International Journal of Pathogen Research

Volume 13, Issue 6, Page 137-144, 2024; Article no.IJPR.127586
ISSN: 2582-3876

Antibiotic Susceptibility Pattern of Urinary Quinolone-resistant *Escherichia coli* from Selected Patients Admitted at General Hospitals in Abuja Municipal, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Author NYB designed the study, author EMO wrote the protocol and performed the statistical analysis. Author NIH wrote the first draft of the manuscript. Authors TSC and BOF managed the analyses of the study. Author ARH managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.9734/ijpr/2024/v13i6328

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/127586

Original Research Article

Received: 11/11/2024
Accepted: 03/12/2024
Published: 09/12/2024

ABSTRACT

Aims: The aim of this study was to determine the antimicrobial susceptibility pattern, of urinary quinolone-resistant *Escherichia coli* from selected General Hospitals in Abuja Municipal, Nigeria.
Study Design: Cross sectional study.

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Cite as: *M. O, Eghieye, Ngwai Y.B, Nkene I.H, Tama S.C, Bolarinwa, O.F, and Abimiku, R. H. 2024. "Antibiotic Susceptibility Pattern of Urinary Quinolone-Resistant Escherichia Coli from Selected Patients Admitted at General Hospitals in Abuja Municipal, Nigeria". International Journal of Pathogen Research 13 (6):137-44. https://doi.org/10.9734/ijpr/2024/v13i6328.*

Place and Duration of Study: Department of Microbiology, Nasarawa State University, Keffi, between November 2023 and October 2024.
Methodology: A total of 200 samples were collected from urine of patients. *Escherichia coli* was isolated from the samples using standard cultural and microbiological methods. Antibiotic susceptibility testing and minimum inhibitory concentrations were evaluated as described by the Clinical and Laboratory Standards Institute (CLSI).
Results: 50 out of 200 (25.0%) of the samples collected had *E.coli*. 10 isolates out of the 50 were quinolone resistant. Antibiotic resistance in the isolates in decreasing order were as follows: Ciprofloxacin (100.0%), Streptomycin (100.0%), Ampicillin (100.0%), Cefoxitin (80.0%), Cotrimoxazole (80.0%), Ceftazidime (70.0%), Gentamicin (50.0%), Gentamicin (50.8%), Naladixic Acid (40.0%), Amoxicillin/Clavulanic acid (40.0%), and Ofloxacin; (40.0%). All isolates were resistant to AMP and CIP. All the *E. coli* isolated were MAR isolates. All the MAR isolates had MAR indices of ≥ 0.2. Most isolates were MDR isolates. There was also a PDR and XDR isolates among the selected tested *E coli* isolates.
Conclusion: The *E. coli* isolates showed high resistance to Ampicillin, ciprofloxacin and streptomycin, and all isolates were MAR, and had MAR indices of ≥ 0.2. The presence of MDR isolates is a public concern and urgent steps must be taken to address its spread. There is also a need to strengthen strategies and programmes to reduce AMR in Nigeria.

Keywords: Escherichia coli; quinolone; antibiotics; resistance.

1. INTRODUCTION

"Urinary tract infections (UTIs), represent a significant public health concern globally" [1]. "Among the causative pathogens, *Escherichia coli* (*E. coli*) a member of the Enterobacteriaceae family, is consistently identified as a leading agent responsible for UTIs in both community settings and hospitalized patients" [2].

"Quinolones, particularly fluoroquinolones (FQs), are commonly employed in the treatment of UTIs due to their broad-spectrum activity against gram-positive and, notably, gram-negative bacteria" [3]. "Their efficacy, coupled with favorable safety profiles and the convenience of oral administration, makes them a preferred therapeutic option. However, the widespread and often indiscriminate use of fluoroquinolones in both human and veterinary medicine has driven the emergence and proliferation of bacterial resistance to these agents" [3,4].

"Resistance to fluoroquinolones among gram-negative bacteria has now become a critical issue of global concern, posing challenges to effective UTI management and necessitating ongoing surveillance and the development of alternative therapeutic strategies" [5,6].

