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Investigating the prevalence of multidrug-resistant enterobacterales at a quaternary hospital in KwaZulu-Natal, South Africa: a retrospective cross-sectional study of ESBL-producing isolates.

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ABSTRACT

Background:
The emergence of multidrug-resistant Enterobacterales (MDRE) presents a major challenge in healthcare settings due to limited therapeutic options and increased morbidity. Extended-spectrum β-lactamases (ESBLs) confer resistance to multiple β-lactam antibiotics and are widely disseminated through plasmid-mediated mechanisms, compromising the effectiveness of commonly used antimicrobial agents. This study aimed to evaluate the prevalence of ESBL-producing Enterobacterales (ESBL-PE) and describe associated antimicrobial susceptibility patterns at a quaternary hospital in KwaZulu-Natal, South Africa.

Methods:
A retrospective cross-sectional descriptive study was conducted using laboratory data from 2,421 Enterobacterales isolates recovered from clinical specimens of infected patients at a quaternary hospital in KwaZulu-Natal, South Africa, between January 2023 and December 2023. Data were analysed to determine the prevalence of ESBL-producing Enterobacterales, identify predominant ESBL-producing species, and describe their antimicrobial susceptibility profiles.

Results:
ESBL-producing Enterobacterales accounted for 27.8% (672/2 421) of all Enterobacterales isolates. *Escherichia coli* and *Klebsiella pneumoniae* species were the predominant ESBL producers. Antimicrobial susceptibility testing demonstrated high levels of resistance to β-lactam antibiotics and fluoroquinolones among ESBL-producing Enterobacterales. Carbapenems remained active against the majority of ESBL-producing isolates; however, reduced susceptibility was identified among a subset of *Klebsiella pneumoniae* isolates.

Conclusion:
This study demonstrates a substantial burden of ESBL-producing Enterobacterales in a quaternary hospital setting. The observed resistance patterns highlight the importance of strengthened antimicrobial stewardship, susceptibility-guided therapy, and ongoing surveillance to limit the spread of multidrug-resistant pathogens.

Recommendations:
Further studies are warranted to investigate molecular resistance mechanisms and potential sources of transmission.

Keywords: *Multidrug-resistant Enterobacterales; extended-spectrum β-lactamase-producing Enterobacterales; antimicrobial resistance; Klebsiella pneumoniae; Escherichia coli; antimicrobial stewardship*
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INTRODUCTION
Antimicrobial resistance (AMR) is a major global public health challenge that threatens the effective prevention and treatment of infectious diseases. The increasing prevalence of multidrug-resistant organisms (MDROs), particularly multidrug-resistant Enterobacterales (MDRE), has resulted in limited therapeutic options, prolonged hospitalisation, increased healthcare costs, and higher morbidity and mortality worldwide (Jernigan et al., 2020; Kakoullis et al., 2021). The emergence and spread of AMR are largely driven by inappropriate and excessive use of antimicrobial agents, which exert selective pressure

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that favours the survival and proliferation of resistant bacterial strains (van Duin et al., 2020; Telhig et al., 2022).

Within the Enterobacterales family, the production of extended-spectrum β-lactamases (ESBLs) represents one of the most clinically significant antimicrobial resistance mechanisms. ESBLs are enzymes capable of hydrolysing penicillins, third-generation cephalosporins, and monobactams, thereby compromising the effectiveness of commonly used β-lactam antibiotics (Hu et al., 2019; Castanheira et al., 2021). These resistance determinants are predominantly plasmid-mediated, facilitating horizontal gene transfer between bacterial species and accelerating the dissemination of resistance in both hospital and community settings (Ota et al., 2019). Infections caused by ESBL-producing Enterobacterales (ESBL-PE) are associated with delayed initiation of effective therapy and poorer clinical outcomes compared to infections caused by non-resistant organisms (Stratmann et al., 2020; Kim et al., 2021).

