

Antibiotic resistance and occurrence of extended-spectrum beta-lactamases, AmpC and carbapenemases in *Klebsiella pneumoniae* from blood cultures in Southern Ghana

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Abstract

Antibiotic-resistant *Klebsiella pneumoniae* presents a significant global health threat, prompting urgent calls for new treatment options. This study determined antibiotic resistance profiles of *K. pneumoniae* isolates from blood cultures in Southern Ghana and characterized the β -lactamase enzymes mediating β -lactam resistance. Archived *K. pneumoniae* isolates stored at -80°C at the Department of Medical Microbiology, University of Ghana Medical School were retrieved and revived for the study. Isolate identities were confirmed using the BD Bruker MALDI-TOF. Antimicrobial susceptibility testing was performed using both the MicroScan AutoSCAN system and Kirby-Bauer disc diffusion method. Of the 109 non-duplicate archived isolates, 95 (87.2%) were confirmed as *K. pneumoniae*. All confirmed isolates exhibited resistance to at least one antibiotic class, with two isolates (2.1%) resistant to all tested antibiotics. High resistance rates were observed for trimethoprim-sulfamethoxazole (85.3%), gentamicin (83.2%), ceftriaxone (80.0%), cefotaxime (78.9%), and ceftazidime (77.9%). Resistance to ertapenem (18.9%), and meropenem (8.4%) was comparatively lower. β -Lactamase enzyme profiles revealed that 77.9% ($n = 74/95$) of screened isolates were extended-spectrum beta-lactamase (ESBL) producers, 51.6% ($n = 47/91$) were AmpC producers, 26.6% ($n = 17/64$) were carbapenemase-producers, and 12.5% ($n = 6/48$) exhibited resistance to colistin. Notably, 12.5% of isolates concurrently produced ESBL, AmpC, and carbapenemase enzymes and were resistant to colistin. The prevalence of ESBL-producing *K. pneumoniae* was higher among children under five years of age compared to adults over sixty, though the difference was not statistically significant ($p = 0.933$). All ESBL-producing isolates were multidrug-resistant (MDR), and 76.2% ($n = 21$) of non-ESBL producers were also MDR. AmpC-producing isolates were significantly more prevalent among children under five than among those aged 5–19 and adults over sixty ($p = 0.023$). The high prevalence of MDR *K. pneumoniae* strains producing ESBLs, AmpCs, carbapenemases, and exhibiting colistin resistance is alarming and significantly narrows treatment options for bloodstream infections. These findings highlight the urgent need for alternative therapeutic strategies and routine surveillance to guide effective clinical management and antimicrobial stewardship.

Introduction

Klebsiella pneumoniae is a Gram-negative, non-motile, encapsulated bacterium that has emerged as a medically significant multidrug-resistant (MDR) pathogen. It is implicated in both community- and hospital-acquired infections (CAIs and HAIs)^{1,2,3}. The World Health Organization (WHO) has classified *K. pneumoniae* as a critical priority pathogen that warrants new antibiotics urgently⁴. Globally, it is the second most common cause of Gram-negative bacteremia⁵ and the leading cause of neonatal sepsis in sub-Saharan Africa.^{6,7} In 2019 alone, drug-resistant *K. pneumoniae* was associated with over 600,000 deaths in the region,⁸ underscoring its major threat to public health in the context of rising antimicrobial resistance (AMR).

AMR remains one of the most pressing threats to global public health. It leads to significant adverse outcomes, including prolonged hospital stays due to failed antimicrobial therapy, increased medical costs for patients and their families, overburdened healthcare systems, and elevated mortality rates.^{4,9,10} In 2017, the WHO underscored the urgent need for low-and middle-income countries (LMICs) to strengthen their healthcare systems to combat AMR through the implementation of surveillance and antimicrobial stewardship programs. These programs aim to optimize antimicrobial use and prevent the further spread of resistant pathogens.^{9,11}

The clinical impact of *K. pneumoniae* is well documented, with increasing resistance observed against key antibiotics. Resistance to third-generation cephalosporins is commonly mediated by ESBLs and AmpC β -lactamases¹². Resistance to last-resort antibiotics such as carbapenems is conferred by carbapenemase enzymes,¹³ while resistance to colistin – a reserve antimicrobial is often linked to polymyxin E resistance.¹⁴ In Enterobacteriaceae, antibiotic resistance mechanisms include drug target modification, efflux pumps, biofilm formation, enzymatic degradation (via ESBLs, AmpCs, and carbapenemases), global cell adaptation, and decreased membrane permeability due to porin loss¹⁵. These mechanisms collectively confer resistance to a broad spectrum of antibiotics, including cephalosporins, fluoroquinolones, and trimethoprim-sulfamethoxazole,¹⁶ ultimately limiting treatment options by restricting, inactivating, or degrading antibiotics before they exert their effect.^{14,15,16} While ESBLs and AmpCs can hydrolyze most penicillins and cephalosporins, they do not typically affect carbapenems^{17,18,19}. However, rising global concern surrounds the increasing resistance to colistin in both human and veterinary settings,²⁰ including documented cases in Ghana.^{21,22} Although MDR-*K. pneumoniae* has been reported worldwide, its prevalence in LMICs is particularly concerning.

