



Antibiotic resistance profiles in Gram-negative bacteria causing bloodstream and urinary tract infections in paediatric and adult patients in Ndola District, Zambia, 2020–2021

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SUMMARY

Background: Bloodstream infections (BSIs) and urinary tract infections (UTIs) caused by antibiotic resistant bacteria (ARB) have unfavourable treatment outcomes and negative economic impacts.

Objectives: The main objective of this study was to determine antibiotic resistance profiles in Gram-negative bacteria (GNB) causing BSIs and UTIs.

Method: A prospective study from October 2020 to January 2021 at Ndola Teaching Hospital and Arthur Davison Children's Hospital in the Ndola district, Zambia. Blood and urine samples collected from inpatients and outpatients presenting with fever and/or urinary tract infection symptoms were submitted for microbiological analysis. Pathogen identification and antibiotic susceptibility was determined by the automated VITEK 2 Compact machine. Resistance genes to commonly used antibiotics were determined using polymerase chain reaction. Data were analysed using SPSS version 28.0.

Results: One hundred and ten GNB were isolated, *E. coli* (45.5%) was predominant, with varying resistance profiles to different antibiotic classes. Resistance to third-generation

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cephalosporin was highest in *Enterobacter cloacae* (75%) and *Klebsiella pneumoniae* (71%), respectively. Emergence of carbapenem resistance was noted with the highest being 17% in *Acinetobacter baumannii*. Notably, the prevalence of multi-drug resistance was 63% and extensively drug-resistance was 32%. Resistance gene determinants identified included *bla*_{CTX-M}, *qnrA* and *bla*_{NDM}.

Conclusion: High level antibiotic resistance was observed in GNB known to be prevalent causative agents of BSIs and UTIs locally in Zambia. Improving microbiology diagnostic capacity, strengthening antimicrobial stewardship programs and enforcing infection prevention and control measures are of utmost importance in promoting rational use of antibiotics and preventing the spread and emergence of resistant pathogens.

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Introduction

Antimicrobial resistance (AMR) is a global crisis with public health and economic impact, the impact of AMR is reported to be severe in low- and middle-income countries (LMICs) with inadequate hospital infrastructure, poorly funded health systems, and insufficient water sanitation and hygiene (WASH) infrastructure [1,2]. These factors have been linked to the rise and spread of AMR, resulting in limited antibiotic treatment options, prolonged hospital stays and increased morbidity, mortality and treatment costs [3]. Bloodstream infections (BSIs) and urinary tract infections (UTIs) caused by resistant bacteria have several negative economic impacts [1,4]. BSIs are also a leading cause of morbidity and mortality among hospitalised patients, with an estimated overall mortality of 15%–30%, especially when preceded by severe sepsis or septic shock [5,6].

BSIs can be classified as primary bacteraemia, defined as bacteraemia without a documented source of infection or secondary bacteraemia, which develops from an evident area of infection as the source, such UTI [7]. BSIs and UTIs can either be community-acquired infections (CAIs) or hospital-acquired infections (HAIs) [8]. HAIs are infectious diseases not present at admission but acquired in a healthcare facility after 48 hours of admission [8]. It has been estimated that approximately 30% of hospital-acquired BSIs are caused by multi-drug resistant (MDR) Gram-negative bacteria (GNB) and are linked to higher mortality [9,10]. UTIs are among the most common infections and the second most common clinical indication for empirical antimicrobial treatment in most primary and secondary healthcare facilities [11]. Due to limited diagnostic capacity in LMICs, UTIs are often treated empirically before culture results are available [12]. Consequently, there is excessive use of antibiotics, and many prescriptions are considered to be inappropriate [13,14].

The rise in AMR poses treatment challenges for BSIs and UTIs, with the major concern being the emergence and global spread of multidrug-resistant organisms (MDRO), such as ESBL producers, carbapenem-resistant *Enterobacterales* (CRE) and MDR non-lactose fermenters such as *Pseudomonas aeruginosa* and *Acinetobacter* species [15]. Several studies have demonstrated high mortality attributable to BSI as a result of MDROs [16–19]. This study aimed at establishing antibiotic resistance profiles in GNB causing BSIs and UTIs at two tertiary hospitals in Ndola district of Zambia.

