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Molecular Epidemiology of Extended-spectrum β-Lactamase-producing *Escherichia coli* in South Korea: A Korean Global Antimicrobial Resistance Surveillance System Report

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Background: Extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* is among the most important multidrug-resistant pathogens causing bloodstream infections (BSIs). Cefotaximase (CTX-M) enzymes are the most common and highly diverse ESBL family in *E. coli*. CTX-M-15 in group CTX-M-1 and CTX-M-14 in group CTX-M-9 are the most extensively disseminated enzymes. Multidrug-resistant *E. coli* strains complicate empirical therapy and increase healthcare burden globally and in Korea. We investigated the molecular epidemiology, sequence types (STs), and ESBL genotypes of *E. coli* bloodstream isolates in Korea and identified clinical risk factors for cefotaxime resistance.

Methods: We collected all non-duplicated isolates of *E. coli* and related clinical information from patients with BSIs at eight sentinel hospitals in the Korean Global Antimicrobial Resistance Surveillance System (Kor-GLASS) collection network during 2017–2021. Duplicate isolates were removed to ensure representativeness of the data. Antimicrobial susceptibility was tested using disk diffusion tests, and multilocus sequence typing and beta-lactamase genotyping were performed.

Results: Among 9,232 *E. coli* blood isolates, resistance rates to cefotaxime and ceftazidime were 36.4% and 11.4%, respectively. Among the clinical factors, age >65 yrs (adjusted odds ratio [aOR], 1.36), hospital-origin infection (aOR, 2.55), and admission type (intensive care unit [ICU] vs. general ward; aOR, 1.34) were significant cefotaxime resistance risk factors. ST131 was the most prevalent among cefotaxime-resistant *E. coli* (64.8%, 2,180/3,363), followed by ST1193 (5.3%, N=177), and ST69 (5.1%, N=170). ST131, ST648, ST405, and ST410 cefotaxime-resistant *E. coli* isolates frequently harbored $bla_{\text{CTX-M-15}}$, whereas ST1193 and ST68 showed a high proportion of $bla_{\text{CTX-M-27}}$ carriers, and most ST457 and ST5150 isolates carried $bla_{\text{CTX-M-55}}$.

Conclusions: Continuous monitoring of ESBL-producing *E. coli* is required to prevent further dissemination, guide empirical therapy, inform infection control policies, and ensure early detection of multidrug-resistant clones with the potential for widespread transmission.

Key Words: Antibiotic resistance, *Escherichia coli*, Extended-spectrum beta-lactamase, Monitoring

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INTRODUCTION

Escherichia coli has been the most common pathogen involved in community- and healthcare-associated bloodstream infections (BSIs) since the early 2000s, accounting for approximately 20% of BSIs worldwide and in Korea [1, 2]. The prevalence of antimicrobial resistance (AMR) in *E. coli* has increased recently, and extended-spectrum β-lactamase (ESBL)-producing isolates are disseminating [2, 3]. *E. coli* isolates showing resistance to third-generation cephalosporins, primarily because of ESBL production, are associated with a delayed appropriate treatment, high mortality rate, and prolonged hospital stay [4–6].

ESBLs show hydrolytic activity toward a broad range of β-lactam antimicrobials, including penicillins, cephalosporins, and monobactams, but not cephamycins and carbapenems [7]. Plasmid-mediated ESBL genes are primarily found in Enterobacterales such as *E. coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis* [8]. CTX-M enzymes are the most common ESBL family in *E. coli* worldwide, including the United States, European countries, and South Korea [9–11].

Cefotaximase (CTX-M) genes originate from the mobilization of chromosomal β-lactamase genes in *Kluyvera* spp. [12] and are incorporated into mobile genetic elements, resulting in rapid dissemination [13]. CTX-M enzymes historically showed higher hydrolytic activity toward cefotaxime than toward ceftazidime; however, point mutations such as P167S and D240G have resulted in enhanced hydrolytic activity toward ceftazidime [14, 15]. The CTX-M family is highly diverse and is classified into five major groups: CTX-M-1, CTX-M-2, CTX-M-8, CTX-M-9, and CTX-M-25 [16]. CTX-M-15 in group CTX-M-1 and CTX-M-14 in group CTX-M-9 are the most widely disseminated globally [10].

The Korean Global Antimicrobial Resistance and Use Surveillance System (Kor-GLASS) is Korea's national adoption of the WHO GLASS, which is a global collaborative effort to standardize AMR surveillance, established in 2016 [17]. The Kor-GLASS network collects isolates from clinical settings to investigate their AMR phenotypes and genotypes to provide representative national AMR data [2]. We characterized the molecular epidemiology of cefotaxime-resistant *E. coli* BSIs in Korea using Kor-GLASS surveillance data, focusing on the sequence types (STs) and ESBL genotypes, with the aim to address the critical gap in understanding the nationwide distribution and molecular features of resistant isolates.

