Infection and Drug Resistance

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ORIGINAL RESEARCH

Distribution Patterns and Antibiotic Resistance Profiles of Bacterial Pathogens Among Patients with Wound Infections in the Jiaxing Region from 2021 to 2023

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Purpose: To systematically assess the distribution and antimicrobial susceptibility of pathogens in wound infections, and analyze risk factors associated with multidrug resistance (MDR).

Patients and Methods: Retrospectively analyzing Jiaxing-region medical records between January 2021 and December 2023, we identified a cohort of 461 wound infection patients. Cultures were grown on various agars, with bacteria identified via Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry. The antimicrobial susceptibility of the organisms were conducted by VITEK 2 system, Kirby-Bauer disk diffusion method and Epsilometer test. Statistical Package for the Social Sciences (SPSS) version 22 was used for statistical analysis. Multivariable logistic regression models were developed to pinpoint risk factors for multidrug-resistant organism (MDRO) infections and predict occurrences.

Results: From 461 patients, 549 bacterial pathogens were isolated, predominantly consisting of *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Acinetobacter baumannii, Enterobacter cloacae*, and *Enterococcus faecalis*. Vancomycin, linezolid, and tigecycline maintained their efficacy against *Staphylococcus aureus* and *Enterococcus species*, while *Pseudomonas aeruginosa* demonstrated sensitivity to aminoglycosides. Conversely, *Escherichia coli* exhibited high amoxicillin resistance (85.4%). More than half of the isolates were resistant to levofloxacin, ceftriaxone, cotrimoxazole, and gentamicin, with *Acinetobacter baumannii* strains showing considerable resistance (65.8–68.4%) to advanced cephalosporins and carbapenems. Within this group, 58 MDROs were detected, primarily originating from Burn Plastic Surgery, Emergency, and Intensive Care Unit (ICU) departments. Multivariate logistic regression identified hyperglycemia, hypoalbuminemia, surgery, extended hospitalization, and exposure to multiple antibiotic classes as independent risk factors for MDRO wound infections. Based on these findings, a predictive model for MDRO occurrence in wounds was constructed, which had a sensitivity of 0.627, specificity of 0.933, and an Area Under the Curve (AUC) of 0.838.

Conclusion: *Staphylococcus aureus* and *Pseudomonas aeruginosa* dominated in wound infections with differential antibiotic resistance. Independent risk factors included hyperglycemia, hypoalbuminemia, surgery, extended hospitalization, and polyantibiotic use. We urge prioritizing culture, susceptibility tests, and personalized antibiotic strategies to address MDRO risks and improve wound infection management specificity and efficacy.

Keywords: antibiotic resistance, wound infection, pathogenic bacteria, risk factor, prediction model

Introduction

Wound infection is a complex pathology that may manifest either as a rapid onset acute condition, or as a prolonged chronic condition.[1] Wounds present serious health problems in humans. Importantly, if left untreated, wound infections will inevitably result in prolonged treatment durations.[2] The inappropriate use and costs of antibiotics place significant challenges globally and put a heavy burden on the health budget of all countries.[3] The projection for the global wound care market indicates a potential expansion to $18.7 billion by the end of 2027, underpinned by a Compound Annual

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Growth Rate (CAGR) of 6.6% throughout the analytical period extending from 2020 to 2027.[4] Of particular interest, China's segment is predicted to achieve a market size of $4 billion by 2027, reflecting a robust CAGR of 10%.[4] Wound infections are a multidisciplinary challenge which should be diagnosed as early as possible and adequately treated.[2]

Wound infections frequently arise from the ingress of bacterial pathogens into skin breaches from either other body sites or environmental sources, with the potential for involvement of adjacent tissue depending on the specific pathogen type. Once established, these pathogens survive and multiply within the necrotic and devitalized tissues of the wound, exacerbating and disseminating the infection.[5,6] Notable bacterial species commonly implicated in wound infections include *Pseudomonas aeruginosa (P. aeruginosa), Staphylococcus aureus (S. aureus), Klebsiella pneumoniae*, and *Acinetobacter baumannii (A. baumannii)*.[7,8] A variety of antibiotics, such as carbapenems, aminoglycosides, colistin, and β-lactam/β-lactamase inhibitors, have been employed to mitigate bacterial wound infections.[9] However, prolonged antibiotic usage can lead to both minor and severe complications, including diarrhea, the development of antibiotic resistance, and potentially lethal leukopenia. The emergence of multidrug-resistant (MDR) bacteria further complicates wound management.[10] These infections could progress into life-threatening diseases if not treated quickly and efficiently, especially in developing countries. The recent update of the World Health Organization's (WHO) 2024 Bacterial Priority Pathogens List (BPPL) highlights the escalating global health threat posed by multidrug-resistant organisms (MDROs), particularly carbapenem-resistant *Acinetobacter baumannii* and *Enterobacterales*, which are frequently implicated in wound infections.[11] These pathogens, with their tenacious resistance to standard treatments and high transmissibility within healthcare environments, underscore the pressing need for enhanced clinical attention. Thus, comprehensively understanding the risk factors associated with MDRO-infected wounds is vital, as these organisms can evade preventative measures and pose significant challenges to healthcare institutions. Therefore, it is crucial to regularly investigate the microbial pathogens that cause wound infections and assess their susceptibility to antibiotics and understand the risk factors of multidrug-resistant infection in wounds.

