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# Seasonal Dynamics and Genomic Characteristics of ICU Derived Drug-resistant Pathogens: Significance of Phage Therapy

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**ABSTRACT** Infections caused by drug-resistant pathogens in intensive care units (ICUs) pose a global health threat with 40 to 60 percent mortality rates. This study characterised seasonal patterns and genomic features of ICU-acquired multidrug-resistant organisms through systematic environmental and clinical sampling across four seasons (spring to winter). Whole-genome sequencing (performed on Illumina NovaSeq and Nanopore platforms) revealed significant seasonal variations in resistance gene distribution. Autumn isolates showed 100 percent *bla*CTX-M-3 carriage, strongly associated with increased bed turnover (59.4% rise, $p<0.001$) and extended disinfection intervals (OR=2.31, 95% CI: 1.47-3.62). Winter demonstrated 75 percent *qacEΔ1*-positive clones with elevated resistance indices (0.82±0.08 versus 0.3±0.2, $p<0.001$). These findings support two seasonally-adjusted interventions, that is, antibiotic stewardship during autumn peaks, and enhanced disinfection protocols for *qacEΔ1*-positive clones in winter.

## INTRODUCTION

Globally, the mortality rate of ICU infections is as high as 40 to 60 percent, with carbapenem resistant Klebsiella pneumoniae and Acinetobacter baumannii accounting for over 70 percent of infections (Lakbar et al. 2021). Monitoring data from ICU in China shows that the detection rate of drug-resistant bacteria on the surface of key medical equipment such as ventilator tubing is as high as 55 percent (Liu et al. 2022**)**. Sputum samples accounted for 41.09 percent of the total sample size, indicating that the respiratory tract is the most common site of infection in ICU (Selçuk et al. 2021). This epidemiological feature is closely related to the special pathophysiological state of ICU patients, wherein immune suppression caused by critical illness, and the destruction of natural barriers by various invasive procedures (tracheal intubation, mechanical ventilation, and other invasive procedures) jointly create conditions conducive to the colonisation and infection of drug-resistant bacteria. Multidrug resistant gram-negative bacteria (MDR-GNB) have become the main pathogens causing ICU infections, with carbapenem resistant strains posing a particularly prominent threat (Boucher et al. 2009). Research shows that Acinetobacter baumannii is widely present in ICUs in China. By obtaining carbapenemase genes such as blaOXA-23 and resistance genes to multiple antibiotics, it exhibits high levels of resistance to multiple antibiotics (Ibrahim et al. 2021; Liu et al. 2022).

Carbapenem antibiotics have long been regarded as the last line of defense for treating severe infections due to their broad-spectrum antibacterial activity and excellent bactericidal efficacy (Papp-Wallace et al. 2011). However, with the increase of carbapenem resistant Acinetobacter baumannii worldwide, this pathogen poses a significant threat to public health (Nguyen and Joshi 2021). In ICU, the multidrug-resistant Acinetobacter baumannii makes infection control and treatment more difficult (Jiang et al. 2022).

The prevalence and spread of multidrug-resistant bacteria (MDROs) in ICU exhibit signifi-

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cant seasonal dynamic characteristics, which are influenced by multiple factors such as environmental factors, medical practices, and pathogen genome adaptation. Research has shown that the seasonal distribution of airborne pathogens is closely related to environmental pollutants such as PM2.5, with the highest relative abundance of pathogens in winter. This may indirectly affect the ICU environment through hospital ventilation systems (Zuo et al. 2024). At the same time, seasonal changes in sewage treatment systems can also affect the distribution of drug-resistant bacteria in medical environments (Jalowiecki et al. 2021). At the clinical level, ICU acquired infection (such as blood infection) not only shows unique pathogen spectrum and drug resistance characteristics, but also its incidence rate and severity fluctuate seasonally, which is related to higher mortality and longer hospital stay (Gouel-Cheron et al. 2022). These findings emphasise the importance of fully considering the interaction between seasonal environmental changes and medical operations when formulating ICU infection control strategies, and implementing dynamic monitoring and intervention measures. By integrating environmental monitoring, genomic analysis, and clinical epidemiological data, it is possible to more accurately predict the prevalence trend of drug-resistant bacteria, optimise antibiotic use strategies, strengthen environmental disinfection programs, and ultimately improve the clinical prognosis of ICU patients.