MATERIALS AND METHODS

Collection of clinical data and *E. coli* blood isolates

All patients who underwent blood culture examinations for suspected BSI between January 2017 and December 2021 were analyzed in eight sentinel hospitals in the Kor-GLASS collection network: Gangnam Severance Hospital, National Health Insurance Service Ilsan Hospital, Wonju Severance Christian Hospital, Chungbuk National University Hospital, Chonnam National University Hospital, Inje University Busan Paik Hospital, Hallym University Dongtan Sacred Heart Hospital, and Jeju National University Hospital. The Kor-GLASS system includes patients with laboratory-confirmed BSIs caused by nine target pathogens, including *Staphylococcus aureus*, *Enterococcus faecalis*, *Enterococcus faecium*, *Streptococcus pneumoniae*, *E. coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter* spp., and *Salmonella* spp., and those with *E. coli* BSIs were enrolled in this study. Initial *E. coli* isolates were collected and transferred to Gangnam Severance Hospital for microbiological assessment, and duplicate isolates were removed. Demographic data, including age and sex, were also collected. Older individuals were defined as those >65 yrs of age for further analyses. Admission types were classified as outpatient department (OPD), general ward (GW), and intensive care unit (ICU). Infection cases were categorized into hospital-origin (HO) and community-origin (CO) infections, based on the WHO GLASS criteria [18]. HO infection was defined as a case diagnosed from a blood culture performed 2 days after hospitalization.

Ethics statement

All analyses were conducted in accordance with the ethical standards of the institutional and national research committees, the 1964 Helsinki Declaration, and comparable ethical standards. This study was approved by the Institutional Review Boards of Gangnam Severance hospitals and all other participating hospitals (approval No.: 3-2020-0140). The requirement for informed consent was waived because we used clinical data collected via retrospective chart review.

Microbiological analysis

Clinical isolates identified as *E. coli* at the sentinel hospitals were transferred to the Gangnam Severance Hospital analysis center, where species identity was confirmed using MALDI-TOF MS (Bruker Biotyper; Bruker Daltonics, Bremen, Germany) and further validated via 16S rRNA sequencing. Antimicrobial susceptibility to ampicillin, piperacillin, ampicillin-sulbactam, cefazolin, cefotaxime, ceftazidime, cefepime, aztreonam, cefoxitin, imipenem, meropenem, ertapenem, amikacin, gentamicin, ciprofloxacin, trimethoprim-sulfamethoxazole, and tigecycline was determined using the disk diffusion method, and zone diameters were interpreted according to the clinical breakpoints established in CLSI M100-S26 [19]. For the cefotaxime-resistant *E. coli* isolates, resistance genes encoding CTX-M, sulfhydryl variable (SHV), and Temoneira (TEM) ESBLs were PCR-amplified and identified using sequencing with previously reported primers [2], using previously characterized ESBL-carrying strains as positive controls and *E. coli* ATCC 29212 as a negative control. Sequencing quality was verified by inspecting chromatogram peak clarity. In addition, multilocus sequence typing (MLST) was performed for cefotaxime-resistant isolates by sequencing the partial sequences of seven housekeeping genes (*adk*, *fumC*, *gyrB*, *icd*, *mdh*, *purA*, and *recA*) and comparing them with the *E. coli* MLST database according to the Achtman scheme [20].

External QC

The microbiological analysis results were validated by the Kor-GLASS Quality Control Center [21]. In brief, quarterly interlaboratory proficiency testing was conducted by comparing the results obtained in the analysis and by QC centers for 5% of randomly selected *E. coli* isolates, with a categorical agreement rate >90%, major error rate <3%, and very major error rate <1.5% considered acceptable. The analysis center was certified through an external quality assurance program every three months during the study period.

Statistical analysis

All statistical analyses were performed using the R software v.4.3.1 (updated on July 16, 2023; http://www.R-project.org/). Continuous variables were analyzed using the Mann–Whitney U or Kruskal–Wallis tests, and categorical variables were analyzed using Fisher's exact test. Logistic regression was used to calculate the odds ratio (OR) for each risk factor for cefotaxime resistance. Variables with $P<0.05$ in univariate analysis were included in the multivariate logistic regression model to calculate adjusted (a)ORs. The variance inflation factor was calculated to evaluate multicollinearity. Statistical significance was set at $P<0.05$.

RESULTS

Prevalence of *E. coli* BSIs

In total, 398,814 patients underwent blood culture testing at eight sentinel hospitals during the study period. The number of patients who underwent blood culture examination was the lowest in the age group 15–24 yrs and increased with age, peaking in the age group 74–84 yrs (Fig. 1A). Among all patients, 5.3% (21,206/398,814) were diagnosed as having BSIs caused by the nine Kor-GLASS target pathogens, among which the proportion of *E. coli* was 43.5% (9,232/21,206) from 2017 to 2021, ranging from 41.7% (1,724/4,131) to 45.8% (1,949/4,254).

