Infection and Drug Resistance

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ORIGINAL RESEARCH

Epidemiological and Antimicrobial Resistance Trends of *Klebsiella Pneumoniae* Pre-, During, and Post-COVID-19 Pandemic in a Teaching Hospital in Southwest China

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Purpose: To quantify phase-specific changes in antimicrobial resistance (AMR) of *Klebsiella pneumoniae* and carbapenem-resistant *Klebsiella pneumoniae* (CRKP) across the pre-, during, and post-pandemic phases to inform post-pandemic antimicrobial stewardship and infection prevention and control (IPC).

Patients and Methods: We performed a retrospective study at a tertiary hospital in Southwest China (2018–2024), quantifying AMR and isolate distribution by patient age, sex, specimen type, and clinical department for *Klebsiella pneumoniae* and CRKP across the pre-, during, and post-pandemic phases.

Results: We identified 7073 non-duplicate *Klebsiella pneumoniae* isolates; CRKP comprised 4.9%. Among patients aged <18 years, the *Klebsiella pneumoniae* isolation rate declined during the pandemic and rebounded in the post-pandemic phase ($P < 0.001$), mirroring the trend in blood specimens ($P < 0.05$). In contrast, isolation rates of *Klebsiella pneumoniae* and CRKP rose during and post-pandemic among patients aged ≥65 years, in sputum, and in intensive care units (ICUs) and respiratory department ($P < 0.05$). Resistance to ceftazidime in *Klebsiella pneumoniae* decreased from 25.3% pre-pandemic to 16.2% during the pandemic and rebounded to 19.9% in the post-pandemic ($P < 0.001$). Similar decrease–rebound trends were observed for other cephalosporins, β-lactam/β-lactamase inhibitor combinations, carbapenems, monobactams, and aminoglycosides ($P < 0.05$). Notably, fluoroquinolone resistance rose steadily during the pandemic and post-pandemic phases ($P < 0.001$). Among CRKP isolates, resistance to fluoroquinolones, aminoglycosides, and monobactams increased from 70.0%, 75.0%, and 90.0% in 2018 to 94.9%, 90.8%, and 96.9% in 2024, respectively.

Conclusion: *Klebsiella pneumoniae* resistance temporarily declined during the pandemic but rebounded in the post-pandemic phase, whereas fluoroquinolone resistance continued to rise throughout. In the post-pandemic phase, CRKP exhibited markedly elevated resistance to aminoglycosides, fluoroquinolones, and monobactams, highlighting the urgent need for sustained AMR surveillance, AMS, and targeted IPC in the post-COVID-19 era.

Keywords: *Klebsiella pneumoniae*, carbapenem-resistant *Klebsiella pneumoniae*, antimicrobial resistance, multidrug-resistant bacteria, COVID-19

Introduction

Klebsiella pneumoniae (*K. pneumoniae*) is a common Gram-negative opportunistic pathogen responsible for hospital-acquired infections (HAIs), including pneumonia, urinary tract infections, and bloodstream infections (BSIs), particularly in immunocompromised or long-term hospitalized patients.[1] According to the Global Burden of Disease Study 2019,

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K. pneumoniae ranks among the top bacterial pathogens contributing to infection-related mortality worldwide.[2] The global rise in CRKP, now listed by the World Health Organization (WHO) as a critical priority pathogen,[3] poses serious clinical and public health challenges due to limited treatment options, high transmissibility, and substantial hospital containment burdens.

Since early 2020, the COVID-19 pandemic has profoundly impacted healthcare systems, altering patient demographics, infection control practices, and antimicrobial prescribing behaviors.[4,5] Because of overlapping respiratory symptoms between COVID-19 and bacterial pneumonia, empirical antibiotic use increased substantially during the pandemic, intensifying selective pressure on bacterial populations.[6] A meta-analysis revealed that, among patients with COVID-19, antimicrobial use was 89% in low- and middle-income countries (LMICs), compared to 58% in high-income nations.[7] Antibiotic misuse is a well-established driver of AMR evolution.[8] WHO surveillance further indicated that 37% (13/35) of countries experienced increased HAIs caused by multidrug-resistant organisms (MDROs) during the pandemic,[9] while data from the US Centers for Disease Control and Prevention (CDC) showed that carbapenem-resistant *Acinetobacter* and Enterobacterales infections rose by 78% and 35%, respectively.[10]

As a hospital-associated pathogen, *K. pneumoniae* exhibited dynamic shifts in prevalence, clonal structure, and resistance profiles throughout the pandemic, likely influenced by altered host immunity, hospital operations, and antimicrobial exposure.[11,12] Moreover, a systematic review of 55 studies—including 25 specifically focused on *K. pneumoniae*—highlighted divergent resistance trends.[13] Some studies reported increased resistance to piperacillin–tazobactam and carbapenems, with multidrug-resistant *K. pneumoniae* (MDR-KP) rates rising from 67% to 94%.[14–17] Conversely, others observed reductions in resistance to aminoglycosides and ceftazidime, and a decline in extended-spectrum β-lactamase (ESBL)-producing and CRKP strains—possibly attributable to enhanced infection prevention and control efforts.[18–22] These discrepancies underscore the region-specific, drug-specific, and multifactorial nature of AMR evolution.[13,23]

Although several studies have examined the impact of the COVID-19 pandemic on AMR, most have focused on early pandemic phases, with limited data extending beyond 2022. In China, the comprehensive relaxation of control measures in 2023 led to rapid normalization of healthcare services, alongside shifts in patient composition and antibiotic prescribing behaviors that may have reshaped AMR dynamics. Recent reports have also documented a post-pandemic resurgence of respiratory pathogens such as *Mycoplasma pneumoniae, Streptococcus pneumoniae*, and *Streptococcus pyogenes*.[24–26] The post-pandemic surge in respiratory infections may have driven renewed increases in antibiotic use, thereby exacerbating selective pressure for resistance. However, evidence from Southwest China remains scarce. Moreover, few studies span the full pre-, during, and post-pandemic continuum and extend into 2023–2024 to characterize post-pandemic resistance patterns, particularly for *K. pneumoniae* and CRKP. Therefore, evaluating the epidemiological and resistance trends of *K. pneumoniae* and CRKP during the post-pandemic phase—particularly in LMICs, where surveillance remains constrained by limited geographic coverage and reporting delays—is essential for understanding long-term AMR evolution and informing resource allocation for infection control and antimicrobial stewardship.[27]

In this context, we examined whether the isolate distribution of *K. pneumoniae* and CRKP differed across the pre-, during, and post-pandemic phases (2018–2024), within strata defined by age, sex, specimen type, and clinical department. In addition, we evaluated resistance rates by drug class and individual agents to determine whether there were phase-specific changes, and we presented year-to-year trends for 2018–2024. To address these questions, we conducted a 7-year retrospective analysis (2018–2024) of clinical isolates from a tertiary hospital in Southwest China. Our findings provide data to guide empirical antibiotic selection, strengthen AMR surveillance, and support targeted IPC, particularly in resource-limited settings facing escalating CRKP threats.

