

RESEARCH ARTICLE



Analysis of ESKAPE pathogens in clinical isolates in a tertiary care hospital in China from 2018 to 2023

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ABSTRACT

The widespread use of antimicrobial agents correlated with the increasing incidence of nosocomial infections and bacterial antibiotic resistance. These have become major challenges in the prevention and control of hospital-acquired infections worldwide. The aims of this study were to analyze the distribution and characteristics of ESKAPE pathogenic bacteria and their antibiotic resistance profile among clinical isolates from a tertiary hospital in China from 2018 to 2023. The results showed that a total of 20,472 non-duplicated pathogenic bacteria were isolated from clinical specimens in this hospital between 2018 and 2023, of which the top five pathogenic bacteria were *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Acinetobacter baumannii*. In case of *E. coli* the main detected resistance genes were *bla*_{CTX-M}, *bla*_{TEM} and *bla*_{OXA}. *K. pneumoniae* mainly carried *bla*_{OXA}, *bla*_{KPC} and *bla*_{NDM} genes. *P. aeruginosa* was mainly positive for *bla*_{OXA}, AmpC type beta-lactamases and *bla*_{VIM} genes. *A. baumannii* mainly carried *ArmA*, *bla*_{TEM} and *cas3* genes. *S. aureus* was mainly positive for *mecA*, *erm*(C) and *erm*(A) genes. In this study, we have found that the antibiotic resistance of common pathogens from clinical isolates in a tertiary hospital in China in the past 6 years is severe, and *A. baumannii* was particularly a prominent pathogen. There is an urgent need to strengthen the prevention and control of nosocomial infections and antimicrobial drug management in order to curb the spread of multidrug-resistant bacteria.

KEYWORDS

hospital-acquired infections, clinical strains, antibiotic resistance analysis

1. INTRODUCTION

In recent years, with the aging of society and the development of medicine, the increase of various invasive operations and interventional therapies, and the long-term and extensive use of antimicrobial drugs in the clinical departments, the problem of bacterial resistance and hospital-acquired infections caused by antibiotic resistant bacteria have received increasing attention [1]. Antibiotic resistant bacterial infections not only threaten human health but also bring serious economic burden to global public health and healthcare by prolonging hospitalization time while increasing medical costs and mortality [2, 3]. According to the findings of the European Union, more than 25,000 deaths per year are caused by multidrug-resistant bacterial infections, with a consequent loss of up to 1.5 billion euros in health care and social productivity [4]. On the other hand, in the United States alone there are more than 2 million cases of bacterial infections that have become resistant to at least first-line antibiotics and US medical and healthcare organizations spend more than \$20 billion to address the antibiotic resistance problem [5]. A recent report by the World Bank and the Food and Agriculture Organization of the United Nations (FAO) states that if the problem of antibiotic resistance is not solved by 2050, the annual global GDP will fall by 1.1%–3.8%, equivalent to

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the impact of the 2008 financial crisis [6]. A high-volume, long-term combination of broad-spectrum antimicrobials will lead to increased resistance in pathogenic bacteria, making the choice of anti-infective therapeutic agents increasingly limited. There is a strong demand in some clinical departments for drug-resistant outcomes in pathogenic bacterial infections. Antibiotic resistance monitoring of bacteria is an effective method to understand the change of drug-resistant bacteria and to curb the spread of drug-resistant bacteria. Bacterial antibiotic resistance testing in hospitals can assist the clinic in the timely understanding of the types of common pathogens and the change of antibiotic resistance, adjust the therapeutic strategy and rationalize the use of medication, and reduce the burden of disease on patients. According to the Ministry of Health of China, the use of antibiotics in China is twice as high as that in Europe and the United States, and the irrational use of antibiotics in clinical treatment is widespread [7]. Since the variation of bacterial resistance is affected by the use of antimicrobial drugs in the region, it is of great significance to understand bacterial resistance and the use of antimicrobial drugs in the region for clinical diagnosis and treatment and the rational use of medication, which is one of the main tasks of China's National Action Plan for Containment of Microbial Antibiotic Resistance (2022–2025) [8]. In this study, we analyzed the distribution of major pathogenic bacteria and antibiotic resistance trends of clinical isolates in our hospital in the past 6 years aiming to provide a reference basis for clinical diagnosis and treatment and rational use of antimicrobial drugs. The antibiotic resistant pathogens isolated from patients admitted to Affiliated Danyang Hospital of Nantong University during the period of 2018–2023 were analyzed as follows.

2. MATERIALS AND METHODS

2.1. Strain origin of pathogenic bacteria

Clinical specimens from outpatients and inpatients of Affiliated Danyang Hospital of Nantong University from January 2018 to December 2023 were selected and sent to the Microbiology Laboratory of the Department of Laboratory Medicine for specimen culture and isolation. The types of specimens were mainly sputum, urine, blood, pleural and abdominal fluid, vaginal secretions, wound secretions, bile and pus.

2.2. Bacterial culture identification and antibiotic susceptibility testing

Clinical specimens from outpatients and inpatients of Affiliated Danyang Hospital of Nantong University from January 2018 to December 2023 were selected and sent to the Microbiology Laboratory of the Department of Laboratory Medicine for specimen culture and isolation. The types of specimens were mainly sputum, urine, blood, pleural and abdominal fluid, vaginal secretions, wound secretions, bile

and pus. Specimens sent for testing by clinical departments need to be cultured, isolated, and identified for bacteria in strict accordance with the National Clinical Laboratory Practice Protocols, 4th edition [9]. Primary strains were isolated from Columbia blood medium, MacConkey medium, and chocolate medium, and thereafter passaged culture and pure culture were performed with Columbia blood medium or chocolate medium. The test results were all interpreted according to the requirements of the National Technical Program for Bacterial antibiotic Resistance Surveillance and reported to the National Bacterial antibiotic Resistance Surveillance Network (CHINET) [10]. Identical strains isolated multiple times consecutively from the same patient were excluded. Bacterial identification and antibiotic susceptibility testing were carried out by using the VITEK MS mass spectrometer of bioMérieux, France, and the supporting reagents. For the antibiotic susceptibility testing, the culture medium of Shanghai Comarca Microbial Technology Co., Ltd. was used, and the isolates were identified in detail by using the VITEK-2Compact automatic bacterial identifier of bioMérieux, France. The strains were identified by the Kirby-Bauer disk diffusion method (K-B method) and Minimum inhibitory concentration method (MIC method) using the matching identification cards [Gram-negative bacterial drug sensitivity card (AST-GN13), Gram-positive bacterial drug sensitivity card (AST-GP67)] and the drug sensitivity paper tablets of Oxoid Limited. Inhibitory concentration method (MIC method). The antibiotic susceptibility testing and interpretation of the results were performed concerning the methods recommended by the Clinical and Laboratory Standards Institute (CLSI) 2022 edition [11]. The antibiotic susceptibility testing were performed according to the antimicrobial drugs commonly used in our clinic, and the quality control test strains were *Pseudomonas aeruginosa* ATCC27853, *Escherichia coli* ATCC25922, *Staphylococcus aureus* ATCC29213, *Enterococcus faecalis* ATCC29212, *Streptococcus pneumoniae* ATCC49619, and *Haemophilus influenzae* ATCC49247. No CLSI folds were judged by reference to the (FDA) recommended folds. Piperacillin/tazobactam for *Acinetobacter baumannii* refers to the CLSI Enterobacteriaceae piperacillin fold-point judgment [12].