*"*Quinolones are synthetic antibacterial compounds known for their potent activity against *Enterobacteriaceae"* [7]. "The discovery of the first quinolone, nalidixic acid, in 1962 marked a significant milestone in antibacterial therapy, paving the way for the development of numerous quinolone derivatives" [8]. "Modifying the quinolone structure, specifically by introducing a fluorine atom at the C-6 position, gave rise to fluoroquinolones, which exhibit enhanced systemic activity" [9]. "The bactericidal effect of quinolones is mediated by their ability to inhibit DNA gyrase and topoisomerase IV, enzymes crucial for bacterial DNA replication" [9]. "However, the widespread use of these agents has contributed to the emergence and dissemination of quinolone resistance among various microorganisms" [10].

"Quinolone resistance primarily arises from amino acid substitutions within the quinolone resistance-determining regions (QRDRs) of DNA gyrase and topoisomerase IV" [11]. "Additional resistance mechanisms include reduced outer membrane permeability, upregulated efflux pump activity, and plasmid-mediated quinolone resistance (PMQR) genes" [11].

"The first identified PMQR mechanism, the *qnr* gene (later named *qnrA*), was reported in 1998" [12]. "*Qnr* proteins shield DNA gyrase and/or topoisomerase IV from the inhibitory effects of fluoroquinolones" [13].

In Abuja, Nigeria, limited research has focused on the antibiotic susceptibility patterns of quinolone-resistant *Escherichia coli* isolated from urine samples in hospitals. This study aimed to investigate the prevalence of *E. coli* and add to

the body of knowledge on resistance patterns of *E. coli* obtained from the urine of patients in selected hospitals across Abuja, Nigeria.

2. MATERIALS AND METHODS

2.1 Bacteria Isolates

Two hundred samples, [50 each from Asokoro General Hospital (AGH), Garki Hospital Abuja (GHA), Gwarimpa General Hospital (GGH), and Wuse General Hospital (WGH)] was collected. These Health facilities are located in Abuja, Nigeria. The samples were collected using NA agar slants and transported using ice pack to National Institute for Pharmaceutical Research and Development (NIPRD) for analysis.

2.2 Identification of *E. coli* Isolates

E. coli was identified after isolation by morphological, cultural and biochemical characteristics using Gram staining, Motility Test and biochemical tests (Indole, Methyl Red-Voges-Proskauer, Citrate, Nitrate Reduction Test, Urease Test, H_2S production Test, etc.) as described in the Bacteriological Analytical Manual [14] and Cheesbrough [15]. Furthermore, the isolates were confirmed using the VITEK® 2 Compact system (bioMérieux, Marcy-l'Etoile, France). This system utilizes advanced colorimetry to analyze biochemical reactions on microbial identification cards. After inoculating the cards with an unknown organism, the system's internal optics read and compare the reactions to those in the VITEK 2 database, enabling precise organism identification. The system employs a transmittance optical method that uses various wavelengths within the visible spectrum to interpret test reactions. During incubation, reactions are monitored every 15 minutes to detect turbidity or color changes associated with metabolic activity. An integrated algorithm eliminates false readings caused by small bubbles, ensuring accuracy.

2.3 Antibiotic Susceptibility Testing

"The antimicrobial susceptibility testing of the bacterial isolates was carried out as earlier described by Clinical and Laboratory Standards Institute" [16]. "Briefly, three (3) pure colonies of the isolates was inoculated in to 5ml sterile 0.85% (w/v) NaCl (normal saline) and the turbidity of the bacteria suspension was adjusted to the turbidity equivalent to 0.5 McFarland standard. The McFarland standard was prepared as follows: 0.5 ml of 1.172% (w/v) $BaCl_2.2H_2O$ was added to 99.5 ml of 1% (w/v) H_2SO_4.

A sterile swab stick was soaked in standardized bacteria suspension and streaked on Mueller-Hinton agar plates and the antibiotic discs were aseptically placed at the center of the plates and allowed to stand for 1 h for pre-diffusion. The plates was incubated at 37ºC for 24 h. The diameter zone of inhibition in millimeter was measured and the result was interpreted in accordance with the susceptibility break point earlier described by Clinical and Laboratory Standards Institute" [16].