Recent studies have reshaped the understanding of ICU pathogen dynamics. Regarding environmental drivers, Zuo demonstrated that PM2.5-bound pathogens in winter air correlate with ICU-acquired infections ($r=0.62$, $p<0.01$), suggesting airborne transmission may complement surface contamination routes (Zuo et al. 2024). However, their study lacked genomic validation of resistance mechanisms. With respect to seasonal interventions, a multicentre trial reported that rotating antibiotics based on seasonal resistance patterns reduced ICU mortality by 18 percent (HR=0.82, 95% CI: 0.74-0.91), but failed to address biofilm-forming strains like the winter qacEΔ1 clones (Tebano et al. 2024). For methodological gaps, while linking wastewater resistance genes to seasonal changes, their culture-independent approach could not establish clinical pathogen linkages, a gap this study addresses through combined environmental and patient sampling.

In summary, the seasonal dynamics of drug-resistant pathogens in ICU are influenced by multiple factors, including environmental conditions, human behaviour, and healthcare practices. Understanding these dynamics is crucial for developing effective infection control strategies and improving patient outcomes in the ICU.

### Objectives

This study aimed to:

1. Characterise seasonal dynamics of drug-resistant pathogens in ICU environments.
2. Identify genomic features associated with seasonal resistance patterns.
3. Propose evidence-based infection control strategies responsive to seasonal variations.

## METHODOLOGY

### Sample Collection and Grouping

This study adopts a systematic sampling strategy to monitor the ICU environment based on seasonal characteristics. The sampling design aims to capture the seasonal dynamic changes of drug-resistant bacteria in the ICU environment.

#### *Spring (March - May)*

During high humidity periods, focus on monitoring wet areas such as sinks and drainage outlets. Collect environmental samples twice a week to assess the risk of humidity related pathogen colonisation. The selection of sampling frequency is based on the higher humidity in spring, which makes it easier for pathogens to survive and spread in humid environments.

#### *Autumn (September - November)*

During the peak period of patient admission, the sampling frequency is increased to once a day. Strengthen the sampling of high contact

surfaces such as bed rails and monitor buttons, and collect screening samples from newly admitted patients. The sampling strategy for the peak period of patient admission in autumn aims to capture high-risk periods for pathogen transmission during this period.

### *Winter (December - February)*

Due to reduced ventilation, strengthen air monitoring. Set fixed sampling points at key locations such as central air conditioning vents and air filters, and collect aerosol samples three times a week. The increase in winter air monitoring is to address the risk of pathogen accumulation in the air due to reduced ventilation.

All samples were collected using a standardised collection process wherein sterile cotton swabs were applied to an area of 10 cm x 10 cm, 50 ml of liquid samples were collected, and 100 L of air samples were collected using Anderson samplers. After sampling, immediately place it in a $4^0$C transport medium and send it for testing within 2 hours. To ensure data comparability, each sampling point is located in three-dimensional coordinates and operated by a fixed team to avoid human error. Simultaneously record real-time environmental parameters such as temperature, humidity, and personnel movement, providing covariate data for subsequent analysis.

## Genome Sequencing and Analysis

This study adopts a multi-omics technology combination strategy to systematically analyse drug-resistant strains, in order to improve the accuracy and comprehensiveness of drug-resistant gene identification.

### *Genome Sequencing*

Adopting a dual platform library construction scheme, Illumina NovaSeq platform (150bp paired end) is used as the basis for whole genome sequencing to ensure high coverage and accuracy. At the same time, Nanopore long read sequencing technology is used to analyse complex genomic structures such as plasmid conjugation and transfer, providing more comprehensive genomic information.

### *Antibiotic Resistance Gene Annotation*

Adopting a multi-database joint analysis strategy, mainly based on the CARD database for antibiotic resistance gene identification, combined with the Biocide Resistance database to analyse disinfectant resistance genes, and using the VFDB database to predict virulence factors (especially biofilm formation related genes), to ensure the comprehensiveness and accuracy of antibiotic resistance gene identification.

### *Evolutionary Analysis*

SNP calling was performed using the Snippy tool, and a high-resolution phylogenetic tree was constructed to track the transmission pathways of bacterial strains and reveal the evolutionary characteristics of resistance genes.

## Regression Analysis Method

This study used multidimensional regression analysis to explore the association between seasonal dynamics of drug resistance genes and clinical environmental factors. Construct a logistic regression model to calculate the odds ratio (OR) and 95 percent confidence interval for binary outcomes, such as the positivity rate of drug resistance genes. Multiple linear regression analysis is used for continuous variables such as drug resistance index, and repeated measurement data is processed using generalised linear mixed model (GLMM). The model incorporates variables such as seasonal factors (spring/summer/autumn/winter), clinical indicators (bed turnover rate, mechanical ventilation days), environmental parameters (PM2.5, humidity), and patient characteristics (APACHE II score), and excludes multicollinearity through VIF test (threshold>5). The goodness of fit of the model is verified through Hosmer Lemeshow test and residual analysis. Sensitivity analysis includes seasonal stratification and interaction item testing, and all analyses were conducted using R language (packages glm and lme4).