There are many reports in the literature describing the distribution and resistance of pathogenic bacteria in wound infections.[12–15] However, due to the influence of research population, regional differences and other related factors, the distribution and drug resistance of wound infection pathogens reported in different regions are also different. In the Jiaxing region, the pathogen spectrum and drug resistance analysis of wound infection have not been comprehensively studied in recent years. The First Hospital of Jiaxing, situated in Nanhu District, Jiaxing City, Zhejiang Province, stands as the largest comprehensive medical institution in Jiaxing. It boasts a comprehensive structure comprising 35 clinical departments, 15 medical technology divisions, and a dedicated infection control unit responsible for overseeing and managing hospital-acquired infections. These cases encompass the city of Jiaxing and its surrounding areas, rendering it a pivotal site for investigating the microbiological characteristics of wound infections and the risk factors for multidrug-resistant organisms in this region.

Accordingly, the primary objective of this investigation was to systematically analyze the distribution patterns and antibiotic susceptibility profiles of pathogenic bacteria isolated from wound cultures obtained from patients at our institution between January 2021 and December 2023. This endeavor sought to furnish empirical evidence that would inform strategies for the prevention and management of wound infections, promote the judicious use of antibiotics, and thereby serve as a foundation for formulating evidence-based recommendations for empirical antibiotic therapy regimens tailored to our local context.

Materials and Methods

Sample Collection and Data Recording

This retrospective study utilized routine wound culture data collected from inpatients at Jiaxing First Hospital between January 2021 and December 2023. A total of 461 patients' wound specimens were subjected to bacterial culture, and subsequent identification and antimicrobial susceptibility testing were performed on the isolated microorganisms. Comprehensive patient data were systematically recorded, encompassing both general clinical data and laboratory data. The data was downloaded from the Haiti Electronic Medical Record System, which is consistently updated in real-time by physicians and nurses at the First Hospital of Jiaxing adhering to standardized protocols, for the purpose of

maintaining accurate patient medical records. General clinical data included the patient's name (anonymized for privacy), gender, age, hospital department, comorbidities, previous medical history, and primary diagnosis. Laboratory data encompassed drug susceptibility profiles, antibiotic resistance patterns, and detailed culture outcomes.

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: (1) patients diagnosed with skin wound infections; (2) positive microbial cultures obtained from wound samples; and (3) availability of complete clinical records. Exclusion criteria comprised: (1) duplicate bacterial strains isolated from the same patient within the study period; and (2) bacterial culture results that could not definitively exclude contamination or cases lacking documented microbial drug sensitivity tests.

Patient Classification

Based on the results of microbial culture and antimicrobial susceptibility testing, patients were categorized into two groups: (i) the MDRO (Multidrug-Resistant Organism) group, comprising patients with infections caused by MDROs; and (ii) the NMDRO (Non-Multidrug-Resistant Organism) group, consisting of patients without MDRO infections. Notably, when both drug-resistant and susceptible bacteria were concurrently isolated from a single patient, such patients were assigned to the MDRO group.

Bacterial Culture

Each sample was cultivated using uniform and standardized microbiological techniques, including specimen collection, specimen transport, specimen acceptability, MALDI-TOF, antimicrobial susceptibility testing, quality assurance, quality control and laboratory records.[16] The process involved cleansing the wound with sterile saline, followed by gentle swabbing of the secretion using a sterile cotton swab, which was then placed into a disposable sterile container. These samples were promptly transported to the microbiology laboratory of our clinical facility within one hour post-collection. Then, the samples were inoculated onto blood agar plates, MacConkey agar plates and nalidixic acid cetrimide (NAC) agar plates. McConkey agar plate is a weakly selective medium used for the isolation and culture of enteric pathogens and the identification of non-fermenting bacteria, including *Pseudomonas* and *Acinetobacter*. NAC agar plate is used for the isolation and culture of *Pseudomonas aeruginosa*. The plates were incubated aerobically at 35°C for 18–24 hours until the size and shape of the colonies were observed. Based on the difference in colonies morphology and color, single colonies were picked and inoculated separately onto blood agar plates using sterile inoculation loops for isolation and purification.

Bacteria Identification and Antimicrobial Susceptibility Testing

Isolated bacterial strains underwent identification and antimicrobial susceptibility assessment through conventional and standardized microbiological protocols. Microbial identification was carried out using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF), while the VITEK 2 system was employed for the drug sensitivity assays using AST-GN13/GP67 cards. Some drugs were not included in the VITEK 2 system, and some drug susceptibility results were inaccurate by VITEK 2 system. This was further complemented by the Kirby-Bauer disk diffusion method and the Epsilometer test (E-test) as needed. The following drugs were tested for susceptibility: penicillin G, oxacillin, ampicillin, streptomycin, gentamicin, vancomycin, linezolid, tigecycline, tetracycline, erythromycin, levofloxacin, moxifloxacin, clindamycin, quinupuddin/dafupudin, amoxicillin-clavulanic acid, cefoperazone/sulbactam, piperacillin/tazobactam, amikacin, tobramycin, meropenem, imipenem, ciprofloxacin, compound sulfamethoxazole, aztreonam, ceftriaxone, ceftazidime, cefepime. For *Enterobacteriaceae* in general, such as *Escherichia coli*, we added ampicillin, gentamicin, cefazolin, aztreonam, ampicillin/sulbactam, meropenem for susceptibility using the Kirby-Bauer disk diffusion method. If the results done for *Enterococcus* on the VITEK 2 system were vancomycin or linezolid resistant, then we had to review them with the E-test, because vancomycin or linezolid resistance in *Enterococcus* was very rare. The interpretation of antimicrobial susceptibility testing data was conducted according to Clinical and Laboratory Standards Institute (CLSI) guidelines. According to the CLSI criteria, the antibiotic susceptibility reports were classified into three distinct categories: susceptible (S), intermediate (I), and

resistant (R). To ensure the reliability and accuracy of these tests, the Shanghai Clinical Laboratory Center provided the following quality control strains: *Escherichia coli* ATCC25922, *Staphylococcus aureus* ATCC25923, *Pseudomonas aeruginosa* ATCC27853, *Enterococcus faecalis* ATCC700327, and *Klebsiella pneumoniae* ATCC700324. After all the assays were completed, the bacterial isolates would be stored at −80 °C in cryopreservative solution.

