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Research Article
Characteristics and Drug Resistance Analysis of Nosocomial Infections with Multidrug-Resistant Bacteria in the Intensive Care Unit

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Abstract

Background and Objective: The Intensive Care Unit (ICU) provides specialized care for critically ill patients with compromised immunity, undergoing invasive treatments and frequently receiving broad-spectrum antibiotics, resulting in a high incidence of multidrug resistance. This study aimed to analyze the characteristics of nosocomial infections with multidrug-resistant bacteria in the ICU and to examine their drug resistance. **Materials and Methods:** A total of 968 patients treated in the ICU of Hospital of Chengdu University of Traditional Chinese Medicine from January, 2021 to December, 2023 were retrospectively selected as the study subjects. The distribution of pathogens in infected cases, changes in major pathogens in different years, antibiotic resistance of major pathogens and changes in drug resistance of major pathogens were analyzed and the differences in drug resistance of major pathogens in different years were compared. **Results:** Among 968 patients, 1244 bacterial strains were cultured. The detection rate of *Klebsiella pneumoniae* showed a decreasing trend over the years, while the detection rate of *Enterococcus faecium* exhibited an increasing trend ($p<0.05$). *Escherichia coli* exhibited the highest resistance to cefazolin, *Klebsiella pneumoniae* showed the highest resistance to ampicillin and *Pseudomonas aeruginosa* had the highest resistance to ceftazidime. **Conclusion:** The pathogens in the ICU are diverse, with *Escherichia coli* and *Enterococcus faecium* being the most prevalent. The antibiotic resistance of these pathogens is concerning and has shown an increasing trend annually. It is recommended to judiciously select antibiotics for treatment in clinical settings.

Key words: Intensive care unit, multidrug-resistant bacteria, nosocomial infection, drug resistance rate, drug resistance change, pathogen distribution

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

In recent years, there have been numerous incidents of nosocomial bacterial infections, with the phenomenon of multidrug resistance becoming increasingly prominent and the emergence of superbugs has even left physicians with no effective treatments available[1]. Nosocomial infections have become a major global public health concern, encompassing a multidisciplinary issue involving hygiene, microbiology, clinical medicine and epidemiology[2]. Modern medical research has confirmed that nosocomial infections not only prolong patients' hospital stays and increase their treatment costs but also significantly elevate mortality rates[3]. In the United States, for instance, the annual incidence of nosocomial infections is approximately 5 to 10%, resulting in additional medical expenses amounting to 17.5 to $35 billion[4]. The Intensive Care Unit (ICU) provides specialized medical care for critically ill patients, who often exhibit compromised immunity upon admission, undergo invasive therapeutic interventions and frequently receive broad-spectrum antibiotics, leading to a high incidence of multidrug-resistant cases[5]. Infection characteristics and drug resistance analysis of multidrug-resistant bacteria in the ICU aids in reducing the incidence of nosocomial infections and provides a basis for the control of nosocomial infections.

The irrational use of antibiotics is a significant factor in the onset of nosocomial infections. Data indicate that prophylactic use of antibiotics accounts for approximately 30-40% of the total antibiotic consumption[6]. Multivariate logistic regression analysis indicates that the risk of nosocomial infections in patients receiving prophylactic antibiotics is approximately 1.98 times higher than in those without prophylactic treatment[7]. The ICU primarily provides specialized medical care for critically ill patients who are often in critical condition upon admission, with rapidly progressing ailments and poor prognoses. Such patients typically exhibit hypoimmunity, necessitating invasive treatments and frequent antibiotic use and they are at risk of colonization by drug-resistant bacteria. Relevant literature indicates that the rate of nosocomial infections in the ICU is 5-10 times higher than in general wards[8,9]. Therefore, it is recommended to implement focused infection surveillance in the ICU. This study was conducted to investigate the characteristics of nosocomial infections with multidrug-resistant bacteria in the ICU and analyze their drug resistance through retrospective analysis, to provide a practical reference for reducing the incidence of nosocomial infections in the ICU, preventing hospital-acquired infection events and controlling the spread of multidrug-resistant bacteria.