Clinical studies have reported ESBL-producing *K. pneumoniae* rates of 77.1% in Northeastern Thailand,²³ 80% in Bangladesh,²⁴ and 84% in Côte d'Ivoire.²⁵ In Colombia, carbapenem resistant *K. pneumoniae* prevalence reached 91.5% in clinical isolates.²⁶ Across Africa, hospital-based studies have reported prevalence of carbapenemase-producing organisms ranging from 2.3% to 67.7% in North Africa, and 9% to 60% in sub-Saharan Africa.² Despite this, routine detection and characterization of resistance mechanisms are often lacking in diagnostic laboratories across LMICs, including Ghana – a situation that is common in many resource-constrained settings.²⁷ This gap in diagnostic capacity limits effective antimicrobial therapy and infection prevention efforts. To address these knowledge gaps, the present study evaluated the prevalence of ESBLs, AmpCs, carbapenemases, and colistin resistance; characterizes AMR patterns; and maps the distribution of these resistance traits among MDR-*K. pneumoniae* isolated from blood cultures in Ghana. The findings aim to inform empirical therapy and clinical decision-making through the rapid identification of resistance traits and their associated antibiotic resistance profiles, thereby enhancing patient care and treatment outcomes.

Material and Methods

Study design and isolate recovery

Archived *K. pneumoniae* isolates preserved at -80°C in the Department of Medical Microbiology, University of Ghana Medical School, were retrieved and revived on July 4, 2023 for the study. The isolates had been collected between April and December 2021. A total of 109 freezer skimmed-milk tryptone glucose glycerol stock of the non-duplicate *K. pneumoniae* isolates were aseptically scraped using sterile pipette tips and inoculated into tryptic soy broth (TSB) (Oxoid, UK). After 24 ± 1 h incubation at 37°C, a loopful was plated onto nutrient agar (NA) (Oxoid, UK) and incubated at 37°C for 20 ± 1 h. Ninety-five (95) isolates were successfully revived and confirmed using the BD MALDI-TOF analyzer, Version 4.2.100 (BRUKER Daltonics, Germany). Patient demographics (age, sex), clinical diagnoses, and contributing health facilities from which the isolates emanated were extracted from the associated anonymized database.

Antibiotic susceptibility testing and determination of resistance phenotypes

Antibiotic susceptibility testing (AST) was conducted using the Kirby-Bauer disc diffusion method and the minimum inhibitory concentration (MIC) method on the MicroScan AutoSCAN-4 system (American MicroScan, USA) in accordance with the manufacturer's instructions and interpreted using the clinical and laboratory standards institute (CLSI) M100 guidelines.²⁸ The AutoSCAN-4 was performed in the 96-well microplates as described previously.²⁹ Briefly, the isolates were inoculated into the microdilution panels containing preloaded antibiotics. The inoculated plates were then incubated for 20 ± 1 h at 37°C and scanned for absorbance representing growth. The AutoSCAN-4 performs automated AST in a 96-well microbroth dilution plate and is read by measuring the amount of light passing through the wells.²⁹ With the disc diffusion method, susceptibilities of isolates were examined against the following clinically relevant antibiotics: ampicillin (10 µg), ceftazidime (30 µg), cefotaxime (30 µg), ceftriaxone (30 µg), ciprofloxacin (5 µg), ertapenem (10 µg), meropenem (10 µg), tetracycline (30 µg), chloramphenicol (30 µg), gentamicin (10 µg), azithromycin (15 µg), and trimethoprim-sulfamethoxazole (1.25/23.75 µg) (Oxoid, UK). Reference strains *Escherichia coli* ATCC 25922 and *K. pneumoniae* NCTC 13438 were included as quality controls in each susceptibility assay and phenotypic test.

The confirmed isolates were tested for the presence of resistance phenotypes, including ESBLs, AmpCs, and carbapenemases as well as resistance to colistin. The isolates were screened for presumptive presence of ESBLs using cefotaxime (30 µg), and ceftazidime (30 µg) antibiotic discs (MAST, UK). Isolates with zone inhibition diameters ≤ 27 mm for cefotaxime and ≤ 22 mm for ceftazidime were recorded as ESBL screened-positive. Confirmation for ESBL production was performed using the combined-discs method. Zones of inhibition were determined for each isolate to antibiotic disc containing 30 µg of cefotaxime, and 30 µg of ceftazidime either alone or in combination with 10 µg of clavulanic acid (MAST, UK). All zones of inhibition which differed by ≥ 5 mm between at least one of the standard antibiotic discs and its corresponding clavulanic combination disc were phenotypically confirmed as ESBL producers.