Materials and Methods

Data Source and Pandemic Phase Definitions

This single-center retrospective study was conducted at a large tertiary teaching hospital in Southwest China with 3,241 open beds. The hospital was designated as a non–COVID-19 treatment facility, continuing routine clinical microbiology services throughout the pandemic. Clinical data and *K. pneumoniae* isolates from routine specimens collected between January 1, 2018, and December 31, 2024, were included. According to epidemic control policies issued by the National Health Commission of China, the study period was divided into three phases: pre-pandemic (n = 2,001; January 1, 2018–

January 19, 2020), pandemic (n = 2,804; January 20, 2020–January 7, 2023),[28,29] and post-pandemic (n = 2,268; January 8, 2023–December 31, 2024).

Institutional IPC Measures Across the Pre-, During, and Post-Pandemic Phases

Prior to the COVID-19 pandemic (2018-01-01–2020-01-19), our hospital implemented routine IPC measures, including standard precautions, hand hygiene, environmental and surface cleaning and disinfection, and medical waste management. During the pandemic (2020-01-20–2023-01-07), in accordance with national policies,[30] we reinforced IPC and hospital operations by increasing the frequency of staff training and supervision; strengthening personal protective measures and management of high-exposure posts; intensifying environmental and surface cleaning and disinfection; implementing zoned patient care with isolation and transfer procedures as required; and imposing staged restrictions on visitation and caregiving. Since 2023-01-08, when COVID-19 management in China was adjusted from "Category B under Category A control" to "Category B under Category B control",[29] routine clinical services have been gradually restored under a normalized management framework. The hospital has continued to enforce standard precautions, hand hygiene, and environmental/surface disinfection, accompanied by ongoing training and monitoring. Throughout the study period, antimicrobial use complied with national policy and institutional regulations, with no major changes to antimicrobial stewardship practices.

Isolate Inclusion and Exclusion Criteria

A total of 7,073 non-duplicate clinical isolates of *K. pneumoniae* were included, retaining only the first isolate per patient. Demographic data—including sex, age, specimen type, and submitting department—were extracted from the hospital's Laboratory Information System (LIS) and anonymized before analysis. Exclusion criteria included: (1) repeat isolates from the same patient; (2) incomplete antimicrobial susceptibility testing (AST) results or missing demographic information; and (3) isolates considered as contaminants.

Bacterial Identification and AST

Bacterial identification was performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS; Bruker, Germany). AST was primarily conducted using the MicroScan WalkAway 96 system (Siemens, USA). Additional agents were tested using the disk diffusion method or Etest when necessary. Susceptibility interpretations followed the Clinical and Laboratory Standards Institute (CLSI) guidelines for each year (2018–2024). Quality control strains included *Pseudomonas aeruginosa* ATCC 27853 and *Escherichia coli* ATCC 25922.

Antimicrobial Classification and Resistance Definitions

Sixteen antimicrobial agents were analyzed, categorized as follows: cephalosporins (cefuroxime, ceftazidime, ceftriaxone, cefotaxime, cefepime); β-lactam/β-lactamase inhibitor combinations (piperacillin-tazobactam, ampicillin-sulbactam); carbapenems (imipenem, meropenem, ertapenem); fluoroquinolones (levofloxacin, ciprofloxacin); aminoglycosides (gentamicin, amikacin); monobactams (aztreonam); and sulfonamides (trimethoprim-sulfamethoxazole). Resistance classification was defined as follows:[31] If any agent within a drug class was interpreted as resistant, the isolate was considered resistant to that class (eg, resistance to either levofloxacin or ciprofloxacin was defined as fluoroquinolone resistance). CRKP was defined as resistance to any of the following: imipenem, meropenem, or ertapenem. The overall study workflow is illustrated in Figure 1.

Statistical Analysis

Statistical analyses were performed using SPSS software (version 27.0; IBM Corp., Armonk, NY, USA). Graphs were created using GraphPad Prism (version 10.4; GraphPad Software Inc., San Diego, CA, USA). Categorical variables were expressed as counts (n) and percentages (%). Comparisons of demographic characteristics and resistance rates among different pandemic phases were conducted using the chi-square (χ^2) test. A two-sided P-value < 0.05 was considered statistically significant.

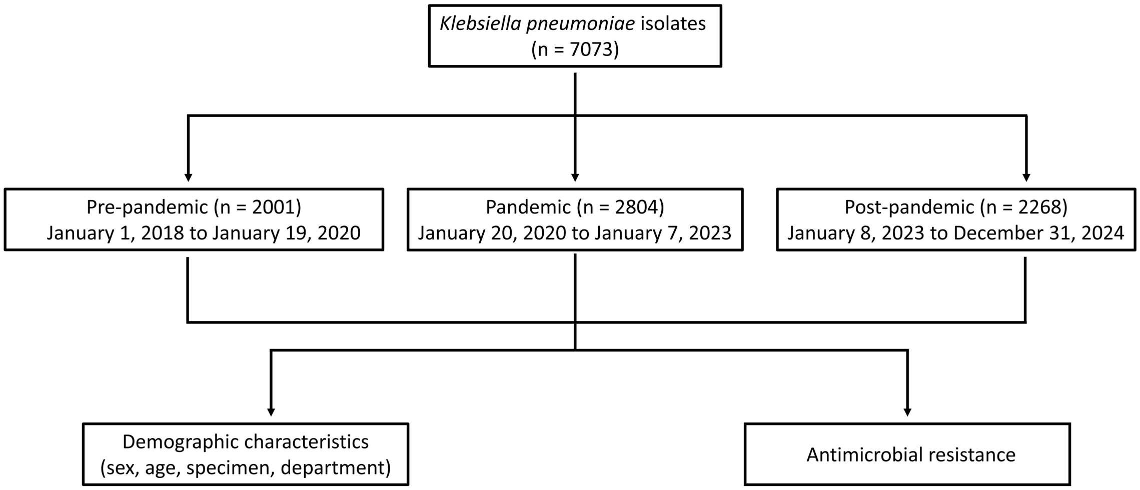

Figure 1 Study design and classification of *Klebsiella pneumoniae* isolates across the pre-, during, and post-pandemic phases.

Notes: A total of 7073 non-duplicate *Klebsiella pneumoniae* isolates were collected between January 1, 2018, and December 31, 2024. Based on the COVID-19 pandemic timeline, isolates were stratified into three phases: pre-pandemic (n = 2001, January 1, 2018–January 19, 2020), pandemic (n = 2804, January 20, 2020–January 7, 2023), and post-pandemic (n = 2268, January 8, 2023–December 31, 2024). Subsequent analyses focused on demographic characteristics (sex, age, specimen type, and clinical department) and antimicrobial resistance profiles.