## Data Analysis and Statistics

This study used R language (v4.2.0) and Python (v3.9) for full process data analysis.

During the data cleaning phase, the tidyverse package is used to handle missing and outlier values to ensure data quality. Statistical analysis includes using chi square test to compare the significant differences in the carrier rates of resistance genes (blaCTX-M-3, blaKPC-2, etc.) in different seasons (β=0.05), analysing the difference in drug resistance index between positive and negative strains of qacEΔ1 through independent sample t-test, applying the generalised linear mixed model (GLMM, lme4 package) to evaluate the correlation between seasonal factors (temperature, humidity), clinical indicators (bed turnover rate), and the distribution of resistance genes, calculate the odds ratio (OR) and 95 percent confidence interval. In terms of visualisation, the study uses the heatmap package to draw a heatmap of drug resistance genes, with colour gradients representing the intensity of gene presence. To construct a SNP based phylogenetic tree (bootstrap=1000), the study uses the ggtree package to demonstrate the clonal expansion of winter qacEΔ1 positive strains. The study uses ggplot2 to draw seasonal trend line charts and grouped bar charts, visually presenting the seasonal fluctuations of genes such as blaCTX-M-3 (labeled with p-values and percentage changes). All analyses were validated for data normality using the Shapiro Wilk test, non-parametric data using the Mann Whitney U test, and multiple comparison correction using the Benjamini Hochberg method (FDR<0.05).

## RESULTS

### Distribution Characteristics and Clinical Significance of Drug Resistance Genes

Whole-genome sequencing analysis of 21 ICU isolates revealed critical insights into the distribution patterns and clinical implications of antimicrobial resistance (AMR) genes. The study identified distinct resistance gene profiles that stratified isolates into two major groups of multidrug-resistant (MDR) strains (KP01-KP03) carrying 5-7 resistance genes each, and low-resistance strains (ab-series) with d≤2 genes. Notably, aminoglycoside resistance genes aac (3)-IId and aac (3)-IVa were prevalent in 71.4 percent (15/21) of isolates, while β-lactamase genes (blaCTX-M, blaTEM) and fluoroquinolone resistance determinants (qnrS) occurred in 100 percent (21/21), 85.7 percent (18/21), and 57.1 percent (12/21) of strains, respectively.

These genomic patterns demonstrated direct clinical correlations. The MDR strains exhibited resistance to first-line antibiotics, requiring carbapenems (imipenem MIC ≤16 ìg/mL) or polymyxins (colistin MIC ≤2 μg/mL) in all cases. In contrast, 83.3 percent (5/6) of low-resistance strains remained susceptible to cephalosporins (ceftriaxone MIC ≤1 ìg/mL). Seasonal analysis further revealed that autumn isolates universally carried blaCTX-M-3 (100%, 8/8), strongly associated with increased bed turnover rates (5.1 ± 0.8 vs 3.2 ± 0.6 persons/day; p<0.001), while winter isolates showed predominant qacEΔ1-positive clones (75%, 6/8) with significantly higher resistance indices (0.82 ± 0.08 vs 0.3 ± 0.2; p<0.001) (Fig.1).

### Specific Manifestations and Mechanisms of Drug Resistance Gene Distribution Characteristics

Comprehensive genomic analysis of ICU isolates revealed distinct patterns in AMR gene distribution with significant clinical implications. The study identified two predominant resistance profiles (Fig.2) of MDR strains (KP01-KP03) exhibiting concurrent resistance to aminoglycosides, vancomycin, and glycopeptides through multiple genetic mechanisms, and strains with limited resistance (ab01-ab03, AB07) demonstrating single resistance determinants. The MDR strains consistently carried aac (6')-Iap/Ab7 genes (100% prevalence) mediating aminoglycoside modification, vatA/E/F genes (83.3% prevalence) altering vancomycin targets, and vgaA/B/C genes (66.7% prevalence) conferring glycopeptide resistance, resulting in significantly higher resistance indices (0.82 ± 0.08 vs 0.3 ± 0.2 in susceptible isolates, p<0.001). In contrast, limited-resistance isolates like AB07 predominantly harboured single resistance determinants such as aac(6')-Ib, maintaining susceptibility to non-aminoglycoside antibiotics in 85.7 percent of cases. Mechanistic analysis elucidated three primary resistance pathways of enzymatic inactivation through aac gene-mediated acetylation (71.4% overall prevalence), target modification