2.3. Antibiotic resistance gene detection

Primer design was used from Primer-BLASTS provided by the National Center for Biotechnology Information (NCBI). The designed primers were synthesized and purified by Bioengineering (Shanghai) Co. DNA extraction of *E. coli*, *Klebsiella pneumoniae*, *P. aeruginosa*, *S. aureus*, and *A. baumannii* was performed in strict accordance with the kit instructions. The prepared 1 mL of different colony suspensions were pipetted into sterilized Eppendorf tubes respectively, and 50 µL of proteinase K was taken into the above Eppendorf tubes, and then 100 µL of 20% SDS buffer was aspirated and mixed with it, and placed in a centrifuge at 4 °C for 10 min at 2,500 rpm, the droplets on the walls of the tubes were removed, and the supernatant was retained to

obtain the DNA templates of these strains. We checked that the A260/A280 value is 1.6–2.0, and the optimal concentration of DNA is 30–50 ng μL^{-1} , and stores in the refrigerator at -80°C . PCR amplification was performed by polymerase chain reaction, and the reaction system was 5 μL of template, 33.75 μL of Nuclease-Free Water, 4 μL of dNTP Mixture, 0.25 μL of TaKaRa Taq™ HS Perfect Mix, and 5 μL of $10 \times$ PCR Buffer, totaling 48 μL . The PCR reaction conditions were preheating at 95°C for 5 min; denaturation at 95°C for 30 s, annealing at 58°C for 30 s, and extension at 72°C for 40 s for a total of 40 cycles; and reaction at 72°C for 5 min, followed by 4°C storage. The above PCR amplification products were subjected to 1% agarose gel electrophoresis, stained with ethidium bromide for 20 min, and then read by gel imaging system. When the target band appeared, the test result was positive for the gene. The primer sequences and product lengths of the main target genes are shown in Table 1.

2.4. Statistical analysis

The results of bacterial identification and drug sensitivity were statistically analyzed using WHONET 5.6 software, and the data were analyzed using SPSS 26.0 statistical software, the count data were expressed as n/% with 2 test, and the trend was judged by 2 test Linear-by-Linear Association, and the difference was considered statistically significant with $P < 0.05$.

3. RESULTS

3.1. Types and distribution of bacteria

3.1.1. Results of detection of major pathogenic bacteria. A total of 14,252 clinical non-duplicate strains were isolated from January 1, 2018, to December 31, 2023, at the hospital, and the number of specimens cultured in the calendar year was 25,627, 34,333, 26,976, 29,183, 30,159, and 35,231, respectively. The number of isolated bacteria was 3,015, 3,374, 3,413, 3,403, 3,245, and 4,196, respectively. The isolation positivity rates were 11.765%, 9.828%, 12.656%, 11.661%, 10.760%, and 11.910%, respectively. The isolation rate of gram-negative bacteria among the positive strains ranged from 60.31% to 69.75%, with the percentage in the past years being 29.32% (475/1,620), 25.5% (627/2,458), 24.38% (593/2,432), 25.94% (661/2,548), 26.08% (636/2,439), 24.67% (767/3,109); the isolation rate of Gram-positive bacteria ranged from 24.38% to 29.32%, and the percentage of the calendar year was 69.75% (1,130/1,620), 64.01% (1,574/2,458), 65.25% (1,587/2,432), 66.01% (1,682/2,548), 63.96% (1,560/2,439), and 60.31% (1,875/3,109) (see Fig. 1A). The top 10 common pathogenic bacteria isolated during the 6 years were *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. aureus*, *A. baumannii*, *Enterobacter cloacae*, *Staphylococcus epidermidis*, *E. faecalis*, *S. pneumoniae*, and *Stenotrophomonas maltophilia*, as shown in Table 2.

3.1.2. Characteristics of isolated bacteria. The number of non-duplicated pathogenic bacterial strains isolated from

sputum, urine, pus, secretions, blood, and other (bile, pleural fluid, ascites, etc.) samples during the period 2018–2023 were 4,477, 2,991, 1,562, 1,269, 1,141, and 747 strains, respectively, and the specifics of the bacteria isolated from each sample type (see Fig. 1B). Among the clinically isolated pathogens, the percentages of sputum specimens in the past years were 10.63% (476/4,477), 21.96% (983/4,477), 15.90% (712/4,477), 15.08% (675/4,477), 14.61% (654/4,477), and 21.82% (977/4,477), respectively; and the percentages of urine specimens in the past years were 12.64% (378/2,991), 15.58% (466/2,991), 16.32% (488/2,991), and 17.92% (536/2,991), respectively. In abdominal fluid samples the positivity were 12.64% (378/2,991), 15.58% (466/2,991), 16.32% (488/2,991), 17.92% (536/2,991), 16.42% (491/2,991), and 21.13% (632/2,991), and the percentage of pus specimens in the past year was 8.96% (140/1,562), 8.90% (134/1,562), and 8.90% (134/1,562) respectively. In pleural fluid samples the positivity were 8.90% (139/1,562), 19.14% (299/1,562), 20.36% (318/1,562), 23.37% (365/1,562), and 19.27% (301/1,562) respectively, and the percentage of secretion specimens in the past years was 13.87% (176/1,269), 14.89% (189/1,269), 16.71% (212/1,269), 18.20% (231/1,269), 16.31% (207/1,269), and 20.02% (254/1,269), and the percentage of blood specimens in the calendar year was 14.46% (165/1,141), 17.44% (199/1,141), 17.79% (203/1,141), 17.88% (204/1,141), 14.11% (161/1,141), 18.32% (209/1,141).

3.1.3. Distribution of pathogenic bacteria in different types of samples. The top 3 pathogenic bacteria isolated from respiratory specimens during 2018–2023 were *K. pneumoniae* (21.17%, 948/4,477), *A. baumannii* (18.00%, 806/4,477), *P. aeruginosa* (13.78%, 617/4,477), and the top 3 from urinary tract specimens were *E. coli* (45.64%, 1,365/2,991), *K. pneumoniae* (9.73%, 291/2,991), and *E. faecalis* (7.45%, 223/2,991). The top 3 urinary tract specimens were *E. coli* (45.64%, 1,365/2,991), *K. pneumoniae* (9.73%, 291/2,991), and *E. faecalis* (7.45%, 223/2,991); the top 3 pus specimens were *E. coli* (35.40%, 553/1,562), *K. pneumoniae* (11.01%, 172/1,562), and *P. aeruginosa* (10.43%, 163/1,562). In secretions the top 3 specimens were *S. aureus* (25.37%, 322/1,269), *E. coli* (10.00%, 127/1,269), and *P. aeruginosa* (9.46%, 120/1,269); the top 3 blood specimens were *E. coli* (23.05%, 263/1,141), *K. pneumoniae* (14.99%, 171/1,141), and *S. aureus* (10.52%, 120/1,141).