Clinical information of patients with *E. coli* BSIs

The number of patients with *E. coli* BSIs and the positive rate of *E. coli* in BSIs by age group showed J-shaped curves, similar to the pattern observed in the number of patients with suspected BSIs (Fig. 1B and 1C). Of the 9,232 (2.3%) patients diagnosed as having *E. coli* BSIs (Table 1), nearly 6,791 (73.6%) were elderly individuals aged >65 yrs, with a median age of 75 yrs (1st–3rd interquartile range, 64–82 yrs). Notably, the proportion of patients aged >65 yrs significantly increased from 1,238 (69.9%) in 2017 to 1,420 (76.8%) in 2021 ($P=0.003$). Approximately two-thirds of the patients (59.8%, 5,525/9,232) were female. CO infection was more frequent (80.8%, N=7,456) than HO infection (19.2%, N=1,776). According to the admission type, 4,172 (45.2%) patients were outpatients or emergency room visitors, 4,284 (46.4%) were GW patients, and 776 (8.4%) were intensive care patients.

Antimicrobial susceptibility of *E. coli* blood isolates

The ampicillin resistance rate among the *E. coli* blood isolates was 66.6% (6,149/9,232), whereas that of ampicillin-sulbactam resistance was 24.1% (2,226/9,232). Among third-generation cephalosporins, the resistance rate to cefotaxime (36.4%, 3,363/9,232) was more than three times higher than that to ceftazidime (11.4%, 1,053/9,232). The resistance rates to carbapenems were 0.2% (17/9,232) to ertapenem, 0.1% (8/9,232) to imipenem, and 0.1% (6/9,232) to meropenem.

AMR rates did not differ by year during the study period (Fig. 2A). The cefotaxime and ceftazidime resistance rates in HO infection cases (56.0% and 20.1%, respectively) were substantially higher than those in CO infection cases (31.8% and 9.3%, respectively) (Fig. 2B). By admission type, the resistance rates increased progressively from OPD to GW to ICU for all antimicrobials tested (Fig. 2C). The ampicillin resistance rate was 63.9% in *E. coli* blood isolates from OPDs, 67.6% in those from GWs, and 75.9% in those from ICUs. Similarly, the cefotaxime resistance rates were 32.5%, 38.0%, and 48.7% in OPD, GW, and ICU cases, respectively. The resistance rates to broad-spectrum

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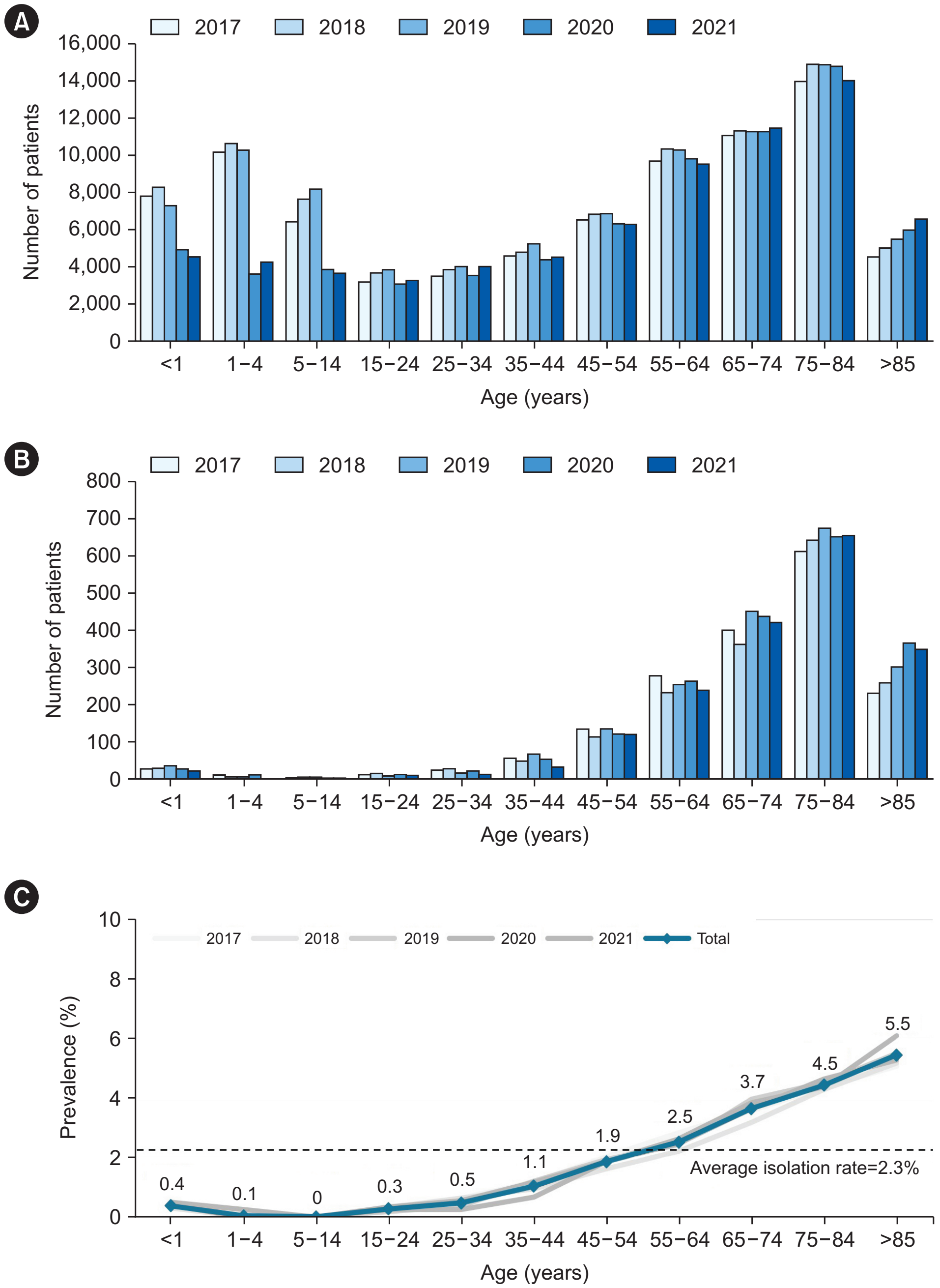