The modified carbapenem inactivation method (mCIM), as described by Pierce *et al.*³⁰, was used to detect carbapenemase production using meropenem (10 µg). Briefly, 1 µl of the *K. pneumoniae* isolate was mixed in a tube containing 2 ml of TSB using a sterile inoculation loop and vortexed for 10 to 15 s. Thereafter, a 10 µg meropenem disc was aseptically added into the bacterial suspension and incubated at 37°C for $4 \text{ h} \pm 15 \text{ m}$. Shortly before completing the 4-h carbapenem inactivation step, a suspension of the mCIM indicator organism (*E. coli* ATCC 25922, a carbapenem-susceptible strain) adjusted to a 0.5 McFarland standard turbidity was prepared. The surface of a mueller hinton agar (MHA) plate was then inoculated following the standard disc diffusion susceptibility testing method.²⁸ The meropenem disc was then removed from the TSB bacterial suspension using a 10 µl inoculating loop, placed at the center of the inoculated MHA plate, and incubated aerobically at 37°C for 20 ± 1 h. The diameter of the zone of inhibition around each meropenem disc was measured and interpreted. A zone diameter of 6 to 10 mm was considered positive (carbapenemase production detected), a zone diameter of 11 to 19 mm was considered an indeterminate, and a zone diameter of ≥ 20 mm was considered as negative (no carbapenemase production detected) as previously reported.^{31,32} Colistin resistance and AmpC were determined using the MicroScan AutoSCAN-4 system.

Data analysis

Data were entered into a Microsoft Excel® (2016) spreadsheet and exported into the IBM Statistical Products and Services Solutions (SPSS), Version 25 (IBM Corp., USA), for analysis. Descriptive statistics were computed, including means and standard deviation or medians and interquartile ranges for continuous variables, and frequencies and percentages for categorical variables. Differences in the prevalence of multidrug resistance by gender, age group, healthcare facility, region, and city were examined using Fisher's exact test or the independent-samples t-test, as appropriate. Bar charts were generated using Microsoft Excel® (2016) to visualize antibiotic resistance profiles. Ninety-five percent confidence intervals (95% CIs) were calculated using the modified Wald method with the GraphPad QuickCalcs online calculator (<https://www.graphpad.com/quickcalcs/confinterval2/>). A *p-value* < 0.05 was considered statistically significant.

Results

General characteristics of the study participants

Of the 109 archived isolates, 95 (87.2%) were successfully revived and confirmed as *K. pneumoniae*. The mean age of the individuals from whom the isolates were recovered was 17.66 ± 24.68 years. Among patients with available sex data, 32 were male (mean age = 17.03 ± 24.57 years) and 31 were female (mean age = 17.84 ± 24.77 years). Data on sex and age were missing for 33.7% (32/95) and 27.4% (26/95) isolates, respectively. The majority of

isolates were obtained from patients with a clinical diagnosis of sepsis (84.2%, 80/95), followed by bacteremia and chronic kidney disease (2.1%, 2/95 each). Eleven patients (11.6%) had other clinical conditions (Table 1).

Table 1
Characteristics of study participants and phenotypic resistant traits among *K. pneumoniae* isolates from blood cultures

