P-ISSN: 2811-1516
E-ISSN: 2811-1524

AL-HIKMAH JOURNAL OF HEALTH SCIENCES (AJOHS)

Official Publication of Faculty of Basic Medical Sciences

Al-Hikmah University Ilorin, Nigeria

https://alhikmahuniversity.edu.ng/AJOHS/index.php/journal

Original Article

Co-resistance to Aminoglycosides and Fluoroquinolones in Carbapenemase-Producing Bacteria from Nigerian Hospital Sewage

Faari Babatunde Usman[1]*, Abdul-Razak Nuhu[2], Umar Asiya Imam[2], Ahmed Bayo Opalekunde[3], Aisha Bello Ibrahim[4] and Yazid Muhammad Bakkuyum[2]

[1]Department of Medical Laboratory Science, Federal Neuro-Psychiatric Hospital (FNPH), Budo-Egba Asa LGA, Kwara State, Nigeria
[2]Department of Medical Microbiology, School of Medical Laboratory Science, Usmanu Danfodiyo University, Sokoto (UDUS), Nigeria
[3]Department of Medical Laboratory Science, Faculty of Allied Health Sciences, Kwara State University, Malete, Kwara State, Nigeria
[4]Department of Microbiology and Parasitology, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria.

ARTICLE INFO

Article History
Received: 28th March, 2026
Accepted: 3rd May, 2026
Available online: 1st June, 2026

Keywords:
Co-resistance
Aminoglycosides
Fluoroquinolones
bla NDM
Hospital Sewage

Corresponding Author:

Faari Babatunde Usman
Department of Medical Laboratory Science, Federal Neuro-Psychiatric Hospital (FNPH), Budo-Egba, Asa LGA, Kwara State, Nigeria.
Phone number: +2348053194919
Email: faariusman@gmail.com

ABSTRACT

Background: Hospital sewage systems function as high-kinetic biological reactors that accelerate the convergence of diverse resistance determinants. This study investigated the phenotypic and genotypic landscapes of carbapenemase-producing bacteria (CPB) in effluent from a Nigerian tertiary hospital, focusing on the critical co-resistance between aminoglycosides and fluoroquinolones.

Methods: Environmental surveillance at the University of Ilorin Teaching Hospital (UITH) yielded 196 isolates. Identification and susceptibility profiling were conducted via VITEK® 2 and Kirby-Bauer methods. Carbapenemase activity was confirmed using the Modified Carbapenem Inactivation Method (mCIM). Molecular characterization of resistance genes (*bla* NDM, *bla* OXA–48, *bla* VIM, *bla* KPC, *bla* IMP) and the colistin-resistance marker (mcr−1) was achieved through multiplex PCR and genomic sequencing.

Results: While Enterobacteriaceae predominated (81.6%), significant carbapenem-resistant non-fermenters, including *Burkholderia cepacia* and *Stenotrophomonas maltophilia*, were recovered. A defining finding was the extensive co-resistance to fluoroquinolones and aminoglycosides; ciprofloxacin resistance was rampant (up to 50.0%), whereas amikacin efficacy remained robustly preserved (>90%), identifying a narrow therapeutic window. Genotypically, *bla* NDM (64.0%) was the primary driver. Notably, the co-carriage of *bla* NDM and mcr−1 in *E. coli* signaled a transition toward total-drug resistance (TDR). Genomic analysis established 100% clonal synteny between ICU clinical strains and environmental isolates.

Conclusion: Hospital sewage acts as a stable gateway for the dissemination of co-resistant "superbugs." The convergence of carbapenemase and fluoroquinolone resistance markers proves that clinical pathogens are actively seeding the environmental interface.

Please cite this article as: Faari, B.U., Nuhu, A., Umar, A.I., Olalekan, A.O., Opalekunde, A.B., Ibrahim, A.B. & Bakkuyum, Y.M. (2026). Co-resistance to Aminoglycosides and Fluoroquinolones in Carbapenemase-Producing Bacteria from Nigerian Hospital Sewage *Al-Hikmah Journal of Health Sciences, 5*(2), 30-36.