Fig. 1. Number of cases and prevalence of *Escherichia coli* bloodstream infections stratified by age. (A) The number of patients who underwent blood culture examination according to the age group, (B) the number of patients with *E. coli* bloodstream infection according to the age group, and (C) the prevalence of *E. coli* bloodstream infection according to the age group.

cephalosporins, including cefotaxime, ceftazidime, and cefepime, were significantly higher in the older age group than in the other age groups (Fig. 2D).

Risk factors for cefotaxime resistance in *E. coli* blood isolates

cefotaxime resistance was observed in 36.4% (3,363/9,232) of *E. coli* isolates from BSIs. In univariate logistic regression incorporating clinical information, age >65 yrs (OR, 1.35; 95% confidence interval [CI], 1.22–1.49), HO infection (OR, 2.68; 95% CI,

Table 1. Baseline demographic and clinical characteristics of patients with *Escherichia coli* bloodstream infections

Variables	Total (N = 9,232)	2017 (N = 1,772)	2018 (N = 1,724)	2019 (N = 1,939)	2020 (N = 1,949)	2021 (N = 1,848)	*P**
District							< 0.001
Seoul	570 (6.2)	120 (6.8)	96 (5.6)	114 (5.9)	124 (6.4)	116 (6.3)	
Gyeonggi	2,575 (27.9)	454 (25.6)	537 (31.1)	555 (34.6)	528 (27.3)	497 (26.9)	
Gangwon	1,077 (11.7)	222 (12.5)	206 (11.9)	243 (12.5)	218 (11.2)	188 (10.2)	
Chungbuk	788 (8.5)	160 (9.0)	166 (9.6)	171 (8.8)	135 (6.9)	156 (8.4)	
Chonnam	1,801 (19.5)	337 (19.0)	344 (20.0)	351 (18.1)	406 (20.8)	363 (19.6)	
Busan	1,384 (15.0)	258 (14.6)	219 (12.7)	323 (16.7)	319 (16.4)	265 (14.3)	
Jeju	1,037 (11.2)	221 (12.5)	156 (9.0)	182 (9.4)	215 (11.0)	263 (14.2)	
Age, median (1st–3rd interquartile range)	75.0 (64.0–82.0)	74.0 (61.0–81.0)	75.0 (63.0–82.0)	75.0 (64.0–82.0)	75.0 (64.0–82.0)	76.0 (65.0–83.0)	< 0.001
Old age (> 65 yrs)	6,791 (73.6)	1,238 (69.9)	1,262 (73.2)	1,422 (73.3)	1,449 (74.3)	1,420 (76.8)	0.003
Sex							0.737
Female	5,525 (59.8)	1,073 (60.5)	1,033 (59.9)	1,168 (60.2)	1,157 (59.4)	1,094 (59.2)	
Male	3,707 (40.2)	699 (39.4)	691 (40.1)	771 (39.8)	792 (40.6)	754 (40.8)	
Infection type							0.463
Community-origin	7,456 (80.8)	1,426 (80.5)	1,385 (80.3)	1,546 (79.7)	1,596 (81.9)	1,503 (81.3)	
Hospital-origin	1,776 (19.2)	346 (19.5)	339 (19.7)	393 (20.3)	353 (18.1)	345 (18.7)	
Admission type							< 0.001
Outpatient	4,172 (45.2)	697 (39.3)	792 (45.9)	907 (46.8)	903 (46.3)	873 (47.2)	
General ward	4,284 (46.4)	895 (50.5)	788 (45.7)	881 (45.4)	882 (45.3)	838 (45.3)	
Intensive care unit	776 (8.4)	180 (10.2)	144 (8.4)	151 (7.8)	164 (8.4)	137 (7.4)	

Values are presented as number (%) or median (1st–3rd interquartile range).
**P*-values were calculated using the chi-square test for categorical variables and the Kruskal–Wallis test for continuous variables.

2.41–2.98), and admission type (OPD, OR: 0.79; ICU, OR: 1.52 vs. GW) were significantly associated with cefotaxime resistance (Table 2). In multivariable logistic regression, the risk factors age >65 yrs (aOR, 1.36; 95% CI, 1.23–1.51), HO infection (aOR, 2.55; 95% CI, 2.28–2.85), and admission type (ICU vs. GW, aOR: 1.34, 95% CI 1.14–1.58) still showed significant associations with cefotaxime resistance in *E. coli*, except in the OPD group (aOR, 0.96; 95% CI, 0.87–1.05).