Gram-negative bacteria such as *Escherichia coli* and *Klebsiella pneumoniae* are among the most frequently implicated ESBL-producing pathogens. These organisms are common causes of urinary tract infections, bloodstream infections, pneumonia, wound infections, and intra-abdominal infections, particularly among hospitalised patients (Zhang et al., 2021; Acolatse et al., 2022). Their ability to acquire multiple resistance mechanisms, including resistance to non-β-lactam antimicrobials, has contributed substantially to the increasing burden of multidrug-resistant infections globally (Yan et al., 2022).

The burden of ESBL-producing Enterobacterales is particularly pronounced in low- and middle-income countries, including those in sub-Saharan Africa, where limitations in diagnostic capacity, antimicrobial stewardship implementation, and infection prevention infrastructure may exacerbate resistance transmission (Arias et al., 2020; Founou et al., 2019). In South Africa, surveillance data and local studies have documented rising resistance among Enterobacterales, with ESBL production emerging as a dominant resistance mechanism in both hospital-acquired and community-associated infections (Quan et al., 2026; Ntshonga et al., 2026). Despite this, institution-specific data from quaternary referral hospitals remain limited, despite their central role in managing complex and severe infections.

Quaternary hospitals manage patients with prolonged hospital stays, extensive prior antimicrobial exposure, significant comorbidities, and frequent use of invasive medical devices, all of which increase the risk of acquisition and transmission of multidrug-resistant organisms (Rhoden et al., 2021; Willems et al., 2023). Understanding the local epidemiology of ESBL-PE and their antimicrobial susceptibility profiles in such settings is critical for informing empirical therapy, guiding antimicrobial stewardship programmes, and strengthening infection prevention and control strategies.

This study, therefore, aimed to evaluate the prevalence of multidrug-resistant Enterobacterales, with a particular focus on ESBL-producing Enterobacterales, at Inkosi Albert Luthuli Central Hospital, a quaternary referral hospital in KwaZulu-Natal, South Africa. The objectives were to determine the prevalence of ESBL-PE among Enterobacterales isolates, identify the predominant ESBL-producing species, and describe their antimicrobial susceptibility patterns. By addressing these objectives, the study contributes locally relevant evidence to support clinical decision-making, antimicrobial stewardship efforts, and surveillance initiatives aimed at mitigating the spread of antimicrobial resistance.

RESEARCH METHODOLOGY

Study design and setting

This retrospective cross-sectional descriptive study was conducted at Inkosi Albert Luthuli Central Hospital (IALCH) in Durban, South Africa. IALCH is a government-funded quaternary referral and academic hospital that receives complex and specialised cases from healthcare facilities across the KwaZulu-Natal province. Diagnostic pathology services at the hospital are provided by the National Health Laboratory Service (NHLS). Laboratory data generated between 1 January 2023 and 31 December 2023 were utilised for the study. Data analysis and reporting were conducted between July 2024 and December 2024.

Data collection and sampling

Laboratory data were retrospectively extracted from the NHLS Laboratory Information System (LIS). Before data collection

n, formal permission was obtained through the NHLS Academic Affairs Research Management System (AARMS). A purposive census sampling approach was employed to include all Enterobacterales isolates identified from microscopy, culture, and sensitivity (MC&S) testing performed at the hospital's Microbiology laboratory during the study period.

A total of 2,421 Enterobacterales isolates meeting the inclusion criteria were identified and included in the analysis. Data extraction was achieved by filtering LIS

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records to capture all Enterobacterales isolates reported within the defined study period.

Inclusion and exclusion criteria

The study included all Gram-negative Enterobacterales isolates obtained from clinical specimens of patients tested at IALCH between 1 January 2023 and 31 December 2023. Isolates that were not classified as Enterobacterales, records with incomplete or missing MC&S results, and duplicate entries were excluded from the analysis.

Diagnostic criteria and case definition

The prevalence of multidrug-resistant Enterobacterales, including ESBL-producing isolates, was determined using standard microbiological laboratory procedures. Initial assessment included Gram staining performed using a manual Gram stain technique. Bacterial identification and antimicrobial susceptibility testing were carried out using the VITEK® 2 automated system (bioMérieux, France).

ESBL production was determined using the VITEK® 2 Advanced Expert System, based on minimum inhibitory concentration (MIC) patterns for third-generation cephalosporins tested with and without clavulanic acid, in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines. Isolates demonstrating reduced susceptibility to extended-spectrum cephalosporins together with a clavulanic acid effect were classified as ESBL producers.