3.2. Antibiotic sensitivity of major isolates

3.2.1. Antibiotic resistance in *E. coli*. A total of 2,992 strains were isolated and obtained from 2018 to 2023, which accounted for 20.99% (2,992/14,252) of the total number of bacteria isolated and ranked No. 1. The resistance rate of *E. coli* to ampicillin and ciprofloxacin was detected to be relatively stable during the 6 years, with an average rate of resistance of 78.43% and 63%, respectively, and a low sensitivity rate; the resistance rate to cefotaxime was 40.47%, showing a decreasing trend. In comparison, the average resistance rate to imipenem and ertapenem was less than 1%, with a high sensitivity rate, as shown in Table 3.

Table 1. Primer sequences of genes

Resistance type	Primers	Primer sequences	Fragment size/bp
β -lactam	AmpC	F:TCAGCCTGCTGCACTTAGCCAC R:GTGGATCCC GTTTATGCACCC	198
	<i>bla</i> _{KPC}	F:CGGAACCTGCGGAGTGTATGG R:CGCTGTGCTTGTCATCCTTGTTA	119
	<i>bla</i> _{IMP}	F:AAGAAGTTAACGGGTGGGGC R:CTTTCAGGCAGCCAAACCAC	385
	<i>bla</i> _{VIM}	F:TAGCCGAGGTAGAGGGGAAC R:TGCCTGCTACTCAACGACTG	383
	<i>bla</i> _{NDM}	F:GCATTAGCCGCTGCATTGAT R:TGGCTCATCACGATCATGCT	704
	<i>bla</i> _{OXA}	F:ATTATCGGAATGCCAGCGGT R:GCAGCCCTAAACCATCCGAT	706
	<i>bla</i> _{TEM}	R:CTCGTCGTTTGGTATGGC F:AGGAAGAGTATGATTCAACA	535
	<i>bla</i> _{CTX-M}	F:GCGTTGTTGTTGTTGTTGTTG R:CGTTGTTGTTGTTGTTGTTG	204
	<i>mecA</i>	F:TGAAGTTGTTGTTGTTGTTGTTG R:TTCGTTGTTGTTGTTGTTGTTG	178
aminoglycoside	<i>aph3'-III</i>	F:GATGTTGTTGTTGTTGTTGTTG R:CGTTGTTGTTGTTGTTGTTG	187
	<i>APH(6)-Id</i>	F:ATGCGTTCGTTGCTGTTGTT R:CGTTGCGTTGCTGTTGTTG	185
	<i>aph(3')-III</i>	F:GCTGTTGTTGTTGTTGTTGTTG R:CGTTGTTGTTGTTGTTGTTG	211
	<i>aac(6')-Ib</i>	F:GTTGCTGATGTTGCTGATGTTG R:CGTTGTTGTTGTTGTTGTTG	210
	<i>aac(3')-II</i>	F:ATGCGTTCGTTGCTGATGTTG R:CGTTGTTGTTGTTGTTGTTG	196
quinolone	<i>gyrA</i>	F:CGTACACCGGCTTCAGAATAC R:CTTCGCCCTCTTGTGGCTTTA	154
	<i>parC</i>	F:ATGCGTTCGTTGCTGATGTTG R:CGTTGTTGTTGTTGTTGTTG	195
	<i>fyrA</i>	F:TGGAGAAGGCGGTTGATGTT R:CCGTTGCGTTGCTGTTGTTG	238
macrolide	<i>erm(C)</i>	F:GCGTTGTTGTTGTTGTTGTTG R:CGTTGTTGTTGTTGTTGTTG	140
	<i>erm(A)</i>	F:ATGTTGTTGTTGTTGTTGTTG R:CTTGTTGTTGTTGTTGTTGTTG	219
	<i>mph(E)</i>	F:TGGAGAAGGCGGTTGATGTT R:CCGTTGCGTTGCTGTTGTTG	240
other	<i>cas3</i>	F:TCGACGCTGTTGCTGATGTT R:AGCGTTCGTTGTCGTTGTTG	276
	<i>tetM</i>	F:TTGTTGTTGTTGTTGTTGTTG R:CGTTGTTGTTGTTGTTGTTG	184
	<i>AdeB</i>	R:GTCTTTAAGTGTGCTAAAAGCCAC F:TACCGGTATTACCTTTGCCGGA	729
	<i>OprD</i>	F:TCAGCCTGCTGCACTTAGCCAC R:GTGGATCCC GTTTATGCACCC	213
	<i>sul1</i>	F:ATGCACCGTGTTGATCGACAG R:GAAGGTGACCGGTGCGGGTGGC	206
	<i>ArmA</i>	R:TTATTTCTGAAATCCACTAGTAATTA F:ATGGATAAGAATGATGTTGTTAAG	774
	<i>carO</i>	R:TTACCAGTAGAATTCNACACCAAC F:ATGAAAGTATTACGTGTTTATGACAAC	530
	<i>cfr</i>	F:GCGTTGTTGTTGTTGTTGTTG R:CGTTGTTGTTGTTGTTGTTG	225