MATERIALS AND METHODS

Clinical data: A total of 968 patients treated in the ICU of the Hospital of Chengdu University of Traditional Chinese Medicine from January, 2021 to December, 2023 were retrospectively selected as the study subjects. Among the patients, 628 were male and 340 were female, with a male-to-female ratio of 1.85:1. The ages ranged from 18 to 68 years, with an average age of (55.02±23.65) years. Of these patients, 221 (22.83%) had diabetes, 113 (11.67%) had chronic kidney disease, 103 (10.54%) had prostate diseases and 5 (0.52%) were pregnant.

Ethical consideration: This study has been approved by the Ethics Committee of the Hospital of Chengdu University of Traditional Chinese Medicine. All study participants provided written informed consent before participating in the study.

Inclusion criteria: (1) All subjects underwent pathogen detection during ICU treatment; (2) Age $\geq$18 years and (3) All patients included received bacterial resistance testing in the hospital.

Exclusion criteria: (1) Incomplete clinical data; (2) Sample contamination; (3) Immunodeficient individuals and (4) Recent (within 1 month) use of immunosuppressants.

Detection methods: Specimens from included patients, including sputum, urine, blood, throat swabs, skin tissue and serous cavity fluid, were all isolated and cultured in our hospital's laboratory, strictly adhering to the protocols outlined in the "National Guide to Clinical Laboratory Procedures"[10].

The cultured colonies were analyzed using a fully automated bacterial identification system (referencing the MIC method recommended by the Clinical and Laboratory Standards Institute[11]). The antibiotic susceptibility results were conducted in accordance with CLSI standards[12]. The quality control strains included *Escherichia coli* ATCC25922, *Pseudomonas aeruginosa* ATCC27853, *Klebsiella pneumoniae* ATCC13883, *Enterococcus faecalis* ATCC29212 and *Enterococcus faecium* ATCC35667. The interpretation of antimicrobial susceptibility results followed the CLSI M100-S24 performance standards in 2014[13].

Statistical methods: Data collection for this study was conducted using Excel and statistical analysis was performed with SPSS 26.0. The measurement data (e.g., patients' average age) conformed to a normal distribution and were expressed as Mean±Standard Deviation. Counting data were represented by rates and Chi-square tests were used for intergroup comparisons. The $p<0.05$ indicated statistical significance.

RESULTS

Distribution of common pathogens in infected cases: A total of 1244 bacterial strains were cultured from 968 patients, including 777 Gram-negative bacteria (62.46%) (Fig. 1a) and 467 Gram-positive bacteria (37.54%) (Fig. 1b) and no fungal strains were detected. *Escherichia coli* was the most commonly isolated pathogen among Gram-negative bacteria, accounting for 61.39% (477/777). *Enterococcus faecium* was the most commonly isolated pathogen among Gram-positive bacteria, accounting for 68.74% (321/467). The top three detected strains by proportion were *Escherichia coli* (43.28%), *Enterococcus faecium* (29.13%) and *Klebsiella pneumoniae* (10.07%) (Table 1, Fig. 1).

Analysis of changes in major pathogens: In 2021, 348 strains were detected, in 2022, 405 strains were detected and in 2023, 491 strains were detected. The comparative analysis of the changes in the major pathogens over different years revealed that the detection rate of *Klebsiella pneumoniae*, a Gram-negative bacterium, showed a decreasing trend over the years, with statistically significant differences observed in detection rates in different years ($p<0.05$) (Fig. 2a). The detection rate of *Enterococcus faecium*, a Gram-positive bacterium, exhibited an increasing trend over the years, with statistically significant differences observed in detection rates in different years ($p<0.05$) (Fig. 2b). However, the detection rates of other pathogens in different years did not exhibit statistically significant differences ($p>0.05$) (Table 2, Fig. 2).