STs and ESBL genotypes of *E. coli* blood isolates

The most prevalent ST in cefotaxime-resistant *E. coli* blood isolates was ST131 (64.8%, 2,180/3,363), followed by ST1193 (5.3%, N = 177), ST69 (5.1%, N = 170), ST38 (2.6%, N = 88), and ST648 (2.0%, N = 66) (Fig. 3A). The remaining 682 isolates (20.3%) were from 160 different STs, each comprising < 50 isolates.

Among the 3,363 cefotaxime-resistant *E. coli* isolates, 3,168 isolates harbored one (N = 3,041) or two $bla_{\text{CTX-M}}$ type ESBL genes (N = 127), whereas the remaining 195 isolates were negative for CTX-M, SHV, and TEM ESBL genes. Among *E. coli* isolates with one ESBL gene, 52.0% (N = 1,582) carried CTX-M-1 group ESBL genes, including $bla_{\text{CTX-M-15}}$ (N = 1,265) and $bla_{\text{CTX-M-55}}$ (N = 253), whereas 47.9% (N = 1,457) carried CTX-M-9 group ESBL genes, including $bla_{\text{CTX-M-27}}$ (N = 672) and $bla_{\text{CTX-M-14}}$ (N = 656). Two isolates carried CTX-M-2. Of the 127 isolates harboring two CTX-M-type ESBL genes, 90 harbored both $bla_{\text{CTX-M-15}}$ and $bla_{\text{CTX-M-14}}$.

The correlations between STs and ESBL genotypes are shown in Fig. 3B and Supplemental Data Fig. S1. ST131, ST648, ST405, and ST410 cefotaxime-resistant *E. coli* isolates frequently harbored $bla_{\text{CTX-M-15}}$. In contrast, ST1193 and ST68 showed a high proportion of $bla_{\text{CTX-M-27}}$ carriers, and most ST457 and ST5150 isolates carried $bla_{\text{CTX-M-55}}$.

Longitudinal trends revealed shifts in the prevalence of the CTX-M-1- and CTX-M-9-group ESBL genes (Fig. 4). In 2017, CTX-M-1-group ESBLs were more common than those in the CTX-M-9