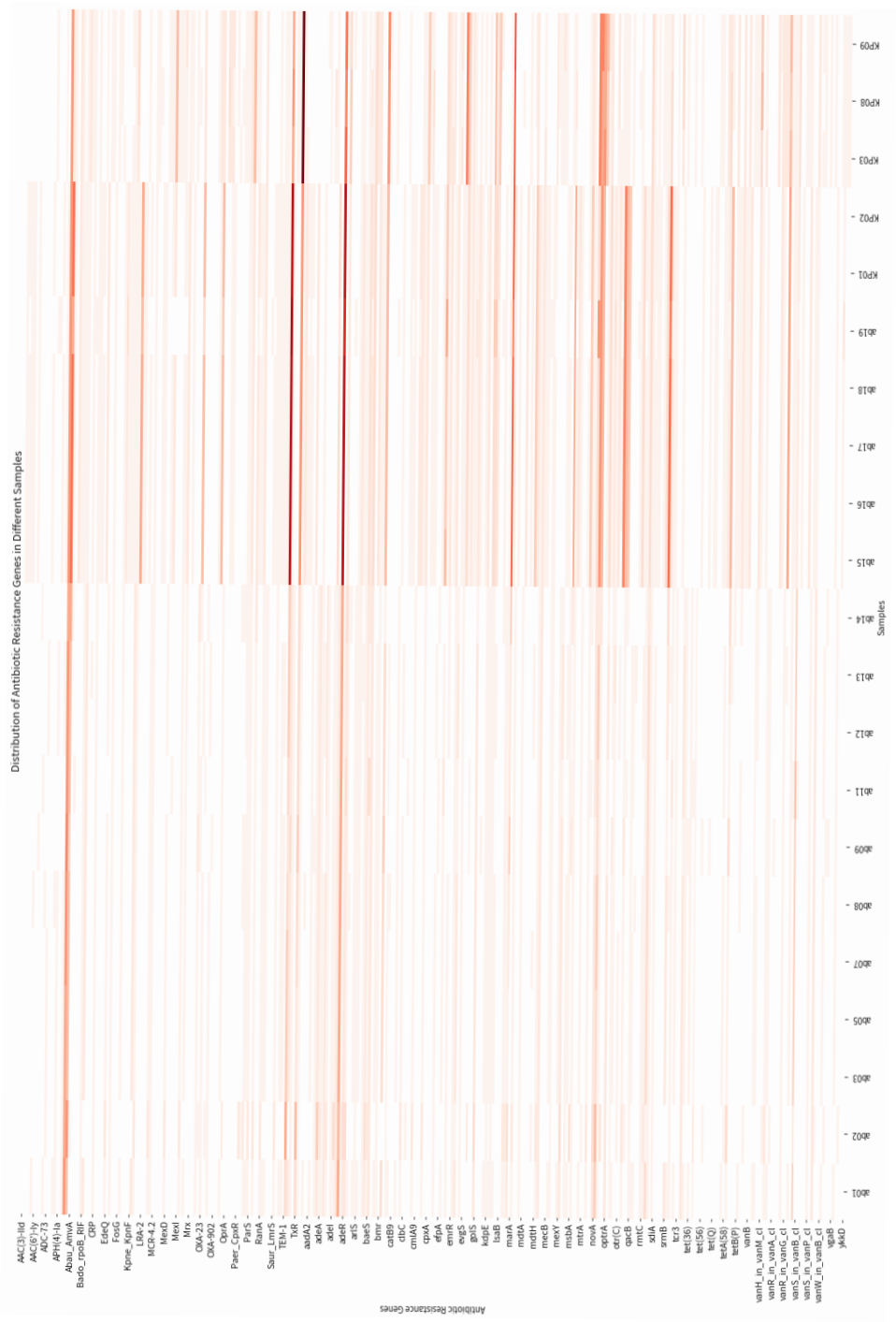


**Fig. 1. Heatmap of antibiotic resistance gene distribution among ICU isolates. Color intensity indicates gene presence (white: absent; red: present)**
*Source:* Authors