P-ISSN: 2811-1516
E-ISSN: 2811-1524

Introduction

The unchecked escalation of antimicrobial resistance (AMR) represents a paramount threat to global public health, fundamentally undermining decades of progress in modern medicine (Murray *et al*., 2022). At the epicentre of this crisis are carbapenemase-producing Enterobacteriaceae (CPE). The World Health Organization (WHO) classifies these pathogens as "Priority 1: Critical," given their ability to hydrolyze carbapenems, the historical last-resort agents for life-threatening Gram-negative infections (WHO, 2021). As the utility of the carbapenem class wanes, clinicians are increasingly reliant on alternative classes, primarily fluoroquinolones and aminoglycosides, as salvage or combination therapies. Consequently, understanding the complex co-occurrence of resistance determinants against these distinct pharmacological classes within single bacterial lineages is critical (Tamma *et al*., 2021).

Whilst global AMR surveillance has traditionally been patient-centric, focusing almost exclusively on clinical isolates, this reactive paradigm fails to account for the dynamic environmental reservoirs that drive resistance evolution. Hospital sewage, in particular, is a dense, high-kinetic bio-ecosystem. Commensal and pathogenic bacteria within this matrix are constantly exposed to sub-lethal concentrations of antibiotics, disinfectants, and heavy metals (Larsson *et al*., 2022). This environment exerts immense selective pressure, accelerating the horizontal gene transfer (HGT) of mobile genetic elements, such as plasmids bearing bla_{NDM}, $bla_{\text{OXA-48}}$, and bla_{KPC} genes, across diverse microbial taxa (Adekanmbi *et al*., 2021).

In resource-constrained settings such as Nigeria, where the infectious disease burden is severe and the healthcare infrastructure is routinely overstretched, the untreated discharge of hospital effluent poses a profound epidemiological risk. The escape of pan-resistant pathogens into municipal water systems transfigures localized nosocomial challenges into regional community outbreaks (Okeke *et al*., 2023). As the clinical exhaustion of Carbapenems shifts the therapeutic burden to Fluoroquinolones and aminoglycosides, understanding the co-occurrence of resistance to these agents in environmental reservoirs is of critical public health importance.

This study aimed to characterize the prevalence, molecular architecture, and phenotypic co-resistance profiles of CPE in the sewage matrix generated at the University of Ilorin Teaching Hospital (UITH), North-Central Nigeria. By integrating culture-dependent susceptibility data with genome sequencing, we evaluated the critical co-occurrence of fluoroquinolone and aminoglycoside resistance, ultimately tracing the evolutionary and transmission linkage between clinical ward outbreaks and environmental contamination.

Implications of all the available evidence

The unregulated discharge of viable, multi-drug resistant clones and mobile genetic elements (including the Colistin-resistant mcr-1 gene) into municipal water matrices constitutes an acute public health crisis. Clinical laboratories in the region must adopt an "Ertapenem-first" screening paradigm to successfully detect stealth OXA-48 producers. Therapeutically, Fluoroquinolones must be reconsidered for empirical salvage therapy in suspected hospital-acquired Gram-negative sepsis, with Amikacin repositioned as a strategic sparing agent. Hospital administrations must urgently implement point-of-source sewage disinfection infrastructures to sever the transmission link between clinical wards and community water systems.

Methods

Study Design and Setting

This descriptive, cross-sectional, observational study was conducted at the University of Ilorin Teaching Hospital (UITH), a major Federal Tertiary Referral Centre in Kwara State, Nigeria, serving a catchment population exceeding 3.5 million. The study protocol was approved by the UITH Ethical Review Committee with ethical approval number (UITH/CAT/189/21B/565).

Environmental Sampling Strategy

A strategic, two-tier environmental sampling framework was employed over four weeks. Tier I (Targeted Surveillance) involved triplicate grab samples (500 mL) collected at 2-hour intervals from maintenance holes receiving direct sewage from high-risk clinical units, including the Intensive Care Unit (ICU), Neonatal Intensive Care Unit (NICU), Gynecology ward and Labour wards. Tier II (Composite Surveillance) comprised 24-hour composite sampling at the hospital's main terminal sewage outflow, representing the institution's aggregate microbial burden.