Table 1: Distribution of common pathogens in infected cases

Pathogens	Strains (n = 1244)	Proportion of Gram-negative/Gram-positive bacteria (%)	Total proportion (%)
Gram-negative bacteria (n = 777)			
Escherichia coli	477	61.39	43.28
Klebsiella pneumoniae	111	14.29	10.07
Pseudomonas aeruginosa	52	6.69	4.72
Proteus mirabilis	41	5.28	3.72
Enterobacter cloacae	25	3.22	2.27
Enterobacter aerogenes	24	3.09	2.18
Acinetobacter baumannii	20	2.57	1.81
Serratia fonticola	15	1.93	1.36
Burkholderia cepacia	12	1.54	1.09
Enterococcus faecium	321	68.74	29.13
Enterococcus faecalis	53	11.35	4.81
Gram-positive bacteria (n = 467)			
Staphylococcus haemolyticus	42	8.99	3.81
Staphylococcus aureus	25	5.35	2.27
Staphylococcus epidermidis	20	4.28	1.81
Others	6	1.28	0.54

Table 2: Analysis of changes in major pathogens

Pathogens	Year 2021 (n = 348)	Year 2022 (n = 405)	Year 2023 (n = 491)	χ^2	p-value
Gram-negative bacteria					
Escherichia coli	136 (39.08)	156 (38.52)	185 (37.68)	3.485	0.175
Klebsiella pneumoniae	53 (15.23)	40 (9.88)	18 (3.67)	7.014	0.030
Pseudomonas aeruginosa	9 (2.59)	16 (3.95)	27 (5.50)	1.478	0.478
Proteus mirabilis	10 (2.87)	11 (2.72)	20 (4.07)	1.236	0.151
Gram-positive bacteria					
Enterococcus faecium	52 (14.94)	96 (23.70)	173 (35.23)	16.208	0.000
Enterococcus faecalis	15 (4.31)	11 (2.72)	27 (5.50)	1.233	0.540
Staphylococcus haemolyticus	11 (3.16)	9 (2.22)	22 (4.48)	0.639	0.415
Staphylococcus aureus	6 (1.72)	5 (1.23)	14 (2.85)	1.036	0.369

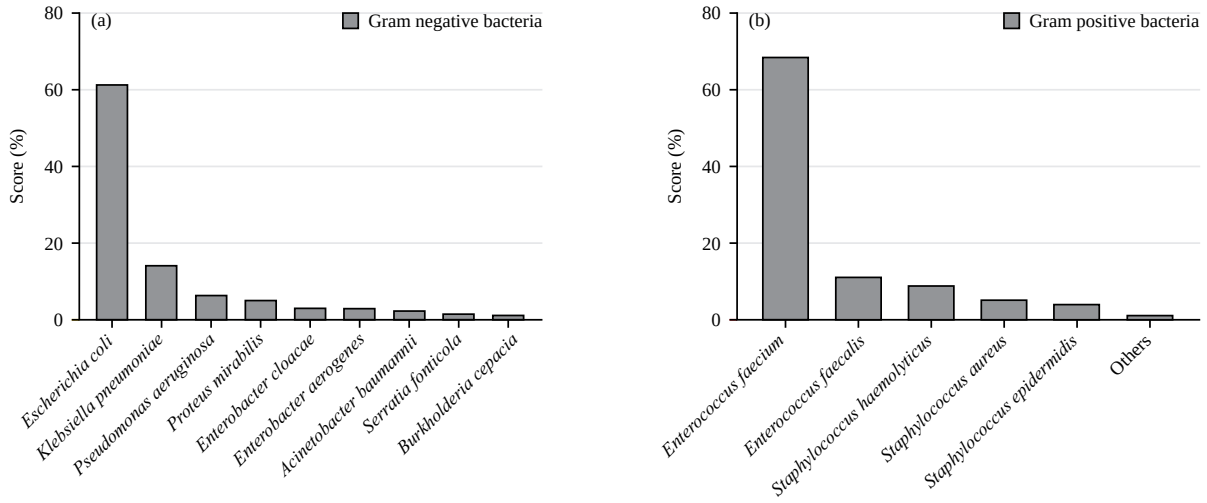

Fig. 1(a-b): Distribution of common pathogens in infected cases, a total of 1244 bacterial strains were detected, including (a) 777 Gram-negative bacteria (62.46%) and (b) 467 Gram-positive bacteria (37.54%)
Top three strains detected were *Escherichia coli* (43.28%), *Enterococcus faecium* (29.13%) and *Klebsiella pneumoniae* (10.07%)

