

Seven-Year Surveillance and AI-Based Forecasting of Antimicrobial Resistance in Pediatric *Escherichia coli* Infections in Northern China (2018–2024)

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Background: Pediatric *Escherichia coli* infections are a major cause of morbidity, and increasing antimicrobial resistance (AMR) complicates empirical treatment. Long-term local surveillance combined with trend forecasting may support rational antimicrobial use and stewardship in northern China.

Methods: We retrospectively analyzed 2021 pediatric *E. coli* isolates collected at Baoding Hospital of Beijing Children's Hospital, Capital Medical University (2018–2024), calculated annual resistance rates to 14 commonly used antibiotics and the prevalence of extended-spectrum β -lactamase (ESBL) producers, defined an overall resistance indicator as the mean annual resistance across these agents, and used χ^2 -tests, linear regression, and autoregressive integrated moving average (ARIMA) and long short-term memory (LSTM) models to evaluate temporal trends and generate exploratory forecasts for 2025–2027.

Results: Nearly half of isolates were from children <2 years and about two-thirds from boys; pus, sputum, and urine were the predominant specimen types. Resistance to ampicillin and trimethoprim–sulfamethoxazole remained high, whereas resistance to several β -lactams, including ampicillin/sulbactam and third-generation cephalosporins, declined significantly over time. ESBL-producing isolates accounted for 45.93% of all strains, with annual detection rates >50% in 2018–2020 and around 40% thereafter, while carbapenems and amikacin maintained very low resistance rates. Both ARIMA and LSTM models suggested a modest further decline in the overall resistance indicator through 2027, with LSTM showing slightly better fit and lower prediction errors.

Conclusion: Pediatric *E. coli* isolates in our center exhibited high resistance to several common oral agents but encouraging declines in ESBL prevalence and cephalosporin resistance, likely reflecting local antimicrobial stewardship. Exploratory AI-based time-series models may help anticipate resistance trajectories and support pediatric antibiotic policies and stewardship, although forecasts from a short annual series should be interpreted cautiously.

Keywords: *Escherichia coli*, pediatric infections, antimicrobial resistance, extended-spectrum β -lactamase, ESBL, time-series forecasting, LSTM

Introduction

Antimicrobial resistance (AMR) has become an urgent global public health challenge. Recent modeling studies project that, absent effective interventions, cumulative deaths directly attributable to bacterial AMR could reach 39 million by 2050, with AMR-associated deaths rising to 169 million, underscoring its long-term impact on health systems and socioeconomics.^{1,2} In pediatrics, *Escherichia coli* (*E. coli*) is a major pathogen of both community- and hospital-acquired infections and is among the most common etiologies of pediatric urinary tract infection (UTI), sepsis, pneumonia, and diarrheal diseases. Multicenter surveillance indicates that *E. coli* is the leading cause of pediatric UTI, with resistance patterns varying by age and region; neonates and infants are particularly susceptible to invasive *E. coli* infection, and their incidence and outcomes are strongly

influenced by host immune maturation. In addition to urinary tract infections, *E. coli* is also a major cause of bloodstream, lower respiratory tract, and skin and soft-tissue infections in hospitalized children. Therefore, in this study, we included isolates from urine, sputum, pus, blood, and other clinically relevant specimens to comprehensively reflect the burden of pediatric *E. coli* infections and severe hospital-associated infections in our center. Within the diarrheal disease spectrum, diarrheagenic *Escherichia coli* remains a major cause of morbidity in young children in several low- and middle-income countries, particularly in settings with limited sanitation and vaccine coverage.^{3,4} In recent years, carriage and infection due to extended-spectrum β -lactamase (ESBL)–producing *E. coli* have shown sustained increases or persistently high, fluctuating prevalence in both community and healthcare settings, challenging empiric regimens such as third-generation cephalosporins.^{5,6} Nevertheless, pediatric multicenter data and clinical studies suggest that reserve agents—exemplified by carbapenems—retain high in vitro activity for severe/complex infections; amikacin also demonstrates high susceptibility across multiple resistance phenotypes (including some ESBL or carbapenemase-producing strains) and, where pharmacokinetic/pharmacodynamic (PK/PD) considerations and safety are satisfied, may serve as an alternative in selected scenarios to reduce unnecessary carbapenem exposure.^{3,7–9} In parallel, pediatric antimicrobial stewardship (AMS) has continued to advance. Systematic reviews show that AMS in pediatric settings (including PICUs) can reduce antibiotic consumption, promote guideline-concordant prescribing, and improve medication safety, although current intervention models, metrics, and reporting still vary across institutions and warrant standardization and optimization.^{10,11} Given the availability of local primary surveillance data in the present study, and in light of the favorable performance of ARIMA and machine-learning approaches for forecasting resistance and antibiotic use, it is both feasible and practically meaningful to perform trend extrapolation, optimize regimen structure, and locally calibrate empiric therapy strategies.^{2,12–14} To provide forward-looking, locally tailored evidence for pediatric antimicrobial stewardship, we combined a classical autoregressive integrated moving average (ARIMA) model with a long short-term memory (LSTM) neural network. ARIMA has been widely used to model linear temporal patterns in antimicrobial resistance surveillance data, whereas LSTM can capture potential nonlinear dependencies in short time series. In this study, both models were evaluated using one-step-ahead forecasts and standard error metrics (mean absolute error and root mean squared error) to compare their performance, and the observed resistance levels were briefly benchmarked against national surveillance and WHO GLASS reports to ensure plausibility.