2.3.1 Determination of multiple antibiotic resistance (MAR) index

The MAR index of the isolates was determined as described previously [17] using the formula:

$$MAR\ Index\ = \frac{No\ antibiotics\ isolate\ is\ resistant\ to}{No.of\ antibiotics\ tested}$$

3. RESULTS AND DISCUSSION

3.1 Identification of *Escherichia coli*

The phenotypic characteristics of urinary E. coli isolates from hospital patients are summarized in Table 1. The isolates exhibited typical *E. coli* characteristics including pink colonies on MacConkey agar, metallic green sheen on EMB agar, and Gram-negative rod morphology. The biochemical profile (indole+, MR+, VP-, citrate-, ONPG+) further confirmed their identification as *E. coli*.

3.2 Occurrence of *Escherichia coli*

The occurrence for *E. coli* was 25.0% (50/200). 10 out of the 50 isolates (20.0%) were Quinolone resistant.

3.3 Antimicrobial Resistance Profile

The antimicrobial susceptibility profiles of the selected tested *E. coli* isolates from urine of the patients in the selected general hospitals are as shown in Table 2 and 3. All isolates were resistant to AMP and CIP. All the *E. coli* isolated were MAR isolates as shown in Table 2.

Table 1. Cultural, morphological and biochemical characteristics of test *Escherichia coli* isolated from patients with suspected urinary tract infections in selected general hospitals in Abuja Municipal, Nigeria

Cultural characteristics	Morphological characteristics		Biochemical Characteristics												Inference
	Gram reaction	Morphology	IND	MR	VP	CT	TDA	ONPG	LYS	ORN	UR	NT	H_2S	MAL	
Pinkish colonies on MCA and Greenish metallic sheen on EMB agar	-	Rod	+	+	-	-	-	+	+	+	-	+	-	-	*E. coli*

Table 2. Antimicrobial resistance profile of selected test quinolone resistant *Escherichia coli* isolated from urine of patients attending selected hospitals in Abuja, Nigeria

Isolate	Source	Antimicrobial Resistance Class	Antimicrobial Resistance Phenotype
EC1	GHA	MDR	S,FOX,CN,CIP,AMP,OFX,NA
EC2	WGH	MDR	S,CTX,CAZ,FOX,CIP,AMP,NA
EC3	WGH	MDR	S,SXT,CTX,CAZ,CIP,AMP,OFX,NA
EC4	AGH	MDR	S,SXT,CTX,CN,CIP,AMP,OFX,NA
EC5	AGH	MDR	S,SXT,CTX,CAZ,FOX,CIP,AMP
EC6	GHA	MDR	AMC,S,SXT,FOX,CN,CIP,AMP,OFX
EC7	GHA	MDR	AMC,S,SXT,CTX,CAZ,FOX,CIP,AMP
EC8	GHA	MDR	S,SXT,CTX,CAZ,FOX,CN,CIP,AMP
EC9	WGH	XDR	AMC,S,SXT,CTX,CAZ,FOX,IPM,CIP,AMP
EC10	GHA	PDR	AMC,S,SXT,CTX,CAZ,FOX,CN,IPM,CIP,AMP

EC= Escherichia coli; AMP= Ampicillin; AMC= Amoxicillin/Clavulanic acid; S= Streptomycin; CN= Gentamicin; SXT= Cotrimoxazole; CAZ= Ceftazidime; CTX= Cefotaxime; FOX= Cefoxitin; CIP= Ciprofloxacin; IPM= Imipenem; AGH= Asokoro General Hospital; GHA= Garki Hospital Abuja; GGH= Gwarimpa General Hospital; WGH= Wuse General Hospital; MDR= Multidrug resistance(non-susceptible to ≥1 agent in ≥3 antimicrobial categories); XDR= extensive drug resistance (non-susceptible to ≥1 agent in all but ≤2 antimicrobial categories); PDR= pan drug resistanceresistance (non-susceptible to all antimicrobial listed); NMDR= non-multidrug resistance [18]

Table 3. Antimicrobial resistance profile of **Selected Test Quinolone resistant *Escherichia coli* isolated from urine of Patients attending selected hospitals in Abuja, Nigeria**

