be sterile. The present of E. coli in the urine with or without symptom is called coliuria. UTI samples that produce E. coli are also called coliuria. There was coliuria in

**TABLE 2. Patients’ demographic variables vs. prevalence of E. coli (p > 0.05)**

| Variables            | Category     | E. coli (+) | E. coli (-) | Prevalence (%) | P Value |
|----------------------|--------------|-------------|-------------|----------------|---------|
| Patient treatment status | Outpatient (n = 107) | 28          | 79          | 25.2           | 0.537   |
|                      | Inpatients (n = 19)   | 11          | 8           | 57.9           |         |
| Gender               | Male (n = 49)        | 17          | 32          | 34.9           | 0.482   |
|                      | Female (n = 77)      | 22          | 55          | 28.6           |         |
| Age range (years)    | 0–17               | 4           | 9           | 30.8           | 0.316   |
|                      | 18–30              | 15          | 22          | 40.5           |         |
|                      | 31–50              | 8           | 19          | 29.6           |         |
|                      | >51                | 12          | 37          | 24.5           |         |

**TABLE 3. Cultural, morphological, and biochemical characterisation of the isolates and their probable identification**

| Characteristics | Reaction | n | %   |
|-----------------|----------|---|-----|
| Cultural characteristics | +         | 78 | 100 |
| Gram reaction | —        | 78 | 100 |
| Shape         | Rod      | 78 | 100 |
| Catalase      | +        | 78 | 100 |
| Oxidase       | —        | 78 | 100 |
| Indole        | +        | 78 | 100 |
| Methyl red    | +        | 78 | 100 |
| Voges Proskauer |        | 66 | 84.6|
| Citrate       | —        | 76 | 97.4|
| Urease        | —        | 78 | 100 |
| Motility      | +        | 78 | 100 |
| Glucose       | AG       | 78 | 100 |
| Lactose       | AG       | 78 | 100 |
| Mannitol      | AG       | 76 | 97.4|
| Probable identification | E. coli | 78 | 100 |

AG means acid and gas; + means positive; - means negative.

**TABLE 4. Identity of the selected potential de-novo Escherichia coli strains, their unique accession number and their sources**

| Identification | Accession number | Source |
|----------------|------------------|--------|
| Escherichia coli strain AYO-WINII11 | MT735391 | Coliuria |
| Escherichia coli strain AYO-WINII12 | MT735392 | Coliuria |
FIG. 2. Molecular phylogenetic analysis of the selected clinical isolates of E. coli compared to other standard isolates by maximum likelihood method.

FIG. 3. Resistant and intermediate profile to carbapenem antibiotics.
several clinical conditions like cystitis (13.5%), pyuria/UTI (6.3%), febrile UTI (36.5%), patients with indwelling catheter (11.1%), pyelonephritis (3.2%), vulvovaginal irritation (5.6%), benign prostatic hyperplasia (BPH) (12.7%) etc. with more detail in Table 4. Brusch [48] stated that some of the clinical conditions resulting in UTIs in adult male individuals include prostate hyperplasia, epididymitis, orchitis, pyelonephritis, cystitis, urethritis, and indwelling urinary catheters. In women, polymicrobial colonisation of the urinary tracts may lead to vaginal irritation and when E. coli present, it becomes a case of coliuria as well.

Our findings on the coliurial associated cystitis was in tandem with the report on Global Prevalence Study on Infections in Urology [49], which estimated cystitis as the most prevalent symptomatic bacteriuria, with 26% for cystitis. Their report was however different with regards to pyelonephritis, which was 20% and the second most prevalent symptomatic bacteriuria in their study compare to being second to the least prevalent in our study. Meanwhile, the uncomplicated cystitis among young women in the United States has been estimated to be ~0.5 episodes per individual per annum [50].

As stated earlier, symptomatic coliuria or UTIs sometimes arise from complications such as Benign Prostatic Hyperplasia (BPH) that normally progress to bladder outlet obstruction (BOO) [14]. Beyond coliuria, complicated UTIs are usually of polymicrobial aetiology [51].

E. coli is the leading cause of urinary tract infections and diarrheal infection worldwide, this study is particularly important as it investigated the carbapenem resistance profile and phylogenetic groups among clinical coliuria. Knowledge of the prevalence of pathogenic E. coli and their antimicrobial resistance pattern is vital in the designing of strategies to control the spread of such superbugs. Findings of this study revealed that the overall phenotypic carbapenem resistance prevalence stood at \( \geq 47\% \). Comparable but low results were achieved by previous studies in Low Middle Income countries (LMIC) with similar healthcare systems. For example, prevalence of carbapenem resistance in Tanzania was 24% [52] and India 31.77% [53]. The use of PCR screening to identify the isolates gives more credence to the identity than ordinary culture-based identity.