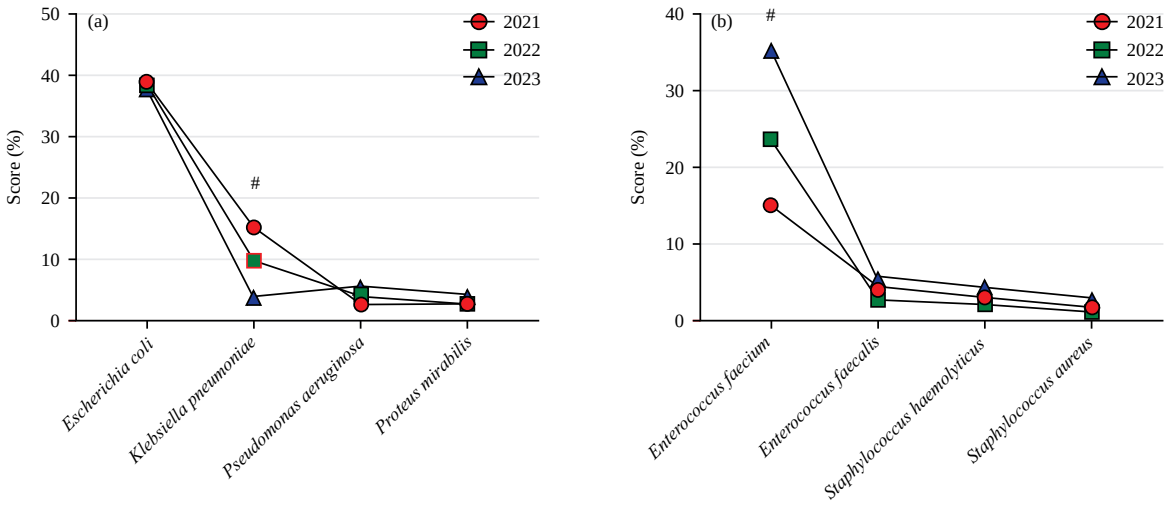

Fig. 2(a-b): Analysis of changes in major pathogens, (a) Detection rate of *Klebsiella pneumoniae*, a Gram-negative bacterium, showed a decreasing trend annually ($p<0.05$), while (b) Detection rate of *Enterococcus faecium*, a Gram-positive bacterium, exhibited an increasing trend annually ($p<0.05$)
[#]Statistically significant difference between groups

Analysis of drug resistance of major pathogens to common antibiotics: Among Gram-negative bacteria, *Escherichia coli* exhibited the highest resistance to cefazolin (90.57%), followed by ampicillin (88.68%), cefuroxime (82.81%) and cefotaxime (75.89%). *Klebsiella pneumoniae* showed the highest resistance to ampicillin (95.50%), followed by cefazolin (89.19%), amoxicillin (77.48%) and cefotaxime (71.17%). *Pseudomonas aeruginosa* demonstrated the highest resistance to ceftazidime (23.08%), followed by cefepime (19.23%), piperacillin (11.54%), meropenem (11.54%) and ciprofloxacin (9.62%) (Table 3, Fig. 3). Among Gram-positive bacteria, *Enterococcus faecium* exhibited 100% resistance to levofloxacin, followed by erythromycin (90.97%), ampicillin (81.31%) and gentamicin (78.78%). *Enterococcus faecalis* showed the highest resistance to erythromycin (75.47%) and gentamicin (73.58%), followed by tetracycline (71.70%), ampicillin (67.92%), penicillin (67.92%) and rifampin (66.04%) (Table 4, Fig. 4).