Methods

Materials and methods

Ethical approval

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics committee at ERES Converge Research Ethics Board (Ref. No. 2019-Aug-017). The regulatory approval was obtained from the National Health Research Authority (NHRA) of Zambia. Informed consent was sought and obtained from all participants. The study participants were assured of confidentiality by pseudonymisation. In order to ensure safety, the collection of samples was performed by a qualified health professional when clinically indicated.

Study design and site

A prospective study conducted at the Ndola Teaching Hospital (NTH) and Arthur Davison Children's Hospital (ADCH) in the Ndola district in the Copperbelt Province of Zambia. Between October 2020 and January 2021, GNB isolated from blood and urine samples routinely submitted to microbiology laboratories as part of the routine investigation and patient care were included. NTH is a national tertiary hospital with a bed capacity of approximately 800, offering health care services to the adult population, while ADCH is a paediatric hospital with a bed capacity of 250, offering specialised care to paediatric population.

According to the 2020 Zambia standard treatment guidelines, ampicillin/amoxicillin, nitrofurantoin, ciprofloxacin or ceftriaxone are the first line and empiric treatment options for UTIs and pyelonephritis while ceftriaxone is the drug of choice for empiric treatment in cases of bloodstream infections [22,23].

Specimen collection and processing

As per hospital policy and routine healthcare provision, consent was obtained from admitted patients to collect blood and urine samples from (inpatients who presented with fever and/or other symptoms suggestive of BSI and UTI. Similarly, urine samples were collected from outpatients that presented with symptoms suggestive of UTI. Laboratory request forms

were filled in for demographic data. Blood was inoculated in automated or manual aerobic blood culture bottles (Becton Dickinson). The blood culture bottles were transported to the microbiology laboratories and incubated in the BD BACTEC™ FX blood culture machine (BD BACTEC™ FX 9050, Wokingham, Berkshire, United Kingdom). All blood culture samples that flagged positive were sub-cultured on MacConkey, blood, and chocolate agar plates (Oxoid, Basingstoke, UK). Blood and chocolate agar plates were incubated for 18–24 hours in a 5% carbon dioxide incubator, while MacConkey agar plates were incubated aerobically at 35–37 °C for 18–24 hours.

Urine samples were collected in two 2ml sterile containers; one was used for urinalysis and the other for culture. This was done to observe the sterile aseptic procedure and prevent contamination. The urine was sub-cultured on blood and CLED agar plates (Oxoid, Basingstoke, UK). The incubation condition was set as per the standard protocol documented for the blood culture samples above. After incubation, MacConkey and CLED plates were then examined for lactose- and non-lactose fermenters suggestive of GNB. A Gram stain was performed to confirm Gram-negative morphology. For urine samples, all pure growths of GNB and those that met the laboratory's standard operating procedure criteria of significant GNB growth in mixed growths were processed. The inclusion and exclusion criteria for the culture growths was based on whether growth was pure or mixed. Additionally, bacterial quantification was used to determine between infection and contamination. A bacterial count of 10^5 organisms/ml or more from fresh clean catch urine was considered as true infection, while those between 10^4 – 10^5 /ml and less than 10^4 were interpreted based on clinical details provided. Where clinical details were missing, a repeat specimen was requested. The samples processed did not include urinary catheter samples and/or catheter tips. The white cell count threshold was not included as a qualification for eligibility in this study. Additionally, only GNB from one specimen type per patient were included in this study.

Identification, antimicrobial susceptibility testing (AST)

All the GNB isolates were stored in glycerol at -80°C and transported to the University Teaching Hospitals (UTHs) Microbiology Reference Laboratory in Lusaka, Zambia. Identification and AST was achieved by using the VITEK® 2 Compact instrument (bioMérieux). VITEK GN and AST-GN83/GN86 cards were used for identification and AST, respectively. Each batch of Vitek cards was quality-controlled using ATCC *Escherichia coli* 25922 control strain. Results were entered into WHONET 2020, where the proportion of resistant (R %), intermediate (I %), susceptible (S %) and MDR %, XDR %, and PDR % were estimated. MDR isolates were defined as any GNB isolate resistant to at least one agent in three or more antibiotic classes; XDR as bacteria resistant to at least one agent in all but two or fewer antimicrobial categories and pan drug-resistant (PDR) was defined as bacteria resistance to all agents in all antimicrobial categories [20].