Characteristics of study participants and phenotypic resistant traits among <i>K. pneumoniae</i> isolates from blood cultures														
Demographic Characteristics		ESBL Producers (n = 74)				AmpC Producers (n = 47)			Carbapenemase Producers (n = 17)			Colistin Resistant (n = 6)		
Category	n = 95 (%)	Frequency (%)	95% CI*	P-Value	Frequency (%)	CI* (%)	P-value	Frequency (%)	CI* (%)	P-Value	Frequency (%)	CI* (%)	P-value	
Sex														
Male	33.7	32.4	22.8–43.8	0.621	25.5	15.1–39.6	0.055	17.7	5.4–41.8	0.506	33.3	9.3–70.4	0.233	
Female	32.6	35.1	25.2–46.5		27.7	16.8–41.9		29.4	13.0–53.4		50.0	18.8–81.2		
Unknown	33.7	32.4	22.8–43.8		46.8	33.3–60.8		52.9	30.9–73.8		16.7	1.1–58.2		
Age groups														
Under 5 years	40	40.5	30.1–51.9	0.933	25.5	15.1–39.6	0.023	17.6	5.4–41.8	0.210	33.3	9.3–70.4	0.272	
5–19 years	8.4	9.5	4.4–18.5		8.5	2.8–20.5		17.6	5.4–41.8		33.3	9.3–70.4		
20–59 years	13.7	13.5	7.3–23.3		17.0	8.6–30.4		5.9	0.0–28.9		16.7	1.1–58.2		
60 + years	10.5	9.5	4.4–18.5		8.5	2.8–20.5		11.8	2.0–35.6		0.0	0.0–44.3		
Unknown	27.4	27.0	18.2–38.2		40.4	27.6–54.7		47.1	26.2–69.0					
Diagnosis Queried														
Sepsis	84.2	90.5	81.5–95.6	0.879	93.6	82.2–98.5	0.822	100.0	78.4–100.0	0.715	100.0	55.7–100.0	0.715	
Bacteremia	2.1	2.7	0.2–9.9		4.3	0.4–15.0		0.0	0.0–21.6		0.0	0.0–44.3		
Chronic kidney disorder	2.1	1.4	0.0–8.0		0.0	0.0–9.0		NT	-		NT	-		
Others	11.6	5.4	1.7–13.5		2.1	0.0–12.1		0.0	0.0–21.6		0.0	0.0–44.3		
Study site														
KATH	23.2	29.7	20.5–41.0	0.002	36.2	23.9–50.5	< 0.001	35.3	17.2–58.8		50	18.8–81.2	NA	
GARH	22.1	14.9	8.3–24.9		10.6	4.2–23.0		0.0	0.0–21.6		0.0	0.0–44.3		
KBTH	17.9	16.2	9.4–26.4		25.5	15.1–39.6		35.3	17.2–58.8		0.0	0.0–44.3		
ERH	12.6	10.8	5.3–20.2		17.0	8.6–30.4		23.5	9.1–47.8		50	18.8–81.2		
37 MH	10.5	13.5	7.3–23.3		2.1	0.0–12.1		5.9	0.0–28.9		0.0	0.0–44.3		
PMLCH	6.3	8.1	3.5–16.9		2.1	0.0–12.1		0.0	0.0–21.6		0.0	0.0–44.3		
HTH	3.2	4.1	0.9–11.7		6.4	1.6–17.8		0.0	0.0–21.6		0.0	0.0–44.3		
Private Lab	3.2	1.4	0.0–8.0		0.0	0.0–9.0		0.0	0.0–21.6		0.0	0.0–44.3		
LEKMA Hospital	3.2	1.4	0.0–8.0		0.0	0.0–9.0		0.0	0.0–21.6		0.0	0.0–44.3		

Demographic Characteristics		ESBL Producers (n = 74)				AmpC Producers (n = 47)			Carbapenemase Producers (n = 17)			Colistin Resistant (n = 6)		
Category	n = 95 (%)	Frequency (%)	95% CI*	p-Value	Frequency (%)	CI* (%)	p-value	Frequency (%)	CI* (%)	p-Value	Frequency (%)	CI* (%)	p-value	
Sex														
Regional Summary														
Greater Accra	61.1	55.4	44.1–66.2	0.021	40.4	27.6–54.7	0.001	41.2	21.6–64.1		0.0	0.0-44.3	0.010	
Ashanti	23.2	29.7	20.5–41.0		36.2	23.9–50.5		35.3	17.2–58.8	50.0	18.8–81.2			
Eastern	12.6	10.8	5.3–20.2		17.0	8.6–30.4		23.5	9.1–47.8	50.0	18.8–81.2			
Volta	3.2	4.1	0.9–11.7		6.4	1.6–17.8		0.0	0.0-21.6		0.0	0.0-44.3		

ESBL – Extended Spectrum Beta-Lactamase, KATH - Komfo Anokye Teaching Hospital, GARH - Greater Accra Regional Hospital, KBTH - Korle Bu Teaching Hospital, ERH - Eastern Regional Hospital, 37 MH – 37 Military Hospital, PMLCH - Princess Marie Louise Children's Hospital, HTH – Ho Teaching Hospital, LEKMA - Ledzokuku-Krowor Municipal Assembly, n – Number, % - Percentage, NA – Not applicable, NT – Not tested, CI* - Confidence interval.

Antibiotic susceptibility patterns of the isolates

All isolates demonstrated resistance to at least one class of antibiotic, and two isolates (2.1%) were resistant to all antibiotics tested. Of the twelve antibiotics evaluated, nine exhibited resistance rates exceeding 50.0%, while resistance to chloramphenicol, ertapenem, and meropenem was 49.5%, 18.9%, and 8.4%, respectively. All isolates were resistant to ampicillin (100.0%). High resistance rates were also observed for trimethoprim-sulfamethoxazole (85.3%), gentamicin (83.2%), ceftriaxone (80.0%), cefotaxime (78.9%), and ceftazidime (77.9%) (Fig. 1). Multidrug resistance, defined as resistance to at least one agent in three or more antimicrobial classes, according to Magiorakos *et al.*,³³ was identified in 94.7% (90/95) of the isolates.