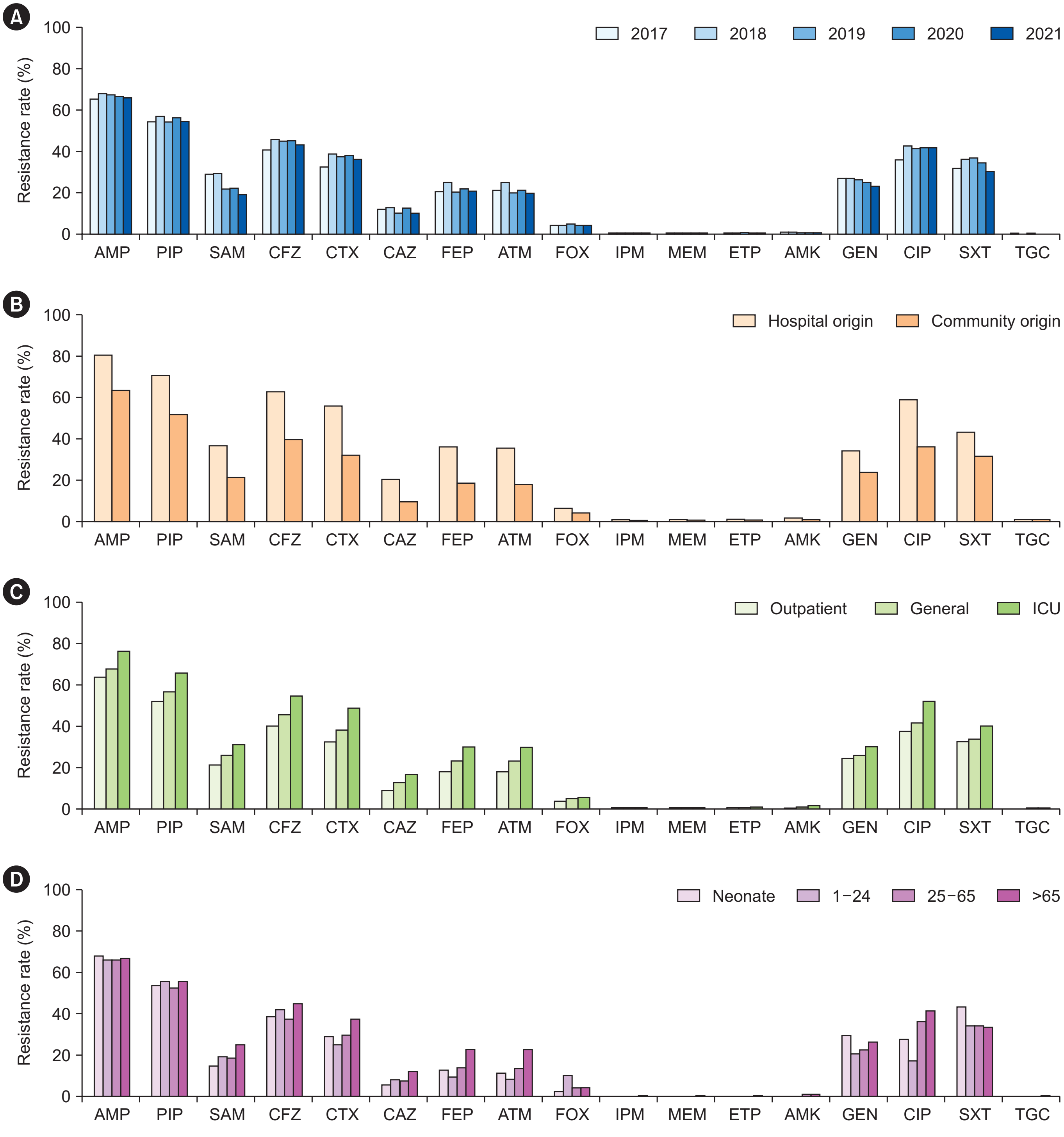

Fig. 2. Antimicrobial resistance rates of *Escherichia coli* blood isolates by year (A), infection origin (B), admission type (C), and age group (D). Abbreviations: AMP, ampicillin; PIP, piperacillin; SAM, ampicillin-sulbactam; CFZ, cefazolin; CTX, cefotaxime; CAZ, ceftazidime; FEP, cefepime; ATM, aztreonam; FOX, cefoxitin; IPM, imipenem; MEM, meropenem; ETP, ertapenem; AMK, amikacin; GEN, gentamicin; CIP, ciprofloxacin; SXT, trimethoprim-sulfamethoxazole; TGC, tigecycline.

Table 2. Risk factors for cefotaxime resistance of causative *Escherichia coli* isolates in patients with bloodstream infections

Variables	Univariate logistic regression		Multivariate logistic regression*		
	OR (95% CI)	*P*	aOR (95% CI)	*P*	VIF
Male	1.06 (0.97–1.16)	0.171	-	-	-
Age group					
Neonates	0.91 (0.62–1.32)	0.639	0.76 (0.51–1.13)	0.183	1.07
1–24 yrs	0.77 (0.47–1.22)	0.280	0.91 (0.50–1.32)	0.437	1.03
25–65 yrs	Reference		Reference	-	-
> 65 yrs	1.35 (1.22–1.49)	< 0.001	1.36 (1.23–1.51)	< 0.001	1.07
District					
Seoul	Reference		-	-	-
Gyeonggi	0.91 (0.75–1.10)	0.308	-	-	-
Gangwon	1.06 (0.86–1.31)	0.587	-	-	-
Chungbuk	1.01 (0.80–1.26)	0.933	-	-	-
Chonnam	1.13 (0.93–1.37)	0.232	-	-	-
Busan	1.03 (0.84–1.26)	0.789	-	-	-
Jeju	0.94 (0.76–1.17)	0.588	-	-	-
Hospital-origin infection	2.68 (2.41–2.98)	< 0.001	2.55 (2.28–2.85)	< 0.001	1.10
Admission type					
Outpatient	0.79 (0.73–0.87)	< 0.001	0.96 (0.87–1.05)	0.351	1.14
General ward	Reference		Reference		
Intensive care unit	1.52 (1.31–1.77)	< 0.001	1.34 (1.14–1.58)	< 0.001	1.13

*Variables with $P < 0.05$ in univariate logistic regression were included in multivariate logistic regression.
Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; VIF, variance inflation factor

group (52.2% vs. 44.1%). However, with the increasing incidence of $bla_{\text{CTX-M-27}}$-harboring *E. coli* isolates during the study period, the proportion of CTX-M-9-group ESBL-harboring isolates surpassed that of CTX-M-1-group ESBL-harboring isolates in 2021 (CTX-M-1 group: CTX-M-9 group = 46.4%: 47.7%).

DISCUSSION

E. coli is the most common pathogen causing BSIs, and the multidrug-resistant trait of ESBL-producing *E. coli* can delay appropriate antimicrobial treatment, leading to increased mortality and prolonged hospital stays [4–6]. Previous exposure to cephalosporin antimicrobials, admission history to hospitals or healthcare facilities, and older age of patients have been reported to be risk factors for infection caused by ESBL-producing *E. coli* [22, 23]. In our study, the proportion of *E. coli* among the BSI cases caused by Kor-GLASS target pathogens was 43.5%. The number of BSI patients > 60 yrs increased from 69.9% in 2017 to 76.8% in 2021, resulting in an increased burden of ESBL-producing *E. coli* on public health. Moreover, old age and HO infection were identified as independent risk factors for cefotaxime resistance. These findings indicate that the public burden of *E. coli* BSIs is substantial and may highlight the need for careful consideration of broad-spectrum antimicrobial coverage in elderly patients and those with HO *E. coli* BSIs.