Results

Isolation of *K. Pneumoniae* and CRKP From 2018 to 2024

A total of 7,073 *K. pneumoniae* isolates were recovered from 2018 to 2024. The annual number declined from 929 in 2018 to 874 in 2021, followed by a rebound starting in 2023 and peaking at 1,206 in 2024 (Figure 2A). Of these, 344 isolates were identified as CRKP, accounting for 4.9% of the total. The CRKP isolation rate rose from 2.2% in 2018 to 6.3% in 2019, declined steadily to 3.3% in 2022, and then surged to 8.1% in 2024 ($\chi^2 = 56.059$, $P < 0.001$) (Figure 2B). These findings highlight temporal fluctuations in both the overall number of *K. pneumoniae* isolates and the proportion of CRKP strains, suggesting evolving epidemiological dynamics that warrant further demographic and resistance profiling in subsequent analyses.

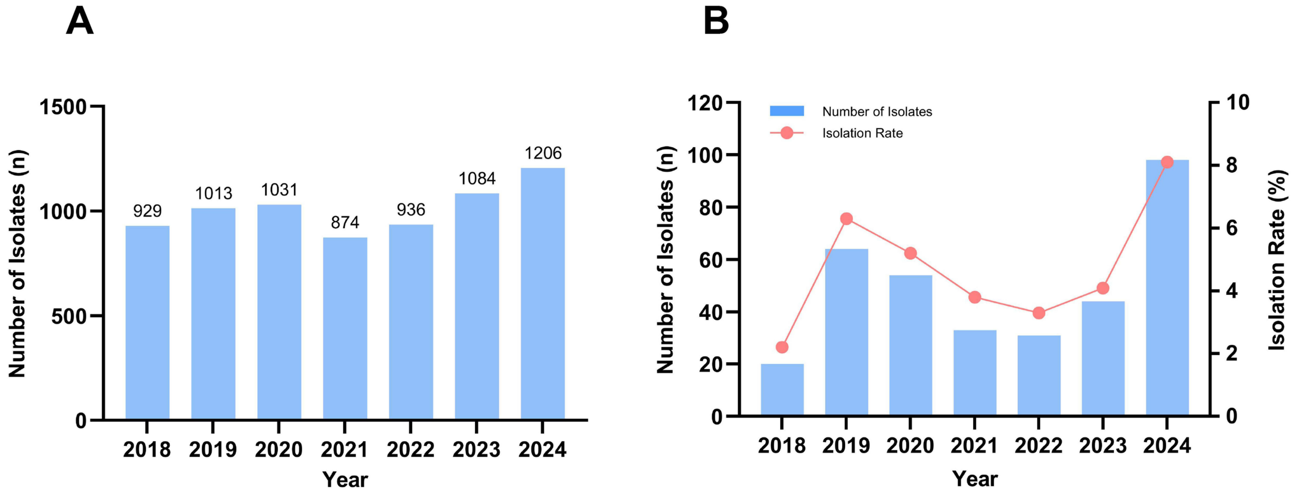

Figure 2 Annual trends in *Klebsiella pneumoniae* and CRKP isolation from 2018 to 2024. (**A**) Annual number of *Klebsiella pneumoniae* isolates; (**B**) Annual number and isolation rate of CRKP.

Abbreviation: CRKP, carbapenem-resistant *Klebsiella pneumoniae*.

Demographic Characteristics of Patients with *K. Pneumoniae* Across the Pre-, During, and Post-Pandemic Phases

To assess differences in patient characteristics across the pre-, during, and post-pandemic phases, stratified analyses were performed based on sex, age group, specimen type, and clinical department. The male-to-female ratio remained stable across the three phases (68.1% vs 31.9%), with no statistically significant difference ($\chi^2 = 0.500$, $P > 0.05$). However, significant differences were observed in age group distribution. The isolation rate in patients under 18 years decreased from 16.4% in the pre-pandemic phase to 8.7% during the pandemic, then rebounded to 12.0% post-pandemic ($\chi^2 = 65.721$, $P < 0.001$). In contrast, the isolation rate in patients aged ≥65 years increased significantly during and after the pandemic ($\chi^2 = 10.341$, $P < 0.05$).

Regarding specimen types, sputum consistently accounted for the majority of isolates, increasing to 66.1% during the pandemic and slightly declining to 62.0% post-pandemic ($\chi^2 = 166.916$, $P < 0.001$). The proportion of urine specimens increased from 10.7% pre-pandemic to 13.3% post-pandemic ($\chi^2 = 7.019$, $P < 0.05$), while blood specimen rates significantly decreased during the pandemic and partially rebounded afterward ($\chi^2 = 10.879$, $P < 0.05$). The proportions of *K. pneumoniae* isolates from ICUs, the respiratory department, and neurosurgery increased significantly during and after the pandemic. Specifically, the proportion from ICUs rose markedly from 5.1% in the pre-pandemic phase to 10.8% during the pandemic and 13.3% post-pandemic ($\chi^2 = 83.275$, $P < 0.001$). Similarly, respiratory department isolates increased from 12.6% to 14.8% and further to 15.6% across the three phases ($\chi^2 = 8.273$, $P < 0.05$). In neurosurgery, the proportion rose from 4.3% to 9.8% during the pandemic, followed by a slight decline to 7.2% post-pandemic ($\chi^2 = 51.761$, $P < 0.001$) (Figure 3A; Supplementary Table 1). These findings demonstrate a notable shift in the demographic and clinical distribution of *K. pneumoniae* infections across pandemic phases, particularly among pediatric and elderly patients, and in specimen and departmental profiles.

Demographic Characteristics of Patients with CRKP Across the Pre-, During, and Post-Pandemic Phases

Among the 344 CRKP isolates, the age-specific distribution revealed a sharp decline in the proportion of isolates from patients under 18 years, dropping from 53.8% in the pre-pandemic phase to 20.7% during the pandemic and further to 2.8% post-pandemic ($\chi^2 = 84.083$, $P < 0.001$). In contrast, the proportions of CRKP isolates from patients aged 18–64 years and those aged ≥65 years significantly increased during and after the pandemic, rising from 27.5% to 47.9% and from 18.7% to 49.3%, respectively ($\chi^2 = 10.223$, $P < 0.05$; $\chi^2 = 22.900$, $P < 0.001$).