Analysis of changes in drug resistance of major pathogens: The drug resistance analysis of antibiotics in a common Gram-negative bacterium, *Escherichia coli*, revealed an overall increasing trend from 2021 to 2023, though the resistance rates did not show a statistically significant difference over the three years (p>0.05) (Table 5, Fig 5). Similarly, the major Gram-positive bacterium, *Enterococcus faecium*, displayed an increasing resistance trend over the three years, but the changes were not statistically significant (p>0.05) (Table 6, Fig. 6).

Table 3: Analysis of drug resistance of major Gram-negative bacteria to common antibiotics (%)

	Gram-negative bacteria		
Antibacterial agents	*Escherichia coli*	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*
Ampicillin	88.68	95.50	-
Amoxicillin	73.58	77.48	-
Piperacillin	42.14	35.14	11.54
Ciprofloxacin	63.94	26.13	9.62
Levofloxacin	56.39	27.93	5.77
Cefazolin	90.57	89.19	-
Cefuroxime	82.81	64.86	-
Cefotaxime	75.89	71.17	-
Ceftazidime	58.07	58.56	23.08
Cefepime	68.34	50.45	19.23
Imipenem	-	4.50	-
Meropenem	-	8.11	11.54
Nitrofurantoin	28.51	32.43	-

Table 4: Analysis of drug resistance of major Gram-positive bacteria to common antibiotics (%)

	Gram-positive bacteria	
Antibacterial agents	*Enterococcus faecium*	*Enterococcus faecalis*
Penicillin	77.88	67.92
Ampicillin	81.31	67.92
Piperacillin	44.55	47.17
Ciprofloxacin	48.60	37.74
Levofloxacin	100.00	30.19
Tetracycline	75.70	71.70
Erythromycin	90.97	75.47
Rifampin	70.40	66.04
Gentamicin	78.82	73.58
Vancomycin	0.00	0.00
Teicoplanin	0.00	0.00
Linezolid	0.00	0.00

Table 5: Analysis of changes in drug resistance of major Gram-negative bacterium

	Escherichia coli				
Antibacterial agents	Year 2021	Year 2022	Year 2023	χ^2	p-value
Ampicillin	88.89	82.91	93.98	3.723	0.155
Amoxicillin	68.63	75.32	76.51	3.179	0.204
Piperacillin	40.52	41.14	44.58	1.746	0.418
Ciprofloxacin	62.09	59.49	69.88	4.554	0.103
Levofloxacin	56.86	56.33	56.02	0.312	0.855
Cefazolin	88.89	89.87	92.77	1.75	0.417
Cefuroxime	79.08	78.48	90.36	5.795	0.056
Cefotaxime	75.16	72.78	79.52	2.395	0.302
Ceftazidime	52.94	60.76	60.24	3.26	0.196
Cefepime	65.36	63.92	75.30	5.531	0.063
Imipenem	0.00	0.00	0.00	-	-
Meropenem	0.00	0.00	0.00	-	-
Nitrofurantoin	25.49	27.22	32.53	3.993	0.136

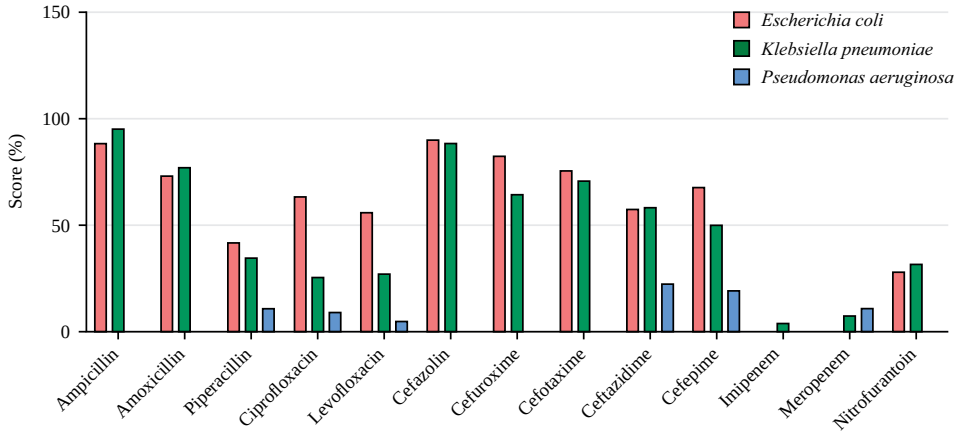

Fig. 3: Analysis of drug resistance of major Gram-negative bacteria to common antibiotics