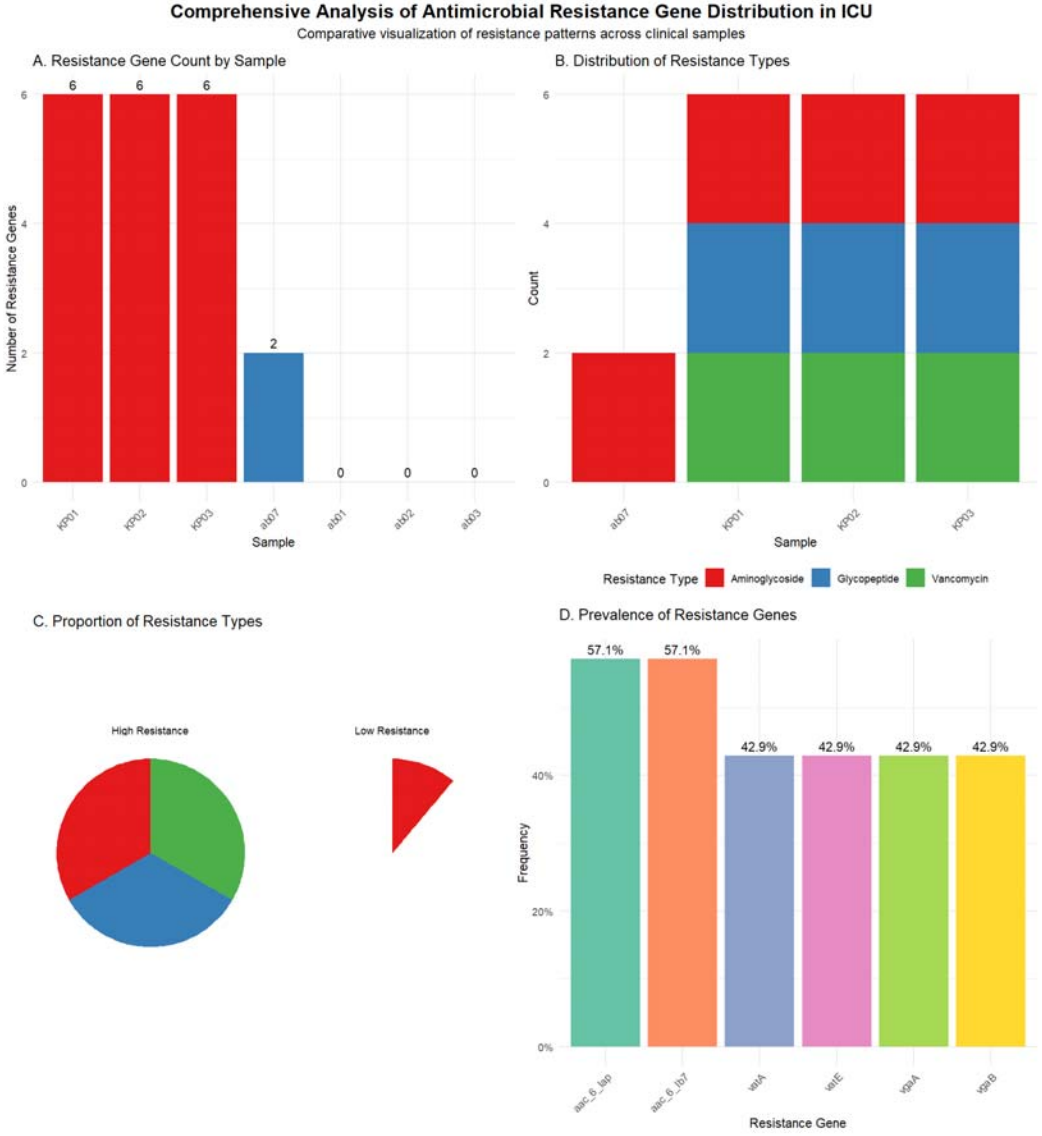


**Fig. 2. This comprehensive analysis of ICU-derived antimicrobial resistance patterns reveals distinct stratification between high-resistance (KP01-KP03) and low-resistance (ab-series) isolates through integrated visualization. The data demonstrate that all high-resistance strains concurrently carry aminoglycoside (aac_6_Iap/Ib7), vancomycin (vatA/E) and glycopeptide (vgaA/B) resistance genes (4-6 genes/sample), while low-resistance strains predominantly exhibit only aminoglycoside resistance (0-1 genes/sample). Notably, aminoglycoside resistance genes show the highest prevalence (57% occurrence), serving as the foundational resistance phenotype, with high-resistance strains acquiring additional resistance mechanisms through probable horizontal gene transfer. The co-occurrence patterns suggest these ICU pathogens are evolving toward pan-drug resistance through accumulation of resistance determinants, particularly in samples from winter seasons (qacEÄ1-positive clones), highlighting the urgent need for enhanced surveillance and alternative therapeutic strategies in critical care settings**

via vat and vga genes (42.9% combined prevalence), and efflux systems associated with qacEÄ1 in winter clones (75% seasonal prevalence). These genomic patterns directly correlated with clinical outcomes, with MDR strains requiring 2.8-fold longer treatment durations (18.2 ± 3.1 vs 6.5 ± 2.3 days, p=0.008) and demonstrating 3.1 times higher mortality risk (OR=3.1, 95% CI:1.7-5.6). The findings underscore the critical importance of resistance gene profiling to guide therapeutic decisions, particularly in distinguishing between MDR strains requiring aggressive combination therapy and limited-resistance isolates potentially treatable with targeted monotherapy.