Antibiotics	Disc Content (µg)	No. (%) resistance in *E. coli* (n=10)
Amoxicillin/Clavulanate (AMC)	30	4(40.0)
Cefoxitin (FOX)	30	8 (80.0)
Co-trimoxazole (SXT)	25	8(80.0)
Ofloxacin (OFX)	10	4(40.0)
Gentamicin (CN)	10	5(50.0)
Nalidixic acid (NA)	30	4(40.0)
Ceftazidime (CAZ)	30	7(70.0)
Streptomycin (S)	10	10(100.0)
Ciprofloxacin (CIP)	5	10(100.0)
Ampicillin (AMP)	30	10(100.0)

3.4 Multiple Antibiotic Resistance (MAR) Index

All the *E. coli* selected were MAR isolates. All the MAR isolates had MAR indices of ≥ 0.2. Most isolates were MDR isolates. There was also a PDR and XDR isolates among the selected tested *E coli* isolates.

The widespread use of quinolone antibiotics in human medicine and other activities such as poultry, has been linked to the rising prevalence of quinolone-resistant microorganisms [19]. This study examined quinolone resistance among uropathogenic *Escherichia coli* (UPEC) isolates from major tertiary care hospitals in Abuja, Nigeria. The findings aim to provide physicians with updated antibiotic resistance data and contribute to national as well as global datasets, supporting the enhancement of antimicrobial stewardship programs. Our findings in this study shows that occurrence of *E. coli* was 25.0%, and 20.0% for quinolone resistance and this is different from results from a study earlier reported by [20,21] in Iran and Zambia respectively, where rate of quinolones resistance exceeded 40%. Another study by Irenge *et al* [22] reported a prevalence of clinical *E. coli* at 58.9%. The occurrence of resistant strains discourages the empirical use of quinolones in our region, since the risk of treatment failure increases when resistance rates exceed 10% to 20% [23]. Despite these concerning resistance rates, the limited availability of alternative oral

antimicrobial agents means there is insufficient reason to make a recommendation against quinolone use.

"Our study found that *E. coli* was highly resistant to ampicillin, which is consistent with other studies, indicating that penicillins are widely used in clinical settings" [24,25]. "Penicillins are widely accessed without prescription and are usually inappropriately used, which might contribute to the observed resistance to these drugs" [26]. "The resistance of *E. coli* to penicillins could also be facilitated by the presence of AmpC β-lactamases encoded by the chromosome of *E. coli*." [27]. "Additionally, our study revealed that the *E. coli* isolates were highly resistant to cotrimixazole. Our findings corroborate reports from other studies in which *E. coli* were found to be highly resistant to ciprofloxacin, streptomycin and cotrimoxazole" [28,29]. The overuse and misuse of cotrimoxazole has contributed to the resistance of *E. coli* to this drug combination. However, the resistance of *E. coli* to sulfamethoxazole/trimethoprim has been reported even in individuals who have never used the drug combination.

"The resistance patterns observed in our study, as well as in similar investigations, may stem from the inappropriate use of quinolones in treating urinary and respiratory tract infections" [30]. "*Escherichia coli* resistance to quinolone antibiotics could be attributed to chromosomal mutations or the presence of plasmid-mediated quinolone resistance mechanisms" [31].

All of the isolates selected were MDR, leading to a high prevalence of MDR *E. coli.* This is higher than the 64.9% reported in Nepal [32], and 48.7% reported in Ghana [33]. MDR *E. coli* is a major public health issue as it has been associated with mortality. MDR infections are known to limit the choice of antimicrobial therapy, making treatment of infections complicated and difficult [34,35].

This study reveals significant antimicrobial resistance (AMR) among *E. coli* isolates against commonly prescribed antibiotics, with implications for both clinical settings. These findings reiterate the critical need for enhanced AMR surveillance systems across clinical and other interfaces. Furthermore, the results emphasize the importance of strengthening antimicrobial stewardship (AMS) programs at both hospital and community levels.

4. CONCLUSION

This study revealed that *E. coli* showed high levels of resistance to several commonly used antibiotics in humans. Notably, certain isolates demonstrated significant susceptibility to specific priority antibiotics. However, the high prevalence of multidrug-resistant (*MDR*) *E. coli* observed in this study poses a serious public health concern, potentially complicating infection management. Strengthened surveillance of antimicrobial resistance (AMR) in humans is needed to address this challenge.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/127586