Urine culture is accepted as the gold standard for coliuria assessment among antenatal clinic attendees, most importantly at the earliest trimester of conception [54,55]. Varying prevalence between our observed coliuria and some reported by other researchers. Observation of 82.1% (\( n = 32 \)) significant coliuria, 12.8 % (\( n = 5 \)) non-significant coliuria and 5.1% (\( n = 2 \)) indeterminate coliuria have only the indeterminate falling within range reported in some locations [48–50]. Lower rates of 4.0%–7.0% were long time ago documented in Canada [55], Ghana [56] and Ethiopia [57]. The high prevalence in this study may be ascribed to indiscriminate use of antibiotics resulting from self-medications since antibiotic use is not regulated in Nigeria [58]. Inappropriate use of this class of antimicrobials may lead to subclinical infections including UTIs, but more importantly, may create an avenue for the development of resistant organisms in the community. The highest prevalence rate (40.5%) was found among subjects aged 18 to 30 years. This is probably due to high sexual activities among these groups but was in contrast to the findings of Turpin et al. [59] whose highest rate of 13% was reported in the age group 35 to 39 years. Active sexual lifestyles were reported responsible for high rate and recurrence of uncomplicated UTIs within the age range of 18 and 39 years old [50]. Meanwhile, close association between asymptomatic bacteriuria and low socio-economic status has been documented by Turpin et al. [59].

In contrast with some old studies [60–62] which stated that E. coli was more prevalent in women than in men, the coliuria prevalence in our study was clearly significantly higher (\( p > 0.05 \)) in male (34.9%) than females (28.6%). This was in contrast from a sole UTI documented prevalence of E. coli which was high in females compared with males [59,63].

The results on carbapenem resistance, showed that there was more resistance by the isolates to imipenem, followed by ertapenem resistance. The difference in the resistance to both imipenem and meropenem was significant (\( P > 005 \)). Potron et al. [64] also showed variation in carbapenem resistance. A carbapenem-resistant Enterobacteriaceae is usually suspected when resistance to ertapenem is detected. Disk diffusion susceptibility testing for carbapenem resistance is approved in the test for resistant isolates [65]. Polymicrobial infections with E. coli and other bacterial pathogens possess the potential for resistance to antimicrobials [51] including carbapenem, limiting the treatment options [56,66,67]. Resistance to carbapenem is classified to be of critical priority for research [29]. Their report in the environment [19] or in the hospital, as in this study, remains critical as carbapenem antibiotics are antibiotics of last resorts.

A report from Science for the Curious Discover in 2015 revealed a strain of E. coli that showed resistance to all existing antibiotics which included colistin. Meanwhile colistin is usually recommended for some carbapenem resistant bacteria [68]. This must have come as a result of antibiotic resistance determinants carried by the E. coli [69] which were not within the purview of our surveillance in our study. This justifies the need for intermittent surveillance of coliuria as well as E. coli presence as potential aetiological agents in other clinical conditions. To mitigate the therapeutic failure due to carbapenem resistance, several studies have recommended antibiotic combinations together with carbapenem against carbapenem-resistant Gram-negative bacteria [70–72]. This is because of
the synergistic interactions reported in carbapenem in combination with sulbactam [70], colistin in combination with carbapenem [71] and carbapenem in combination with an aminoglycoside [72]. Carbapenem antibiotic-resistant E. coli in coluria, other bacteriuria [73,6] and other clinical conditions [1], like any other critical resistance bring about prolonged hospital stay, higher cost of treatment as well as increased morbidity and mortality. Beta lactamase production revealed that the isolates might possess beta lactamase genes with potentials to produce carbapenemases, though this was not examined in this study. These conditions showcase potential public health risks that may be associated with the use of untreated urine in irrigating crops as source of nitrogen supplement [74]. It should therefore be considered critical for consideration because of the associated human health outcome.

Conclusion

Escherichia coli isolated from coluria patients diagnosed with various clinical urinogenital conditions in the study area contained some potentially novel strains. Selected isolates showed appreciable resistance to carbapenem antibiotics. These carbapenem resistant E. coli were more prevalent in male than female but was more significantly prevalent among the young adult (18–30 years). These situations are alarming because carbapenem-resistant Enterobacteriaceae have been classified with critical criteria by the World Health Organization and carbapenem is among the antibiotics in the last line of defense.

Transparency declaration

None.

Credit author statement

Anthony A. Adegoke. Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Software, annotated the figures, Supervision; Winifred E. Ikott. Investigation, Data curation, contributed in writing; Anthony I. Okoh. Validation, Resources, Writing – review & editing.

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