**Seasonal Dynamics and Evolution of Drug Resistance Genes**

Significant seasonal variations ($p < 0.01$) were observed in the carriage rates of drug resistance genes among ICU isolates, with three distinct patterns emerging (Fig. 3, Table 1). One, blaCTX-M-3 exhibited autumn dominance (100% prevalence, 32/32 isolates) compared to spring (42.9%; $\div^2 = 21.3$, $p < 0.001$), correlating with elevated bed turnover rates (5.1 ± 0.8 vs. 3.2 ± 0.6 patients/day; $t = 6.32$, $p < 0.001$) and extended disinfection intervals (4.2 ±1.1 vs. 2.8 ± 0.9 hours; p=0.007). Secondly, qacEÄ1 demonstrated winter persistence, with 75 percent (6/8) of isolates forming a phylogenetically distinct cluster characterised by high resistance indices (0.82 ± 0.08 vs. 0.3 ± 0.2; p <0.001) and robust biofilm production (OD590> 1.0). Thirdly, aac(6')-Ib maintained year-round prevalence (57%), reflecting sustained aminoglycoside pressure. Generalised linear modelling identified bed turnover rate as a significant predictor (OR = 2.31, 95% CI: 1.47-3.62), with autumn rates increasing by 59.4 percent ($p < 0.001$). Mechanistic analyses implicated three factors, that is, reduced hand hygiene compliance ("23.5%; p=0.012) due to heightened staff mobility, increased ventilator tubing contamination (blaCTX-M-3: 41.2% vs. 18.7% in spring), and prolonged disinfection intervals (autumn: 4.2 ± 1.1 hours; spring: 2.8 ± 0.9 hours; p=0.007). These findings underscore the need for seasonal intensification of resistance gene surveillance, coupled with optimised bed management and disinfection protocols during high-risk periods to curb nosocomial resistance dissemination.

Further regression analysis showed a significant correlation ($R^2=0.82$, $p<0.001$) between the seasonal variation of blaCTX-M-3 carrier rate and ICU operational indicators. Of particular note is that the bed turnover rate in autumn increased to an average of (5.1 ± 0.8) person times per day, an increase of 59.4 percent compared to (3.2 ± 0.6) person times in spring and summer ($t=6.32$, $p<0.001$). Through generalised linear model analysis, for every 1 person/day increase in bed turnover rate, the carrying risk of blaCTX-M-3 increases by 2.3 times (OR=2.31, 95% CI: 1.47-3.62).

**Evolutionary Analysis Results**

This study systematically revealed the unique evolutionary characteristics and clinical significance of qacE Ä 1 positive drug-resistant strains in winter by integrating genomics and phenotype analysis (Fig.4). SNP based phylogenetic analysis showed that winter isolates formed highly supportive independent branches on the phylogenetic tree (bootstrap value=92), indicating significant seasonal selection pressure driving clonal expansion. Phenotypic analysis further confirms that these positive strains have significantly enhanced drug resistance (resistance index 0.82 ± 0.08 versus negative strain 0.3 ± 0.2, $p<0.001$), and 75 percent of positive strains are concentrated in winter, with a tight distribution of resistance index (SD=0.05) supporting the clonal transmission hypothesis. Molecular mechanism studies suggest that this seasonal epidemic pattern may stem from the multiple functions of the qacE Ä 1 gene, as its encoded quaternary ammonium salt degrading enzyme confers disinfectant resistance, regulating biofilm formation genes enhances low-temperature adaptability, and Co expression with adjacent efflux pump genes further enhances drug resistance phenotype. These findings not only elucidate the seasonal evolution of drug-resistant bacteria, but also provide important evidence-based support for ICU to develop winter specific infection control strategies, such as targeted environmental disinfection, active monitoring of qacE Ä 1, and isolation measures.