Deoxyribonucleic acid (DNA) extraction and molecular analysis

Following the AST analysis, DNA was extracted from bacterial isolates resistant to a third-generation cephalosporin (3GC,

cefotaxime), a fluoroquinolone (ciprofloxacin), and a carbapenem (imipenem/meropenem) using the Nuclisense Bio-merieux easyMAG as described in the easyMAG user manual. PCR was performed using Sigma-Aldrich primers. The following resistance gene determinants were screened; ESBL determinants (*bla*TEM, *bla*SHV, *bla*CTX-M), *AmpC* β-lactamase (*ampC*), fluoroquinolone resistance determinants [plasmid-mediated quinolone resistance (PMQR) genes *qnrA*, *qnrB* and *qnrS*] and carbapenem resistance determinants (*bla*OXA, *bla*NDM, *bla*-VIM)]. The primer selection and PCR protocol used was based on the study by Farkas *et al.* [21]. PCR reactions were carried out using the following protocol: 2 µL of extracted DNA was combined with 12.5 µL of 2X master mix, 1 µL forward and 1 µL reverse primer, and the mixture was made up to a 25 µL volume with nuclease-free water. PCR amplification using the Veriti 96 Well Thermal Cycler-Applied Biosystems (Pittsburgh, PA, USA) was initiated at 96 °C (1 min), followed by 35 cycles at 96 °C denaturation (1min), annealing (1min), extension at 72 °C (2mins) and final extension was at 72 °C (10mins). Positive samples were used as positive controls, and nuclease-free water was included in each amplification reaction as a negative control. The PCR products (1/10 volume) were analysed by gel electrophoresis (Bio-Rad, Hercules, CA, USA) at 100 volts for 30 minutes using 1.5 % agarose gels (BD Difco™) in 1X TAE buffer (Tris-acetate EDTA). The gels were stained with ethidium bromide (Sigma, St. Louis, MO, USA), and PCR products were visualised under ultraviolet light. A single band with amplicon sizes as was demonstrated by Farkas *et al.* [21].

Statistical analysis of AST data

Laboratory data and results were collected using the CSPro 7.6 and then exported to Excel® spreadsheets, where pseudonymisation was done before being exported to SPSS® version 28.0 (International Business Machines Corporation) for statistical analysis. Descriptive statistics were summarised as frequencies and percentages.

The AST analysis was done for all the GNB, for *E. coli* (n = 50) and *Klebsiella Pneumoniae* (n = 28). The antibiotic susceptibility analysis excluded intrinsic resistance and those that lacked CLSI breakpoints. An example of intrinsic resistance is ampicillin resistance in *Klebsiella pneumoniae* isolates.

Results

Demographic characteristics of patients and specimen type

The descriptive characteristics of study participants are shown in Table I. The age group 10–16 years was the most predominant in the paediatrics group and 36–54 years in the adult group. In the under-five age group, only two were neonates (≤30 days). Urine accounted for 80.9% (89/110), of the total samples collected; Most patients were inpatients 74% (81/110) (Table I).

Distribution of pathogens

A total of 110 GNB were isolated from blood and urine samples during our study period, and the prevalence of isolated GNB is described in Table II. Thirteen GNBs from blood culture

Table I
Descriptive characteristics of study participants (n=110)

Variables	Levels	Frequency/ Percentage(n)/%
Age (years)	< 5 years	7 (6.4)
	5–9 years	5 (4.50)
	10–16 years	12 (10.9)
	17–35 years	27 (24.5)
	36–54 years	34 (30.9)
	≥ 55 years	25 (22.7)
Patient categories	Neonates	2 (1.8)
	Paediatrics	24 (21.6)
	Adults	85 (76.6)
Sex	Female	58 (52.7)
	Male	52 (47.3)
Specimen type	Blood	21(19.1)
	< 5 years	6 (29)
	5–9 years	3 (14)
	10–16 years	4 (19)
	17–35 years	3 (14)
	36–54years	5 (24)
	≥ 55 years	0
	Urine	89 (80.9)
	< 5 years	2 (2)
	5–9 years	1(1)
	10–16 years	8 (9)
	17–35 years	23 (26)
	36–54 years	30 (34)
	≥ 55 years	25 (28)
Hospital department	In-patient	81(73.6)
	Out-patient	29 (26.4)
Hospital	Children's Hospital	21 (19.1)
	Adult Hospital	89 (80.9)

were from ADCH, while eight were from NTH, 81 GNBs from urine were from NTH, and eight were from ADCH. *E. coli* was the most prevalent in urine and blood specimens (Table II). *Acinetobacter baumannii* and *Pseudomonas aeruginosa* were isolated from inpatients exclusively (Table II).