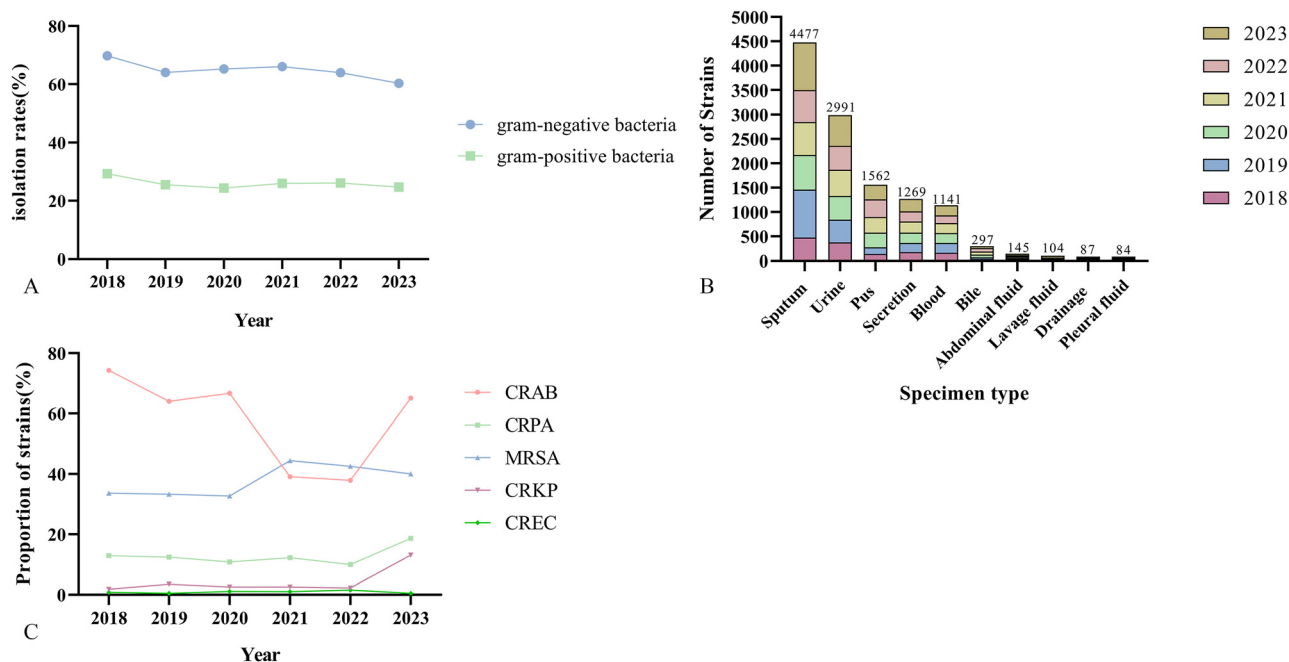


Fig. 1. Distribution of pathogenic bacteria and resistance of multidrug-resistant bacteria, 2018–2023. A: Distribution of gram-negative and gram-positive bacteria, 2018–2023; B: Distribution of bacteria in the top 10 different types of specimens from 2018 to 2023; C: Variation of drug resistance in five surveillance bacteria, 2018–2023

3.2.2. Antibiotic resistance in *K. pneumoniae*. A total of 1,935 strains were isolated from 2018 to 2023, accounting for 13.58% (1,935/14,252) of the total number of bacteria isolated, which ranked No. 3. The average resistance rate of *K. pneumoniae* to cefuroxime detected during the six years was 21.12%, with a high rate of sensitivity and this resistance rate increased year by year, while the average resistance rate to amikacin was only 1.67% with a high rate of sensitivity. There was a significant decrease in the rate of resistance to gentamicin in 2023, from 10.8% in 2019 to 2.8%, with a high rate of sensitivity. The rates of resistance to ceftazidime, piperacillin/tazobactam, cefuroxime, ceftriaxone, and cefepime in 2018 increased from 8.3%, 1%, 16.3%, 10.3, and 3.6%, respectively, to 14.3%, 11.8%, 24.6%, 18.6% and 13.4% in 2023, as shown in Table 4.

3.2.3. Antibiotic resistance in *P. aeruginosa*. A total of 884 strains were isolated and obtained in 2018–2023, accounting for 6.20% (884/14,252) of the total number of bacteria isolated, which ranked No. 3. The resistance rates of *P. aeruginosa* to piperacillin/tazobactam, ceftazidime, imipenem, and levofloxacin were 5.9%, 12.9%, 9.7%, and 19.4%, respectively, in 2018. Its resistance rate to the four drugs increased to 16.1%, 14.8%, 10.9%, and 22.8% in 2023, with a yearly increasing trend to piperacillin/tazobactam. The average resistance rate of *P. aeruginosa* to ciprofloxacin was 19.23% and this resistance rate was decreasing year by year the 6-year average resistance rate to amikacin, tobramycin, and gentamicin did not exceed 5.00%, as shown in Table 5.

3.2.4. Antibiotic resistance in *S. aureus*. A total of 849 strains of *S. aureus* were isolated in 6 years, accounting for

5.96% (849/14,252) of the total number of bacteria isolated, which ranked 4th. *S. aureus* had a high rate of resistance to penicillin G and a low rate of sensitivity, which were maintained at 91.8–94.4% during 2018–2023, respectively; and to ciprofloxacin, which increased from 16.2% to 32.7% in 2018; the resistance rate to vancomycin, linezolid, and rifampicin was low, maintained at 0–0.8%, 0–0.8%, and 0–2%, respectively, during the 6-year period, but the sensitivity rate was high, as shown in Table 6.

3.2.5. Antibiotic resistance in *A. baumannii*. A total of 838 strains were isolated and obtained from 2018 to 2023, which accounted for 5.88% (838/14,252) of the total number of total bacteria isolated and ranked 5th. The average resistance rate of *A. baumannii* to piperacillin/tazobactam detected during the 6 years was 66.12%, which was a low susceptibility rate with an upward trend. While the resistance rate to ceftazidime, cefepime, gentamicin, tobramycin, cephalothin, ciprofloxacin, and levofloxacin decreased from 70.4%, 68.9%, 67.5%, 66.1%, 73.3%, and 66% in 2018 by 65.8%, 64.9%, 50%, 5.3%, 65.1%, and 52%; the detection rate of carbapenemase-resistant *A. baumannii* decreased from 70.6% (in 2018) to 36.8% (in 2021) year and then showed an increasing trend, see Table 7.

3.2.6. Analysis of antibiotic resistance gene detection in 5 main pathogens. The top 5 genes detected within 2,992 *E. coli* strains were: β -lactam resistance genes *bla*_{CTX-M} 1,622, *bla*_{TEM} 1,527, and *bla*_{OXA} 940; aminoglycoside resistance genes *aph*(3')-III 933; and quinolone resistance genes *gyrA* 825. The top 5 resistance genes among 1,935 *K. pneumoniae* strains were: carbapenem resistance gene *bla*_{OXA} 1,104,

Table 2. Distribution of main bacteria isolated from clinical specimens, 2018–2023

viruses	2018 Year (n = 1,704)		2019 Year (n = 2,447)		2020 Year (n = 2,318)		2021 Year (n = 2,584)		2022 Year (n = 2,377)		2023 Year (n = 2,822)		Total (n = 14,252)	
	Strains	Proportion/%	Strains	Proportion/%	Strains	Proportion/%	Strains	Proportion/%	Strains	Proportion/%	Strains	Proportion/%	Strains	Proportion/%
<i>E. coli</i>	367	21.54	409	16.71	541	23.34	580	22.45	516	21.71	579	20.52	2,992	20.99
<i>K. pneumoniae</i>	218	12.79	315	12.87	309	13.33	348	13.47	311	13.08	434	15.38	1,935	13.58
<i>P. aeruginosa</i>	101	5.93	129	5.27	120	5.18	180	6.97	161	6.77	193	6.84	884	6.2
<i>S. aureus</i>	107	6.28	123	5.03	162	6.99	144	5.57	148	6.23	165	5.85	849	5.96
<i>A. baumannii</i>	175	10.27	164	6.7	168	7.25	92	3.56	87	3.66	152	5.39	838	5.88
<i>E. cloacae</i>	47	2.76	38	1.55	61	2.63	82	3.17	74	3.11	61	2.16	363	2.55
<i>S. epidermidis</i>	66	3.87	48	1.96	57	2.46	59	2.28	61	2.57	71	2.52	362	2.54
<i>E. faecalis</i>	52	3.05	56	2.29	61	2.63	60	2.32	59	2.48	65	2.3	353	2.48
<i>S. pneumoniae</i>	36	2.11	95	3.88	43	1.86	28	1.08	17	0.72	43	1.52	262	1.84
<i>S. maltophilia</i>	27	1.58	34	1.39	48	2.07	38	1.47	42	1.77	63	2.23	252	1.77
Other strains	508	29.81	1,036	42.34	748	32.27	973	37.65	901	37.9	996	35.29	5,162	36.22