Statistical Analysis

Multidrug-resistance (MDR) specifically refers to bacteria or other microorganisms that have acquired (as opposed to innate) resistance to at least one agent within three or more different classes of antibiotics.[17] The analysis of the antimicrobial susceptibility test results was conducted using WHONET 5.6 software, developed by the World Health Organization (WHO), Geneva, Switzerland. Statistical analyses were performed using IBM SPSS Statistics 22.0 (IBM Corp., Chicago, Illinois, USA). Clinical data had been downloaded from the Haiti Electronic Medical Record System, from which potential risk factor data were subsequently identified and compiled. To assess the normality of the data, the Shapiro–Wilk test was applied. Continuous variables that conformed to a normal distribution were expressed as mean ± standard deviation (SD) and analyzed using independent sample *t*-tests for intergroup comparisons, such as hemoglobin at admission. Non-normally distributed continuous variables were presented as median (interquartile range, Q1–Q3) and compared between groups using the non-parametric Mann–Whitney *U*-test, such as hospital stays. Categorical data, such as gender, age, and hypertension, were expressed as counts and compared between groups via chi-square (χ^2) tests, continuity correction chi-square tests, or Fisher's exact probability method. For multivariate analysis, variables showing a significance level of $P < 0.10$ in the univariate analysis were entered into a binary logistic regression model to capture the maximum number of potential influential factors. Subsequently, based on the β coefficients, odds ratios (ORs), and 95% confidence intervals (CIs) associated with each factor included in the regression model, a risk prediction model was mathematically derived. Lastly, the discriminatory capability of this predictive model was assessed using the Receiver Operating Characteristic (ROC) curve, with an area under the curve (AUC) indicating its discriminative power. Throughout all statistical assessments, a significance threshold was set at $p < 0.05$.

Results

Pathogenic Characteristics of Patients with Wound Infections

In total, 549 strains of pathogenic bacteria were isolated from 461 patients, among which 396 cases (84.8%) were infected by a single bacterial strain and 71 cases (15.2%) had mixed bacterial infections. As detailed in Table 1, *S. aureus* emerged as the most prevalent pathogen, being detected in 92 strains (16.8%). Following *S. aureus*, the pathogens ranking next in frequency were *P. aeruginosa, Escherichia coli (E. coil)*, and *A. baumannii*. Among the Gram-positive cocci, *S. aureus* was the most common, trailed by *Enterococcus faecalis* (*E. faecalis)* and other *Enterococcus* species, contributing to 16.8%, 5.3%, and 2.4% of the isolates respectively. As for the Gram-negative bacilli, *P. aeruginosa, E. coil*, and *A. baumannii* dominated, representing 10.0%, 7.5%, and 6.9% of the total isolates respectively. The distribution and proportions of these pathogenic microorganisms derived from wound culture samples are comprehensively illustrated in Table 1.

Among the 549 pathogenic bacterial isolates, 58 (10.6%) were identified as MDROs. These MDROs comprised 35 strains of Gram-negative bacilli, making up 60.3% of the total MDROs, while 23 strains were Gram-positive cocci, representing 39.7% of the MDROs. Among the Gram-negative bacilli, carbapenem-resistant *Acinetobacter baumannii* (CRAB) was the most prevalent, with 26 strains detected, and methicillin-resistant *Staphylococcus aureus* (MRSA) was the predominant Gram-positive cocci species, accounting for 22 strains. As depicted in Figure 1, the comparative analysis of data involving NMDROs over the years 2021 and 2022 revealed that in 2023, the absolute quantities and relative proportions of MDROs reached their lowest point. Notably, the difference in numbers between MDROs and NMDROs was relatively insignificant during 2021 and 2022.

Table 1 Distribution of Main Pathogenic Bacteria Among Patients with Wound Infections from 2021 to 2023

Pathogenic Bacteria	Number of Isolates (Strains)	Composition Ratio (%)
Staphylococcus aureus	92	16.8%
Pseudomonas aeruginosa	55	10.0%
Escherichia coli	41	7.5%
Acinetobacter baumannii	38	6.9%
Enterobacter cloacae	33	6.0%
Enterococcus faecalis	29	5.3%
Corynebacterium striatum	24	4.4%
Klebsiella pneumoniae	23	4.2%
Proteus mirabilis	22	4.0%
Enterococcus faecium	13	2.4%
Proteus vulgaris	10	1.8%
Morgan morganella	8	1.5%
Enterobacter aerogenes	7	1.3%
Candida albicans	6	1.1%
Klebsiella oxytoca	5	0.9%
Serratia marcescens	5	0.9%
Alcaligenes faecalis	4	0.7%
Pseudomonas putida	4	0.7%
Streptococcus agalactiae	4	0.7%
Pseudomonas maltophilia	4	0.7%
Other	122	22.2%
Total	549	100.0%

Antibiotic Resistance Patterns of Pathogens

The resistance rates for various antibiotics among bacterial strains are as follows (Table 2): *S. aureus* exhibited the highest resistance rate to penicillin G at 84.8%, trailed closely by erythromycin (45.7%) and clindamycin (45.2%). In the case of *E. faecalis*, erythromycin had the highest resistance rate at 69.0%, succeeded by a high concentration of gentamicin (37.9%) and high concentration of streptomycin (31.0%). Regarding *Enterococcus faecium (E. faecium)*