Materials and Methods

General Information

This retrospective study included a total of 2021 *Escherichia coli* isolates recovered from clinical specimens of hospitalized children at Baoding Hospital of Beijing Children's Hospital, Capital Medical University, Baoding between January 2018 and December 2024. Basic information collected comprised the number of submitted specimens, patient sex and age, specimen types, and clinical diagnoses. The study was approved by the Ethics Committee of Baoding Hospital of Beijing Children's Hospital, Capital Medical University, Baoding, and written informed consent was obtained from the legal guardians of all participants.

Instruments and Reagents

Instruments

A carbon dioxide (CO₂) incubator (Shanghai Lishen Scientific Instruments Co., Ltd., Shanghai, China); a BacT/ALERT 3D blood culture system (bioMérieux, Marcy-l'Étoile, France); and a VITEK 2 Compact microbial identification and antimicrobial susceptibility testing system (bioMérieux, Marcy-l'Étoile, France).

Principal Reagents and Strains

Blood agar plates (Zhengzhou Antu Bioengineering Co., Ltd. [Autobio], Zhengzhou, China); China blue agar plates (Zhengzhou Antu Bioengineering Co., Ltd. [Autobio], Zhengzhou, China). The quality-control strain was *Escherichia coli* ATCC 25922.

Methods

Isolation and Culture of Strains

In accordance with the *National Clinical Laboratory Procedures* (China), clinical specimens (eg, sputum, pus, urine) were inoculated onto blood agar and China blue agar plates and incubated at 37°C with 5% CO₂ for 18–24 h. For blood specimens, samples were injected into blood culture bottles and loaded into the BacT/ALERT 3D system; once flagged positive, they were subcultured onto blood agar and China blue agar plates and incubated at 37°C with 5% CO₂ for 18–24 h.

Identification of Strains

Following the *National Clinical Laboratory Procedures* (China), isolates were identified and confirmed using the VITEK 2 Compact automated microbial identification system.

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing (AST) for all *Escherichia coli* isolates was performed using the VITEK 2 Compact system (bioMérieux, Marcy-l'Étoile, France). Susceptibility categorizations were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) M100, 2024 edition. For each antimicrobial agent, minimum inhibitory concentration (MIC)-based breakpoints for susceptible (S), intermediate (I), and resistant (R) were applied exactly as recommended by CLSI. *Escherichia coli* ATCC 25922 was used as the quality-control strain in all AST runs. Isolates showing resistance or non-susceptibility to third-generation cephalosporins, suspicion of ESBL production, carbapenem non-susceptibility, or other discordant phenotypes were re-tested and confirmed by the disk diffusion method and/or CLSI-recommended ESBL confirmatory tests. Routine isolates without unusual or discrepant results were not systematically duplicated by disk diffusion. This approach ensured both adherence to international standards and reliability of the final susceptibility data.

Amikacin: susceptible ≤ 4 µg/mL; intermediate: 4–16 µg/mL; resistant ≥ 16 µg/mL

Ampicillin: susceptible ≤ 8 µg/mL; intermediate: 8–32 µg/mL; resistant ≥ 32 µg/mL

Aztreonam: susceptible ≤ 4 µg/mL; intermediate: 4–16 µg/mL; resistant ≥ 16 µg/mL

Ceftazidime: susceptible ≤ 4 µg/mL; intermediate: 4–16 µg/mL; resistant ≥ 16 µg/mL

Ceftriaxone: susceptible ≤ 1 µg/mL; intermediate: 1–4 µg/mL; resistant ≥ 4 µg/mL

Cefuroxime: susceptible ≤ 8 µg/mL; intermediate: 8–32 µg/mL; resistant ≥ 32 µg/mL

Cefepime: susceptible ≤ 2 µg/mL; intermediate: 2–16 µg/mL; resistant ≥ 16 µg/mL

Gentamicin: susceptible ≤ 2 µg/mL; intermediate: 2–8 µg/mL; resistant ≥ 8 µg/mL

Imipenem: susceptible ≤ 1 µg/mL; intermediate: 1–4 µg/mL; resistant ≥ 4 µg/mL

Levofloxacin: susceptible ≤ 0.5 µg/mL; intermediate: 0.5–2 µg/mL; resistant ≥ 2 µg/mL

Meropenem: susceptible ≤ 1 µg/mL; intermediate: 1–4 µg/mL; resistant ≥ 4 µg/mL

Ampicillin/sulbactam: susceptible ≤ 8 µg/mL; intermediate: 8–32 µg/mL; resistant ≥ 32 µg/mL

Tobramycin: susceptible ≤ 2 µg/mL; intermediate: 2–8 µg/mL; resistant ≥ 8 µg/mL

Trimethoprim-sulfamethoxazole: susceptible $\leq 2/38$ µg/mL; intermediate: 2/38–4/76 µg/mL; resistant $\geq 4/76$ µg/mL

Statistical Analysis

All data were managed using WHONET 5.6 and analyzed in SPSS Statistics 28.0 (IBM Corp., Armonk, NY, USA) and Python 3.10. Categorical variables were summarized as counts (n) and percentages (%). The annual resistance rate for each antibiotic was calculated as: number of isolates categorized as resistant (R) divided by the total number of isolates tested for that agent in the corresponding year $\times 100\%$. Intermediate (I) isolates were reported descriptively and were not counted as resistant in the primary analysis. Sensitivity analyses considering non-susceptible (I+R) categories were explored where relevant.

The overall resistance rate for each year was defined as the arithmetic mean of the resistance rates of the 14 routinely tested antibiotics and was used as an aggregate indicator to describe temporal changes in the overall antimicrobial resistance burden among pediatric *E. coli* isolates at our center.