Of the 95 isolates, 12.5% were concurrently ESBL-, AmpC-, and carbapenemase-producing, and were resistant to colistin. Overall, 77.9% (74/95) of isolates were ESBL-producing *K. pneumoniae* (77.9%). Although ESBL production appeared more frequent among isolates from children under five years of age (40.5%) compared with adults older than 60 years (9.5%), this difference was not statistically significant ($p = 0.933$) (Table 1). The majority of ESBL-producing isolates originated from the Greater Accra Region (55.4%). At the facility level, ESBL producers were most prevalent at KBTH (16.2%), followed by GARH (14.9%), 37 MH (13.5%), PMLCH (8.1%), Private Lab (1.4%), and LEKMA Hospital (1.4%) (Table 1). ESBL-producing isolates demonstrated high resistance rates (often > 60%) to most antibiotics tested, including ampicillin, trimethoprim-sulfamethoxazole, ceftriaxone, gentamicin, cefotaxime, ceftazidime, tetracycline, azithromycin, ciprofloxacin, and chloramphenicol (Fig. 2A). All ESBL-producing isolates (74/74; 100%) were MDR, compared with 76.2% (16/21) of non-ESBL-producing isolates. The majority of the isolates remained susceptible to meropenem and ertapenem. Detailed antimicrobial susceptibility and phenotypic test results are presented in supplementary table S1.

Of the 91 isolates tested for AmpC production, 51.6% (47/91) were confirmed as AmpC-producers. Among these, 27.7% were recovered from females and 25.5% from males, while sex data were missing for 46.8% of isolates. The proportion of AmpC-producing *K. pneumoniae* was relatively higher among children under five years of age compared with individuals aged 5–19 years and adults older than 60 years (Table 1). Most AmpC-producing isolates originated from the Greater Accra Region (40.4%). At the facility level, AmpC-producers were most prevalent at KBTH (25.5%), followed by GARH (10.6%), PMLCH (2.1%), and 37 MH (2.1%). No AmpC-producing isolates were recorded from LEKMA Hospital or the Private Lab (Table 1). AmpC producing isolates demonstrated high resistance rates (> 60%) to most antibiotics tested, whereas non-AmpC producers exhibited moderate to high resistance across the antibiotics evaluated (Fig. 2B). With the exception of one isolate, all AmpC producers (97.9%; 46/47) were MDR. Among non-AmpC producers, 90.9% (40/44) were MDR.

Carbapenemase testing was performed on 64 isolates (due to resource constraints), of which 26.6% were confirmed as carbapenemase-producers. Among these, 29.4% were recovered from females and 17.6% from males, while sex data were missing for 52.9% of isolates. There was no statistically significant difference in carbapenemase-producing *K. pneumoniae* across the different age groups (Table 1). Most carbapenemase-producing isolates originated from the Greater Accra Region (41.2%). At the facility level, carbapenemase producers were most prevalent at KBTH (35.3%), followed by 37 MH (5.9%). However, none were recorded from GARH, PMLCH, Private Lab, and LEKMA (Table 1). Generally, carbapenemase producers demonstrated high resistance to the various antibiotics, while non-carbapenemase producers showed slightly high resistance to the antibiotics (Fig. 2C). With the exception of one isolate, 94.1% (16/17) of carbapenemase producers were MDR. Similarly, 97.9% (46/47) of non-carbapenemase producers were MDR.

Colistin susceptibility testing was performed on 48 isolates (due to resource constraints), of which 12.5% were confirmed as colistin-resistant. Among these, 50.0% were recovered from females, 33.3% from males, and sex data were missing for 16.7% of isolates. The proportion of colistin-resistant *K.*

pneumoniae was similar among children under five and other age groups (5–19 years), with no statistically significant difference observed ($p = 0.272$) (Table 1). No colistin-resistant isolates were identified from the Greater Accra Region. Colistin-resistant isolates exhibited very high resistance to most antibiotics tested, whereas colistin-susceptible isolates showed moderately high resistance across the same antibiotics. Although all colistin-resistant isolates (6/6; 100%) were MDR, they remained susceptible to meropenem and ertapenem (Fig. 2D). Among colistin-susceptible isolates, 97.6% (40/41) were MDR.

Discussion

This study investigated the prevalence of antibiotic resistance and β -lactam-degrading enzymes specifically ESBLs, AmpCs, and carbapenemases among *K. pneumoniae* isolates recovered from blood cultures in Southern Ghana. A high prevalence of resistance was observed across nearly all antibiotics tested, except for meropenem and ertapenem, aligning with previous findings from Ghana,^{34,35} and other regions.^{36,37} Resistance to third-generation cephalosporins, including cefotaxime, ceftazidime, and ceftriaxone, is often linked to ESBL production.³⁸ Consequently, even if an isolate appears susceptible *in vitro*, treatment failure may occur if it harbors ESBL genes³⁸.