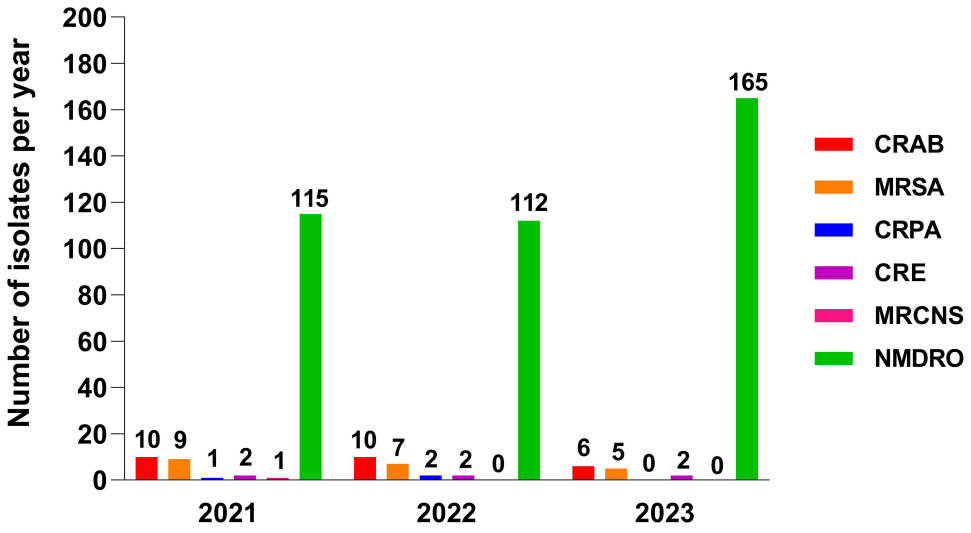

Figure 1 Detection of MDROs and NMDROs from 2021 to 2023 (strains).
Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; CRE, carbapenem-resistant *Enterobacteriaceae*; CRPA, carbapenem-resistant *Pseudomonas Aeruginosa*; MRCNS, methicillin-resistant coagulase-negative *Staphylococci*; NMDRO, non-multidrug-resistant organism.

Table 2 The Resistance Rates of Major Gram-Positive Cocci [Number of Strains (%)]

Antibacterial Drugs	Antibiotics Classes	*S. aureus* (N=92)	*E. faecalis* (N=29)	*E. faecium* (N=13)
Penicillin G	β-Lactams	78 (84.8%)	5 (17.2%)	12 (92.3%)
Oxacillin	β-Lactams	22 (23.9%)	N/A	N/A
Ampicillin	β-Lactams	N/A	0 (0.0%)	12 (92.3%)
High concentration of streptomycin	Aminoglycosides	N/A	9 (31.0%)	7 (53.8%)
High concentration of Gentamicin	Aminoglycosides	N/A	11 (37.9%)	3 (23.1%)
Vancomycin	Glycopeptides	0 (0.0%)	0 (0.0%)	0 (0.0%)
Linezolid	Oxazolidinones	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tigecycline	Glycylcyclines	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tetracycline	Tetracyclines	14 (15.2%)	N/A	N/A
Erythromycin	Macrolides	42 (45.7%)	20 (69.0%)	12 (92.3%)
Levofloxacin	Fluoroquinolones	11 (12.0%)	N/A	N/A
Moxifloxacin	Fluoroquinolones	9 (9.8%)	N/A	N/A
Clindamycin	Lincosamides	37 (40.2%)	N/A	N/A
Quinupuddin/Dafupudin	Streptogramins	0 (0.0%)	N/A	N/A

Abbreviation: N/A, not applicable.

isolates, the antibiotic resistance rates exceeded 90.0% for penicillin G, ampicillin, and erythromycin (Table 2). It is noteworthy that no vancomycin-resistant, linezolid-resistant, or tigecycline-resistant strains were detected among the Gram-positive cocci, including *E. faecium* isolates.

The overall resistance rate of *P. aeruginosa* to the majority of drugs was notably low, with all values being under 10.0% (Table 3). In contrast, *E. coil* displayed substantial resistance, particularly to ampicillin at 85.4%, as well as to levofloxacin, ceftriaxone, cotrimoxazole, and gentamicin, with resistance percentages exceeding 50.0%. However, its resistance to carbapenems, amikacin, piperacillin/tazobactam was relatively low, registering at 2.4% across the board (Table 3). Notably, no strains of *E. coil* exhibited resistance to tigecycline (Table 3). Regarding *A. baumannii*, resistance rates to third-and fourth-generation cephalosporins, along with carbapenems, ranged from 65.8% to 68.4% (Table 3). This pathogen also demonstrated resistance to tigecycline, amikacin, tobramycin, and gentamicin, with individual resistance rates of 18.4%, 21.1%, 42.1%, and 47.4%, respectively (Table 3).