Comparisons of proportions between groups (eg, age, sex, specimen types) were performed using the chi-square (χ^2) test or χ^2 goodness-of-fit test, with $P < 0.05$ considered statistically significant. Linear regression was applied to assess trends in annual resistance rates over time.

Time-series forecasting models were constructed for antibiotics with complete annual resistance data from 2018 to 2024. For each antibiotic and for the overall resistance indicator, an autoregressive integrated moving average (ARIMA) model was fitted using a Box–Jenkins approach. Candidate (p, d, q) orders were selected based on autocorrelation and partial autocorrelation plots and by minimizing the Akaike information criterion (AIC) and Bayesian information criterion (BIC). Model adequacy was confirmed by inspection of residuals and the Ljung–Box test to ensure no significant autocorrelation remained. One-step-ahead forecasts and corresponding 95% prediction intervals were generated for 2025–2027.

In parallel, a univariate long short-term memory (LSTM) neural network was implemented to explore potential nonlinear temporal patterns. For the overall resistance rate, a single hidden LSTM layer with 50 units followed by a fully connected output layer was used. A 3-year sliding window (eg, years $t-2$ to t as input to predict year $t+1$) was adopted. Input data were normalized before training. The model was trained using the Adam optimizer (learning rate 0.001), mean squared error as the loss function, and up to 200 epochs with early stopping based on validation loss. For antibiotics with complete annual resistance data (2018–2024), autoregressive integrated moving average (ARIMA) models were fitted following a Box–Jenkins approach. Candidate (p, d, q) orders were selected using autocorrelation and partial autocorrelation functions and by minimizing the Akaike information criterion (AIC) and Bayesian information criterion (BIC). Model adequacy was confirmed through residual diagnostics and the Ljung–Box test to ensure no remaining autocorrelation. One-step-ahead forecasts with 95% prediction intervals were generated for 2025–2027. In parallel, a univariate long short-term memory (LSTM) neural network was implemented to explore potential nonlinear temporal patterns in the annual series. A single hidden LSTM layer (50 units) with a fully connected output layer was used. A 3-year sliding window (years $t-2$ to t as input to predict $t+1$) and input normalization were adopted. The model was trained with the Adam optimizer (learning rate 0.001), using mean squared error (MSE) as the loss function for up to 200 epochs with early stopping based on validation loss. Given the limited number of annual observations, one-step-ahead rolling-origin validation was applied. Predictive performance was summarized using mean absolute error (MAE) and root mean squared error (RMSE) for both ARIMA and LSTM to enable direct comparison. Because of the short series length, all forecasts are reported and interpreted as exploratory. All forecasts are reported and interpreted as exploratory, owing to the short time series length.

Results

Age-Group Distribution of *E. coli* Isolates

From 2018 to 2024, a total of 2021 *E. coli* isolates were recovered from clinical specimens of hospitalized pediatric patients. By age group, there were 1003 isolates from children <2 years (49.63%), 350 from those 2–5 years (17.32%), and 668 from those >5 years (33.05%). Chi-square testing showed a significant difference in isolation composition across age groups ($\chi^2=167.05$, $df=2$, $P<0.0001$). See Table 1.

Table 1 Age-Specific Distribution of *Escherichia coli* Isolates Among Pediatric Inpatients from 2018 to 2024

Age Group	No. of Isolates	Proportion (%)	χ^2 Value	Degrees of Freedom (df)	P value
<2 years	1003	49.63			
2–5 years	350	17.32			
>5 years	668	33.05			
Total	2021	100.00	167.05	2	<0.0001

Notes: The highest proportion was observed in children under 2 years of age. Chi-square analysis revealed a statistically significant difference among age groups ($P < 0.0001$).

Table 2 Gender-Specific Distribution of *E. coli* Isolates

Gender	No. of Isolates	Proportion (%)	χ^2 Value	Degrees of Freedom (df)	P value
Male	1312	64.9			
Female	709	35.1			
Total	2021	100.0	91.40	1	<0.0001

Notes: The number of isolates was significantly higher in male patients than in female patients. Goodness-of-fit chi-square test indicated a statistically significant deviation from the expected 1:1 distribution ($P < 0.0001$).

Sex Distribution

Overall, 1312 isolates were from male children (64.9%) and 709 from female children (35.1%), yielding a male-to-female ratio of approximately 1.85:1. A χ^2 goodness-of-fit test indicated that this difference was statistically significant ($\chi^2=91.40$, $df=1$, $P<0.0001$), suggesting a higher isolation proportion among males. See [Table 2](#).

Annual Isolate Counts and Specimen-Source Characteristics

From 2018 to 2024, yearly isolate counts were relatively stable with minor fluctuations ([Figure 1](#)). The highest count occurred in 2019 ($n=344$), and the lowest in 2022 ($n=245$). All isolates were obtained from clinical specimens submitted from hospitalized children, with documented source information and antimicrobial susceptibility testing (AST) results.

Regarding specimen sources, pus accounted for the largest proportion (47.35%, 957/2021), followed by sputum (22.17%) and urine (21.62%); together these comprised >91% of all specimens, indicating that extraintestinal *E. coli* infections in inpatients predominantly involved skin/soft-tissue infections, lower respiratory tract infections, and urinary tract infections. Isolates from blood (4.06%) and throat swabs (3.22%) were comparatively fewer, suggesting lower proportions related to bloodstream or pharyngeal infections ([Figure 2](#)).

Analysis of AST results for 14 commonly used antibiotics showed the highest resistance to ampicillin, generally >75%, whereas susceptibility remained favorable for reserve agents such as amikacin, imipenem, and meropenem, with resistance rates $\leq 5\%$. The S/I/R (susceptible/intermediate/resistant) breakdown by agent and overall resistance rates are presented in subsequent sections.