An anonymised dataset containing laboratory results was obtained from the NHLS Corporate Data Warehouse (CDW) following approval through the AARMS application process. Only data relevant to the study objectives were extracted and analysed.

Data analysis

Data were cleaned and filtered using Microsoft Excel (version 2409), and statistical analysis was performed using IBM SPSS Statistics (version 30.0). Descriptive statistics were used to summarise the data. The prevalence of ESBL-producing Enterobacterales was calculated as the proportion of ESBL-positive isolates among all Enterobacterales isolates analysed and presented graphically. The distribution of Enterobacterales species was summarised using frequencies and percentages and presented in tabular format.

Antimicrobial susceptibility patterns of ESBL-producing isolates were analysed descriptively and reported as proportions of isolates classified as susceptible, intermediate, or resistant to each antimicrobial agent. Species distribution and antimicrobial susceptibility results were presented using tables.

Ethical considerations

Ethical approval for the study was obtained from the Mangosuthu University of Technology (MUT) Research Ethics Committee (REF: RD5/22/2024). Permission to access NHLS laboratory data was granted through the NHLS AARMS system (Permission number: PR2455063).

The study involved a retrospective review of laboratory records, and no direct patient contact was required. Patient identifiers were not collected, and all data were analysed in anonymised form to ensure confidentiality. The study utilised existing laboratory data only and posed no additional risk or harm to patients. No personal or sensitive patient information was disclosed at any stage of the research.

RESULTS

Overview of findings

This section presents the findings of the study describing the prevalence, organism distribution, and antimicrobial susceptibility patterns of extended-spectrum β-lactamase-producing Enterobacterales isolated at Inkosi Albert Luthuli Central Hospital during the study period. Results are presented descriptively using tables and figures to summarise key findings.

A total of 2,421 Enterobacterales isolates met the inclusion criteria and were included in the analysis.

Prevalence of ESBL-producing Enterobacterales

Figure 1 illustrates the proportion of Enterobacterales isolates identified as extended-spectrum β-lactamase (ESBL) producers among all isolates analysed during the study period.

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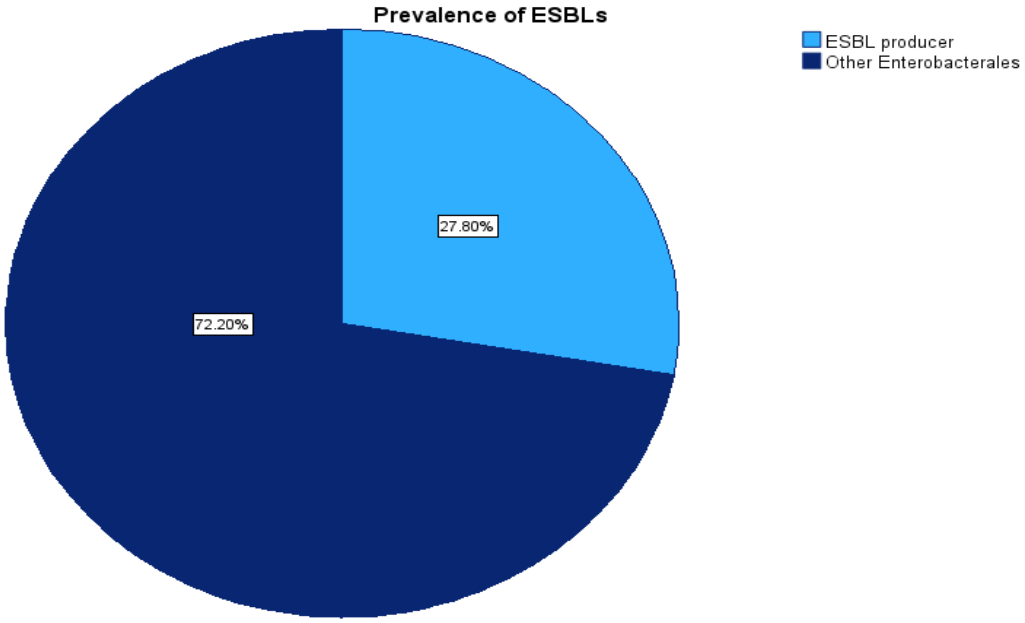