The high resistance rate to gentamicin, an aminoglycoside, observed in this study may be attributed to several mechanisms, including: (1) enzymatic inactivation by aminoglycoside-modifying enzymes such as acetyltransferases, nucleotidyltransferases, or phosphotransferases; (2) increased efflux; (3) reduced permeability; and (4) alterations in the 30S ribosomal subunit that prevent drug binding³⁹. This is especially concerning given the widespread and often empiric use of aminoglycosides in Ghana, where they are among the most commonly prescribed antibiotics^{40,41,42}. A six-year review at a Ghanaian secondary healthcare facility found gentamicin usage at a rate of 13.1 defined daily doses per 100 patients, with no significant reduction from 2016 to 2021⁴³. The overuse and misuse of antibiotics particularly aminoglycosides, cephalosporins, and fluoroquinolones is a key driver of AMR and highlight the urgent need for stricter prescribing practices and improved surveillance.

In contrast, meropenem and ertapenem retained relatively high effectiveness against MDR strains, consistent with reports from other settings.^{44,45} Their limited use is likely attributable to their high cost, intravenous administration, and their designation as last-resort agents in national treatment guidelines. Although these carbapenems have been available in Ghana since 2002, their lower consumption compared with older antibiotics such as aminoglycosides, may have contributed to the preservation of their efficacy. Nevertheless, judicious use remains essential, and routine monitoring of carbapenem use should be emphasized as a key component of antimicrobial stewardship programs.

The prevalence of ESBL production in this study (77.9%) was significantly higher than previous reports from China (12.1%)⁴⁶, Italy (30%)⁴⁵, and sub-Saharan Africa (45.5%)⁴⁷. The elevated rate may reflect long-standing but under-recognized community circulation of ESBL-producing strains in Ghana, exacerbated by limited laboratory capacity and lack of awareness¹⁹. The prevalence reported here is comparable to studies in Egypt (76.2%)⁴⁸, and Ghana (71.2%)⁴⁹, (75.6%)⁵⁰, though lower than figures from Bangladesh (80%)²⁴, Belgium (89.3%)⁵¹, Egypt (80%)⁵², and Côte d'Ivoire²⁵. Variations in ESBL prevalence likely stem from geographic, methodological, and temporal differences. ESBL prevalence was notably higher among children under five, though not statistically significant ($p = 0.933$), likely due to increased empirical antibiotic use in this age group.

MDR is strongly associated with ESBL production, and the high prevalence of MDR *K. pneumoniae* observed especially among ESBL producers is consistent with earlier findings from Ghana^{53,54}, and other regions^{55,56}. Resistance was particularly high for penicillins, trimethoprim-sulfonamide combinations, aminoglycosides, third-generation cephalosporins, tetracyclines, macrolides, and fluoroquinolones. This is alarming, as these antibiotics are frequently used empirically for syndromic treatment⁵⁷. The increasing ineffectiveness of these drugs against MDR pathogens necessitates urgent, multifaceted public health interventions, including enhanced diagnostics, refined treatment protocols, and robust infection control measures.

AmpC production was detected in 51.6% of isolates significantly higher than previous reports from Saudi Arabia (5.5%)⁵⁸, Libya (6.7%)⁵⁹, and Ghana (19.4%)⁴⁹, (17%)⁶⁰, but comparable to a study from Iran (52.9%)⁶¹. AmpC prevalence remains underdefined in sub-Saharan Africa due to the absence of rapid, validated detection methods⁵⁸. Consequently, its burden may be underestimated, underscoring the need to develop and implement standardized detection protocols⁶².

Carbapenemase production was detected in 26.6% of isolates – significantly higher than previously reported rates in Ghana: 5.6% by Dwomoh et al.⁵³, 2.9% by Codjoe et al.⁶³, and 7.2% by Hackman et al.⁶⁴. The present study's focus on *K. pneumoniae* from blood cultures in secondary and tertiary hospitals in Southern Ghana may account for this higher prevalence. The findings align with a recent Ghanaian study reporting 26.4% prevalence⁴⁹, and with similar findings from Uganda⁶⁵, though still lower than those from Egypt (54.1%)⁶⁶. Elsewhere, reported carbapenemase rates vary 4.9% in Argentina⁶⁷, 5.74% in Malaysia⁶⁸, and 9.1% in Nepal⁶⁹, but collectively point to a global rise in carbapenem resistance, requiring urgent, coordinated responses.