These findings provide a descriptive overview of the clinical distribution of *E. coli* over the past seven years at our center and establish a basis for subsequent trend analyses and targeted interventions.

Comparative in vitro Activity of Antimicrobial Agents Against *Escherichia coli*

This study systematically reviewed the in vitro susceptibility profiles of 14 commonly used antimicrobial agents against *E. coli* isolates recovered from hospitalized children between 2018 and 2024. Overall, susceptibility varied markedly

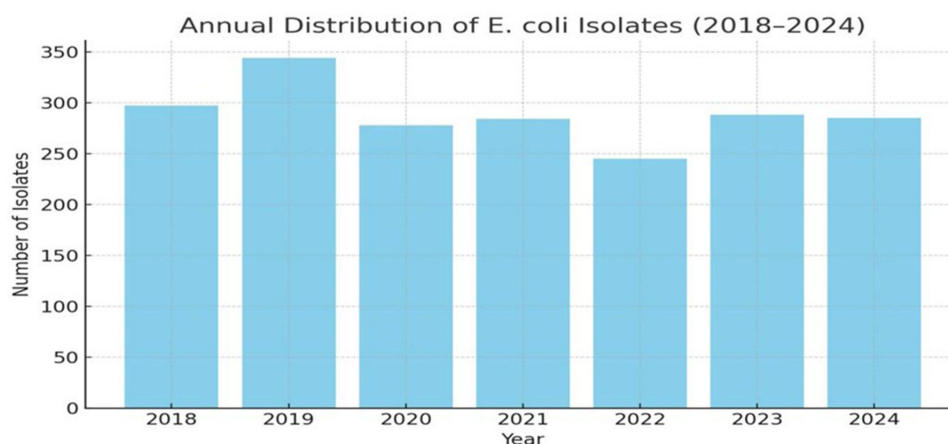


Figure 1 Annual distribution of *Escherichia coli* isolates collected from pediatric inpatients between 2018 and 2024.

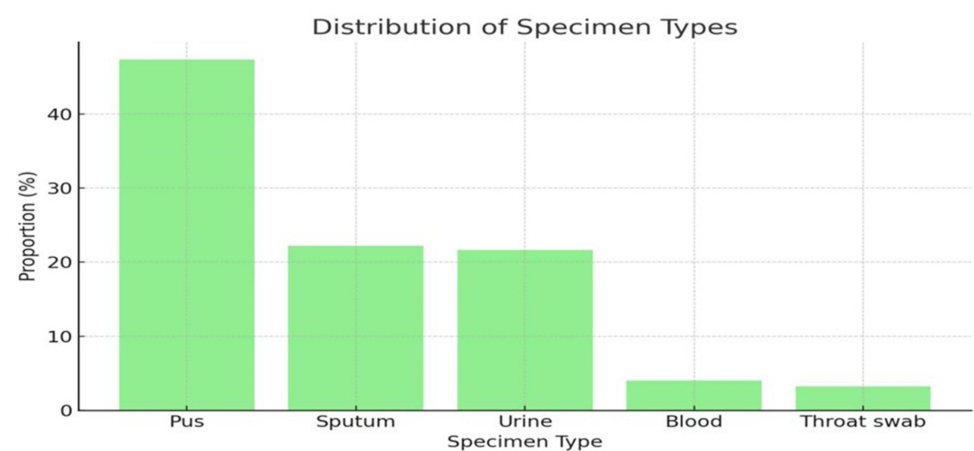


Figure 2 Distribution of specimen sources for *Escherichia coli* isolates among pediatric inpatients from 2018 to 2024.

across agents, with wide heterogeneity in resistance rates (Table 3). To verify the statistical significance of these differences, we applied chi-square tests to the S/I/R (susceptible/intermediate/resistant) categories for all drugs. The distribution of susceptibility differed highly significantly among agents ($\chi^2=12,739.08$, $P<0.001$), indicating substantial differences in their in vitro activity against *E. coli*.

Prevalence and Annual Detection Rates of ESBL-Producing *E. coli* (2018–2024)

From 2018 to 2024, a total of 943 out of 2021 pediatric *E. coli* isolates were identified as ESBL producers, yielding an overall prevalence of 45.9%. The annual proportions of ESBL-producing isolates were 54.43% in 2018, 55.81% in 2019,

Table 3 The Susceptibility Profiles of *E. coli* Isolates to 14 Antibiotics Showed Marked Variability Across Drug Classes

Antibiotic	Sensitive (S)	Intermediate (I)	Resistant (R)	χ^2 Value	df	P value
Ampicillin	103	15	1903			
Cefotaxime	325	58	1638			
Amikacin	1872	42	107			
Ciprofloxacin	812	83	1126			
Gentamicin	1273	137	611			
Imipenem	1941	27	53			
Meropenem	1922	24	75			
Piperacillin-tazobactam	1583	107	331			
Cefepime	999	139	883			
Ceftazidime	1093	123	805			
Ceftriaxone	876	132	1013			
Trimethoprim-sulfamethoxazole	1201	172	648			
Tetracycline	835	133	1053			
Chloramphenicol	1330	98	593			
Overall Comparison	–	–	–	12,739.08	26	< 0.001

53.20% in 2020, 39.14% in 2021, 36.32% in 2022, 38.34% in 2023, and 44.27% in 2024 (Table 4). ESBL prevalence therefore remained above 50% during 2018–2020, followed by a decline to approximately 40% from 2021 onwards, suggesting a partial but incomplete alleviation of the ESBL burden among pediatric *E. coli* infections in our center and highlighting the need for ongoing surveillance and targeted antimicrobial stewardship interventions.