Antimicrobial susceptibility results

Resistance profiles for all the tested GNB revealed the highest resistance to co-trimoxazole and ampicillin, both at 85%. Resistance to ampicillin-sulbactam, cefazolin, commonly used ciprofloxacin, and cefotaxime was 63%, 60%, 59% and 51%, respectively. Resistance was lowest to meropenem (4%) and piperacillin-tazobactam (3%), and no resistance to amikacin was recorded with very few (3%) intermediate isolates (Figure 1).

The highest resistance in *E. coli* isolates was observed to ampicillin (92%), co-trimoxazole (92%) and ciprofloxacin (72%). Resistance to cefotaxime, piperacillin-tazobactam and meropenem was 52%, 14% and 2% respectively. There was no resistance to the two tested aminoglycosides, amikacin and gentamicin (Figure 2).

Resistance to third-generation cephalosporins [cefotaxime (71%) and ceftazidime (64%)], nitrofurantoin (57%), fourth-generation cephalosporins [cefepime (42%)] and meropenem (7%) was higher in *Klebsiella pneumoniae* isolates compared to

E. coli isolates. Resistance to piperacillin-tazobactam was 4%, lower than what was observed in *E. coli* with gentamicin resistance at 4%. Resistance to co-trimoxazole and ciprofloxacin was at 79% and 68%, respectively, lower than recorded in *E. coli* isolates (Figure 3).

There was no meropenem and piperacillin-tazobactam resistance in *Proteus mirabilis* and *Enterobacter cloacae* isolates. *Enterobacter cloacae* isolates were highly resistant to co-trimoxazole (88%), cefotaxime (75%) and ciprofloxacin (75%). *Acinetobacter baumannii* isolates had the highest resistance to piperacillin-tazobactam (33%) and meropenem (17%) compared to all the other GNBs in this study. There was no resistance to third and fourth-generation cephalosporin, meropenem and piperacillin-tazobactam in *Morganella morganii* isolates.

Notably, resistance to first line and empiric treatment antibiotic options was relatively high (Figures 1–3). Additionally, there was resistance to antibiotics used to treat invasive infections in isolates from outpatients. The resistance was categorized as MDR (69), Possible XDR [35], True XDR [3] and PDR [1]. *E. coli* had the most MDR strains (35/69), followed by *K. pneumoniae* (22/69). Only *Klebsiella pneumoniae* had a PDR strain (Table II).

ESBL resistance gene determinants (*bla*_{CTX-M}, *bla*_{SHV}, *bla*_{TEM}) were identified in *E. coli*, *Klebsiella pneumoniae*, and *Enterobacter cloacae* isolates. *bla*_{CTX-M} was the most prevalent, compared to *bla*_{TEM} and *bla*_{SHV}. *E. coli* had the most *bla*_{CTX-M} and *bla*_{TEM} resistance gene determinants, while *Klebsiella pneumoniae* had the most *bla*_{SHV}. Only *E. coli* had an *ampC*-producing isolate. Plasmid-mediated quinolone resistance (PMQR) gene *qnrA* was found in all GNB tested (Table II). Carbapenem resistance gene determinants were identified in *Acinetobacter baumannii* (*bla*_{VIM} and *bla*_{NDM}) and *Klebsiella pneumoniae* (*bla*_{NDM} and *bla*_{OXA-48}) only (Table II).

Discussion

This study aimed to establish the antibiotic resistance profiles in GNB isolated from BSIs and UTIs at two tertiary hospitals in Ndola, Zambia. Despite the high burden of infectious diseases and associated morbidity and mortality in LMICs, the availability of diagnostic microbiology services for bloodstream infections is frequently limited by cost and infrastructure, as well as frequent lack of stock of blood culture bottles [24]. This may partly explain why urine cultures outnumbered blood cultures in this study. Comparably, a study done in 2019 at NTH found urine specimens (59%) to outnumber blood cultures (13%) of all samples processed [25]. UTIs are the primary source in approximately 10–30% of all BSIs resulting in sepsis, with high morbidity and mortality, and patients with community-acquired UTIs or BSIs are among the leading cause of empirical outpatient antibiotic prescriptions [26,27]. It is, therefore, important to assess antimicrobial resistance profiles of pathogens causing UTIs as this may help formulate empiric treatment options, especially in areas where blood culture services are unavailable.