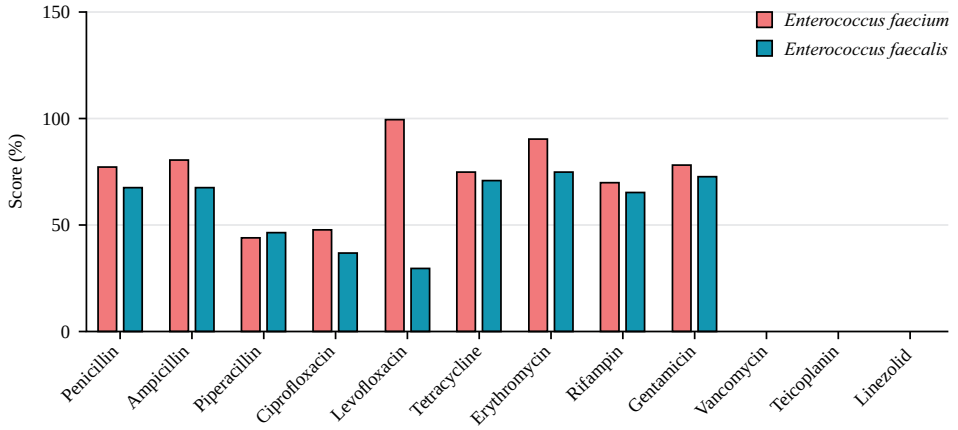

Fig. 4: Analysis of drug resistance of major Gram-positive bacteria to common antibiotics