Linear Regression Trend Analysis of Resistance Rates (2018–2024)

To further assess the statistical significance of year-to-year changes, we performed linear regression on resistance rates for 14 commonly used antibiotics from 2018 to 2024 (Figure 3a–d and Supplementary Figure 1). Multiple agents exhibited significant downward trends, most notably ampicillin/sulbactam (slope = -4.20 percentage points/year, $P = 0.00126$, $R^2 = 0.943$), indicating an average annual decrease exceeding 4 percentage points with high trend stability. Significant declines were also observed for cefepime (slope = -2.894 percentage points/year, $P = 0.00750$, $R^2 = 0.789$), ceftazidime (slope = -2.310 percentage points/year, $P = 0.02944$), and tobramycin (slope = -1.24 percentage points/year, $P = 0.03059$). Some agents (eg, aztreonam) did not show statistically significant changes, though the overall tendency was downward. These trend analyses are consistent with the preceding descriptive results and provide quantitative support for effective resistance control of *Escherichia coli* in our local pediatric population.

Temporal Trends in Resistance to Commonly Used Antibiotics

The annual resistance rates of commonly used antibiotics against pediatric *Escherichia coli* isolates from 2018 to 2024 are summarized in Figure 4. Overall, resistance to ampicillin and trimethoprim-sulfamethoxazole remained high throughout the study period, while several β -lactams, including ampicillin/sulbactam and third-generation cephalosporins, showed gradual declines in resistance. In contrast, resistance to amikacin, piperacillin-tazobactam, and carbapenems remained consistently low. Notably, cefotaxime, ceftriaxone, and cefepime exhibited encouraging downward trends, which paralleled the reduction in ESBL-producing isolates. Presenting these data in a single summary table allows straightforward comparison of temporal patterns across agents without redundant narrative descriptions for each antibiotic.

AI Modeling and Comparative Analysis of Overall Pediatric Resistance Trends

Based on analysis of our hospital's antimicrobial susceptibility data for pediatric *E. coli* infections from 2018 to 2024, we built a time-series deep learning model using long short-term memory (LSTM) to forecast changes in overall resistance rates for the next three years (2025–2027). The model input comprised the annual overall resistance-rate data, and the output was the predicted resistance rate for subsequent years.

Table 4 Seven-Year Trends in the Prevalence of ESBL-Producing *Escherichia coli* Isolates Inpediatric Patients (2018–2024)

	n	ESBL-Producing Isolates	Non-ESBL-Producing Isolates	Detection Rate of ESBL-Producing Isolates
2018	316	172	144	54.43%
2019	344	192	152	55.81%
2020	297	158	139	53.20%
2021	304	119	185	39.14%
2022	245	89	156	36.32%
2023	253	97	156	38.34%
2024	262	116	146	44.27%
Total	2021	943	1078	45.93%