E. coli was the leading pathogen in this study, this was similar to the finding in a study that assessed phenotypic and genotypic antibiotic susceptibility profiles of GNB isolated from BSIs at the University Teaching Hospital in Lusaka, Zambia [28]. Although a study at Livingstone Central Hospital in Zambia, located about 500 km from UTH, recorded *Staphylococcus*

Table II
Isolated pathogens per ward, specimen type, resistance type/genes

Isolate type	<i>E. coli</i>	<i>K. Pneumoniae</i>	<i>P. mirabilis</i>	<i>E. cloacae</i>	<i>A. baumannii</i>	<i>M. morgannii</i>	<i>P. aeruginosa</i>
Location							
In-patient	33	23	9	4	6	2	4
Out-patient	17	5	1	4	-	2	-
Total	50	28	10	8	6	4	4
Specimen type							
Blood	7	6	0	1	3	1	3
Urine	43	22	10	7	3	3	1
Total	50	28	10	8	6	4	4
Resistance type							
MDR	35	22		5	2	3	-
Possible XDR	12	15		5	2	1	-
True XDR	1	2		-	-	-	-
PDR	-	1		-	-	-	-
Resistance genes							
<i>bla</i> CTX-M	21	16		5	-		
<i>bla</i> SHV	4	13		1	-		
<i>bla</i> TEM	10	7		4	-		
<i>ampC</i>	1	-		-	-		
<i>qnrA</i>	7	1		2	1		
<i>qnrB</i>	14	6		4	-		
<i>qnrS</i>	8	9		1	-		
<i>bla</i> VIM	-	-		-	1		
<i>bla</i> NDM	-	1		-	1		
<i>bla</i> OXA-48	-	1		-	-		

Key: The criteria for multiple drug resistance patterns was defined as follows.

Multi-drug resistance (MDR): Non-susceptible to ≥ 1 agent in ≥ 3 antibiotics.

Extensive drug resistance (XDR): Non-susceptible to ≥ 1 agent in all but ≤ 2 categories.

Pan drug resistance (PDR): Non-susceptible to all antibiotic agents listed.

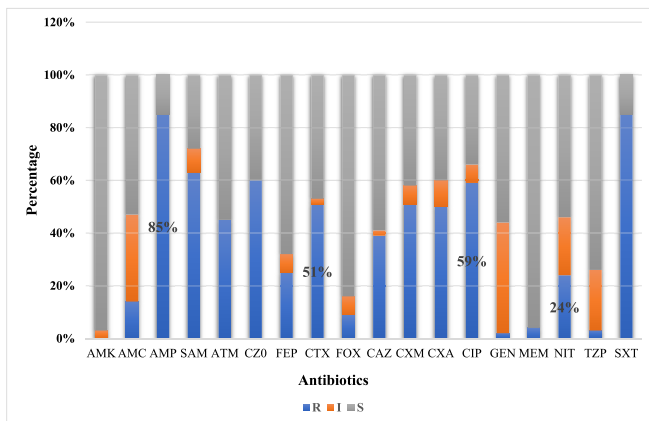


Figure 1. Antibiotic susceptibility profiles for all the GNB tested. Abbreviations: AMK - Amikacin, AMC - Amoxicillin-clavulanate, AMP - Ampicillin, SAM - Ampicillin-sulbactam, ATM - Aztreonam, CZO - cefazolin, FEP - Cefepime, CTX - Cefotaxime, FOX - Cefoxitin, CAZ - Ceftazidime, CXM - Cefuroxime, CXA - Cefuroxime axetil, CIP - Ciprofloxacin, GEN - Gentamicin, MEM - Meropenem, NIT - Nitrofurantoin, TZP - Piperacillin-tazobactam, SXT - Co-trimoxazole. *Ampicillin (85% resistance), ciprofloxacin (59% resistance) and nitrofurantoin (24% resistance) are the commonly used antibiotics as first line treatment for UTIs. *Ceftriaxone (51% resistance) is the commonly used antibiotic as first line treatment for pyelonephritis and BSIs.