Colistin resistance was identified in 12.5% of isolates comparable to rates from Kuwait (12.0%)³⁷, and Spain (13.1%)⁵⁵, but lower than those reported in India (33.3%)¹⁴, Italy (43%)⁵⁶, and Ghana (57%)²². These variations may reflect differences in antibiotic use practices, population demographics, resistance trends, and detection methods. The absence of standardized, rapid colistin resistance testing and lack of consistent antimicrobial use guidelines compounded by limited public awareness remains a challenge, especially given colistin's role as a last-resort antibiotic for MDR Gram-

negative infections. Many healthcare facilities in resource-limited settings lack the diagnostic capacity to detect colistin resistance²⁷, leading to its underreporting. Although the prevalence found here is relatively low, regular nationwide surveillance is essential.

This study has certain limitations. Archived isolates were used, limiting access to detailed clinical data such as underlying conditions or comorbidities. Nonetheless, inclusion of isolates from both secondary and tertiary care facilities across Southern Ghana enhances the study's representativeness and generalizability.

Conclusion

This study reveals a high prevalence of ESBL, AmpC, carbapenemase production, and colistin resistance among *K. pneumoniae* isolates from blood cultures in Southern Ghana. Notably, a subset of isolates harbored all three β -lactamase enzymes and were concurrently resistant to colistin, presenting a significant therapeutic challenge.

Routine detection and characterization of resistance mechanisms, coupled with robust laboratory surveillance, are urgently needed to guide effective clinical management and containment strategies. The responsible use of last-resort antibiotics such as meropenem and ertapenem must be prioritized, while the overuse of third-generation cephalosporins, aminoglycosides, and fluoroquinolones should be strictly regulated.

The widespread presence of MDR *K. pneumoniae* in both ESBL-producing and non-ESBL-producing isolates, as well as AmpC-producing and non-AmpC-producing isolates, and carbapenemase-producing and non-carbapenemase-producing isolates underscores the urgent need to enhance infection-prevention and control measures. Strengthening antimicrobial stewardship programs within both healthcare facilities and communities is essential to curb the spread of resistance and preserve the efficacy of available antibiotics.

Declarations

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Author contributions

Conceptualization: FKMT, WB, KOD, and ES-D. Methodology: FKMT, MMO, FCNK, BD, and KOD. Validation: FKMT, MMO, FCNK, BD, KOD, and ES-D. Formal analysis: FKMT, WB, BD, and KOD. Investigation: FKMT. Data curation: FKMT, WB, MMO, FCNK, and BD. Writing - original draft preparation: FKMT. Writing - review and editing: FKMT, WB, KOD, and ES-D. Visualization: FKMT, WB, MMO, FCNK, BD, KOD, and ES-D. Supervision: KOD, and ES-D. Resources: FKMT, MMO, FCNK, and ES-D. Project administration: FKMT, MMO, FCNK, and ES-D. All authors reviewed final draft of the manuscript and approved for submission.

Declaration of competing interests

The authors declare no competing interests.

Data availability

All data generated or analyzed during the study are included in this article. Further inquiries can be directed to the corresponding authors.

Ethical approval

The Ethical and Protocol Review Committee (EPRC) of the College of Health Sciences, University of Ghana, approved the research study (protocol identification number: CHS-Et/M.2-P4.6/2021-2022). Approval was also obtained from the respective study sites. Informed consent was waived by the ethics committee because there was no contact with patients. Archived bacterial isolates were retrieved and used. The isolates had been de-identified prior to retrieval. All methods were performed in accordance with the relevant standard guidelines and regulations.

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Figures

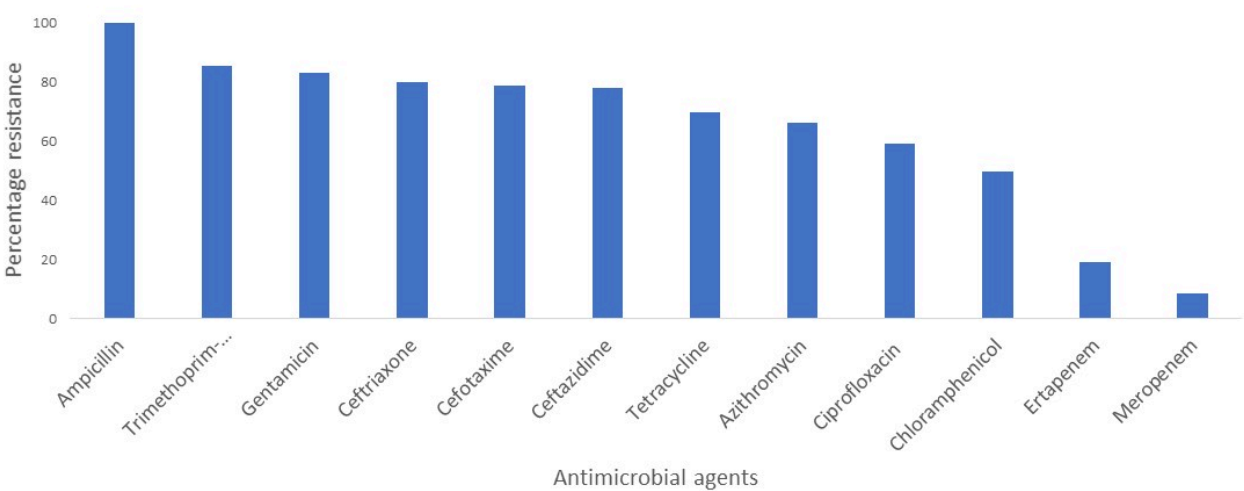


Figure 1. Antibigram profiles of the *K. pneumoniae* isolates from blood cultures.