Table 3 The Resistance Rates of Major Gram-Negative Bacilli [Number of Strains (%)]

Antibacterial Drugs	Antibiotics Classes	*P. aeruginosa* (N=55)	*E. coli* (N=41)	*A. baumannii* (N=38)
Ampicillin	β-Lactams	N/A	35 (85.4%)	N/A
Amoxicillin-clavulanic acid	β-lactam/β-lactamase inhibitors	N/A	9 (21.9%)	N/A
Cefoperazone/sulbactam	β-lactam/β-lactamase inhibitors	3 (5.4%)	3 (7.3%)	23 (60.5%)
Piperacillin/tazobactam	β-lactam/β-lactamase inhibitors	3 (5.4%)	1 (2.4%)	22 (57.9%)
Amikacin	Aminoglycosides	0 (0.0%)	1 (2.4%)	8 (21.1%)
Tobramycin	Aminoglycosides	1 (1.8%)	N/A	16 (42.1%)
Gentamicin	Aminoglycosides	2 (3.6%)	21 (51.2%)	18 (47.4%)
Meropenem	Carbapenems	3 (5.4%)	1 (2.4%)	26 (68.4%)
Imipenem	Carbapenems	2 (3.6%)	1 (2.4%)	26 (68.4%)
Ciprofloxacin	Fluoroquinolones	5 (9.0%)	N/A	25 (65.8%)
Levofloxacin	Fluoroquinolones	4 (7.2%)	25 (60.9%)	25 (65.8%)
Compound sulfamethoxazole	Sulfonamides	N/A	22 (53.6%)	21 (55.3%)
Aztreonam	Monobactams	3 (5.4%)	12 (29.2%)	N/A
Ceftriaxone	Third-Generation Cephalosporins	N/A	25 (60.9%)	26 (68.4%)
Ceftazidime	Third-Generation Cephalosporins	4 (7.2%)	9 (21.9%)	26 (68.4%)
Cefepime	Fourth-Generation Cephalosporins	2 (3.6%)	10 (24.4%)	25 (65.8%)
Tigecycline	Glycylcyclines	N/A	0 (0.0%)	7 (18.4%)

Abbreviation: N/A, not applicable.

Table 4 Distribution of MDROs in Different Departments (Number of Strains)

Clinical Department	MRSA	CRAB	CRE	CRPA	MRCNS	Total Quantity
Burn and Plastic Surgery Department	8	6	2	2	0	18
The Emergency Department (Trauma Center)	5	10	1	0	1	17
ICU	0	10	3	0	0	13

Abbreviations: MDRO, multidrug-resistant organism; MRSA, methicillin-resistant *Staphylococcus aureus*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; CRE, carbapenem-resistant *Enterobacteriaceae*; CRPA, carbapenem-resistant *Pseudomonas Aeruginosa*; MRCNS, methicillin-resistant coagulase-negative *Staphylococci.*

MDR wound infections

The distribution of MDROs had been notably prominent in various clinical settings, particularly within the departments of Burn and Plastic Surgery, the Emergency Department (Trauma Centre), and Intensive Care Unit (ICU). In the Burn and Plastic Surgery unit, a total of 18 MDRO isolates were obtained, among which there was an incidence of 8 MRSA strains demonstrating methicillin resistance, 6 CRAB strains showing carbapenem resistance, 2 CRE strains exhibiting carbapenem resistance, and 2 CRPA strains that were also carbapenem-resistant (Table 4). In the Emergency Department's Trauma Centre, 17 MDRO cases were documented, including 10 CRAB isolates, 5 MRSA isolates, a single CRE isolate, and one MRCNS (methicillin-resistant coagulase-negative *Staphylococci*) strain (Table 4). In the ICUs, a total of 13 MDRO isolates were recovered, wherein 10 were CRAB and 3 were CRE (Table 4).

Among the possible causes of MDRO causing wound infections, 41 cases were complicated with surgery, followed by 27 cases with high-energy trauma, 11 cases with diabetes, 8 cases with skin ulcer and 6 cases with infection. Figure 2 presented a heat map that shows the distribution of five different types of MDRO across seven different wound etiologies (surgery, diabetes, high-energy trauma, skin ulcer, infection, burn, pressure, and malignant tumor), CRAB was the most prevalent bacterium overall, with the highest frequency observed in surgery-related wounds. MRSA was also relatively common, particularly in diabetic wounds and infections.

Factors associated with MDR wound infections

According to the Results of microbial culture and drug sensitivity test, they were divided into MDRO group and NMDRO group, with 52 patients and 409 patients respectively. Among the factors influencing the occurrence of MDRO infection, 13 possible factors were analyzed by univariate analysis. The results showed that the days of hospitalization, hemoglobin at admission, hypoproteinemia, surgery, open fracture, trauma and types of antibiotics used were related to the occurrence of MDRO infection of wound ($P < 0.05$), as shown in Table 5.

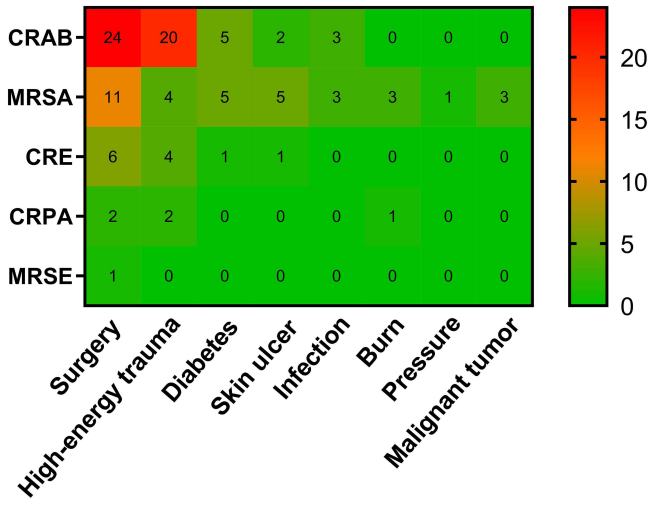

Figure 2 MDROs distribution of different causes (strains). Different colors represent the quantities of various pathogens in wounds of different etiologies.