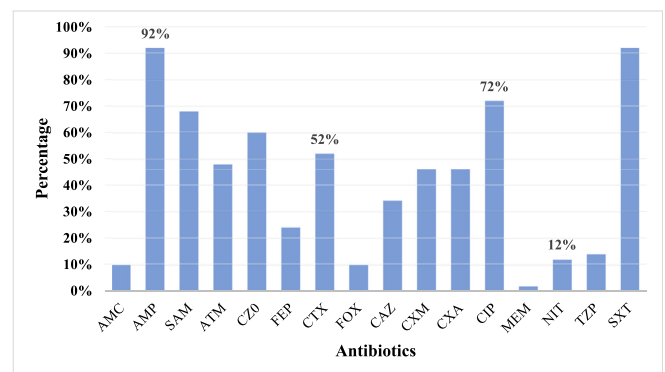


Figure 2. Antibiotic resistance profiles for *E. coli* (n = 50). Abbreviations: AMC - Amoxicillin-clavulanate, AMP - Ampicillin, SAM - Ampicillin-sulbactam, ATM - Aztreonam, CZO - cefazolin, FEP - Cefepime, CTX - Cefotaxime, FOX - Cefoxitin, CAZ - Ceftazidime, CXM - Cefuroxime, CXA - Cefuroxime axetil, CIP - Ciprofloxacin, GEN - Gentamicin, MEM - Meropenem, NIT - Nitrofurantoin, TZP - Piperacillin-tazobactam, SXT - Co-trimoxazole. *Ampicillin (92% resistance). Ciprofloxacin (72% resistance) and Nitrofurantoin (12% resistance) are the commonly used antibiotics as first line treatment for UTIs. *Ceftriaxone (52% resistance) is the commonly used antibiotic as first line treatment for pyelonephritis and BSIs.

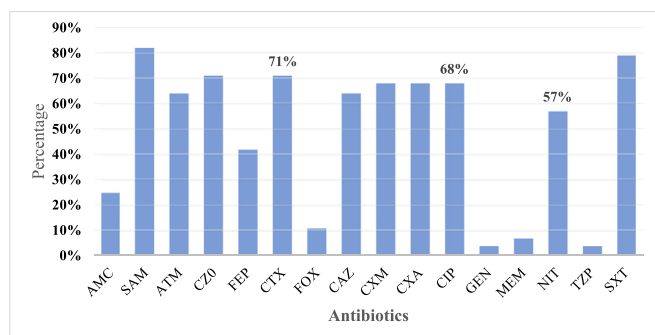


Figure 3. Antibiotic resistance profiles for *Klebsiella pneumoniae* (n = 28). Abbreviation: AMC - Amoxicillin-clavulanate, SAM - Ampicillin-sulbactam, ATM - Aztreonam, CZO - cefazolin, FEP - Cefepime, CTX - Cefotaxime, FOX - Cefoxitin, CAZ - Ceftazidime, CXM - Cefuroxime, CXA - Cefuroxime axetil, CIP - Ciprofloxacin, GEN - Gentamicin, MEM - Meropenem, NIT - Nitrofurantoin, TZP - Piperacillin-tazobactam, SXT - Co-trimoxazole. *Ciprofloxacin (72% resistance) and nitrofurantoin (57%) are the commonly used antibiotics as first line treatment for UTIs. *Ceftriaxone (71% resistance) is the commonly used antibiotic as first line treatment for pyelonephritis and BSIs.

aureus as the leading cause of infections (excluded in this study), *E. coli* was the second leading cause and predominant among GNB [29]. Comparable to our findings, a study that assessed MDR uropathogens causing community-acquired UTIs among patients attending healthcare facilities in Tanzania found *E. coli* to be the predominant causative agent [30]. The 2017–2019 Global Antimicrobial Resistance and Use Surveillance System (GLASS) data from 12 African countries, which included Zambia, revealed *Staphylococcus aureus* and *Klebsiella pneumoniae* as the prevalent cause of BSIs, while *E. coli* was the most frequent etiological agent of UTIs [31]. The predominance of *E. coli* as the causative agent of BSIs and UTIs is a public health concern, owing to undesirable outcomes as was recorded in the global burden of bacterial antimicrobial resistance (GRAM) study, where *E. coli* had the highest deaths attributable to and associated with AMR [32].