*bla*_{KPC} 1,017, *bla*_{NDM} 970, and β -lactam resistance gene *TME* 869. The top 5 resistance genes of 884 *P. aeruginosa* strains were: beta-lactam resistance genes *bla*_{OXA} 472, AmpC 463 and *bla*_{VIM} 327, quinolone *parC* 413, and efflux pumping system *OprD* 306. The top 5 resistance genes of 838 *A. baumannii* strains were: aminoglycoside resistance gene *Arm A* 565, β -lactamase resistance genes *TEM* 518 and *cas3* 436, and class D enzyme resistance genes *car O* 217 and *Ade B* 183. The top 5 resistance genes of 849 *S. aureus* strains were: β -lactamase resistance gene *mecA* 521 strains; macrolide resistance genes *erm(C)* 501 strains and *erm(A)* 497 strains; aminoglycoside resistance gene *aph3'-III* 422 strains; and *tetM* 394 strains, as shown in Table 8. However, it is worth noting that the presence of the *gyrA* and *parC* genes does not directly confer resistance to fluoroquinolones.

3.2.7. Main monitoring of changes in antibiotic-resistant bacteria. A total of 1,304 strains of five multidrug-resistant bacteria were detected during the period 2018–2023, including 515, 342, 323, 96, and 28 strains of (carbapenem-resistant *A. baumannii*, CRAB), (carbapenem-resistant *P. aeruginosa*, CRPA), (methicillin-resistant *S. aureus*, MRSA), (carbapenem-resistant *K. pneumoniae*, CRKP), and (carbapenem-resistant *E. coli*, CREC), respectively, with an overall detection rate of 39.49% (515/1,304), 26.23% (342/1,304), 24.77% (323/1,304), 7.36% (96/1,304), and 2.15% (28/1,304), as shown in Table 9. The detection rates of MRSA strains and CRPA strains showed a trend of increasing compared to 2018. The detection rate of CRAB over the 6 years decreased from 74.28% in 2018 to 37.93% in 2022 and increased to 65.13% in 2023, while for CREC the detection rate was lower, see Fig. 1C.

4. DISCUSSION

In recent years, with the widespread use of antimicrobial drugs and the increase of antibiotic-resistant strains, the composition and antibiotic resistance of pathogenic bacteria are constantly changing, especially multi-drug-resistant bacterial outbreaks have been reported one after another, which has brought great challenges to anti-infective treatment [13, 14]. Enterobacteriaceae bacteria are widely distributed and are important pathogens causing human infections. One of the more important problems in the order Enterobacteriaceae is the issue of carbapenem resistance, where strains are often resistant to multiple antimicrobial drugs, and the detection of carbapenem-resistant Enterobacteriaceae (CRE) puts a great deal of pressure on the treatment of this group of bacteria in the community setting [15, 16]. CRE infections have gradually evolved into a global problem since they were first reported in the 1990s, and the mastery of CRE information relies on real-time monitoring in clinical microbiology laboratories [17]. Therefore, regular antibiotic resistance monitoring of clinical isolates in this hospital can provide a timely and comprehensive understanding of the distribution of common clinical strains and trends in antibiotic resistance, which is of great significance

Table 3. Antibiotic resistance and susceptibility of *E. coli*

Antibiotic	2018 (<i>n</i> = 367)		2019 (<i>n</i> = 409)		2020 (<i>n</i> = 541)		2021 (<i>n</i> = 580)		2022 (<i>n</i> = 516)		2023 (<i>n</i> = 579)	
	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)
Ampicillin	82.6	15.3	79.7	18.9	77.4	20.1	80.8	16.8	73.7	24.4	76.4	20
Piperacillin/tazobactam	0.3	96.8	1.2	97.6	0.4	97.5	0.8	98.2	1.3	96.4	1.9	96.3
Cefuroxime	50.6	44.3	49.4	43.8	48.4	46.9	42.9	49.7	43.5	50.2	41.2	48.8
Ceftazidime	28.1	68	17.3	80.5	13	86.1	16.8	81.8	13.5	85.7	19	76.1
Ceftriaxone	46.4	53	46.6	53.4	38.3	61.6	41.9	57.7	34	65	35.6	64
Cefotaxime	46.2	50.3	45.2	51.7	42.4	55.6	42.8	57.5	40.1	58.4	38.2	60.2
Cefepime	11.1	83.3	9.4	85.7	6.3	85.8	9.3	83.7	6.6	87.2	14.4	77
Cefoperazone/sulbactam	7.1	91.2	5.4	90.2	4.8	92.4	5.1	91.9	4.5	92.4	5	93.1
Aztreonam	32.7	64.6	28.8	70.5	22.2	77.4	27.3	72	19.2	80.4	23.4	76.4
Cefotetan	1.5	97.1	0.7	98.1	1.3	97.6	2.2	97.2	1.7	96.6	2	96.9
Imipenem	0.9	97.9	0.5	99.3	0.4	99.5	0.2	99.7	0.8	99.1	0.3	99.3
Ertapenem	0.6	99.4	0.5	99.5	0.9	98.7	1	98.8	1.1	98.1	0	99.7
Amikacin	2.6	97.4	1.5	98.3	0.5	99.1	1.7	98.2	0.9	98.7	0.3	99.3
Gentamicin	36.4	63.3	37.8	61	30.8	68.6	33.3	65.4	31.9	67	32.2	66.1
Tobramycin	10.5	64.6	7.5	64.2	5.4	72.1	9.2	65.1	6.8	66.9	5.6	67.9
Ciprofloxacin	66.9	23.5	63.1	31.6	61.4	31.2	66.1	25.6	59.1	31.5	61.4	27.1
Levofloxacin	54.4	12.6	53	17.4	50.5	17.6	55.2	9.7	51.7	15.2	50.8	14.9
Cotrimoxazole	51.9	44	51.1	48.7	46.9	52.9	50.1	49.9	44.2	55.8	47.2	52.8