Microbiological Recovery and Identification

Samples were transported with the cold chain maintained at (2–8°C) and processed immediately or within 2 hours after collection. Aliquots were inoculated onto MacConkey and Cysteine Lactose Electrolyte Deficient (CLED) agar to recover presumptive Enterobacteriaceae. Following standard

P-ISSN: 2811-1516
E-ISSN: 2811-1524

18–24-hour aerobic incubation at 35°C, recovered isolates underwent rigorous morphological and biochemical identification (Indole, Citrate, Urease, Motility, and Triple Sugar Iron assays) aligning with the Edwards and Ewing Identification Schema.

Antimicrobial Susceptibility Testing (AST)

Phenotypic susceptibility profiles were established using the Kirby-Bauer disc diffusion method on Mueller-Hinton Agar against a comprehensive panel, including meropenem, imipenem, ertapenem, ceftriaxone, cefepime, ciprofloxacin, and amikacin. Results were interpreted adhering strictly to Clinical and Laboratory Standards Institute (CLSI) M100 criteria.

Vitek 2 Confirmation

To ensure diagnostic precision, we confirmed the identity of each isolate and determined its antibiotic susceptibility using the VITEK® 2 Compact automated system (bioMérieux) to determine precise Minimum Inhibitory Concentration (MIC) values and the zone of inhibition.

Phenotypic CPE Screening and Confirmation

Isolates were screened for carbapenem resistance utilizing the chromogenic medium CHROMagar™ mSuperCARBA. Screen-positive isolates were systematically subjected to the Modified Carbapenem Inactivation Method (mCIM) for the definitive phenotypic confirmation of carbapenemase enzymatic activity.

Molecular Genotyping

High-purity genomic DNA was extracted from mCIM-positive isolates using the QIAamp® DNA Mini Kit. An optimized multiplex PCR assay was deployed to amplify the "Big Five" carbapenem resistance genes (bla_{NDM}, $bla_{OXA\text{-}48\text{-}like}$, bla_{KPC}, bla_{VIM}, bla_{IMP}) and the mobilized colistin resistance gene (mcr-1). PCR amplicons were resolved via 2.0% molecular-grade agarose gel electrophoresis.

Plasmid and Resistance Profiling:

To investigate clonal relatedness, genomic DNA from selected matched pairs of clinical and sewage isolates was subjected to WGS on the Illumina HiSeq 4000 platform. Cleaned paired-end reads were aligned to reference genomes using BWA-MEM. Plasmids and mobile genetic elements were identified utilizing PlasmidFinder and ISfinder, allowing for the comprehensive analysis of genetic synteny and plasmid backbones.

Bacterial Landscape of the Hospital Effluent

A total of 196 pathogenic isolates were successfully recovered from the UITH sewage network. Enterobacteriaceae dominated the microbial landscape, constituting 56.6% (n=111) of the total yield. This fraction was primarily driven by *Escherichia coli* (45.4%, n=89) and *Klebsiella pneumoniae* (11.2%, n=22). Notably, the *Burkholderia cepacia* complex was highly prevalent (24.8%), indicating robust, biofilm-associated colonization within the hospital's aquatic infrastructure.

Table 1: Microbial Landscape and Phenotypic Confirmation of Carbapenemase Production

Bacterial Species	Total Recovered Isolates n (%)	Screen-Positive (CHROMagar™) n (%)	Confirmed True CPE (mCIM) n (%)
Escherichia coli	89 (45.4%)	51 (57.3%)	21 (23.6%)
Klebsiella pneumoniae	22 (11.2%)	7 (31.8%)	4 (18.2%)
Non-Fermenting GNB (*Burkholderia cepacia*)	80 (40.8%)	-	-
Gram-Positive Bacilli	5 (2.6%)	-	-
Total Target *Enterobacteriaceae*	111 (56.6%)	58 (52.3%)	25 (22.5%)

Antimicrobial Susceptibility and Co-resistance Profiles

AST demonstrated severe divergence in susceptibility patterns, indicating intense environmental selective pressure. As detailed in Table 1, 50.6% of *E. coli* isolates exhibited resistance to meropenem. The co-occurrence of fluoroquinolone resistance was highly pronounced; ciprofloxacin resistance was recorded at 37.1% in *E. coli* and 50.0% in *K. pneumoniae*.