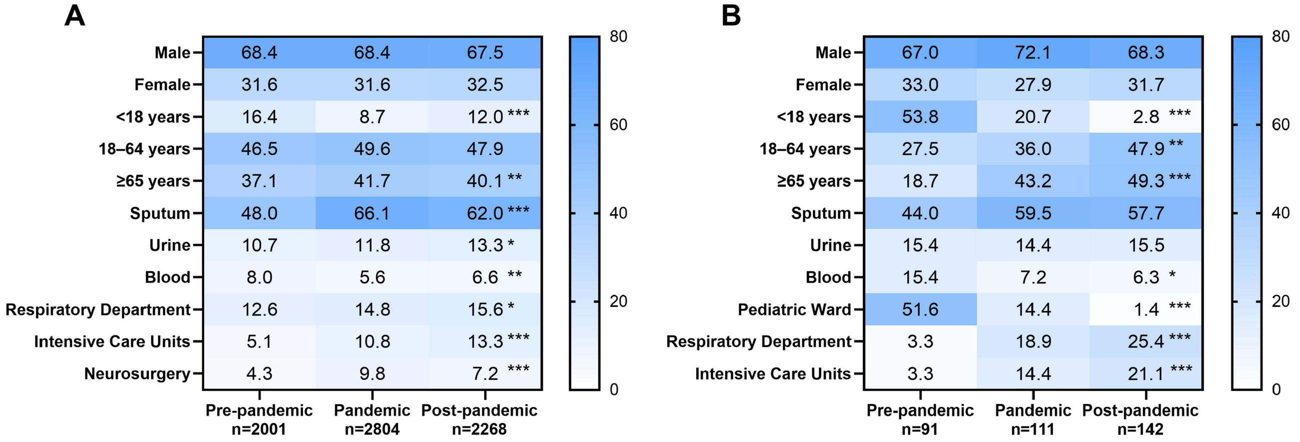

Figure 3 Demographic and clinical distribution of *Klebsiella pneumoniae* and CRKP isolates across the pre-, during, and post-pandemic phases. (**A**) *Klebsiella pneumoniae*; (**B**) CRKP.
Notes: Numerical values represent the isolation rates (%) of *Klebsiella pneumoniae* (A) and CRKP (B). Comparisons across the three pandemic phases were conducted using the chi-square test. *P*-values < 0.05 were considered statistically significant. $P < 0.05$ (*), $P < 0.01$ (**), $P < 0.001$ (***).
Abbreviation: CRKP, carbapenem-resistant *Klebsiella pneumoniae*.

Most CRKP isolates were obtained from sputum specimens, with the proportion rising to 59.5% during the pandemic and slightly decreasing to 57.7% post-pandemic (χ^2 = 5.784, $P > 0.05$). No significant change was observed in the proportion of urine-derived isolates (χ^2 = 0.063, $P > 0.05$), while the proportion of blood-derived isolates declined significantly during and after the pandemic (χ^2 = 6.186, $P < 0.05$). In terms of departmental distribution, the proportion of CRKP isolates from pediatric wards declined from 51.6% pre-pandemic to 14.4% during the pandemic, and further to 1.4% post-pandemic (χ^2 = 93.489, $P < 0.001$). Meanwhile, the proportions of CRKP isolates from the respiratory department and ICUs increased from 3.3% pre-pandemic to 18.9% and 14.4% during the pandemic, and further to 25.4% and 21.1% post-pandemic, respectively (χ^2 = 18.983, $P < 0.001$; χ^2 = 14.438, $P < 0.001$) (Figure 3B; Supplementary Table 2). These findings suggest that the demographic and departmental distribution of CRKP infections changed markedly across pandemic phases. The proportion of pediatric cases declined sharply, while CRKP isolates became increasingly concentrated in adult high-risk departments such as respiratory units and ICUs, reflecting a shift in the clinical epidemiology of CRKP.

AMR Trends of *K. Pneumoniae* Across the Pre-, During, and Post-Pandemic Phases

To assess the impact of the COVID-19 pandemic on AMR in *K. pneumoniae*, we compared resistance rates to commonly used antibiotics (Table 1) and antibiotic classes (Table 2; Figure 4A) across the pre-, during, and post-pandemic phases. Most antibiotic classes—including cephalosporins, β-lactam/β-lactamase inhibitor combinations, carbapenems, aminoglycosides, and monobactams—exhibited a characteristic pattern of decline during the pandemic followed by a rebound in the post-pandemic phase. For instance, resistance to ceftazidime declined from 25.3% in the pre-pandemic phase to 16.2% during the

Table 1 Temporal Comparison of Antimicrobial Resistance Rates of *Klebsiella Pneumoniae* Across the Pre-, Pandemic, and Post-Pandemic Phases

Antimicrobial Agents	Overall N=7073	Pre-pandemic N=2001	Pandemic N=2804	Post-pandemic N=2268	χ^2	*P*-value
Cefuroxime	1990 (28.1)	629 (31.4)	702 (25.0)	659 (29.1)	25.046	**<0.001**
Ceftazidime	1411 (19.9)	506 (25.3)	453 (16.2)	452 (19.9)	60.977	**<0.001**
Ceftriaxone	1825 (25.8)	567 (28.3)	648 (23.1)	610 (26.9)	18.743	**<0.001**
Cefotaxime	1843 (26.1)	561 (28.0)	664 (23.7)	618 (27.2)	13.959	**<0.001**
Cefepime	1645 (23.3)	536 (26.8)	571 (20.4)	538 (23.7)	27.392	**<0.001**
Piperacillin-tazobactam	664 (9.4)	147 (7.3)	201 (7.2)	316 (13.9)	81.121	**<0.001**
Ampicillin-sulbactam	1956 (27.7)	608 (30.4)	692 (24.7)	656 (28.9)	21.692	**<0.001**
Ertapenem	340 (4.8)	88 (4.4)	110 (3.9)	142 (6.3)	16.000	**<0.001**
Imipenem	300 (4.2)	75 (3.7)	94 (3.4)	131 (5.8)	19.806	**<0.001**
Meropenem	311 (4.4)	81 (4.0)	97 (3.5)	133 (5.9)	18.059	**<0.001**
Levofloxacin	1040 (14.7)	223 (11.1)	437 (15.6)	380 (16.8)	29.556	**<0.001**
Ciprofloxacin	1477 (20.9)	342 (17.1)	615 (21.9)	520 (22.9)	25.021	**<0.001**
Gentamicin	1028 (14.5)	321 (16.0)	374 (13.3)	333 (14.7)	6.932	**0.031**
Amikacin	293 (4.1)	75 (3.7)	91 (3.2)	127 (5.6)	18.594	**<0.001**
Aztreonam	1607 (22.7)	520 (26.0)	552 (19.7)	535 (23.6)	27.838	**<0.001**
Trimethoprim-sulfamethoxazole	1680 (23.8)	497 (24.8)	651 (23.2)	532 (23.5)	1.855	0.396

Notes: The total number of *Klebsiella pneumoniae* isolates tested in each phase (N) is indicated in the column headings. Values are presented as number (percentage) of *Klebsiella pneumoniae* isolates. Comparisons across the pre-, pandemic, and post-pandemic phases were conducted using the chi-square test. Bold P-values indicate statistical significance at $P < 0.05$.