Table 4. Antibiotic resistance and susceptibility of *K. pneumoniae*

Antibiotic	2018 (<i>n</i> = 218)		2019 (<i>n</i> = 315)		2020 (<i>n</i> = 309)		2021 (<i>n</i> = 348)		2022 (<i>n</i> = 311)		2023 (<i>n</i> = 434)	
	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)
Piperacillin/tazobactam	1.00	98.50	4.80	93.70	3.20	95.60	2.80	95.80	3.40	93.40	11.80	86.30
Ceftazidime	8.30	89.80	8.30	89.50	7.00	91.80	8.20	90.40	6.30	91.50	14.30	83.40
Cefuroxime	16.30	80.40	19.10	79.80	20.90	77.60	22.70	74.30	23.10	72.50	24.60	71.60
Ceftriaxone	10.80	89.20	16.80	82.50	14.20	85.80	15.40	84.40	13.20	86.50	18.60	81.00
Cefepime	3.40	95.10	5.10	93.00	5.10	93.40	5.60	93.60	3.10	96.20	13.40	85.50
Cefoperazone sulbactam	0.40	98.20	1.10	97.20	1.50	97.10	2.90	96.00	2.80	96.20	3.60	95.40
Cefotetan	1.50	98.00	3.80	94.90	3.20	96.50	3.40	96.10	2.80	96.60	10.30	89.20
Aztreonam	10.40	89.60	12.10	87.90	10.80	89.20	11.50	88.50	7.80	92.20	15.70	83.90
Imipenem	0.50	97.10	2.90	96.20	2.20	95.90	2.50	97.20	2.50	96.20	10.60	87.80
Ertapenem	0.50	99.00	4.10	95.20	4.10	95.90	3.10	96.60	3.40	95.90	13.10	86.90
Amikacin	1.00	99.00	1.90	98.10	1.60	98.40	2.50	97.20	2.50	97.50	0.50	99.50
Gentamicin	6.30	92.70	10.80	88.90	7.60	91.50	9.80	89.70	8.20	90.90	2.80	97.20
Tobramycin	3.40	93.10	4.10	89.20	2.80	89.90	4.50	87.40	50	90.60	4.10	91.70
Sulfamethoxazole	17.20	82.80	23.50	76.50	17.70	82.30	17.90	82.10	16.30	83.70	22.40	77.60

Table 5. Antibiotic resistance and susceptibility of *P. aeruginosa*

Antibiotic	2018 (<i>n</i> = 101)		2019 (<i>n</i> = 129)		2020 (<i>n</i> = 120)		2021 (<i>n</i> = 180)		2022 (<i>n</i> = 161)		2023 (<i>n</i> = 193)	
	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)
Piperacillin	14.60	67.10	11.10	70.50	10.70	72.10	9.80	74.40	9.10	75.20	7.10	78.60
Piperacillin/tazobactam	5.90	83.30	6.10	80.30	8.30	86.70	10.00	80.50	11.20	85.40	16.10	73.10
Ceftazidime	12.90	82.80	7.40	85.90	10.50	83.90	15.20	81.20	5.60	86.70	14.80	77.80
Cefepime	12.90	83.90	9.50	87.60	6.80	89.40	6.20	89.60	2.70	94.00	7.90	85.10
Cefoperazone/sulbactam	7.10	89.30	6.80	89.10	6.30	88.90	5.60	89.60	4.40	90.50	3.10	92.30
Imipenem	9.70	78.50	8.50	79.80	8.90	87.10	7.90	91.10	8.10	89.40	10.90	83.20
Amikacin	4.20	94.80	1.50	97.10	4.70	93.80	2.10	96.40	0.60	99.40	1.90	97.10
Gentamicin	9.80	88.00	3.70	91.90	2.30	96.20	3.60	94.30	1.60	97.30	1.00	94.90
Tobramycin	8.50	90.40	2.20	97.10	1.50	96.90	2.60	95.80	1.10	98.30	1.90	98.10
Ciprofloxacin	26.60	70.20	21.60	71.60	17.20	77.30	13.50	82.80	16.20	78.80	20.30	73.40
Levofloxacin	19.40	66.70	16.10	73.70	13.10	75.40	10.40	78.10	14.90	75.70	22.80	71.40

Table 6. Antibiotic resistance and susceptibility of *S. aureus*

Antibiotic	2018 (n = 107)		2019 (n = 123)		2020 (n = 162)		2021 (n = 144)		2022 (n = 148)		2023 (n = 165)	
	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)
Penicillin G	91.80	8.20	94.30	5.70	94.20	5.80	94.20	5.80	94.40	5.60	92.50	7.50
Oxacillin	34.00	66.00	33.60	66.40	32.10	67.90	44.60	55.40	41.50	58.50	40.70	59.30
Gentamicin	6.10	93.90	4.90	92.70	5.50	92.70	10.80	89.20	3.40	94.60	3.10	96.30
Vancomycin	0.00	100.00	0.80	98.40	0.00	100.00	0.70	97.30	0.00	98.00	0.00	100.00
Linezolid	0.00	100.00	0.80	99.20	0.00	100.00	0.00	100.00	0.00	100.00	0.00	100.00
Erythromycin	60.80	39.20	56.90	43.10	62.30	37.00	62.80	36.50	52.80	47.20	52.80	46.00
Clindamycin	20.50	69.50	14.80	84.40	16.00	84.00	23.60	73.60	13.90	85.40	12.40	87.60
Rifampicin	0.00	100.00	1.60	97.50	1.80	98.20	0.70	99.30	2.00	97.30	0.60	99.40
Tetracycline	21.80	78.20	19.50	79.70	14.60	83.50	22.30	76.40	20.90	78.40	26.90	72.10
Ciprofloxacin	16.20	78.80	12.20	85.40	17.70	79.90	31.80	66.90	20.30	77.70	32.70	63.50

Table 7. Antibiotic resistance and susceptibility of *A. baumannii*

Antibiotic	2018 (n = 107)		2019 (n = 123)		2020 (n = 162)		2021 (n = 144)		2022 (n = 148)		2023 (n = 165)	
	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)
Piperacillin/tazobactam	68.30	26.80	69.00	25.00	68.30	25.40	55.30	43.90	64.20	34.60	71.60	28.40
Ceftazidime	70.40	25.90	64.10	32.30	64.20	32.40	40.40	53.20	46.60	46.60	65.80	32.20
Cefepime	68.90	28.60	64.90	35.30	64.00	34.90	40.00	56.80	46.60	52.30	64.90	33.80
Imipenem	70.60	28.10	64.10	35.90	63.00	37.00	36.80	63.20	38.60	61.40	63.80	36.20
Gentamicin	67.50	28.80	58.10	37.70	60.10	36.40	37.90	57.90	40.90	56.80	50.00	47.60
Tobramycin	66.10	33.30	58.70	40.70	53.80	43.90	22.10	75.80	10.20	88.60	5.30	93.40
Ciprofloxacin	73.30	26.70	65.90	33.50	63.60	36.40	42.10	53.60	43.20	56.80	65.10	34.20
Levofloxacin	66.00	26.50	62.30	34.70	60.70	37.00	27.40	60.00	12.50	59.10	52.00	36.80
Piperacillin/tazobactam	68.30	26.80	69.00	25.00	68.30	25.40	55.30	43.90	64.20	34.60	71.60	28.40
Ceftazidime	70.40	25.90	64.10	32.30	64.20	32.40	40.40	53.20	46.60	46.60	65.80	32.20

in guiding the rational use of antimicrobial drugs, reducing the spread of drug-resistant bacteria, and preventing and controlling nosocomial infections.