Conversely, aminoglycoside susceptibility remained profoundly preserved. Amikacin demonstrated exceptional in vitro activity, retaining efficacy against 97.8% of *E. coli* and 90.9% of *K. pneumoniae* isolates, highlighting a vital therapeutic divergence ($P < 0.001$).

P-ISSN: 2811-1516
E-ISSN: 2811-1524

Table 2: Comparative *In vitro* Susceptibility Profiles of Dominant *Enterobacteriaceae*

Antibiotic Class / Agent	*Escherichia coli* (n=89)		*Klebsiella pneumoniae* (n=22)	
	Susceptible (%)	Resistant (%)	Susceptible (%)	Resistant (%)
Carbapenems				
Meropenem	49.4	50.6	90.9	0.0*
Fluoroquinolones				
Ciprofloxacin	50.6	37.1	40.9	50.0
Aminoglycosides				
Amikacin	97.8	0.0	90.9	0.0
Cephalosporins				
Ceftriaxone (3rd Gen)	65.2	28.1	50.0	40.9
Cefepime (4th Gen)	87.6	7.9	77.3	13.6
**Note: K. pneumoniae isolates demonstrating 90.9% susceptibility to meropenem via standard disk diffusion were subsequently revealed to possess a "stealth" resistance phenotype.*				

Quantitative MIC and the "Stealth" Phenotype

VITEK® 2 MIC determinations quantified the intensity of the resistance. Confirmed CPE *E. coli* isolates exhibited extremely high-level resistance, with Meropenem and Ceftazidime MIC90 values exceeding ≥16 µg/mL and ≥64 µg/mL, respectively. However, *K. pneumoniae* isolates displayed a dangerous "stealth" profile. These isolates were resistant to Ertapenem (MIC90 = 4 µg/mL) whilst appearing largely susceptible to Meropenem (MIC50 = 2 µg/mL) under standard automated optical analysis, complicating routine diagnostic detection.

Table 3: Minimum Inhibitory Concentration (MIC) and Co-Resistance Profiles of Confirmed CPE

Antimicrobial Agent	E. coli CPE (n=21)		K. pneumoniae CPE (n=4)	
	MIC Range (µg/mL)	MIC90 (µg/mL)	MIC Range (µg/mL)	MIC90 (µg/mL)
Meropenem	4 – ≥16	≥16 (R)	≤1 – 4	2 (S/I)*
Ertapenem	≥8	≥8 (R)	2 – ≥8	4 (R)
Ciprofloxacin	≥4	≥4 (R)	NT	NT
Amikacin	≤16	4 (S)	NT	NT
Ceftazidime / Cefepime	≥64 (Ceftazidime)	≥64 (R)	≤1 – 8 (Cefepime)	4 (SDD)
*Note: S/I = Susceptible/Intermediate; R = Resistant; SDD = Susceptible-Dose Dependent; NT = Not Tested on this specific panel. The discordance between Ertapenem (R) and Meropenem (S/I) in K. pneumoniae indicates the stealth OXA-48 phenotype.				

Molecular Architecture of Carbapenem Resistance

While 52.3% of isolates screened positive on the hyper-sensitive CHROMagar™, the mCIM assay confirmed true carbapenemase production in only 22.5% (n=25), highlighting the prevalence of porin-deficient mimics.

Multiplex PCR genotyping of these 25 confirmed isolates identified bla_{NDM} as the absolute dominant resistance determinant, present in 64.0% of the cohort. The $bla_{OXA-48-like}$ gene was the second most frequent (28.0%), identified exclusively within the *E. coli* fraction. The bla_{VIM} gene was confined to *K. pneumoniae* (8.0%). Strikingly, the mobilized Colistin resistance gene, mcr-1, was detected within the effluent, signaling the environmental infiltration of pan-drug-resistant genetic elements.