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Table 2 Comparative Resistance Rates of *Klebsiella Pneumoniae* to Antimicrobial Categories Across the Pre-, Pandemic, and Post-Pandemic Phases

Antimicrobial Categories	Overall N=7073	Pre-pandemic N=2001	Pandemic N=2804	Post-pandemic N=2268	χ^2	P-value
CEP	2036 (28.8)	642 (32.1)	726 (25.9)	668 (29.5)	22.569	**<0.001**
BLI	1969 (27.8)	611 (30.5)	697 (24.9)	661 (29.1)	21.572	**<0.001**
CAR	344 (4.9)	91 (4.5)	111 (4.0)	142 (6.3)	14.966	**<0.001**
FQ	1489 (21.1)	345 (17.2)	622 (22.2)	522 (23.0)	24.902	**<0.001**
AG	1062 (15.0)	342 (17.1)	386 (13.8)	334 (14.7)	10.337	**0.006**
MONO	1607 (22.7)	520 (26.0)	552 (19.7)	535 (23.6)	27.838	**<0.001**
SUL	1680 (23.8)	497 (24.8)	651 (23.2)	532 (23.5)	1.855	0.396

Notes: The total number of *Klebsiella pneumoniae* isolates tested in each phase (N) is indicated in the column headings. Values are presented as number (percentage) of *Klebsiella pneumoniae isolates*. Comparisons across the pre-, pandemic, and post-pandemic phases were conducted using the chi-square test. Bold P-values indicate statistical significance at $P < 0.05$.

Abbreviations: CEP, cephalosporins; BLI, β-lactam/β-lactamase inhibitor combinations; CAR, carbapenems; FQ, fluoroquinolones; AG, aminoglycosides; MONO, monobactams; SUL, sulfonamides.

pandemic, followed by an increase to 19.9% in the post-pandemic phase ($\chi^2 = 60.977$, $P < 0.001$). Similar trends were observed for other agents within these antibiotic classes. In contrast, fluoroquinolone resistance exhibited a continuous upward trend across all three phases. Levofloxacin resistance increased from 11.1% to 15.6%, and further to 16.8% ($\chi^2 = 29.556$, $P < 0.001$), while ciprofloxacin resistance followed a similar trajectory ($\chi^2 = 25.021$, $P < 0.001$). Resistance to sulfonamides remained relatively stable, with no statistically significant changes observed across the three phases ($\chi^2 = 1.855$, $P > 0.05$). Overall, these findings reveal that AMR in *K. pneumoniae* exhibited both phase-dependent and class-specific dynamics, with most antibiotic classes showing a pandemic-related decline–rebound pattern, while fluoroquinolones demonstrated a sustained upward trajectory. These distinct trends underscore the importance of targeted antimicrobial stewardship tailored to drug-specific resistance evolution.

Annual Evolution of AMR of *K. Pneumoniae* From 2018 to 2024

To further characterize the timing and progression of these resistance trends, we analyzed annual variations in resistance across antibiotic classes from 2018 to 2024 (Figure 4B; Supplementary Table 3). The most pronounced reductions were

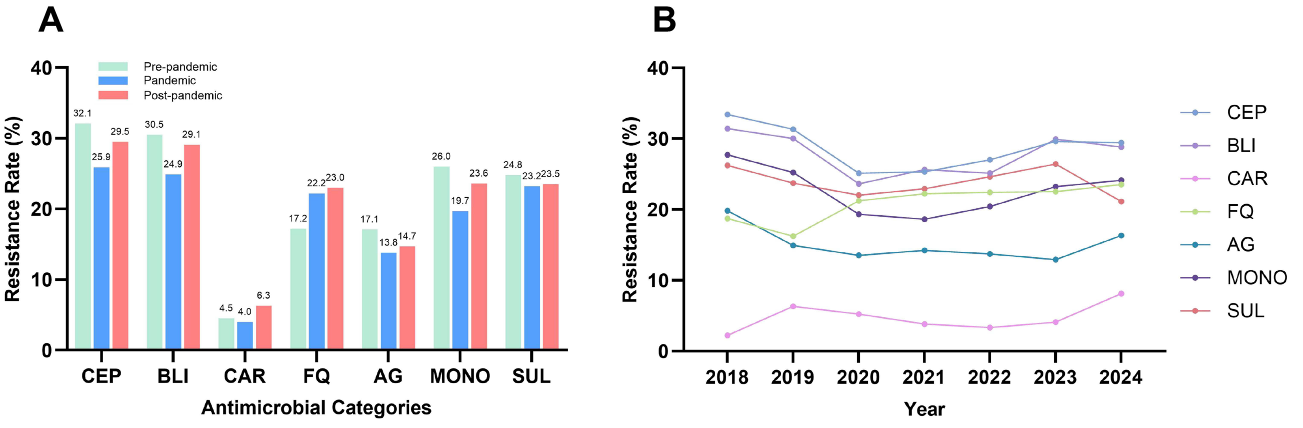

Figure 4 Antimicrobial resistance trends of *Klebsiella pneumoniae*. (**A**) Resistance rates across the pre-, during, and post-pandemic phases; (**B**) Annual resistance rates from 2018 to 2024.

Notes: Numerical values represent the resistance rates (%) of *Klebsiella pneumoniae*.

Abbreviations: CEP, cephalosporins; BLI, β-lactam/β-lactamase inhibitor combinations; CAR, carbapenems; FQ, fluoroquinolones; AG, aminoglycosides; MONO, monobactams; SUL, sulfonamides.

observed in 2020, shortly after the onset of the pandemic. Compared with 2019, resistance to cephalosporins, β-lactam/β-lactamase inhibitor combinations, and monobactams decreased by 6.2%, 6.4%, and 5.9%, respectively. These trends began to reverse starting in 2022. Carbapenem resistance decreased from 6.3% in 2019 to 3.3% in 2022, then surged to 8.1% in 2024 ($\chi^2 = 56.059$, $P < 0.001$). Aminoglycoside resistance declined from 19.8% in 2018 to 12.9% in 2023, subsequently rebounding to 16.3% in 2024 ($\chi^2 = 25.599$, $P < 0.001$). Fluoroquinolone resistance rose steadily from 2020 onward and plateaued after 2022 ($\chi^2 = 25.124$, $P < 0.001$), whereas sulfonamide resistance fluctuated without a consistent trajectory ($\chi^2 = 14.361$, $P = 0.026$). Annual analyses revealed subtle dynamics in resistance trends. Most antimicrobial classes experienced a transient decline in 2020, followed by a rebound beginning in 2022, whereas fluoroquinolone resistance continued to rise throughout the entire study period. These findings underscore the importance of year-by-year surveillance in identifying critical turning points and tracking the evolution of antimicrobial resistance.