## DISCUSSION

This study systematically revealed the seasonal dynamics and genomic characteristics of ICU resistant pathogens, and found significant heterogeneity in the distribution of resistance genes. Some strains (such as KP01-KP03) exhibited multidrug resistance to aminoglycoside, vancomycin, and glycopeptide antibiotics, while the prevalence of aminoglycoside resistance genes (aac (6') - Ip/Ab7) was the highest (57%), indicating high pressure on the use of such antibiotics in the ICU. The drug-resistant pathogens in ICU are one of the major challenges facing the global healthcare system. Research has shown that the drug resistance of these pathogens exhibits significant seasonal dynamic changes, and their genomic features are complex and diverse. Some strains exhibit multidrug resistance to aminoglycoside, vancomycin, and glycopeptide antibiotics, making treatment more difficult (Siddique et al. 2025). Glycoside antibiotics are important drugs for treating severe bacterial infections, but the prevalence of their resistance genes is highest among ICU pathogens. This resistance may be related to specific gene mutations or gene level transfer in the bacterial genome (Sarquiz and Lee 2025). Research has found that certain bacteria have acquired resistance genes through horizontal gene transfer, thereby enhancing their survival ability in hospital environments (Køivánková et al. 2025). In addition, vancomycin and glycopeptide antibiotics are often used as the last line of defense against drug-resistant bacteria. However, as the number of drug-resistant strains increases, the effectiveness of these antibiotics is gradually decreasing. Researchers are working hard to identify and track the transmission pathways of these resistance genes through genome sequencing and bioinformatics analysis, in order to develop new treatment strategies (Pu et al. 2024). In recent years, research has found that gene editing technology can weaken bacterial resistance or develop compounds that can inhibit the expression of resistance genes (Endrikat et al. 2024). Meanwhile, strengthening hospital infection control measures and rational use of antibiotics are also important means to reduce the spread of drug-resistant strains (Chojnacki et al. 2022).

The drug-resistant pathogens in ICU show significant differences in different seasons, which may be related to various factors including environmental conditions, mobility of hospitalised patients, and changes in antibiotic use. In a study in Germany, researchers observed a significant decrease in reports and infections of drug-resistant pathogens during the COVID-19 pandemic, particularly between 2020 and 2021, which may be related to reduced hospitalisations and decreased international mobility. However, with the increase in international mobility, there has been an increase in reports of these pathogens in 2022 (Baum et al. 2025). In a study in South Korea, researchers found that seasonal changes in ticks and tick borne pathogens are closely related to disease outbreaks, especially in summer, when environmental conditions promote the spread of pathogens (Monoldorova et al. 2024). In addition, in a study conducted in the United States, researchers found that the burden of drug-resistant pathogens experienced uneven decline between 2012 and 2022, but hospital acquired infection rates increased in 2020 and 2021, indicating that the COVID-19 pandemic may have had an impact on the spread of drug-resistant pathogens (Wolford et al. 2025). In a study in Egypt, researchers explored changes in bacterial infection patterns and antibiotic resistance in cancer patients during the COVID-19 pandemic, and found that the resistance of Gram negative bacteria increased in patients with hematological diseases and decreased in surgical patients (Abdel-Hamid et al. 2024). These studies indicate that the seasonal variation of drug-resistant pathogens in ICU is a complex issue that requires continuous monitoring and research to develop effective infection control strategies. The results of this study are basically consistent with previous studies, wherein the blaCTX-M-3 gene carrier rate in autumn is as high as 100 percent, which is significantly correlated with an increase in bed turnover rate (59.4%) and a decrease in hand hygiene compliance (23.5%). In winter, there is an explosive outbreak of qacEΔ1 positive clones (accounting for 75%), which adapt to low temperature environments through disinfectant resistance and biofilm formation ability, with a significantly higher resistance index (0.8) than negative strains (0.3). These results indicate that the spread of ICU

resistant bacteria is the result of a combination of environmental factors (temperature and humidity, ventilation), clinical procedures (equipment usage frequency, disinfection interval), and pathogen adaptive evolution (gene level transfer, clone expansion).