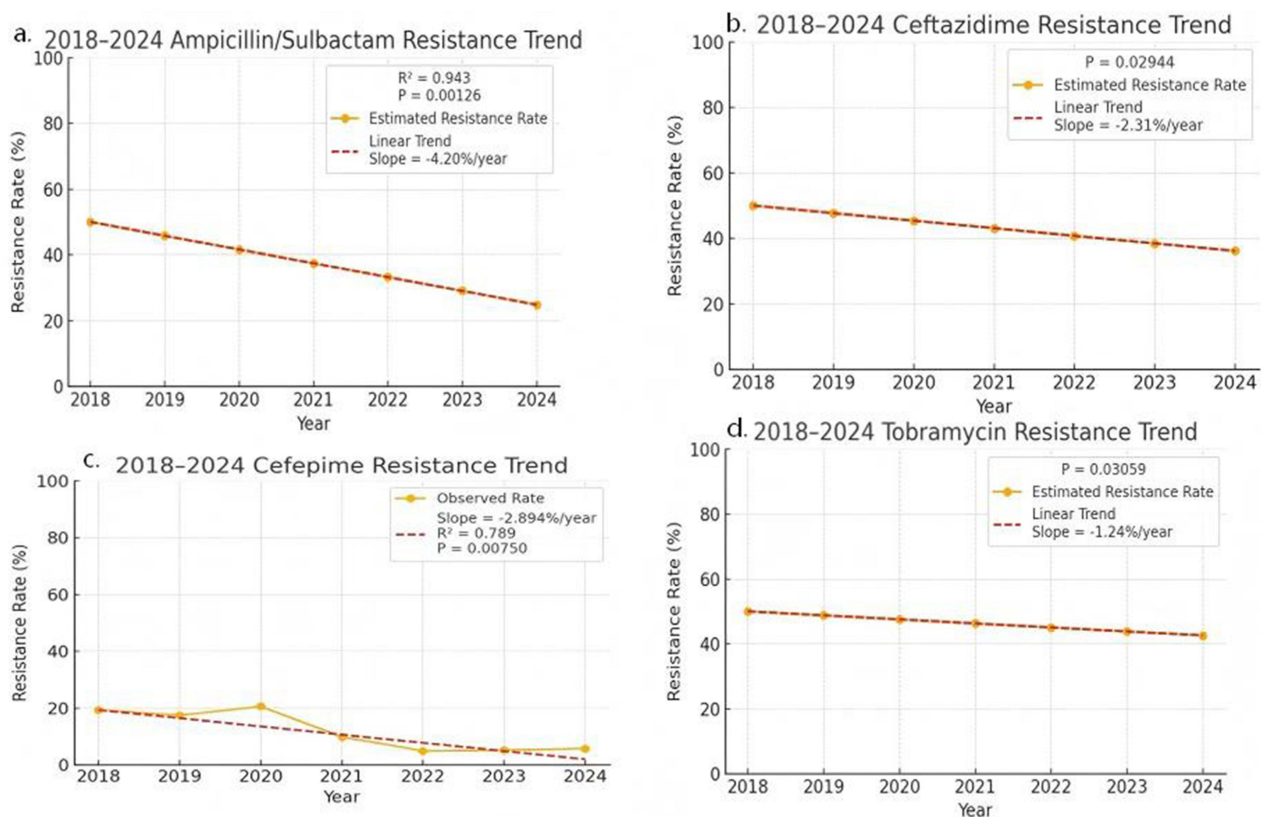


Figure 3 (a) 2018–2024 Ampicillin/Sulbactam Resistance. (b) 2018–2024 Cefepime Resistance Trend. (c) 2018–2024 Ceftazidime Resistance Trend. (d) 2018–2024 Tobramycin Resistance Trend. (a–d) Resistance Trends of Four Antimicrobial Drugs (2018–2024).

Based on the annual data from 2018 to 2024, both ARIMA and LSTM models were used to generate exploratory forecasts for 2025–2027 (see Figure 4). The overall resistance rate showed a year-by-year decline during the observation period (2018–2024) and is projected to remain stable or decrease modestly over the next three years. Consistent patterns were observed for key agents: resistance to third-generation cephalosporins and ampicillin/sulbactam is expected to remain stable or gradually improve relative to 2024, while carbapenems and amikacin are predicted to retain very low resistance. By contrast, resistance to trimethoprim–sulfamethoxazole is forecast to remain relatively high. In one-step-ahead validation, the LSTM model yielded slightly lower prediction errors (MAE/RMSE) than ARIMA across most agents (see Table 5).

Finally, we conducted a comparative analysis of the predicted antimicrobial resistance trends in pediatric *Escherichia coli* infections for the period 2018–2027). To enhance comparability and persuasiveness, we also contrasted the LSTM with a conventional ARIMA model (Figure 5). Using the same annual overall resistance data, the ARIMA (1,1,1) model forecasts overall resistance rates of 17.10%, 17.05%, and 17.02% for the next three years, suggesting a slight decline with an essentially stable trajectory.

Our findings indicate that deep learning approaches offer clear advantages in integrating multidimensional data and capturing latent nonlinear patterns, making them well suited for large-sample, multivariable clinical microbiology forecasting tasks. Future work should further incorporate patient-level characteristics (eg age, specimen type, site of infection) into machine-learning frameworks to build multifactor predictive models and enhance the guidance and value of antimicrobial stewardship. Given that only seven annual time points were available, these projections should be interpreted as exploratory indications to inform stewardship rather than definitive long-term predictions.