Temporal Trends in CRKP Resistance Across Phases and Years (2018–2024)

Given the observed rebound in carbapenem resistance among *K. pneumoniae* in 2024, we further analyzed CRKP resistance patterns across the pre-, during, and post-pandemic phases for commonly used antibiotics (Table 3) and antimicrobial classes (Table 4; Figure 5A). Resistance to cephalosporins remained consistently high (>95%) throughout all three phases, with no statistically significant differences ($\chi^2 = 2.236$, $P > 0.05$). In contrast, resistance to other classes—including β-lactam/β-lactamase inhibitor combinations, monobactams, aminoglycosides, sulfonamides, and fluoroquinolones—increased significantly during and after the pandemic. Notably, aminoglycosides and fluoroquinolones

Table 3 Temporal Comparison of Antimicrobial Resistance Rates of CRKP Across the Pre-, Pandemic, and Post-Pandemic Phases

Antimicrobial Agents	Overall N=344	Pre-pandemic N=91	Pandemic N=111	Post-pandemic N=142	χ^2	*P*-value
Cefuroxime	337 (98.0)	88 (96.7)	108 (97.3)	141 (99.3)	2.236	0.327
Ceftazidime	322 (93.6)	85 (93.4)	100 (90.1)	137 (96.5)	4.256	0.119
Ceftriaxone	335 (97.4)	87 (95.6)	108 (97.3)	140 (98.6)	1.947	0.378
Cefotaxime	336 (97.7)	87 (95.6)	108 (97.3)	141 (99.3)	3.429	0.18
Cefepime	327 (95.1)	85 (93.4)	106 (95.5)	136 (95.8)	0.729	0.695
Piperacillin-tazobactam	314 (91.3)	79 (86.8)	98 (88.3)	137 (96.5)	8.35	**0.015**
Ampicillin-sulbactam	330 (95.9)	84 (92.3)	105 (94.6)	141 (99.3)	7.686	**0.021**
Ertapenem	340 (98.8)	88 (96.7)	110 (99.1)	142 (100.0)	5.342	0.069
Imipenem	300 (87.2)	75 (82.4)	94 (84.7)	131 (92.3)	5.746	0.057
Meropenem	311 (90.4)	81 (89.0)	97 (87.4)	133 (93.7)	3.106	0.212
Levofloxacin	238 (69.2)	37 (40.7)	75 (67.6)	126 (88.7)	60.32	**<0.001**
Ciprofloxacin	251 (73.0)	40 (44.0)	81 (73.0)	130 (91.5)	63.683	**<0.001**
Gentamicin	223 (64.8)	30 (33.0)	70 (63.1)	123 (86.6)	70.237	**<0.001**
Amikacin	179 (52.0)	26 (28.6)	46 (41.4)	107 (75.4)	55.997	**<0.001**
Aztreonam	294 (85.5)	70 (76.9)	93 (83.8)	131 (92.3)	10.866	**0.004**
Trimethoprim-sulfamethoxazole	172 (50.0)	32 (35.2)	62 (55.9)	78 (54.9)	10.914	**0.004**

Notes: The total number of CRKP isolates tested in each phase (N) is indicated in the column headings. Values are presented as number (percentage) of CRKP isolates. Comparisons across the pre-, pandemic, and post-pandemic phases were conducted using the chi-square test. Bold P-values indicate statistical significance at $P < 0.05$.

Abbreviation: CRKP, carbapenem-resistant *Klebsiella pneumoniae*.

Table 4 Comparative Resistance Rates of CRKP to Antimicrobial Categories Across the Pre-, Pandemic, and Post-Pandemic Phases

Antimicrobial Categories	**Overall N=344**	**Pre-pandemic N=91**	**Pandemic N=111**	**Post-pandemic N=142**	χ^2	***P*-value**
CEP	337 (98.0)	88 (96.7)	108 (97.3)	141 (99.3)	2.236	0.327
BLI	330 (95.9)	84 (92.3)	105 (94.6)	141 (99.3)	7.686	**0.021**
FQ	252 (73.3)	40 (44.0)	82 (73.9)	130 (91.5)	64.152	**<0.001**
AG	225 (65.4)	32 (35.2)	70 (63.1)	123 (86.6)	65.293	**<0.001**
MONO	294 (85.5)	70 (76.9)	93 (83.8)	131 (92.3)	10.866	**0.004**
SUL	172 (50.0)	32 (35.2)	62 (55.9)	78 (54.9)	10.914	**0.004**

Notes: The total number of CRKP isolates tested in each phase (N) is indicated in the column headings. Values are presented as number (percentage) of CRKP isolates. Comparisons across the pre-, pandemic, and post-pandemic phases were conducted using the chi-square test. Bold P-values indicate statistical significance at $P < 0.05$.

Abbreviations: CRKP, carbapenem-resistant *Klebsiella pneumoniae*; CEP, cephalosporins; BLI, β-lactam/β-lactamase inhibitor combinations; FQ, fluoroquinolones; AG, aminoglycosides; MONO, monobactams; SUL, sulfonamides.

exhibited the most pronounced escalation: resistance to aminoglycosides increased from 35.2% in the pre-pandemic phase to 63.1% during the pandemic and further to 86.6% post-pandemic ($\chi^2 = 65.293$, $P < 0.001$); fluoroquinolone resistance rose from 44.0% to 91.5% across the same phases ($\chi^2 = 64.152$, $P < 0.001$).

To further evaluate the temporal evolution of CRKP resistance, we analyzed annual resistance rates for each antimicrobial class from 2018 to 2024 (Figure 5B; Supplementary Table 4). Resistance to cephalosporins and β-lactam/β-lactamase inhibitor combinations increased continuously from 2019 onward, reaching 100% by 2024. Notably, resistance to fluoroquinolones, aminoglycosides, and monobactams declined markedly in 2019 compared to 2018—dropping from 70.0% to 35.9%, 75.0% to 23.4%, and 90.0% to 76.6%, respectively—but steadily increased from 2020 onward, peaking in 2024 at 94.9%, 90.8%, and 96.9%. These findings indicate a marked and sustained increase in CRKP resistance across nearly all major antimicrobial classes since 2020, with most peaking by 2024. This suggests that the post-pandemic phase represents a critical period for the intensification of multidrug resistance among CRKP strains.

Discussion

The COVID-19 pandemic profoundly impacted healthcare systems, reshaping patient demographics, clinical practices, and antimicrobial usage patterns, which in turn influenced the epidemiology and resistance profiles of hospital-acquired

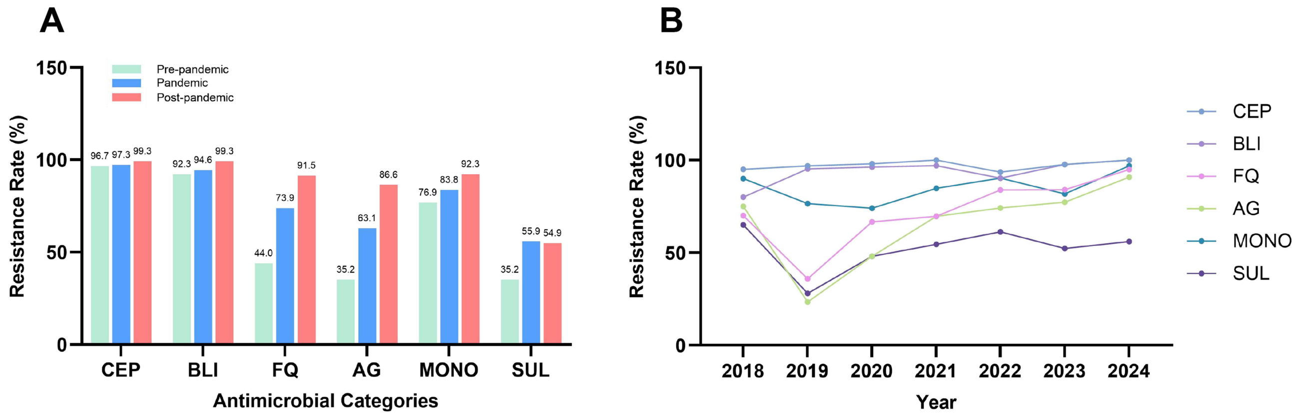

Figure 5 Antimicrobial resistance trends of CRKP. (**A**) Resistance rates across the pre-, during, and post-pandemic phases; (**B**) Annual resistance rates from 2018 to 2024.