In this study, a total of 14,252 clinical non-duplicate strains were collected from a hospital in Jiangsu Province from 2018 to 2023, and the main source specimen types were sputum, urine, secretions, blood, and pus, among which sputum samples were the most common, similar to those reported by Hu Fupin [18]. The top 5 bacteria were *E. coli* (20.99%), *K. pneumoniae* (13.58%), *P. aeruginosa* (6.20%), *S. aureus* (5.96%), and *A. baumannii* (5.88%), which was detected at a higher rate in the present study as compared with that reported by Yang Dan [19] et al. in 2021, which suggests that there is a distribution of clinically pathogenic bacteria with regional differences. Currently, ESBL-producing and carbapenemases remain the most important resistance mechanisms in gram-negative bacilli, especially in Enterobacteriaceae. Although routine laboratory testing for ESBL in *E. coli*, *K. pneumoniae*, and *Proteus mirabilis* is no longer required by CLSI, the resistance rate of these cells to ceftriaxone or cefotaxime can be used as a substitute for this indicator. *E. coli* and *K. pneumoniae* are among the most frequently isolated CREs in China. *E. coli* is a common pathogenic bacterium that predisposes some immunocompromised patients to develop a variety of diseases such as intestinal infections, urinary tract infections, and bloodstream infections. Currently, the most clinically

significant antibiotic resistance mechanisms in *E. coli* are the production of extended-spectrum beta-lactamases (ESBLs) cephalosporinases (AmpC type beta-lactamases), and carbapenemases (e.g. metallo-beta-lactamases) [20]. The results of this study showed that the average resistance rate of *E. coli* to cefuroxime, cefotaxime, and ceftriaxone was higher than 40%, while the average resistance rate of *K. pneumoniae* to cefuroxime was 21.12%, but the resistance rate of *K. pneumoniae* to imipenem was found to have risen from 0.5% in 2018 to 10.6% in 2023, and the rate of CREC resistance was found to be between 0.49% and 1.55%, which is consistent with the significant increasing trend of resistance rate of *K. pneumoniae* to meropenem and imipenem in recent years reported by CHINET [21], and the same results were obtained from the same kind of resistance study in China [22]. This may be related to the fact that the resistance genes of *E. coli* and *K. pneumoniae* in this hospital are mainly the *bla*_{TEM} and *bla*_{OXA} genes. This type of hyperproducing extended-spectrum β -lactamases *E. coli* can hydrolyze cephalosporin antibiotics, leading to resistance against various cephalosporin antibiotics [23]. Overall, the detection rate of carbapenem-resistant Enterobacteriaceae-subject bacteria in this hospital is lower than the national level, but there is still a need to be vigilant for the growth of CRE, which needs to be monitored with a focus on CRE.

In the present study, non-fermenting bacteria were found to be dominated by *P. aeruginosa* and *A. baumannii*.

Table 8. Analysis of the results of antibiotic resistance gene detection of five pathogenic bacteria

<i>E. coli</i> (n = 2,992)			<i>K. pneumoniae</i> (n = 1,935)			<i>P. aeruginosa</i> (n = 884)			<i>A. baumannii</i> (n = 838)			<i>S. aureus</i> (n = 849)		
Genotypes	Strains	Proportion/%	Genotypes	Strains	Proportion/%	Genotypes	Strains	Proportion/%	Genotypes	Strains	Proportion/%	Genotypes	Strains	Proportion/%
<i>bla</i> _{CTX-M}	1,622	54.21	<i>bla</i> _{KPC}	1,017	52.56	<i>AmpC</i>	463	52.38	<i>ArmA</i>	565	67.42	<i>mecA</i>	521	49.59
<i>bla</i> _{TEM}	1,527	51.04	<i>bla</i> _{NDM}	970	50.13	<i>bla</i> _{OXA}	472	53.39	<i>bla</i> _{TEM}	518	61.81	<i>erm</i> (C)	501	61.13
<i>AmpC</i>	601	20.09	<i>bla</i> _{OXA}	1,104	57.05	<i>bla</i> _{IMP}	202	34.62	<i>cas3</i>	436	52.03	<i>tetM</i>	394	46.41
<i>bla</i> _{OXA}	940	31.42	<i>bla</i> _{TEM}	869	44.91	<i>bla</i> _{VIM}	327	36.99	<i>fyrA</i>	352	42	<i>gvrA</i>	319	37.57
<i>aph</i> (3')-III	933	31.18	<i>AmpC</i>	791	40.88	<i>aph</i> 3'-III	192	21.72	<i>aph</i> (6')-Id	95	11.34	<i>erm</i> (A)	497	58.54
<i>aac</i> (3)-II	413	13.8	<i>aph</i> 3'-III	716	37	<i>aac</i> (6')-Ib	207	23.42	<i>carO</i>	217	25.89	<i>aph</i> 3'-III	422	49.71
<i>parC</i>	754	25.2	<i>sulI</i>	504	26.05	<i>parC</i>	413	46.72	<i>AdeB</i>	183	21.84	<i>cfr</i>	326	38.4
<i>gvrA</i>	825	27.57	<i>sulI</i>	—	—	<i>OprD</i>	306	22.85	<i>mph</i> (E)	102	12.17	—	—	—
<i>sulI</i>	554	18.52	—	—	—	—	—	—	—	—	—	—	—	—

Table 9. Detection of 5 multidrug resistant bacteria and their composition ratio

Multidrug-resistant bacteria	Strains (n = 1,304)	Proportion (%)
MDR-AB	515	39.49
MDR-PA	342	26.23
MRSA	323	24.77
CRKP	96	7.36
CREC	28	2.15