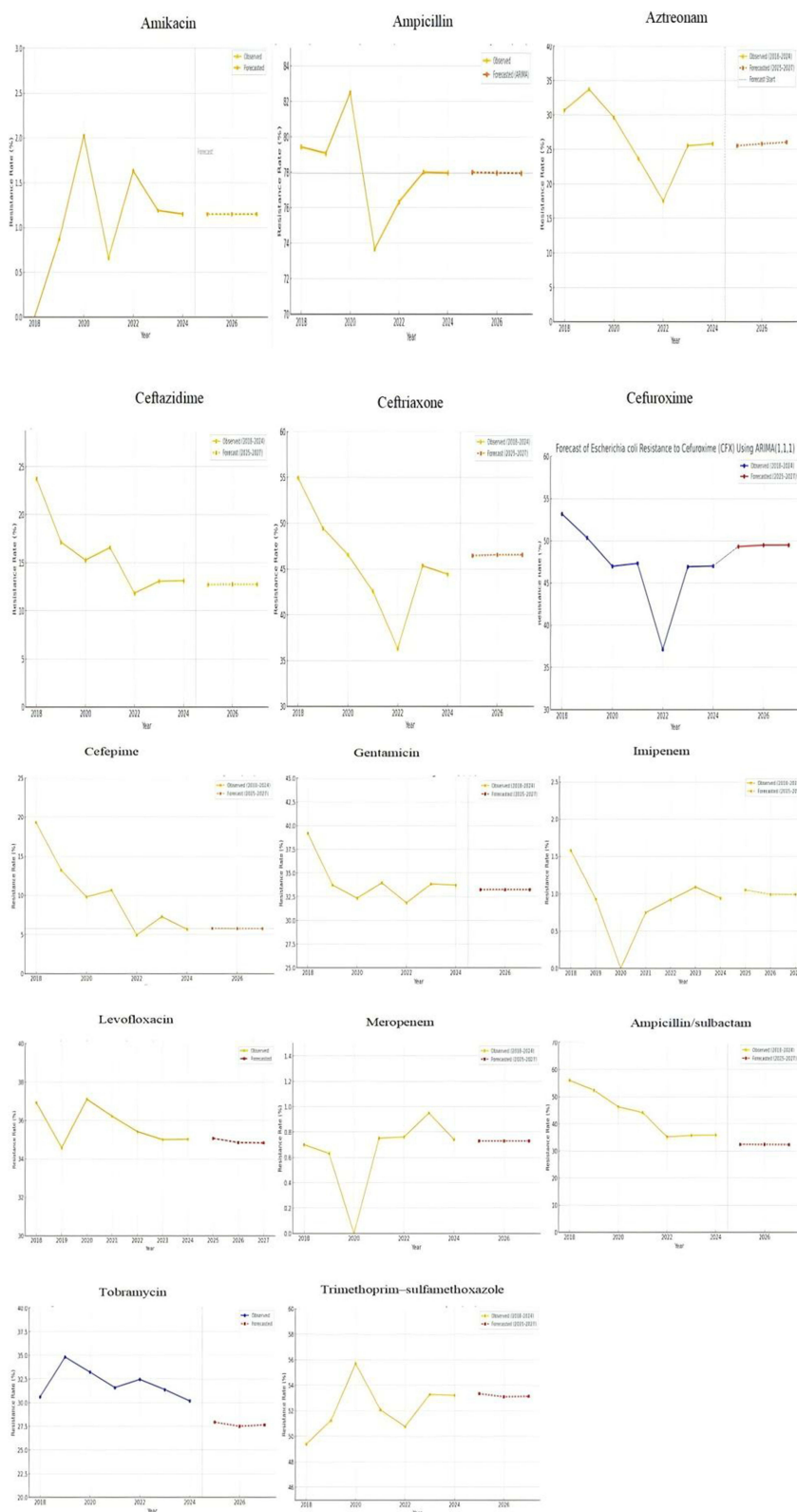


Figure 4 Resistance rates of *Escherichia coli* to 14 antibiotics from 2018 to 2024 (solid lines), and ARIMA-predicted values for 2025–2027. Red dashed lines represent the predicted values.

Table 5 The Overall Trend Predicted by the LSTM Model

Year	LSTM Prediction	ARIMA Prediction
2025	17.02%	17.10%
2026	16.35%	17.05%
2027	15.77%	17.02%

Discussion

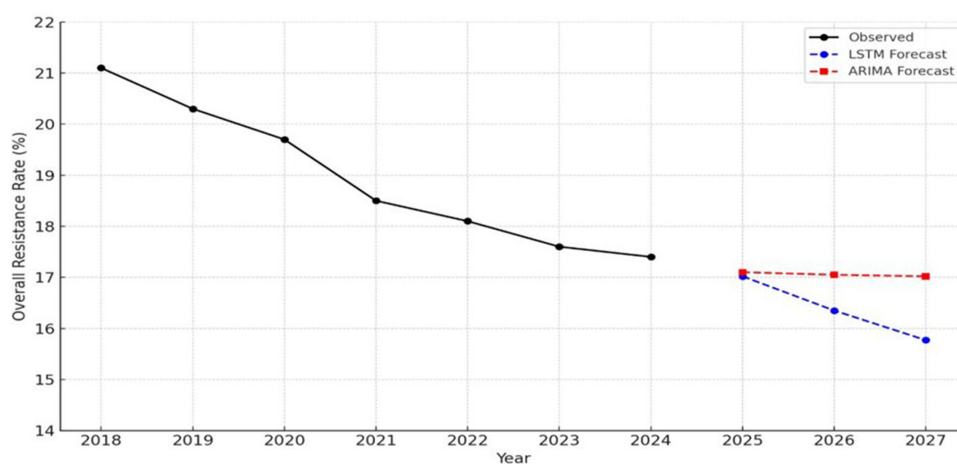
Key Findings and Significance

Drawing on 2021 pediatric clinical *Escherichia coli* isolates collected at Baoding Hospital of Beijing Children's Hospital, Capital Medical University, Baoding between 2018 and 2024, we systematically evaluated resistance patterns and trends across 14 commonly used antimicrobials. Resistance to ampicillin and trimethoprim–sulfamethoxazole remained persistently high (exceeding ~75% and ~50%, respectively), indicating these agents have virtually lost value for empirical therapy. Resistance to ceftriaxone and cefuroxime was also >40%, limiting their clinical utility. In contrast, carbapenems (imipenem, meropenem) and amikacin maintained resistance rates below 5%, supporting their continued role for severe infections. In addition, this study introduced both ARIMA and LSTM models to forecast future resistance trends in a pediatric setting, providing methodological support for resistance surveillance and clinical decision-making. Our seven-year single-center pediatric dataset, combined with dual-model time-series forecasting (ARIMA and LSTM), provides locally actionable AMR insights: notably, declines in ceftazidime and cefepime mirror the drop in ESBL prevalence. Nevertheless, the limited series length, single-center design, and potential changes in testing or prescribing practices warrant cautious interpretation and underscore the need for ongoing surveillance and external benchmarking.

Comparison with Domestic and International Studies

High-Resistance Agents (Ampicillin and Trimethoprim–Sulfamethoxazole)

In our cohort, ampicillin resistance reached 78–82%, aligning closely with multicenter pediatric data from GCC countries (62.7–82.8%).¹⁵ Trimethoprim–sulfamethoxazole resistance remained around 50%, comparable to the 47% reported in Shenzhen.¹⁶ These findings suggest that neither agent is suitable as a first-line empirical option for pediatric infections. Notably, in some regions (eg, South Asia and Gulf countries), trimethoprim–sulfamethoxazole is still used as first-line therapy for pediatric UTI,^{15,17} whereas guidelines in China and most East Asian countries no longer recommend it. This divergence may reflect long-term community use and widespread dissemination of resistance determinants (eg, *sulI*, *dfrA*).

**Figure 5** Comparison of Predicted Trends in Overall Antimicrobial Resistance Rates of Pediatric *Escherichia coli* Infections from 2018 to 2027: LSTM vs ARIMA Models.

Low-Resistance Agents (Carbapenems and Amikacin)

Carbapenems and amikacin maintained very low resistance rates (<5%) in this study, consistent with domestic multi-center and international reports.^{4,16} In a recent pediatric acute pyelonephritis study, amikacin achieved therapeutic outcomes comparable to carbapenems and was considered a potential substitute.⁹ This suggests amikacin can be reserved as an empiric option to reduce overreliance on “last-line” agents.