Notes: Numerical values represent the resistance rates (%) of CRKP.

Abbreviations: CRKP, carbapenem-resistant *Klebsiella pneumoniae*; CEP, cephalosporins; BLI, β-lactam/β-lactamase inhibitor combinations; FQ, fluoroquinolones; AG, aminoglycosides; MONO, monobactams; SUL, sulfonamides.

pathogens.[32,33] In this 7-year retrospective analysis of *K. pneumoniae* isolates from a tertiary hospital in Southwest China (2018–2024), we observed that resistance to most antibiotics declined transiently during the pandemic and rebounded markedly in the post-pandemic phase. In contrast, resistance to fluoroquinolones exhibited a continuous upward trend throughout the study period. Moreover, In the post-pandemic years, CRKP exhibited markedly increased resistance to multiple antimicrobial classes—including aminoglycosides, fluoroquinolones, and monobactams—indicating a potential expansion of its resistance spectrum and further limiting treatment options, highlighting the urgent need for enhanced antimicrobial stewardship and targeted infection control strategies.

The number of *K. pneumoniae* isolates declined during the pandemic and rebounded thereafter, while the CRKP isolation rate decreased to 3.3% in 2022 before rising sharply to 8.1% by 2024. This trend may reflect pandemic-induced changes in specimen collection practices, patient demographics, and infection control measures.[34] Across the pandemic phases, both age-specific and department-specific shifts were evident in the distribution of *K. pneumoniae* and CRKP. Among patients under 18 years, *K. pneumoniae* isolates declined markedly during the pandemic and rebounded in the post-pandemic phase, likely reflecting a reduction in pediatric respiratory infections due to non-pharmaceutical interventions (NPIs) such as lockdowns and school closures, which disrupted the transmission of respiratory pathogens.[35] International studies similarly reported substantial declines in pediatric healthcare utilization and infection burden during the pandemic. In France, pediatric emergency visits and hospitalizations decreased by 68.5% and 44.7%, respectively, while in the Netherlands, the corresponding reductions were 61% and 57%.[36,37] Following the relaxation of NPIs, a resurgence of respiratory infections was observed, potentially supporting the concept of "immunity debt", wherein reduced microbial exposure during the pandemic may have led to increased susceptibility upon re-exposure.[38,39] In contrast, CRKP isolates in children declined significantly during and after the pandemic, likely due to a 2019 outbreak at our hospital involving 29 clonally related *bla*$_{\mathbf{NDM\text{-}5}}$-positive ST2407-K25 strains. The prompt implementation of enhanced isolation protocols, active surveillance, and antibiotic stewardship successfully contained the spread of CRKP in pediatric wards.[40]

Among elderly patients (≥65 years), isolation rates of *K. pneumoniae* and CRKP increased during the pandemic and remained elevated thereafter, likely attributable to increased vulnerability related to age, underlying comorbidities, prolonged hospital stays, and frequent exposure to invasive procedures.[41,42] Sputum consistently accounted for the majority of isolates, and isolation rates increased in respiratory departments, ICUs, and neurosurgery departments. These trends may be associated with the respiratory focus of COVID-19 and the intensified microbiological sampling for secondary bacterial infections.[43,44] International data support this observation: in Mexico, Gram-negative ESKAPE pathogens (*K. pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter species*) causing BSIs during the pandemic were isolated from these departments;[45] in Guangzhou, the proportion of respiratory isolates increased from 11.4% to 14%;[46] and Jeon et al reported a 67.6% increase in *K. pneumoniae* isolations in ICUs in Korea.[47] Collectively, these findings highlight the dual burden of immunity debt in pediatric populations and persistent CRKP risk in elderly and high-risk departments, emphasizing the need for continuous surveillance, early outbreak detection, and tailored infection control strategies in vulnerable groups.

During the COVID-19 pandemic, resistance rates of *K. pneumoniae* to cephalosporins, β-lactam/β-lactamase inhibitor combinations, carbapenems, aminoglycosides, and monobactams decreased significantly at our hospital. This pattern likely reflects the stringent IPC measures implemented during the pandemic—including enhanced isolation with zoned care, standardized use of personal protective equipment (PPE), intensified environmental cleaning and disinfection, and strict visitation policies that reduced patient movement. These measures likely curtailed transmission of resistant strains and paralleled nationwide reinforcement of IPC policies,[30] supporting the premise that strengthened IPC can reduce transmission of antimicrobial-resistant organisms. Consistent with our observations, international and domestic studies also reported declines in *K. pneumoniae* resistance: for example, the proportion of ESBL-producing *K. pneumoniae* in Ireland fell from 19.8% in 2017 to 8.88% in 2020,[18] and at a maternal-and-child hospital in China, the detection rate of CRKP decreased from 13.14% to 4.39%, with the proportion of MDROs falling from 16.86% to 11.42%.[48] Similar declines have been described in Gaza, Saudi Arabia, and Colombia,[19–21] commonly attributed to intensified IPC measures, reductions in elective care, and decreased patient mobility.[18–21,48] Additionally, multiple studies have documented similar declines in antimicrobial resistance among other pathogens during the COVID-19 pandemic. For example, a retrospective study from Italy reported a reduction in MDR ESKAPE isolates in ICUs during the pandemic;[49] *invasive group A Streptococcus* (iGAS) necrotizing soft-tissue infections declined substantially over the same period;[50] and a systematic review noted that five included studies reported 10%–41% decreases in the prevalence or incidence of carbapenem-resistant *Pseudomonas aeruginosa*, including a 25% decline in ICU settings.[51] Taken together, these observations suggest that intensified IPC and AMS efforts during the pandemic may have contributed to the observed reductions in MDROs, further supporting our findings on changes in *K. pneumoniae* resistance. Moreover, stricter infection control during the COVID-19 pandemic played an important role in reducing HAIs, particularly in cardiac care units (CCUs) and pediatric ICUs.[52,53] However, this downward trend was not universal. Studies from Turkey,[16] Egypt,[17] and parts of Latin America reported rising rates of CRKP and carbapenem-resistant Enterobacterales (CRE) during the pandemic,[54] while others observed no significant change in MDRO incidence,[55] highlighting substantial regional heterogeneity driven by variations in healthcare infrastructure, antimicrobial stewardship, infection control policies, and local outbreak dynamics.[13]