ST131 was the most common ST in cefotaxime-resistant *E. coli* blood isolates during the study period, which is consistent with previous findings in other countries, including the United States and European countries [24–26]. *E. coli* ST131 mostly belongs to phylogenetic group B2 and exhibits the *fimH30* type, carrying $bla_{\text{CTX-M-15}}$ and fluoroquinolone resistance, and is designated as subclone H30-Rx [27]. CTX-M-14-producing ST131 *E. coli* is particularly common in Canada, China, Japan, and Spain, and CTX-M-27-producing ST131 *E. coli* strains have been reported in France and Japan [28–30]. In this study, ST131 *E. coli* isolates had diverse of $bla_{\text{CTX-M}}$ genotypes: 47.1% carried $bla_{\text{CTX-M-15}}$, 21.5% carried $bla_{\text{CTX-M-27}}$, and 16.3% carried $bla_{\text{CTX-M-14}}$, in line with previous findings [31]. The observed $bla_{\text{CTX-M}}$ genotype diversity

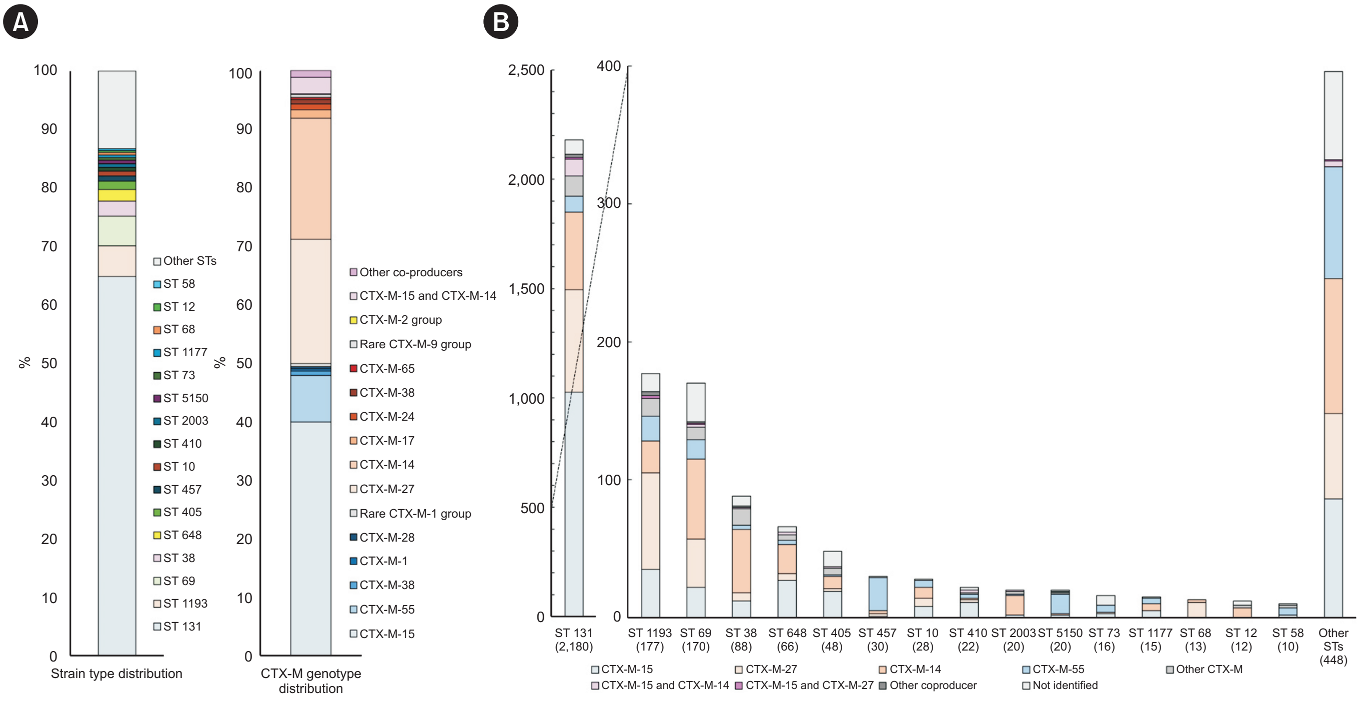

Fig. 3. Distribution of STs and CTX-M genotypes in CTX-resistant *Escherichia coli* blood isolates. (A) Distribution of strain type and *bla*$_{\text{CTX-M}}$ genotype. (B) *bla*$_{\text{CTX-M}}$ genotypes by strain type.
Abbreviations: ST, sequence type; CTX, cefotaxime.