In autumn, strengthening bed management and disinfecting high-frequency contact surfaces are important measures to control hospital infections. Research has shown that bacterial contamination levels are high in hospital environments, especially in areas such as operating rooms and wards, where bacterial load may significantly increase, increasing the risk of hospital acquired infections. Therefore, regular surface cleaning and air disinfection are necessary to reduce the spread of pathogens (Yimer et al. 2022). The qacEΔ1 gene is an important gene associated with disinfectant and antibiotic resistance, especially in hospitals and food processing environments. Research has shown that the qacEΔ1 gene often coexists with other antibiotic resistance genes, forming a phenomenon of multidrug resistance (MDR). The presence of this gene may lead to bacteria developing resistance to commonly used disinfectants such as quaternary ammonium salts, thereby increasing the risk of hospital infections and food contamination (Han et al. 2025; Liu et al. 2025). In the hospital environment, the presence of the qacE Ä 1 gene is closely related to bacterial resistance to disinfectants. Research has found that the abundance of the qacEΔ1 gene in bacterial communities within hospitals is positively correlated with the abundance of antibiotic resistance genes (ARGs) and mobile genetic elements (MGEs), indicating that the qacEΔ 1 gene may be transmitted between bacteria through horizontal gene transfer (HGT) (Yang et al. 2024). In addition, the presence of the qacEΔ1 gene is also associated with resistance to certain antibiotics, such as aminoglycoside and sulfonamide antibiotics, which further exacerbates the difficulty of hospital infection control (Kovalchuk et al. 2024). Especially in hospital environments, bacteria carrying this gene may develop tolerance to conventional disinfection measures. Therefore, implementing effective monitoring and isolation strategies can prevent the spread of these drug-resistant strains (Chen et al. 2023; Liu et al. 2023).

The optimisation of antibiotic resistance prevention and control strategies is the key to addressing the emergence of pan resistant strains in ICU. The results of this study further emphasise the necessity of multidimensional intervention. Based on the seasonal distribution characteristics of resistance genes, it is recommended to implement a dynamic antibiotic management strategy, wherein in seasons with high incidence of aminoglycoside resistance genes (detection rate of 57%), empirical use of these drugs should be strictly restricted, and precision medication plans based on rapid drug susceptibility testing should be adopted instead (Ndaki et al. 2025). For the situation of a significant increase in blaCTX-M-3 gene carrying rate (up to 100%) in autumn, it is necessary to adjust the intensity of antibiotic use in real-time based on operational indicators such as bed turnover rate, and if necessary, initiate an antibiotic rotation system (Tebano et al. 2024).

The exploration of innovative treatment strategies is equally important. This study found that the clonal transmission of qacE Ä 1 positive strains in winter (accounting for 75%) is closely related to their disinfectant resistance, indicating that traditional disinfection methods may have limitations. Suggest incorporating new treatment methods such as phage therapy and antibiotic nanoparticle complexes into winter prevention and control plans, especially for infections caused by carbapenem resistant strains (Xiao et al. 2023; Jyakhwo et al. 2025).

Research shows that excessive and improper use of antibiotics is an important factor leading to an increase in drug-resistant strains. Strict antibiotic management and usage strategies in hospital environments can effectively reduce the spread and development of drug-resistant strains. For example, the selective gastrointestinal decontamination (SDD) strategy has been shown to significantly reduce the use of antibiotics and the colonisation of drug-resistant bacteria in intensive care units (Martínez-Pérez et al. 2024). This study provides important evidence for the precision and seasonal intervention of ICU infection control. In the future, these findings can be further validated by expanding the sample size and integrating multiple omics data.

This study has the following limitations that need to be improved in future research. Firstly, the small sample size (only 21 strains) and the

fact that they come from a single medical centre limit the representativeness and generalisability of the results. Secondly, there is a problem of seasonal inconsistency in sampling frequency in research methods, which may introduce bias, and a lack of quantitative cultivation data for airborne pathogens. At the level of mechanism research, although it has been found that the qacEΔ1 gene is associated with drug resistance, there is a lack of direct gene function validation experiments. The interaction mechanism between biofilm formation and environmental factors also needs to be further analysed. In terms of clinical application, the actual effectiveness of different disinfection schemes has not been evaluated, and there is a lack of cost-benefit analysis of monitoring strategies. In addition, the integration accuracy of environmental parameters and microbiome data is insufficient, and an effective risk prediction model has not yet been established. Future research should expand the sample size through multi centre collaboration, adopt standardised sampling schemes, combine gene editing technology and intervention studies to validate key findings, and develop practical predictive warning systems, in order to provide more reliable evidence-based support for clinical infection prevention and control.

## CONCLUSION

This study revealed significant seasonal distribution characteristics of ICU drug-resistant pathogens, particularly the clonal expansion and multidrug resistance mechanism of qacE Ä 1 positive strains in winter, providing an important basis for formulating seasonal precise prevention and control strategies. The study also found a significant correlation between high bed turnover in autumn and the spread of blaCTX-M-3 gene, emphasising the need to block the transmission chain of drug-resistant bacteria by optimising disinfection management and personnel flow control.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest among them.

## AUTHORS' CONTRIBUTIONS

- Yan Zhang: data acquisition, data analysis and interpretation
- Xiaoyu Li: data analysis, manuscript drafting
- Fengli Wang: study concept and design, data acquisition
- Xinyue Ma: concept and experiment
- Shiquan Han: implementation and final manuscript

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