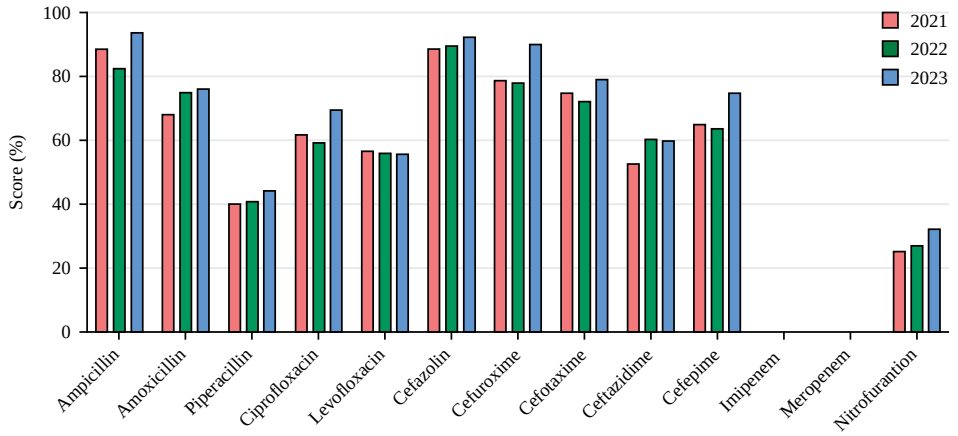

Fig. 5: Analysis of changes in drug resistance of major Gram-negative bacterium

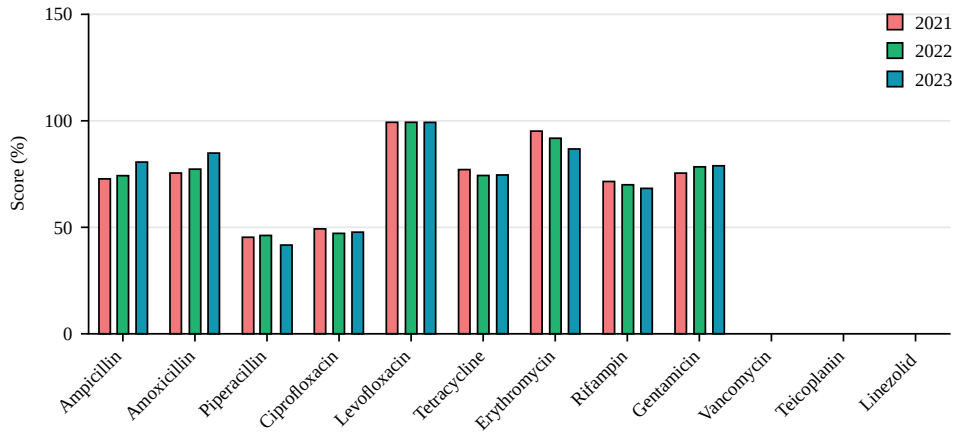

Fig. 6: Analysis of changes in drug resistance of major Gram-positive bacterium

Table 6: Analysis of changes in drug resistance of major Gram-positive bacterium

	Enterococcus faecium				
Antibacterial agents	Year 2021	Year 2022	Year 2023	χ^2	p-value
Penicillin	73.61	75.00	81.70	2.326	0.163
Ampicillin	76.39	78.13	85.62	3.265	0.115
Piperacillin	45.83	46.88	42.48	2.112	0.189
Ciprofloxacin	50.00	47.92	48.37	1.698	0.698
Levofloxacin	100.00	100.00	100.00	-	-
Tetracycline	77.78	77.08	73.86	0.981	0.465
Erythromycin	95.83	92.71	87.58	0.881	0.365
Rifampin	72.22	70.83	69.28	1.036	0.556
Gentamicin	76.39	79.17	79.74	0.669	0.811
Vancomycin	0.00	0.00	0.00	-	-
Teicoplanin	0.00	0.00	0.00	-	-
Linezolid	0.00	0.00	0.00	-	-

DISCUSSION

Critical care medicine is a clinical discipline that studies the onset, progression and treatment methods of life-threatening conditions. The ICU serves as the clinical base for critical care, where patients suffering from single or multiple organ or system dysfunctions, or those with potential high-risk factors, receive essential, appropriate, timely and systematic medical monitoring and treatment; this specialized department within the hospital is dedicated to the centralized monitoring and rescue of critically ill patients[14,15]. The ICU is a specialized area for critically ill patients and a significant site for nosocomial infections. Research indicates that due to its unique environment, host conditions and medical procedures, the ICU is a high-risk place for nosocomial infections[16].

Reports from abroad indicate that the nosocomial infection rate in the ICU for various specialties is approximately 10-30%, significantly exceeding the 6-8% rate in general wards[17]; if patients in the ICU are infected with drug-resistant strains, it can easily lead to severe systemic infections or septic shock, potentially triggering multiple organ dysfunction syndrome and increasing patient mortality rates. The majority of nosocomial infections are caused by bacterial infections, with opportunistic pathogens being the most common. Hospital-acquired microorganisms often exhibit drug resistance, sometimes even multidrug resistance, making anti-infective treatment within hospitals particularly challenging. Currently, extensive research[18,19] suggested significant differences in bacterial resistance between different regions and hospitals and even among different departments within the same hospital. Therefore, understanding the distribution and resistance of multidrug-resistant bacteria is crucial for guiding physicians in the rational use of anti-infective drugs.