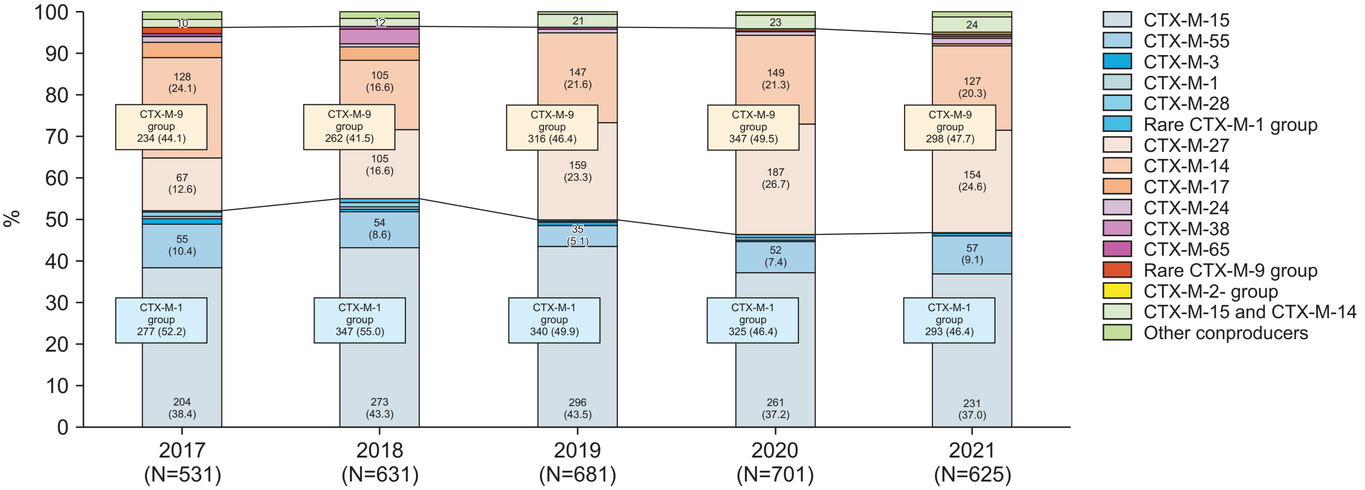

Fig. 4. Distribution of CTX-M genotypes according to the year.
Abbreviation: CTX-M, cefotaximase.

among ST131 isolates suggests an endemic condition.

The ST1193 *E. coli* clone has been increasingly reported over the past decade, particularly in community-associated cases [32]. ST1193 *E. coli* frequently exhibits co-resistance to fluoroquinolones, and non-susceptibility rates to amikacin and carbapenems reportedly are low [33, 34]. ST1193 is the fourth most common ST in South Korea, accounting for 6.5% of all isolates, and its resistance rate to cefotaxime is <20% [31]. In this study, ST1193 was the second most common ST among cefotaxime-resistant isolates and was associated with an increased proportion of CTX-M-27 in the distribution of CTX-M-type ESBLs. CTX-M-27 has a single-nucleotide polymorphism (D240G) compared with CTX-M-14 and exhibits increased hydrolytic activity toward ceftazidime, resulting in broad-range beta-lactam antimicrobial resistance [14]. ST1193 *E. coli* isolates harboring $bla_{\text{CTX-M-27}}$ have been reported in China and Japan [35].

The $bla_{\text{CTX-M-55}}$ gene has been widely reported in many countries, and its prevalence is increasing [36]. CTX-M-55 is a member of group CTX-M-1, exhibiting an amino acid substitution (A77V), and its hydrolytic activity toward ceftazidime of CTX-M-55 is stronger than that toward CTX-M-15 [37]. CTX-M-55 is distributed in a wide range of hosts, including humans, pigs, and chickens, and clonal transmission with few single-nucleotide polymorphisms has been reported in human–pig, human–chicken, and human–environment interactions, suggesting that this enzyme was associated with AMR dissemination in the One Health context [36, 38]. In total, 253 $bla_{\text{CTX-M-55}}$-harboring *E. coli* strains were identified, of which ST131, ST457, ST1193, ST69, and ST5150 were the most common. ST457 *E. coli* is a reservoir of ESBL-producing lineages in food-producing and wild animals in South America and Australia [39]. The WHO has developed an AMR surveillance protocol in the One Health context, focusing on ESBL-producing *E. coli*, known as the Tricycle protocol [40]. $bla_{\text{CTX-M-55}}$ may be an important factor for investigating AMR dissemination from the One Health perspective.

One limitation of this study was that it involved only eight university-affiliated sentinel hospitals, which may not fully represent the national epidemiology, particularly the AMR status in community settings such as local clinics. However, consistent data collection and epidemiological analysis from the same sites over a 5-yr period allowed for the identification of long-term trends in the prevalence of *E. coli* BSIs and AMR status. Another limitation is the lack of clinical information regarding patient outcomes. Further studies are needed to clarify the relationship between AMR genotypes and clinical outcomes.

In conclusion, the molecular epidemiology of ESBL-producing *E. coli* was investigated through AMR phenotyping and genotyping of all isolates collected over 5 yrs at eight sentinel hospitals as part of the national AMR surveillance system. ST131 ESBL-producing *E. coli* was the predominant clone in South Korea, and the prevalence of $bla_{\text{CTX-M-27}}$-carrying ST1193 clones increased during the study period. Further investigation should be conducted in community-associated healthcare settings, and continued research is needed to elucidate the mechanisms of AMR dissemination.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.3343/alm.2025.0145.

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AUTHOR CONTRIBUTIONS

Kim D and Jeong SH contributed to the conceptualization of the study; Hong JS, Choi MH, Kim HS, Kim YR, Kim YA, Uh Y, Shin KS, Shin JH, Kim SH, and Shin JH collected the clinical data and bacterial isolates; Kim D, Yu J, and Hong JS performed bacterial experiments; Kim D conducted the statistical analysis and data visualization; Park JS and Park KU carried out quality assessment of the Kor-GLASS network; Kim D and Jeong SH interpreted the data; Kim D and Lee SY drafted the manuscript; Kim D, Lee SY, and Jeong SH revised and edited the manuscript; Kim D, Kim SH, and Jeong SH acquired funding. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST

None declared.

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