Figure 1: Prevalence of ESBL-producing Enterobacterales among all isolates analysed (n = 2421)

Distribution of ESBL-producing Enterobacterales species

The distribution of ESBL-producing Enterobacterales species is summarised in Table 1. *Escherichia coli* was the most frequently isolated ESBL-producing organism. *Klebsiella pneumoniae* isolates, including identified subspecies, collectively accounted for a substantial proportion of ESBL producers. Other Enterobacterales species were isolated less frequently. These included members of the *Enterobacter cloacae* complex, *Proteus mirabilis*, *Klebsiella oxytoca*, *Citrobacter* species, *Morganella morganii*, and *Serratia marcescens*.

Table 1: Distribution of ESBL-producing Enterobacterales isolated during the study period (n = 2421)

Organism	Count	%
Citrobacter freundii	2	0.3%
Citrobacter koseri	1	0.1%
Enterobacter cloacae	1	0.1%
Enterobacter cloacae complex	6	0.9%
Escherichia coli	299	44.5%
Klebsiella oxytoca	5	0.7%
Klebsiella pneumoniae	168	25.0%
Klebsiella pneumoniae subsp ozaenae	1	0.1%
Klebsiella pneumoniae subsp pneumoniae	178	26.5%
Morganella morganii	2	0.3%
Morganella morganii subsp. morganii	1	0.1%
Proteus mirabilis	6	0.9%
Serratia marcescens	2	0.3%

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Antimicrobial susceptibility patterns of predominant ESBL producers

Antimicrobial susceptibility analysis focused on the three most commonly isolated ESBL-producing organisms: *Escherichia coli*, *Klebsiella pneumoniae*, and *Klebsiella pneumoniae* subsp. *pneumoniae*. Antibiotics tested reflect routine clinical antimicrobial susceptibility panels used for each species.

Antimicrobial susceptibility of ESBL-producing Escherichia coli

The antimicrobial susceptibility profile of ESBL-producing *Escherichia coli* is presented in Table 2. Resistance to penicillins and third-generation cephalosporins was commonly observed. Variable susceptibility was noted for fluoroquinolones and β-lactam/β-lactamase inhibitor combinations. Aminoglycosides and carbapenems demonstrated higher levels of activity.

Table 2: Antimicrobial susceptibility profile of ESBL-producing Escherichia coli

Antibiotic	Resistance	Sensitivity	Intermediate	Not tested
Amoxicillin-clavulanic acid	78	119	102	0
Ampicillin/Amoxicillin	298	0	0	1
Cefotaxime	259	37	3	0
Ceftazidime	152	133	14	0
Ciprofloxacin	228	71	0	0
Amikacin	24	202	72	0
Imipenem	0	298	1	0
Meropenem	0	299	0	0

Antimicrobial susceptibility of ESBL-producing Klebsiella pneumoniae subsp. pneumoniae

The antimicrobial susceptibility patterns of ESBL-producing *Klebsiella pneumoniae* subsp. *pneumoniae* are shown in Table 3. Reduced susceptibility to penicillins and third-generation cephalosporins was observed. Susceptibility to fluoroquinolones and β-lactam/β-lactamase inhibitor combinations varied. Aminoglycosides and carbapenems largely retained activity.

Table 3: Antimicrobial Susceptibility Profile of K. pneumoniae subsp pneumoniae

Antibiotic	Resistance	Sensitivity	Intermediate	Not tested
Amoxicillin-clavulanic acid	93	20	65	0
Ampicillin/Amoxicillin	177	0	1	0
Cefotaxime	171	5	2	0
Ceftazidime	139	16	23	0
Ciprofloxacin	112	65	1	0
Amikacin	4	140	34	0
Imipenem	4	165	8	0
Meropenem	6	169	3	0

Antimicrobial susceptibility of ESBL-producing Klebsiella pneumoniae

Table 4 summarises the antimicrobial susceptibility profiles of ESBL-producing *Klebsiella pneumoniae*. Resistance to penicillins and third-generation cephalosporins was frequently observed. Susceptibility to fluoroquinolones and β-lactam/β-lactamase inhibitor combinations varied. Aminoglycosides and carbapenems demonstrated comparatively higher activity.