The high level resistance of GNB to co-trimoxazole could be attributed to the extensive use of co-trimoxazole for the prevention of *Pneumocystis carinii*, an opportunistic pathogen that causes pneumonia in patients with HIV, a practice that promotes selection pressure as a result of prolonged use, hence increasing the levels of resistance [33,34]. Resistance to third-generation cephalosporins (cefotaxime) was highest in *Enterobacter cloacae* (75%), *Klebsiella pneumoniae* (71%), and *E. coli* (52%); this was similar to the findings in the GLASS 2017–2019 report from the African continent that recorded higher resistance to 3GC in *Klebsiella pneumoniae* (81%) than in *E. coli* (50%) BSI isolates [31]. Another study at the University Teaching Hospital in Lusaka, Zambia, also recorded higher 3GC resistance in *Klebsiella pneumoniae* (67%) than in *E. coli* (54%) [28]. Our findings were, however, different from a Korean study that assessed 3GC resistance of community onset *E. coli* and *Klebsiella pneumoniae* bacteraemia in a secondary hospital, which recorded higher resistance to 3GC and ESBL-producing strains in *E. coli* (6.6% and 6.4%) compared to *Klebsiella pneumoniae* (4.9% and 3.3%) [35]. Notably, there was an increase in 3GC resistance in GNB infections in this study compared to a study done at the

same hospital in 2016–2018, which recorded 3GC resistance below 60% [25]. This indicates continued overuse of 3GC and warrants the development of a facility-specific antibiograms supported by facility-generated microbiology data.

Notable, was resistance to antibiotics used for the treatment of invasive infections and/or MDR pathogens in hospital settings in outpatients, a trend that has been increasing and observed in other countries [36,37]. The rise in resistance in community-acquired infections has been attributed to self-medication, the overuse of antibiotics in some facilities that perform procedures or operations in outpatient settings without hospitalisation, as well as the widespread use of antibiotics of clinical importance in agriculture and the food-producing industry [36,38,39].

Resistance to carbapenems was higher in *Acinetobacter baumannii* (17%) compared to other pathogens such as *Klebsiella pneumoniae* (7%) and *E. coli* (2%). A multinational prospective cohort study (PANORAMA) that assessed the effect of carbapenem resistance on the outcome of BSIs caused by *Enterobacterales* in LMICs established an increased length of hospital stay and mortality in patients with BSIs caused by carbapenem resistance [40]. Additionally, the growing presence of MDR, XDR and PDR pathogens is of utmost concern as they are associated with increased mortality [41].

ESBL and carbapenemase producers pose a substantial threat to many classes of antibiotics [42]. The presence of ESBL resistance genes such as *bla*_{CTX-M} and the occurrence of carbapenem resistance genes such as *bla*_{VIM}, *bla*_{NDM} and *bla*_{OXA-48} leads to expanded resistance to beta-lactam drugs that are the last resort treatment option for infections caused by MDR and ESBL-producing GNB [22,28,42]. To successfully manage infections caused by MDR-GNB, it is essential to distinguish between ESBL and carbapenemase-producing isolates [43]. Additionally, the presence of PMQR that confers resistance to fluoroquinolones, one of the commonly used groups of antibiotics for treating UTIs, further narrows the treatment options, thereby leading to poor outcomes [44]. Accurate and prompt detection of antimicrobial resistance genes can promote appropriate antibiotic use, improve patient outcomes and reduce hospital costs [45].

Conclusion

The high-level antibiotic resistance observed, warrants improved diagnostic capacity, implementation of IPC measures and strengthened antimicrobial stewardship programs. IPC prevents the development and spread of ARB while improved diagnostic capacity supports the development of local antibiograms and treatment guidelines based on facility-generated microbiology data; thereby promoting rational use of antimicrobials. Every infection prevented, reduces the need to use antibiotics.

Credit author statement

Conceptualisation: KY and JBM. Data collection: KY and FM, Laboratory analysis: KY and AM. Data analysis: KY, JBM and AS. Writing original draft: KY. Review and editing: JBM, RC, MM, JYC, DC, SM, MTS, BNC, MF, MC, FM, PM and FNB. All authors have read and approved the final revised manuscript.

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Conflict of interest

The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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