Divergent Trends Among Cephalosporins

Third-generation cephalosporins showed marked heterogeneity: resistance to ceftriaxone and cefuroxime exceeded 40%, limiting their reliability for empirical use; by contrast, resistance to ceftazidime and cefepime was lower and has declined in recent years. Our trends are consistent with a Taiwanese pediatric multicenter survey reporting year-on-year increases in resistance to third-generation cephalosporins, while regional differences imply that prescribing practices and antimicrobial stewardship policies may be key drivers.¹⁸

Multidrug Resistance and the ESBL Challenge

In addition to class-specific resistance patterns, we specifically examined extended-spectrum β -lactamase (ESBL) production among pediatric *E. coli* isolates using VITEK phenotypes and CLSI-recommended confirmatory tests. Overall, ESBL-positive strains accounted for approximately 45.93% of all isolates during 2018–2024, with annual rates ranging from 36.32% to 55.81%. Although the absolute burden remained high, a modest decline was observed in the last few years of surveillance, paralleling the downward trends in resistance to ceftazidime and cefepime.

These findings are broadly consistent with national pediatric data showing increasing or persistently high ESBL rates, such as the reported rise in ESBL-UTI from 12.1% to 21.4% between 2017 and 2021 in a multicenter study.¹⁹ At the same time, our local data suggest that recent antimicrobial stewardship efforts may have begun to curb the expansion of ESBL-producing *E. coli*, at least in the hospital setting. Nevertheless, the substantial ESBL burden underscores the need for continued surveillance, rational use of third-generation cephalosporins, and integration of molecular epidemiology (eg, ESBL gene profiling) to better understand transmission dynamics and support targeted infection control.

Clinical and Public Health Implications

Our findings indicate that ampicillin, trimethoprim–sulfamethoxazole, ceftriaxone, and cefuroxime are no longer suitable for empirical therapy of pediatric infections, whereas carbapenems and amikacin retain clinical value. The observed downward trends in resistance to several agents suggest that recent antimicrobial stewardship policies may be yielding benefits. Given the unique characteristics of pediatric patients (immature immunity and higher susceptibility to infection), empirical guidelines should be continuously updated and grounded in local surveillance to enable precision prescribing.

In Northern China, including our center, pediatric antimicrobial stewardship has been implemented through a combination of formulary restrictions (eg, tiered access to third-generation cephalosporins and carbapenems), mandatory pre-authorization for selected broad-spectrum agents, regular prescription audits with feedback, and updated empirical treatment guidelines for common pediatric syndromes. Against this background, the declining resistance trends to ceftazidime and cefepime, together with the stabilization or slight reduction in ESBL prevalence, likely reflect, at least in part, the impact of these AMS interventions. Our data therefore provide real-world support for the effectiveness of pediatric AMS programs in optimizing antibiotic use while preserving the activity of key agents.

Moreover, by applying AI models (ARIMA and LSTM) to forecast resistance over the next three years, we show that overall resistance is likely to remain stable or decline modestly, underscoring the potential utility of artificial intelligence in AMR trend prediction. This methodological addition provides more forward-looking guidance for clinical decision-making.

Strengths and Considerations

This study has several strengths: (1) a large sample size spanning seven consecutive years, providing a robust basis for elucidating temporal trends; (2) a focus on pediatric patients, a comparatively underrepresented yet clinically important population; and (3) the introduction of a deep-learning forecasting model (LSTM) alongside a traditional time-series model (ARIMA), offering a novel framework for future trend assessment.

Interpretation should consider certain bounds. First, as a single-center retrospective study, generalizability to broader settings requires further validation. Second, molecular epidemiology (eg, resistance genes, strain typing) was not included, as our emphasis was on clinical phenotype surveillance; mechanistic insights warrant follow-up studies. Third, individual-level clinical data (eg, prior antibiotic exposure, comorbidities) were not integrated, limiting deeper analysis of risk factors for resistance. In addition, although the application of ARIMA and LSTM models adds a forward-looking dimension to our analysis, the time series comprised only seven annual data points. As such, the forecasts should be viewed as exploratory, are not intended for precise numerical prediction, and may be sensitive to future changes in testing practices, prescribing behavior, or AMR epidemiology. Longer time series and external validation in multicenter datasets will be essential to refine and confirm these AI-based projections.

Future Research Directions

Future studies should build on multicenter collaborations and integrate molecular epidemiology (eg, whole-genome sequencing) with clinical data to more comprehensively elucidate drivers of resistance. In parallel, the application of artificial intelligence to resistance forecasting should be expanded by developing multidimensional, large-sample integrative models to improve predictive accuracy and clinical utility. For clinical practice, real-world studies are warranted to compare the effectiveness of amikacin versus carbapenems in pediatric infections caused by ESBL-producing *E. coli*, thereby optimizing antimicrobial stewardship and empiric therapy strategies.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Baoding Hospital of Beijing Children's Hospital, Capital Medical University (Approval No. 2025-78). Written informed consent was obtained from the legal guardians of all pediatric participants.

Acknowledgment

Ziqi Song, Yanyan Chen, and Ruihua Di are co-first authors of this work. Yingnan Chen is the corresponding author.

Author Contributions

All authors made significant contributions to the reported work, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or all of these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

Funding

Project No. 20232038, Medical Science Research Program of Hebei Provincial Health Commission. Project No. 2241ZF371, Baoding Science and Technology Program.

Disclosure

The authors declare that this research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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