This study, which included and analyzed 968 patients in the ICU, found that 1244 strains of pathogens were isolated from the patient samples, including 777 strains of Gram-negative bacteria (62.46%) and 467 strains of Gram-positive bacteria (37.54%) and the most common pathogens identified were *Escherichia coli*(43.28%), *Enterococcus faecium*(29.13%) and *Klebsiella pneumoniae* (10.07%), which was consistent

with the findings of other scholars[20,21]. *Escherichia coli* is the normal flora of intestinal tract, possessing strong adaptability. Its flagella, capsules, siderophores and toxins facilitate adhesion to the patient's mucosa, making it the most prevalent in infections. The analysis of the changes in pathogens in this study indicated a yearly decrease in the detection rate of *Klebsiella pneumoniae*, while the detection rate of *Enterococcus faecium* showed a yearly increase. Other scholars also studied the changes in pathogens, but their findings differed slightly from the results of this study. For instance, Zhou *et al.*[22] analyzed children's blood samples from 2017 to 2021 and isolated a total of 7977 bacterial strains, including 70.7% of Gram-negative bacteria and 29.3% of Gram-positive bacteria, with the most prevalent strains isolated being *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella*, *Staphylococcus aureus* and *Streptococcus pneumoniae*; through comparative analysis, they found that the detection rates of different bacterial genera among enrolled children over five years showed no significant differences. The differences in results may be attributed to factors such as regional environment, dietary habits and the ages of the enrolled individuals.

The study further conducted a detailed analysis of the drug resistance of infectious pathogens and the results revealed that the detected major Gram-negative bacteria, such as *Escherichia coli* and *Klebsiella pneumoniae*, exhibited high resistance to cephalosporin drugs, some even exceeding 90%. This suggests that amoxicillin and cephalosporin drugs are not recommended as commonly used drugs for Gram-negative bacterial infections. Shah *et al.*[23] analyzed 105 patients with urinary tract infections and found that the included patients exhibited higher resistance to ampicillin, co-trimoxazole and norfloxacin and comparatively, those who had formed biofilms demonstrated a significantly greater degree of resistance than those who had not formed them. These research findings aligned with the results presented in this study. The results of this study suggested that imipenem and meropenem exhibited superior efficacy in treating Gram-negative bacteria. However, in actual clinical practice, it is advisable to carefully consider their adverse reactions and economic benefits and it is recommended that they be used only in specific treatments for critically ill patients. It is suggested that piperacillin should be considered as the preferred medication due to its minimal adverse effects, economical pricing and good efficacy against major Gram-negative bacteria[24]. In terms of Gram-positive bacteria, *Enterococcus faecium* exhibited a resistance rate of 100% to levofloxacin and a resistance rate of over 90% to erythromycin (except for 87.58% in 2023). Although the results in this study indicated that the major Gram-positive bacteria showed a resistance rate of 0.00% to vancomycin, teicoplanin and linezolid, due to the potential for these antibiotics to disrupt the body flora, they are not recommended as the preferred medications[25]. Instead, piperacillin and ciprofloxacin exhibited relatively higher therapeutic value and could be considered as preferred medications. Finally, the results of this study regarding the changing trends in bacterial resistance in different years suggested that the resistance of various pathogens changed over time. Although this study did not observe significant differences in different years, this may be attributed to the relatively small sample size and short observation period.

CONCLUSION

The pathogens in the ICU are diverse, with *Escherichia coli* and *Enterococcus faecium* being the most prevalent. The antibiotic resistance of these pathogens is concerning and has shown an increasing trend annually. It is recommended to judiciously select antibiotics for treatment in clinical settings. The present study has certain limitations, such as its retrospective nature, limited sample size confined to a single department and fixed sources. Conducting a multi-center prospective study with a larger sample size would aid in refining the research findings, thus providing additional data references for the clinical treatment of patients in the ICU.

SIGNIFICANCE STATEMENT

This study solves the critical issue of nosocomial infections in the Intensive Care Unit (ICU), focusing on the prevalence and drug resistance patterns of multidrug-resistant bacteria. Through a retrospective analysis of 968 ICU patients, *Escherichia coli* and *Enterococcus faecium* were identified as the most common pathogens, exhibiting significant resistance to multiple antibiotics. The findings suggest the necessity of targeted infection surveillance and prudent antibiotic use to mitigate the incidence of nosocomial infections and control the spread of drug-resistant bacteria, thereby contributing to improved patient outcomes and reduced healthcare costs. This research provides valuable insights for developing strategies to manage and prevent nosocomial infections in critical care settings.

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