Figure 1

Antibiogram profiles of the *K. pneumoniae* isolates from blood cultures. This plot presents a summary of the phenotypic antimicrobial susceptibility results, showing the percentage resistance for the various antibiotics tested against the isolates. Each bar presents an antibiotic that denotes the percentage resistance.

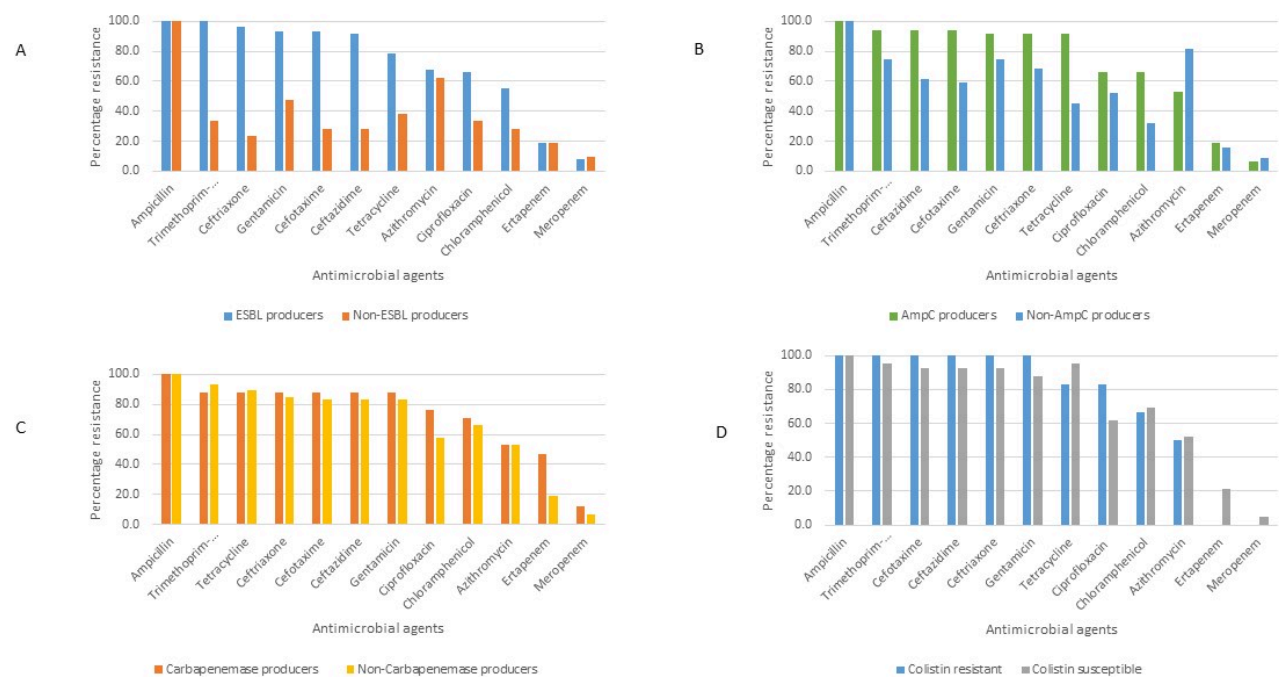


Figure 2. Antibiogram of *K. pneumoniae* phenotypes from blood cultures in Southern Ghana between April and December 2021.

Figure 2

Antibiogram of *K. pneumoniae* phenotypes from blood cultures in Southern Ghana between April and December 2021. (A) Antibiogram of ESBL (n=95), (B) AmpC (n=91), (C) carbapenemase (n=64), and (D) colistin (n=48). Antibiotics: ampicillin (10 µg), ceftazidime (30 µg), cefotaxime (30 µg), ceftriaxone (30 µg), ciprofloxacin (5 µg), ertapenem (10 µg), meropenem (10 µg), tetracycline (30 µg), chloramphenicol (30 µg), gentamicin (10 µg), azithromycin (15 µg), and trimethoprim-sulfamethoxazole (1.25/23.75 µg). *Significant difference between ESBL-producers and non-ESBL-producers.

Supplementary Files

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