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Table 4: Antimicrobial susceptibility profile of ESBL-producing Klebsiella pneumoniae

Antibiotic	Resistance	Sensitivity	Intermediate	Not tested
Amoxicillin-clavulanic acid	86	27	55	0
Ampicillin/Amoxicillin	168	0	0	0
Cefotaxime	161	4	3	0
Ceftazidime	127	20	21	0
Ciprofloxacin	89	79	0	0
Amikacin	5	133	30	0
Imipenem	8	152	8	0
Meropenem	3	163	2	0

Summary of overall results

In summary, ESBL-producing Enterobacterales accounted for a notable proportion of isolates identified at this quaternary hospital during the study period. *Escherichia coli* and *Klebsiella pneumoniae* (including identified subspecies) were the predominant ESBL-producing Enterobacterales. These organisms accounted for the majority of ESBL isolates and demonstrated extensive resistance to β-lactam antibiotics, with variable susceptibility to fluoroquinolones and β-lactam/β-lactamase inhibitor combinations. Carbapenems remained the most active agents against these isolates.

DISCUSSION

Burden of multidrug-resistant Enterobacterales and ESBLs in a quaternary hospital setting

The occurrence of extended-spectrum β-lactamase (ESBL)–producing Enterobacterales in this quaternary hospital reflects a pattern that has been widely documented in tertiary and referral healthcare facilities both in South Africa and internationally. Previous studies have demonstrated that high-level healthcare institutions serve as important reservoirs for antimicrobial resistance due to sustained antibiotic selective pressure, prolonged hospitalisation, frequent invasive procedures, and repeated patient referrals from lower-level facilities (van Duin et al., 2020; Ntshonga et al., 2026). These factors create an ideal environment for the persistence and spread of MDRE.

Comparable studies conducted in South African public-sector hospitals have described ESBL-producing organisms as entrenched pathogens rather than sporadic occurrences, particularly in high-acuity settings such as intensive care units and surgical wards (Quan et al., 2026). Similar observations have been reported across Southern Africa, where ESBL production has become a dominant resistance mechanism among Enterobacterales isolated from hospitalised patients (Ntshonga et al., 2026).

The presence of ESBL-producing Enterobacterales across both inpatient and outpatient clinical services suggests that these organisms are not confined to traditional nosocomial environments. Other authors have also reported increasing detection of ESBL producers in ambulatory care, specialist clinics, and community-linked settings, indicating bidirectional transmission between community and hospital reservoirs (Diorio-Toth et al., 2023; Ramatla et al., 2023). This evolving epidemiological landscape challenges conventional infection control approaches that focus exclusively on inpatient wards.

Predominant ESBL-producing Enterobacterales

The predominance of *Escherichia coli* among ESBL-producing Enterobacterales in this study is consistent with findings from multiple regional and global investigations. Numerous authors have identified ESBL-producing *E. coli* as the leading cause of both community-acquired and healthcare-associated infections, particularly urinary tract and bloodstream infections (Castanheira et al., 2021; Kowalski et al., 2024). Its success is largely attributed to its ability to persist as a gastrointestinal commensal and acquire plasmid-mediated resistance genes that facilitate long-term colonisation and transmission.

Studies have further demonstrated that ESBL-producing *E. coli* circulates across human, animal, and environmental compartments, allowing continuous reintroduction into healthcare settings (Ramatla et al., 2023; Musicha et al., 2026). This broader ecological circulation helps explain the sustained presence of ESBL-producing *E. coli* in tertiary and quaternary hospitals.

Klebsiella pneumoniae, including identified subspecies, also features prominently in ESBL epidemiology, particularly in hospital settings. Previous studies have

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described *K. pneumoniae* as a quintessential nosocomial pathogen with exceptional capacity for acquiring resistance determinants and causing institutional outbreaks (Navon-Venezia et al., 2017). Research from Southern Africa has repeatedly highlighted *K. pneumoniae* as a major contributor to ESBL and carbapenem-resistant Enterobacterales, especially in critically ill patients with prolonged hospital stays (Ntshonga et al., 2026; Quan et al., 2026).