Table 5 Analysis of Influencing Factors of MDRO Infection of Wound

Characteristics	NMDRO group (N=409)	MDRO group (N=52)	χ2/t/U Value	P-value
Gender				
Male	281	37	0.040	0.841
Female	128	15		
Age				
< 60 year	195	30	1.852	0.174
≥ 60 year	214	22		
Hospital stays(days) [d, M (Q1, Q3)]	15.3 (9.0, 19.0)	30.0 (17.5, 37.5)	4.029	<0.001
Hemoglobin at admission (g/L, Mean ± SD)	120.718±20.930	108.510 ± 27.904	2.992	0.004
Complicated with diabetes				
Yes	51	11	2.290	0.130
No	358	41		
Hypertension				
Yes	92	17	2.094	0.148
No	316	35		
Hypoproteinemia				
Yes	54	28	49.371	<0.001
No	355	24		
Malignant tumor				
Yes	15	3	0.127	0.721
No	394	49		
Surgery				
Yes	145	42	37.440	<0.001
No	264	10		
Open fracture				
Yes	32	15	20.031	<0.001
No	377	37		
Trauma				
Yes	117	28	12.486	<0.001
No	292	24		
Burn				
Yes	21	4	0.195	0.658
No	388	48		
Types of antibiotics used				
1–2	348	22	50.621	<0.001
≥ 3	61	30		

Abbreviations: MDRO, multidrug-resistant organism; NMDRO, non-multidrug-resistant organism.

Multifactorial Analysis of Risk Factors for the Occurrence of MDRO Infection

Multifactorial logistic regression analysis revealed that hyperglycemia, hypoproteinemia, surgery, length of stay, and types of antibiotics used ≥3 were the independent risk factors for MDRO infection in wounds (Table 6).

Establishment of Prediction Model of MDRO Infection in Infected Wounds

Based on the five related factors obtained by LOGISTIC regression equation, the prediction model of MDRO in infected wounds was established. The model formula $Z = 1.492 \times$ hyperglycemia $+ 1.154 \times$ hypoproteinemia $+ 1.279 \times$ surgery $+ 0.031 \times$ length of stay $+ 1.512 \times$ antibiotic use type -4.594, the sensitivity and specificity of predicting MDRO infection were 62.7% and 93.3% respectively, and the AUC was 0.838, as shown in Figure 3.

Table 6 Multivariate Logistic Regression Analysis for the Infection of MDRO

Parameters	β	SE	Wald	OR	95% CI	P-value
Constant term	−4.594	0.451	103.529	0.010	N/A	<0.001
Hyperglycemia	1.492	0.472	10.004	4.448	1.740–11.255	0.002
Hypoproteinemia	1.154	0.400	8.332	3.170	1.455–7.019	0.004
Surgery	1.279	0.447	8.174	3.593	1.524–8.956	0.004
Hospital stays	0.031	0.009	10.344	1.031	1.012–1.051	0.001
Types of antibiotics used ≥ 3	1.512	0.372	16.486	4.535	2.193–9.504	<0.001

Abbreviations: MDRO, multidrug-resistant organism; N/A, not applicable; β, Regression Coefficient; SE, Standard Error; Wald, Wald Statistic; OR, Odds Ratio; 95% CI, 95% Confidence Interval.

Discussion

Wound infections pose a pervasive global public health challenge, as evidenced by numerous studies.[18–20] Within the context of China, the exacerbating demographic shift towards an aging population has resulted in a heightened incidence of wound infections due to the expansive patient pool and the involvement of various high-risk surgeries coupled with a complex and diverse array of pathogens. Such infections frequently engender extended rehabilitation periods, escalated healthcare costs, and potentially life-threatening complications, thereby imposing substantial economic burdens on both individual patients and society at large, as highlighted in research of Cheng B.[21] Gaining insight into the pathogen spectrum and antimicrobial resistance patterns of wound infections constitutes a pivotal step in mitigating their impact within hospital environments, as underscored in the study of Bandy A.[22] It is noteworthy that the pathogen spectrum and antimicrobial resistance profiles of wound infections exhibit regional discrepancies.[12,13] Consequently, to ensure the judicious application of antibiotics and preclude the emergence of drug-resistant strains, it is of utmost importance to comprehensively understand the local distribution of pathogens and the antibiotic resistance characteristics associated with bacterial infections. This knowledge serves as a cornerstone for informed decision-making in clinical practice and strategic planning in infection control.

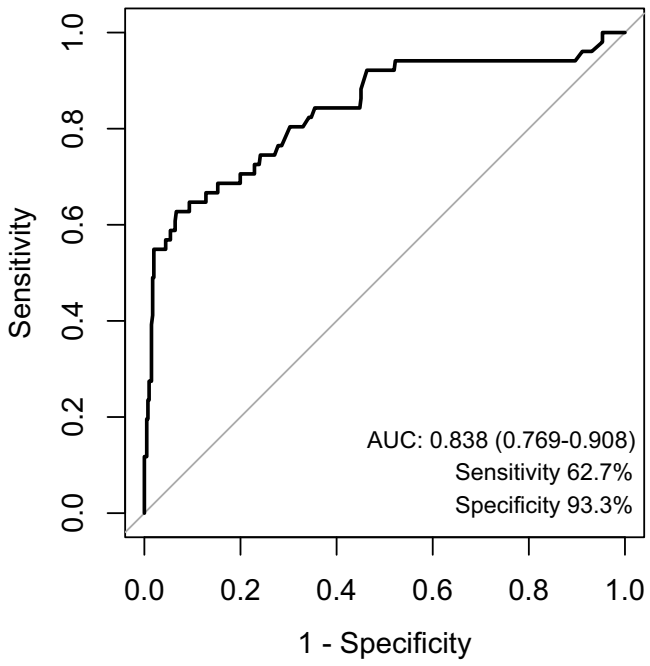

Figure 3 ROC curve for predicting MDRO infection in infected wounds.
Abbreviations: AUC, area under the curve.