The main mechanisms of resistance in *P. aeruginosa* are low outer membrane permeability, active efflux pumps, antimicrobial drug catabolic enzymes, acquired resistance, adaptive resistance, and biofilm-mediated resistance [24]. *P. aeruginosa* was resistant to all antimicrobials monitored below 27.00%, with the highest resistance rate to ciprofloxacin at 19.23% and a higher sensitivity rate, which may be related to the fact that ciprofloxacin is preferred for treatment in clinical therapy. The resistance rate of *P. aeruginosa* to imipenem decreased slightly and was lower than the 2023 national surveillance data [25]. Among all the drugs tested, *P. aeruginosa* had the lowest resistance rate to amikacin, followed by tobramycin and gentamicin, both of which were below 10.00%, but carbapenem *P. aeruginosa* was detected in more than 25% of cases. *A. baumannii* is one of the most common pathogens in hospital-acquired infections, and due to the widespread use of antimicrobial drugs in hospitals, *A. baumannii* has been showing increasing rates of resistance and exhibits multi-drug resistance, making the treatment of *A. baumannii* infections a global problem [26]. Resistance of *A. baumannii* to antimicrobial drugs covers almost all major mechanisms known to date, such as passive production, active efflux pump mechanism, and altered outer membrane permeability. With its broad spectrum of resistance and the existence of multiple resistance mechanisms, resistant strains will choose adaptive survival in an environment where antimicrobial drugs are widely used, increasing the difficulty of clinical treatment [27, 28]. In this study, the resistance rate of *A. baumannii* to antimicrobial drugs was found to be higher than 50% for piperacillin/tazobactam, ciprofloxacin, ceftazidime, cefepime, imipenem, and gentamicin, and 36% for tobramycin and levofloxacin, which made the resistance situation very serious. It is suggested that *A. baumannii* has different resistance to different antimicrobial drugs, and it is necessary to use cephalosporins with high resistance to avoid further development of its resistance. The increase of *A. baumannii* resistance may be related to the wide distribution of this bacterium in the hospital environment, which is easy to be detected on the skin of patients and on the surface of objects in the hospital room, which makes the patients susceptible to repeated infections of *A. baumannii*, and increases its antibiotic resistance rate [29]. *A. baumannii* is a conditionally pathogenic bacterium, and clinical treatment should focus on improving patients' immunity, minimizing the use of antimicrobial drugs, and suggesting that hospitals should strengthen the

cleaning and disinfection of the environment in sick areas. The resistance mechanism of *A. baumannii* is extremely complex, and it is associated with the altered membrane permeability and the absence of penicillin-binding proteins, etc. The main mechanism is the carriage of resistance genes by plasmid- or chromosome-encoded β -lactamases [30]. The results of this study showed that 565 strains of the aminoglycoside resistance gene *ArmA*, 518 strains of the β -lactamase class A resistance gene *bla*_{TEM}, 436 strains of *cas3*, 217 strains of the class D enzyme resistance gene *carO*, and 183 strains of *Ade B* were detected in 838 strains of *A. baumannii*, suggesting that the main resistance genes in *A. baumannii* are *ArmA*, *bla*_{TEM}, and *cas3* genes. The gene encoding β -lactamase class A enzyme is located on the sequence of the resistant plasmid transposon *Tnl*, which can bind to the encoding plasmid through its unique sequence and then transfer to other bacteria, leading to the hydrolysis of the third-generation cephalosporins, which is a major factor in the increasing resistance of *A. baumannii* to cephalosporin antimicrobial drugs [31]. The hospital's hydrocarbon-resistant *A. baumannii* detections from 2018 to 2023 showed a brief downward trend from 2021 to 2022, whereas the detection rates of hydrocarbon-resistant *A. baumannii*, hydrocarbon-resistant *A. baumannii*, and hydrocarbon-resistant *K. pneumoniae* all increased markedly after 2022, and this fluctuation in the temporal trend may be related to changes in antibiotic use patterns, hospital enhanced infection control measures, or changes in the external environment. In addition, it is also related to the importance of respiratory disease transmission in the population triggered by the COVID-19 pandemic in the country during the same period.

The detection rate of gram-positive bacteria in this study ranged from 24.38% to 29.52%, with *S. aureus*, *E. faecalis*, and *S. epidermidis* predominating. *S. aureus* is a common clinical pathogen, characterized by multi-drug resistance and strong pathogenicity, which seriously threatens the life safety of patients [32]. The mechanisms of *S. aureus* antibiotic resistance are enhanced efflux pumps, down-regulation of outer membrane permeability, production of drug-degrading enzymes, biofilm-mediated resistance, and alteration of drug-resistant gene transduction and retention cells [33]. The main mechanism of resistance is a penicillin-binding protein produced by the *mecA* gene encoded on the staphylococcal cassette chromosome *mec* (*SCCmec*) removable genetic element, which results in resistance to all penicillins, cephalosporins, and carbapenems and necessitates the selection of antimicrobial agents such as vancomycin or linezolid for treatment [34–36]. In this study, we found that *S. aureus* had a high rate of resistance to penicillin G and erythromycin of the penicillin group, probably because its main resistance gene was the *mecA* gene, and the rate of resistance to benzoxacillin was 37.75%, while the rate of resistance to vancomycin and linezolid was lower, which is basically in line with the relevant reports in China. However, the resistance rate of *S. aureus* to benzoxacillin in our hospital was 37.7%, which may be related to the high use of antibiotics in the past in the patients received. With the

misuse of antibiotics, the drug-resistant ability of *S. aureus* has gradually increased, and even the emergence of the ultra-resistant bacterium MRSA, which has led to a variety of community- and hospital-acquired infections [37]. MRSA is one of the most important pathogens of clinical infections, and community-acquired MRSA is extremely highly virulent, often causing necrotizing fasciitis, pneumonia, and septicemia [38, 39]. The results of this study showed that the MRSA resistance rate in this hospital increased from 33.64% to 40.00% from 2018 to 2023, which may be related to the extensive use of antibiotics by the population during the COVID-19 pandemic, as well as the decline in immunity against bacterial infections and repeated infections, which made MRSA more resistant. Therefore, after detecting the pathogenic bacteria, drug sensitivity tests should be carried out promptly, and antibiotics should be selected according to the test results to effectively kill the pathogenic bacteria and thus reduce the resistance of antibiotic-resistant strains.

In summary, the results of this study showed that the antibiotic resistance situation of clinical isolates in this hospital is still severe, in which the antibiotic resistance rates of CRAB and MRSA are higher and the antibiotic resistance rate of CRPA has a rising trend, suggesting that the hospital should continue to strengthen the prevention and control of nosocomial infections and the related training and learning, in particular, multidrug-resistant bacteria should be given high priority and should also strengthen the rational use of antimicrobial drugs and sensory control measures and do a good job in the monitoring of antibiotic resistance of pathogenic bacteria monitoring. In this study, the distribution characteristics of pathogenic bacteria isolated from a hospital in Jiangsu Province and changes in antibiotic resistance were analyzed in depth to provide a scientific basis for the hospital to provide reasonable and effective infection prevention and control and medication guidance and to reduce the occurrence of antibiotic resistance. However, there are shortcomings in this study, due to the insufficiency of this monitoring data, the data of different genders and ages of outpatients and inpatients were not analyzed in a more detailed stratified statistical analysis, which should be statistically analyzed in future monitoring.

Conflict of interest statement: The authors declare no financial or non-financial conflicts of interest related to this work.

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