Other Enterobacterales species, including members of the *Enterobacter cloacae* complex, *Citrobacter* species, *Proteus mirabilis*, *Morganella morganii*, and *Serratia marcescens*, were less frequently encountered, a finding also reported by previous studies (Bandy & Tantry, 2021). Although these organisms contribute a smaller proportion of ESBL cases, they often harbour additional resistance mechanisms such as inducible AmpC β-lactamases and porin alterations, which can complicate both detection and treatment.

Antimicrobial resistance patterns in ESBL-producing organisms

The resistance patterns associated with ESBL-producing Enterobacterales observed in this study are consistent with those described in similar investigations. Extensive resistance to penicillins and third-generation cephalosporins is a defining characteristic of ESBL producers and has been widely reported across Africa and other regions (Castanheira et al., 2021; Ntshonga et al., 2026). Continued reliance on these agents in high-prevalence settings has been shown to perpetuate selection pressure and accelerate resistance dissemination.

Co-resistance between ESBL production and fluoroquinolone resistance has been frequently documented in the literature. Wales and Davies (2015) demonstrated that plasmids carrying ESBL genes often simultaneously encode fluoroquinolone resistance determinants, leading to loss of multiple first-line treatment options. Similar observations have been reported in sub-Saharan Africa, where fluoroquinolones remain widely used due to availability and oral formulation (Vink et al., 2020; Kowalski et al., 2024).

β-lactam/β-lactamase inhibitor combinations have shown variable effectiveness against ESBL producers in numerous studies. High-level ESBL expression and coexisting resistance mechanisms often compromise their clinical utility, particularly in serious infections (Castanheira et al., 2021). Consequently, many authors recommend cautious use of these agents and emphasise the importance of susceptibility-guided therapy.

Carbapenems remain the most reliable treatment option for severe ESBL-associated infections; however, increasing reports of reduced susceptibility, particularly among *K. pneumoniae*, are cause for concern. Studies from South Africa and the wider Southern African region have warned that sustained carbapenem use may drive the emergence of carbapenemase-producing Enterobacterales (Ntshonga et al., 2026; Quan et al., 2026). These findings support global calls for judicious carbapenem use and strengthened antimicrobial stewardship.

Implications for antimicrobial stewardship and infection prevention

Consistent with previous research, the findings of this study reinforce the need for robust antimicrobial stewardship programmes that are tailored to local resistance patterns. Evidence suggests that stewardship interventions, when combined with effective infection prevention and control measures, can reduce inappropriate antibiotic use and slow the spread of ESBL-producing organisms (Jernigan et al., 2020; Quan et al., 2026).

Several authors have also advocated for expansion of surveillance beyond inpatient wards to include outpatient services and referral pathways, recognising the role of ambulatory care in resistance dissemination (Ramatla et al., 2023; Musicha et al., 2026). Such integrated approaches are particularly relevant in the South African healthcare context, where patient movement across multiple levels of care is common.

Summary

Overall, the patterns observed in this study are highly consistent with findings reported by other investigators locally, regionally, and globally. The dominance of ESBL-producing *E. coli* and *Klebsiella pneumoniae*, the extensive multidrug-resistant phenotype, and the growing reliance on carbapenems reflect a well-documented and escalating challenge in modern healthcare. Without sustained surveillance, effective antimicrobial stewardship, and integrated infection prevention strategies, further expansion of antimicrobial resistance in quaternary healthcare settings is likely.

Generalizability of the study findings

The findings of this study provide institution-specific insight into the epidemiology and antimicrobial resistance patterns of extended-spectrum β-lactamase-producing Enterobacterales (ESBL-PE) within a quaternary referral hospital in KwaZulu-Natal. When considering the external validity of these findings, several factors should be considered.