Table 4: Molecular Architecture of Carbapenem Resistance Determinants

Species	Total *CPE* (n)	$_{blaNDM}$ n (%)	$bla_{OXA-48-like}$ n (%)	bla_{VIM} n (%)	mcr-1 (Colistin)
Escherichia coli	21	14 (66.7%)	7 (33.3%)	0 (0.0%)	Detected
Klebsiella pneumoniae	4	2 (50.0%)	0 (0.0%)	2 (50.0%)	Detected
Total All CPE	25	16 (64.0%)	7 (28.0%)	2 (8.0%)	Positive

Genomic Concordance and the Spillover Effect

Genomic sequence confirmed direct, unbroken transmission linkages between the clinical wards and

P-ISSN: 2811-1516
E-ISSN: 2811-1524

the hospital sewage. An ICU clinical *E. coli* isolate (C-ICU-Eco-04) and its corresponding sewage counterpart (S-ICU-Eco-14) shared 100% synteny. Both isolates carried the *bla*$_{NDM}$ gene situated on an identical IncFII conjugative plasmid, structurally flanked by IS26 insertion sequences.

Furthermore, the Labour Ward isolates exposed the dynamic nature of mobile genetic elements. While the clinical *K. pneumoniae* isolate carried *bla*$_{KPC}$ and the sewage isolate carried *bla*$_{OXA-48}$, Genomic sequencing revealed that both distinct resistance cassettes were captured and housed within identical Class 1 integrons on a shared IncA/C2 broad-host-range plasmid backbone.

Table 5: Phylogenomic Linkage and Mobile Genetic Element (MGE) Characterization

Source/ Ward	Isolate ID (Species)	Resistance Gene	Plasmid Replicon	MGE Context	Genetic Concordance
Sewage (ICU)	S-ICU-Eco-14 (*E. coli*)	*bla*$_{NDM}$	IncFII (Conjugative)	IS*26* (Truncated *ISAba125*)	Reference
Clinical (ICU)	C-ICU-Eco-04 (*E. coli*)	*bla*$_{NDM}$	IncFII (Conjugative)	IS*26*	100% Synteny (Direct Clonal Match)
Sewage (NICU)	S-NICU-Eco-12 (*E. coli*)	*bla*$_{OXA-48-like}$	IncX3 / IncL/M	Tn*1999.2*	Reference
Clinical (NICU)	C-NICU-Eco-05 (*E. coli*)	*bla*$_{OXA-48-like}$	ColE-type (Non-conj.)	*ISEcp1*	Discordant (Independent Acquisition)
Sewage (Labour)	S-LAB-Kpn-07 (*K. pneumoniae*)	*bla*$_{OXA-48-like}$	IncA/C2 (Broad Host)	Class 1 Integron (*In15*)	Reference
Clinical (Labour)	C-LAB-Kpn-06 (*K. pneumoniae*)	*bla*$_{KPC}$	IncA/C2 (Broad Host)	Class 1 Integron	Plasmid Backbone Match (Cassette Swap)

Discussion

This surveillance study shows the complex and hazardous resistance architecture of the hospital sewage ecosystem at a major tertiary health institution in North-Central Nigeria. The robust recovery of 196 pathogenic isolates, where Enterobacteriaceae (56.6%) and highly resilient non-fermenters like *Burkholderia cepacia* (24.8%) co-exist, confirms that hospital effluent functions as an active biological reactor. Instead of a passive waste stream, it serves as a selective environment that amplifies high-priority pathogens before their release into municipal water networks, aligning with the findings of Adekanmbi *et al*. (2021) in Lagos, where sewage was identified as a critical reservoir for carbapenem-resistant lineages.

In the context of the South-West geopolitical zone of Nigeria, the escalating prevalence of multidrug-resistant (MDR) pathogens has created a precarious clinical landscape. High-level fluoroquinolone resistance in this region is frequently linked to the co-carriage of *bla* $_{CTX-M}$ and *bla* $_{NDM}$ genes, particularly in urban centers within Oyo and Ogun States (Olowo *et al*., 2024; Olalekan *et al*., 2020). Our findings at UITH in North-Central Nigeria mirror this trend, as we observed ciprofloxacin resistance reaching 50.0% in *K. pneumoniae* isolates. This correlation highlights a synchronized regional dissemination of mobile genetic elements, where carbapenemase production is often consolidated with fluoroquinolone resistance determinants on the same conjugative plasmids (Hussain *et al*., 2021).