This study identified *S. aureus, P. aeruginosa, E. coil, A. baumannii, Enterobacter cloacae*, and *E. faecalis* as the most commonly isolated bacterial species in cases of wound infections. Despite variations in their prevalence rankings compared to earlier research, the prevailing organisms implicated in wound infections demonstrated considerable overlap, indicative of potential influences arising from regional specificities and the institutionally variable pathogenic spectra in wounds across diverse locales.[22]

In the present study, it was found that among Gram-positive cocci causing skin wound infections, *S. aureus* and *Enterococcus* species, predominantly *E. faecalis*, were the principal pathogens, with *S. aureus* accounting for the highest proportion, reaching 16.8%. Due to the widespread colonization of *S. aureus* on the skin, when the skin had a wound, it was more susceptible to skin wound infections.[23] Parallel findings from the studies by Hobbs and Petry also highlighted *S. aureus* as one of the commonly isolated pathogens in skin wound infections.[24,25] An increasing prevalence of antibiotic resistance in *S. aureus* has been observed, particularly in chronic wound infections, potentially due to the formation of biofilms by *S. aureus* within these wounds, which can directly contribute to delayed wound healing.[26] In consonance with the results reported by Guan Haonan, no vancomycin-resistant *S. aureus* (VRSA) strains were detected in this investigation.[13] Furthermore, our study showed that following *S. aureus, E. faecalis* was a significant Gram-positive coccus isolated from wound infection samples. Consistent with the research conducted by Ronni A. G. da Silva, *E. faecalis* was demonstrated to be a prevalent conditionally pathogenic bacterium in skin wounds.[27] The drug susceptibility data presented in Table 2 indicated that *E. faecium* displayed a higher resistance rate compared to *E. faecalis*. This observation is corroborated by a survey from Turkey that also suggested *E. faecium* isolates exhibit greater antibiotic resistance than *E. faecalis*.[28] Referring to existing literature, there has been a consistent annual increase in the incidence of nosocomial infections caused by vancomycin-resistant *Enterococci* (VRE).[29] Nevertheless, in the confines of the current study, no VRE strains were identified, a finding that could be attributed to the inherent limitations of the study design where specimens were exclusively obtained from wound surfaces, thereby potentially excluding other sources of bacterial colonization or infection.

In the course of the present research endeavor, we have identified *P. aeruginosa, E. coil*, and *A. baumannii* as the predominant Gram-negative bacterial species implicated in skin wound infections. Global epidemiological data suggest that *P. aeruginosa* constitutes at least one-third of all skin infection cases, presenting across diverse clinical scenarios including traumatic wounds, pressure ulcers, chronic ulcers, and acantholytic or exudative dermatoses.[30] However, it is noteworthy that contrary findings have been reported by Bandy, who in their respective study identified *E. coil* (accounting for 16.3%) as the major Gram-negative bacterial strain.[22] Antimicrobial susceptibility testing results indicated that *P. aeruginosa* exhibits relatively low resistance rates against several common antibiotics, with specific resistance percentages as follows: levofloxacin at 7.2%, ciprofloxacin at 9.0%, piperacillin/tazobactam at 5.4%, ceftazidime at 7.2%, cefepime at 3.6%, imipenem at 5.4%, and meropenem at 3.6%; none of these antibiotic resistance rates exceed 10%. This observation contrasts with a study from Nigeria, which disclosed that among the 69 isolates of *P. aeruginosa* derived from wound infections, 92.8% were sensitive to imipenem, yet displayed resistance to other frequently employed antibiotics.[31] In this scholarly investigation, it was ascertained that the resistance rates of *E. coil* towards ampicillin stood at 85.4%, levofloxacin at 60.9%, and ceftriaxone also at 60.9%, all indicating notably elevated levels of resistance. Conversely, the resistance rates to amikacin, meropenem, imipenem, and piperacillin/tazobactam were relatively low, each measuring below 3.0%. Previous literature has demonstrated that gram-negative bacilli generally exhibit heightened susceptibility to amikacin and imipenem.[13,32] However, in this study, *A. baumannii* exhibited resistance rates of 21.1% and 68.4% to amikacin and imipenem, respectively, which were notably higher than those reported in a Shanghai-based study.[13] *A. baumannii* manifested severe multidrug resistance, with the exception of amikacin (21.1%) and tigecycline (18.4%). The organism displayed significantly high resistance rates against gentamicin (47.7%), ciprofloxacin (65.8%), levofloxacin (65.8%), ceftazidime (68.4%), cefepime (65.8%), and carbapenems (68.4%). These findings suggestively urge clinicians to diligently consider the outcomes of microbial culture and drug susceptibility testing when managing infections caused by various pathogenic bacteria. They further underscore the importance of minimizing the excessive use of empirical antibacterial agents to mitigate the development and spread of antimicrobial resistance.[33]

Gratifyingly, Figure 1 illustrated that the detected prevalence of multidrug resistance in 2023 has been notably reduced compared to those observed in 2021 and 2022. This downtrend could potentially be attributed to the substantial progress achieved by our institution through the diligent implementation of the national policy advocating the rational usage of antibacterial drugs in clinical settings. The hospital's stringent adherence to standardized management protocols for antibacterial agents, coupled with an enhanced emphasis on the rational prescription and administration of these drugs, had seemingly played a pivotal role in mitigating the proliferation of multidrug-resistant bacteria to a considerable extent. Furthermore, the bolstered awareness and practices concerning the prevention and control of drug-resistant bacterial infections within our facility had likely reinforced this positive trend.