Firstly, the study was conducted at a quaternary hospital that manages patients with complex medical conditions,

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prolonged hospitalisation, frequent exposure to broad-spectrum antimicrobials, and extensive use of invasive medical devices. These characteristics are recognised risk factors for the acquisition and persistence of multidrug-resistant organisms. Consequently, the prevalence and resistance patterns observed in this setting are likely to be higher than those seen in primary healthcare facilities, district hospitals, or short-stay institutions. As such, direct extrapolation of the findings to lower-acuity healthcare settings should be undertaken with caution.

Secondly, the patient population at a quaternary referral hospital differs from that in community-based or private healthcare settings, where antibiotic exposure patterns, comorbidity profiles, and healthcare contact frequency may vary. Differences in antimicrobial prescribing practices, diagnostic capacity, and infection prevention and control measures across institutions may further influence resistance profiles. These contextual differences limit the generalizability of the findings to healthcare settings with substantially different patient populations or resource availability.

Nonetheless, the findings are highly generalizable to other tertiary and quaternary referral hospitals in South Africa and similar resource-limited settings that manage comparable case mixes and face analogous antimicrobial stewardship challenges. The resistance patterns described are consistent with those reported in regional and global studies from high-acuity hospital environments, supporting their relevance beyond the study site.

Furthermore, the detection of ESBL-producing Enterobacterales in outpatient and clinic-associated samples suggests that the findings may also have partial relevance to ambulatory care and transitional care pathways, particularly in regions characterised by high antibiotic consumption and frequent patient movement between different levels of care. This highlights the potential applicability of the findings in informing antimicrobial stewardship strategies not only in inpatient settings but across the broader healthcare continuum.

In summary, while the results of this study are most applicable to quaternary and tertiary referral hospitals, they provide valuable insights relevant to similar healthcare settings nationally and regionally. Generalizability to primary care facilities, rural hospitals, private healthcare institutions, and specialised paediatric-only centres is more limited and underscores the need for local surveillance data to guide context-specific antimicrobial stewardship and infection control interventions.

Conclusion

This study evaluated the prevalence of multidrug-resistant Enterobacterales, with a particular focus on extended-spectrum β-lactamase-producing Enterobacterales (ESBL-PE), in a quaternary hospital setting in KwaZulu-Natal, South Africa. In addition, the study identified the predominant ESBL-producing species and described their antimicrobial susceptibility patterns based on routinely tested antibiotics.

The findings demonstrate a substantial burden of ESBL-producing Enterobacterales within the hospital, with *Escherichia coli* and *Klebsiella pneumoniae* identified as the dominant ESBL producers. The resistance profiles revealed extensive resistance to β-lactam antibiotics and fluoroquinolones, limited reliability of β-lactam/β-lactamase inhibitor combinations, and continued dependence on carbapenems as the most effective therapeutic agents. Of particular concern was the detection of reduced carbapenem susceptibility among *Klebsiella pneumoniae* isolates, which may signal the emergence of more advanced resistance mechanisms.

These findings have important implications for clinical management and public health practice. They underscore the critical need for strengthened antimicrobial stewardship programmes, susceptibility-guided therapy, and robust infection prevention and control measures to limit further dissemination of multidrug-resistant organisms. The establishment of effective surveillance systems, alongside investment in diagnostic capacity and antimicrobial resistance awareness initiatives, is essential to support evidence-based decision-making.

Future research should focus on investigating the emergence and spread of carbapenem-resistant Enterobacterales, assessing the role of asymptomatic carriage and environmental reservoirs, and exploring novel therapeutic and non-antibiotic strategies. Overall, this study provides valuable insight into the epidemiology of ESBL-producing Enterobacterales in a quaternary healthcare setting and contributes to the growing body of evidence informing strategies to combat multidrug-resistant infections in resource-limited settings.

Limitations

This study has several limitations that should be considered when interpreting the findings. Firstly, the retrospective design relied on routinely collected laboratory data, which limited control over data completeness and accuracy. Important clinical information, including patient comorbidities, prior antimicrobial exposure, duration of hospitalisation, clinical outcomes, and sources of infection, was not available. The absence of these variables restricted the

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ability to assess patient-level risk factors associated with ESBL production and to evaluate the clinical impact of the observed antimicrobial resistance patterns.