Beyond Nigeria, this pattern of co-resistance is a hallmark of the global "superbug" crisis. In South Africa, environmental surveillance of hospital effluents has similarly documented the convergence of *bla* $_{NDM}$ and fluoroquinolone resistance, effectively neutralizing the utility of oral salvage therapies (Naidoo *et al*., 2023). However, the striking preservation of Amikacin susceptibility (>90% efficacy) in our study provides a critical therapeutic counterbalance. This high efficacy suggests that the local resistome has not yet widely integrated 16S rRNA methyltransferase genes, such as rmtB, which are currently driving pan-aminoglycoside resistance in parts of Asia and Europe (Murray *et al*., 2022). Consequently, Amikacin remains a vital, "last-line" aminoglycoside for managing these environmental clades within the Nigerian healthcare system (Krause *et al*., 2016). Our data document a concerning trajectory: as meropenem resistance breaches 50% in the *E. coli* population, it is firmly accompanied by substantial co-resistance to ciprofloxacin (37.1% in *E. coli* and 50.0% in *K. pneumoniae*). This pattern reflects heavy mutational pressure on DNA gyrase genes (gyrA/parC) combined with the likely plasmid-mediated co-carriage of qnr determinants, a

P-ISSN: 2811-1516
E-ISSN: 2811-1524

phenomenon similarly observed by Hussain *et al*. (2021).

The molecular data establish the endemicity of the *bla* $_{NDM}$ gene (64%), reflecting a broader epidemiological consolidation across West Africa, including Ghana and Benin. More insidiously, the detection of *bla* $_{OXA-48-like}$ genes explains the dangerous "stealth" phenotype observed in *K. pneumoniae.* These isolates appeared deceptively susceptible to meropenem on VITEK® 2 systems (MIC ≤ 2 μg/mL) but were highly resistant to ertapenem. This diagnostic dissociation, often termed the "OXA-48 paradox," is consistent with research from South Africa (Naidoo *et al*., 2023) and Egypt, where automated systems failed to capture low-level carbapenem hydrolysis. Clinical laboratories in Nigeria relying exclusively on meropenem disk diffusion risk silently propagating these lineages into the community.

Our genomic data provide indisputable confirmation of the "Spillover Hypothesis." The 100% clonal synteny between ICU clinical isolates (C-ICU-Eco-04) and sewage counterparts (S-ICU-Eco-14) proves an unmitigated chain of transmission from the patient bedside to the outfall. This direct linkage has been similarly documented in South Africa by Naidoo *et al*. (2023), where identical *bla* $_{NDM}$ clones were tracked from hospital wards to environmental effluents.
Furthermore, the identification of identical IncA/C2 broad-host-range plasmids carrying differing resistance cassettes (*bla* $_{KPC}$ vs. *bla* $_{OXA-48}$) in the Labour Ward highlights the role of integron-mediated recombination. The epidemiological threat lies not solely in specific bacterial clones, but in these promiscuous, highly mobile plasmid vehicles that continuously shuffle resistance traits. The detection of mcr-1 further signals the imminent erosion of colistin, our absolute last-line defense, mirroring the emergence of colistin resistance recently reported in South-East Nigeria (Enugu).

Limitations: The primary limitation is the cross-sectional design, which captures a temporal snapshot and cannot fully account for seasonal dilution (e.g., the rainy season in Ilorin) or fluctuations in hospital antibiotic stewardship. While genomic synteny implies direct shedding, ethical constraints precluded 1:1 matching of individual patients to specific fecal outputs.

Conclusion: The UITH hospital sewage system acts as an active transmission highway for CPB, exhibiting pronounced co-resistance to fluoroquinolones. While Amikacin offers a vital therapeutic window, the detection of mcr-1 indicates a transition toward total-drug resistance.

Recommendation: The installation of point-of-source effluent disinfection (e.g., UV-C or O_3 advanced oxidation) is a non-negotiable requirement to prevent the continuous seeding of the Nigerian ecosystem with untreatable pathogens.

One Health Surveillance: Longitudinal monitoring of both clinical and wastewater resistomes is essential to track the evolution of these high-threat genetic vehicles.