In the present study, patients with wound infections complicated by MDRO infections were predominantly located in the Burn Plastic Surgery Department, the Emergency Department (Trauma Center), and the Intensive Care Unit (ICU). This distribution could be attributed to the fact that the Burn Plastic Surgery Department specializes in wound repair within our hospital, and thus, it attracts complex cases requiring advanced wound management skills. Consistent with previous research, this department was often the first choice for treating refractory or chronic wound infections.[34] Patients admitted to the Emergency Department (Trauma Center) and ICU typically suffer from severe trauma, advanced age, and multiple comorbidities. They undergo various invasive procedures and receive prolonged courses of different antibiotics for infection control, which increases their susceptibility to MDRO infections and polymicrobial infections.[35,36] Our findings indicated that MDRO infections were prevalent among patients with high-energy trauma and those undergoing surgical interventions. The studies by Foschi D highlight how MDROs were increasingly becoming a significant cause of surgical site infections (SSIs), while research conducted by Cleland H emphasizes that MDROs occur more frequently in burn patients compared to other hospitalized patients.[37] These discrepancies may stem from a variety of factors including geographical variation, study population demographics, hospital characteristics, diagnostic and treatment protocols, among others. Our research specifically identified CRAB as the major MDRO encountered. *A. baumannii*, a multidrug-resistant and invasive pathogen, plays a significant role in causing nosocomial infections in today's healthcare environment.[38] Characteristically, *A. baumannii* often carries diverse drug resistance genes that confer resistance to a broad range of antimicrobial agents.[39] Consequently, scrutinizing and examining the dissemination patterns and antibiotic resistance rates of pathogenic bacteria among patients with wound infections, alongside assessing the risk factors associated with MDRO infections, can significantly contribute to furnishing a robust theoretical foundation for informed clinical medication practices. This endeavor is not only crucial but also profoundly impactful in curtailing the emergence and spread of drug-resistant strains.

This study revealed that hyperglycemia, hypoproteinemia, surgical intervention, prolonged hospital stay, and the use of three or more types of antibiotics independently contribute to the risk of MDRO infection in wounds. These findings parallel those of a research conducted in Shandong, China, where hospital length of stay, hypoproteinemia, and open injuries were identified as independent risk factors for MDRO-infected wound complications in orthopedic trauma patients.[15] Diabetes mellitus compromises the phagocytic functions of neutrophils and macrophages, leading to an overall reduction in immune response, thereby predisposing patients to infections. In clinical practice, broad-spectrum antibiotics are frequently employed to manage infections. However, extended usage of broad-spectrum antibiotics can facilitate bacterial gene mutations and heighten drug resistance.[40] Hospital-acquired conditionally pathogenic organisms, such as *A. baumannii*, are ubiquitously present in the hospital environment and can persistently colonize patients' skin, mucosa, and common hospital items over extended periods. When the host's immunity dips to a critical level, whether due to exacerbation of pre-existing comorbidities, hypoproteinemia, or severe trauma, these circumstances favor the translocation of *A. baumannii* from its colonization site to nearby skin injuries, culminating in infection, hindering wound healing, and escalating the risk of MDRO infections.[41,42]

This study acknowledges several limitations that need to be addressed. Firstly, wound samples were collected utilizing swabs, a method that, despite its widespread adoption, only provides an assessment of the microorganisms present on the superficial layer of the wound, failing to capture those residing beneath the surface. In our investigation, we confined our microbial analysis to the sensitivity and drug resistance patterns of primary gram-positive cocci and negative bacilli, leaving out the remainder of the microbiome. Secondly, the retrospective design of this study confined it to a single hospital with a relatively small sample size, thus, the influencing factors derived from medical records might

not entirely represent the comprehensive scenario of wound infections in this region. Moreover, the patient data collection process was marred by the absence of critical parameters such as wound type, wound area, and wound depth. Lastly, although a predictive model for MDRO infection in wounds was constructed, there was an insufficient number of suitable subjects to rigorously validate the model's conformity and predictive capacity. Hence, further validation through a multi-center, prospective study design is essential to bridge the existing evidence gap concerning wound infections.

Conclusion

Our findings will be instrumental for clinicians to gain a deeper understanding of the microbiological characteristics of wound infection pathogens and the status of antibiotic resistance in this area. The study reveals that *S. aureus* and *P. aeruginosa* are the most common pathogens causing wound infections. Burn and Plastic Surgery Departments, Emergency Departments (Trauma Centers), Intensive Care Units are key clinical departments where patients with wound infections are at high risk of acquiring MDRO infections. Hyperglycemia, hypoalbuminemia, surgical procedures, length of hospital stay, and the use of three or more types of antibiotics have been identified as independent risk factors for the occurrence of MDRO infections in wounds. This research has established a predictive model for the development of multidrug-resistant bacterial infections in patients with wound infections. This model can assist clinicians in early recognition of the risk of MDRO infection in wound patients, thereby facilitating the timely identification of high-risk populations for MDRO infections. By doing so, it enables the prompt implementation of comprehensive therapeutic measures, ultimately mitigating disease progression.

Ethics Approval

The study was approved by the ethics committee of the First Hospital of Jiaxing (No. 2024-KY-132). The ethics committee abandoned the requirement for participants to give formal informed permission because of the retrospective nature of this study. Patients' anonymous information was provided from the microbiology hospital laboratory, which isolated the strains. The study completely followed the guiding principles in the Declaration of Helsinki.

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Author Contributions

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

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Disclosure

The authors have no conflicts of interest to declare in this work.

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