Secondly, the analysis was confined to microbiological data from a single quaternary referral hospital. Although the institution serves as a major referral centre for multiple regions within KwaZulu-Natal, the findings may not be fully generalizable to other healthcare settings, such as primary or secondary hospitals, private healthcare facilities, or community-based environments. Differences in patient populations, antimicrobial prescribing practices, diagnostic capacity, and infection prevention and control measures across institutions may result in varying resistance profiles.

Thirdly, the study relied exclusively on phenotypic identification of ESBL production as reported by the diagnostic laboratory. Molecular characterisation of resistance genes was not performed, which limited the ability to identify specific ESBL genotypes or to detect co-existing resistance mechanisms, such as carbapenemase production. Consequently, the genetic diversity, clonal relationships, and transmission dynamics of ESBL-producing Enterobacterales could not be explored.

Finally, antimicrobial susceptibility testing was restricted to antibiotics routinely tested and reported during the study period. Newer or less commonly used antimicrobial agents were not assessed, and potential changes in laboratory testing protocols over time may have influenced susceptibility reporting.

Despite these limitations, the study provides valuable insight into the burden and antimicrobial susceptibility patterns of ESBL-producing Enterobacterales in a quaternary hospital setting. The findings contribute important local data to support antimicrobial stewardship initiatives and identify critical areas for future prospective, multicentre, and molecular-based research.

Recommendations

Empirical antibiotic therapy for suspected infections caused by extended-spectrum β-lactamase-producing Enterobacterales should be guided by regularly updated, unit-specific antibiograms to ensure alignment with local resistance patterns. Carbapenems should remain the first-line agents for severe and invasive ESBL infections, while carbapenem-sparing alternatives should be considered only when supported by reliable susceptibility results and appropriate clinical circumstances. Amoxicillin-clavulanate should be avoided in invasive ESBL-associated infections due to limited reliability.

A structured antimicrobial stewardship approach is essential and should include routine reassessment of antimicrobial therapy with susceptibility-guided de-escalation within 48–72 hours, as well as timely intravenous-to-oral conversion when clinically appropriate. Optimisation of antimicrobial dosing using pharmacokinetic and pharmacodynamic principles, including extended β-lactam infusions and therapeutic drug monitoring for aminoglycosides, should be applied to maximise efficacy and minimise toxicity.

At an institutional level, healthcare facilities should strengthen antimicrobial stewardship programmes, enhance antimicrobial resistance surveillance, and reinforce infection prevention and control practices. Ongoing training and awareness initiatives are also necessary to support sustainable antimicrobial stewardship and limit the further spread of multidrug-resistant Enterobacterales.

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Conflict of interest

The authors declare no conflict of interest.

Data availability statement

The data analysed in this study were obtained from the National Health Laboratory Service Academic Affairs Research Management System under permission number PR2455063. Due to patient privacy and confidentiality requirements, the raw data cannot be made publicly available.

Disclaimer

The views and opinions expressed in this manuscript are purely those of the authors and do not reflect the institution (MUT), hospital (IALCH), nor data supplier (NHLS-AARMS).

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Declaration of artificial intelligence usage

An AI Tool was used for manuscript refining and proofreading.

Author biography

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N.C Mlangeni was responsible for conceptualising the study, conducting data collection, cleaning, and analysis, and drafting the initial version of the manuscript. P.Y Sikosana provided supervision throughout all stages of the research, directed data collection and analysis, and further co-authored the manuscript. K.N Bhengu reviewed and co-authored the manuscript.

List of abbreviations

AMR – Antimicrobial resistance
AARMS – Academic Affairs Research Management System
ASP – Antimicrobial stewardship programme
CDW – Corporate Data Warehouse
CLSI – Clinical and Laboratory Standards Institute
ESBL – Extended-spectrum β-lactamase
ESBL-PE – Extended-spectrum β-lactamase-producing Enterobacterales
IALCH – Inkosi Albert Luthuli Central Hospital
LIS – Laboratory Information System
MC&S – Microscopy, culture, and sensitivity
MDRE – Multidrug-resistant Enterobacterales
MIC – Minimum inhibitory concentration
NHLS – National Health Laboratory Service

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