References

Abbas, R., Chakkour, M., Zein El Dine, H., Obaseki, E. F., Obeid, S. T., Jezzini, A., Ghssein, G., & Ezzeddine, Z. (2024). General overview of *Klebsiella pneumoniae*: Epidemiology and the role of siderophores in its pathogenicity. *Biology*, *13*(2), Article 78. https://doi.org/10.3390/biology13020078

Adekanmbi, A. O., Adejoba, O. R., Makinde, O. M., & Okoh, A. I. (2021). Wastewater as a reservoir for carbapenem-resistant Enterobacteriaceae in Lagos. *Environmental Microbiology Reports*, *13*(4), 389–397. https://doi.org/10.1111/1758-2229.12941

Clinical and Laboratory Standards Institute. (2023). *Performance standards for antimicrobial susceptibility testing* (33rd ed., CLSI supplement M100).

Hussain, A., Ewers, C., Nandan, N., Kamal, R., & Baddam, V. R. (2021). Multiresistant sequence types of *Escherichia coli* producing extended-spectrum beta-lactamases and carrying plasmid-mediated quinolone resistance genes. *Infection and Drug Resistance*, *12*, 107–117. https://doi.org/10.2147/IDR.S191254

Krause, K. M., Serio, A. W., Kane, T. R., & Connolly, L. E. (2016). Aminoglycosides: An overview. *Cold Spring Harbor Perspectives in Medicine*, *6*(6), Article a027029. https://doi.org/10.1101/cshperspect.a027029

Larsson, D. G. J., & Flach, C. F. (2022). Antibiotic resistance in the environment. *Nature Reviews Microbiology*, *20*(5), 257–269. https://doi.org/10.1038/s41579-021-00649-x

Murray, C. J., Ikuta, K. S., Sharara, F., Swetschinski, L., Robles Aguilar, G., Gray, A., Han, C., Bisignano, C., Rao, P., Wool, E., & Naghavi, M. (2022). Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *The Lancet*, *399*(10325),

P-ISSN: 2811-1516
E-ISSN: 2811-1524

629–655. https://doi.org/10.1016/S0140-6736(21)02724-0

Naidoo, R., Essack, S. Y., & Bester, L. A. (2023). Environmental dissemination of *bla* $_{NDM}$-positive Enterobacteriaceae in South African hospital effluents and associated patient colonization. *Journal of Hospital Infection*, *132*, 78–85. https://doi.org/10.1016/j.jhin.2022.10.009

Okeke, I. N., Fayemiwo, S. A., Olayinka, B. O., Eberle, K. N., & Adeyemo, A. T. (2023). Tracking antimicrobial resistance in the Nigerian environment. *Journal of Global Antimicrobial Resistance*, *31*, 230–238. https://doi.org/10.1016/j.jgar.2022.09.014

Olalekan, A. M., Onwugamba, F., Iwalokun, B., Mellmann, A., Becker, K., & Schaumburg, F. (2020). High proportion of carbapenemase-producing *Escherichia coli* and *Klebsiella pneumoniae* among extended-spectrum beta-lactamase-producers in Nigerian hospitals. *Journal of Global Antimicrobial Resistance*, *21*, 8–12. https://doi.org/10.1016/j.jgar.2020.02.009

Olowo, O. A., Ajayi, A. O., & Olalekan, A. M. (2024). Comparative evaluation of the VITEK 2 automated system and molecular methods for detection of carbapenem resistance in clinical and environmental isolates from Nigeria. *Journal of Microbiological Methods*, *216*, Article 106889. https://doi.org/10.1016/j.mimet.2024.106889

Tamma, P. D., Aitken, S. L., Bonomo, R. A., Mathers, A. J., van Duin, D., & Clancy, C. J. (2021). Infectious Diseases Society of America guidance on the treatment of extended-spectrum beta-lactamase-producing Enterobacterales (ESBL-E), carbapenem-resistant Enterobacterales (CRE), and *Pseudomonas aeruginosa* with difficult-to-treat resistance. *Clinical Infectious Diseases*, *72*(7), e169–e183. https://doi.org/10.1093/cid/ciaa1478

World Health Organization. (2021). *Global antimicrobial resistance and use surveillance system (GLASS) report 2021*. https://www.who.int/publications/i/item/9789240027336