In the post-pandemic phase following China's January 8, 2023 policy shift and transition to normalized management,[29] we observed a rebound in *K. pneumoniae* antimicrobial resistance rates at our hospital, coinciding with the relaxation of non-pharmaceutical interventions (NPIs) and the resumption of healthcare activities. Ma et al reported that antibiotic consumption in China returned to 89.5% of pre-pandemic levels in 2023, coinciding with a resurgence of respiratory infections that may have intensified selective pressure.[56] Increased healthcare activity also contributed to a rise in hospital-acquired MDRO infections, particularly *Acinetobacter baumannii*.[57] China Antimicrobial Surveillance Network (CHINET) data indicated that meropenem resistance in *K. pneumoniae* rebounded from 24.2% in 2022 to 26.0% in 2023.[58] Moreover, increasing AMR has been reported in other pathogens, such as invasive group A *Streptococcus*, with clindamycin resistance rising from 13.5% to 19.5%.[26] In Chinese pediatric Acute Respiratory Infection (ARI) cases, *K. pneumoniae* detection increased from 2.76% during the pandemic to 8.52% post-pandemic, surpassing pre-pandemic levels.[59] Notably, *K. pneumoniae* exhibited a distinct resistance trajectory to fluoroquinolones, with resistance rates rising continuously during and after the pandemic, possibly due to the widespread empirical use of fluoroquinolones for respiratory infections throughout the COVID-19 pandemic.[17,60,61] These findings underscore the urgent need for integrated antimicrobial stewardship programs and reinforced infection control strategies within healthcare systems and public health infrastructures, particularly in the context of relaxed pandemic control measures and renewed healthcare activity.

Notably, CRKP exhibited a marked post-pandemic increase in resistance across multiple antimicrobial classes. Resistance to cephalosporins and β-lactam/β-lactamase inhibitor combinations remained persistently high (>90%) throughout the study period. In contrast, resistance to aminoglycosides and fluoroquinolones rose sharply from 75.0% and 70.0% in 2018 to 90.8% and 94.9% in 2024, respectively. This trend likely reflects increased empirical prescribing—especially for respiratory infections with overlapping viral and bacterial presentations—and reduced adherence to infection control protocols in the post-pandemic period. Previous studies have also reported multiple CRKP outbreaks in high-risk areas such as intensive care units during and after the pandemic.[62–64] Notably, this overall pattern was briefly disrupted in 2019 by a localized pediatric outbreak involving 29 clonally related *K. pneumoniae* strains carrying *bla*$_{\text{NDM-5}}$ and identified as ST2407-K25, which were fully susceptible to aminoglycosides, fluoroquinolones, sulfonamides, and monobactams.[40] The predominance of these susceptible strains temporarily diluted the annual CRKP resistance rates, creating an artificial decline that may have affected the interpretation of AMR trends during the pre-pandemic phase. Currently, CRKP maintains high levels of resistance across major antimicrobial classes, particularly in post-pandemic years, underscoring the need for enhanced antimicrobial stewardship and continuous resistance monitoring in clinical settings.

Given the observed rebound in *K. pneumoniae* resistance and the continued increase in CRKP resistance to multiple antibiotics, including aminoglycosides, fluoroquinolones, and monobactams, indicating an expansion of its resistance spectrum, we recommend prioritizing high-risk units and elderly patients and/or those with comorbidities in the post-pandemic phase. We suggest adopting a "trend-trigger-response" strategy: when surveillance detects sustained increases in resistance or clustering of resistance within a unit, initiate screening and isolation for carbapenemase-producing Enterobacterales, optimize empirical therapy using unit-specific cumulative antibiograms and rapid carbapenemase testing, and implement early antibiotic de-escalation strategies.

This study has several limitations. First, regarding study design and applicability: as a single-center retrospective analysis, it only describes phase-specific resistance trends across the pre-pandemic, pandemic, and post-pandemic phases and cannot support causal inference; extrapolation to other regions or institutions should be made with caution. Second, molecular epidemiology was lacking: we did not perform whole-genome sequencing (WGS), multilocus sequence typing (MLST), or carbapenemase typing for CRKP and other isolates, so we could not assess whether the post-pandemic increase in resistance was due to clonal expansion or transmission. Third, key variables were missing: patient-level information (disease severity, antimicrobial therapy, length of stay, invasive procedures, mortality, and complications) and institutional antimicrobial consumption metrics (DDD, DOT) were unavailable, limiting mechanistic interpretation and control for confounding. Nevertheless, our 7-year longitudinal dataset spanning the pre-pandemic, pandemic, and post-pandemic phases provides valuable clues to resistance changes associated with pandemic dynamics. To further elucidate mechanisms, we will conduct multicenter prospective surveillance and cohort studies to link susceptibility results with patient outcomes (eg, severity, treatments, length of stay, and mortality); integrate DDD/DOT; apply mixed-effects and hierarchical modeling, using interrupted time-series analysis and adjusting for seasonality and testing volume where appropriate to improve generalizability and causal interpretability; and, for CRKP isolates, perform WGS, MLST, and carbapenemase typing, supplemented by plasmid analyses and phylogenetic studies, to identify clonal expansion and transmission chains, thereby providing stronger evidence for targeted AMS and IPC.

Conclusion

This study shows that AMR in *K. pneumoniae* declined transiently during the COVID-19 pandemic but rebounded in the post-pandemic phase, while resistance to fluoroquinolones increased continuously throughout the study period. In the post-pandemic years, CRKP exhibited significantly higher resistance to aminoglycosides, fluoroquinolones, and monobactams, further narrowing the options for empirical therapy. Given that this study is a single-center analysis, the generalizability and extrapolation of the results are limited, and further validation through multicenter prospective studies combined with clinical data is necessary. Overall, our findings support the need to strengthen infection control, enhance antimicrobial resistance surveillance, and consolidate antimicrobial stewardship in the post-COVID-19 era, shifting from reactive crisis responses to sustainable, proactive containment of antimicrobial-resistant pathogens.

Data Sharing Statement

Aggregated, de-identified data underlying the results are available from the designated data contact, Dr. Zhangrui Zeng (zengzhangrui@swmu.edu.cn), upon reasonable request and subject to institutional/ethical approvals and a data use agreement.

Ethics Statement

This study was approved by the Ethics Committee of the Affiliated Hospital of Southwest Medical University (Approval No. KY2025385). Given that the study was based on anonymized retrospective data, the requirement for informed consent was waived by the ethics committee. All procedures involving data processing complied with the ethical principles of the Declaration of Helsinki and relevant institutional regulations.

Author Contributions

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

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Disclosure

The authors report no conflicts of interest in this work.

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