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ORIGINAL ARTICLE

Distribution and Drug Resistance of Pathogens of Catheter-Related Blood Stream Infection in a Hospital from 2017 to 2021

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SUMMARY

Background: **We analyzed the clinical distribution and the antibiotic susceptibility of pathogens for catheter-related blood stream infection (CRBSI) in the hospital retrospectively.**
Methods: **The clinical information and pathogens associated with CRBSI were collected from the Microbiology Laboratory of the hospital retrospectively from January 2017 to December 2021. Identification and the antibiotic susceptibility test (AST) were carried out with VITEK-2 Compact. The data were analyzed by WHONET 5.6.**
Results: **A total of 138 isolates (6.4%) associated with CRBSI were found during the 5-year period. Among the pathogens of CRBSI, 89 (64.5%) isolates were coagulase-negative *Staphylococcus*, 6 (4.3%) were strains of *Enterococcus*, and 4 (2.9%) were strains of *Staphylococcus aureus*. *Staphylococci* and *Streptococci* were all sensitive to Linezolid, Vancomycin, Quinuprine/Dafuprine, and Tigecycline. There were 39 (28.3%) Gram-negative bacilli isolates, including 17 strains of *Klebsiella pneumoniae* (12.3%), 6 (4.3%) strains of *Acinetobacter baumannii*, and 6 (4.3%) strains of *Burkholderia cepacia*. The drug resistance rates of Gram-negative bacilli to most drugs were higher than 50%. The main departments where CRBSI pathogens were isolated were Peritoneal Tumor Surgery (86, 62.3%), ICU (20, 14.5%), Emergency Department (6, 4.3%), and Respiratory Department (6, 4.3%).**
Conclusions: **With the emergence of multidrug-resistant (MDR) bacteria, more attention should be paid to the prevention and control of nosocomial infections. At the same time, the use and management of antibiotics should be standardized, and monitoring of multidrug-resistant bacteria should be strengthened in hospitals.**
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KEYWORDS

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INTRODUCTION

Catheters, including central venous catheters (CVC) and peripherally inserted central catheters (PICC), offer several advantages for the treatment of patients. However, these devices can produce iatrogenic diseases resulting in catheter-related bacteremia or candidemia [1]. Catheter-related blood stream infection (CRBSI) refers to the development of bacteremia or candidemia in patients

carrying an intravascular catheter or within 48 hours after catheter withdrawal, accompanied by infectious manifestations such as fever (> 38°C), chills, or hypotension. In addition to the catheter infection, there was no other infection with a clear infection source. Laboratory microbiological examination indicated that the peripheral venous blood culture was positive for bacteria or fungi, or from the catheter segment and peripheral blood culture of the same species, the same drug sensitive results of pathogenic bacteria [2]. Several studies have shown that CRBSI is closely related to high patient morbidity and mortality and prolonged length of stay (LOS) [3-5].

In order to prevent CRBSI effectively, reduce the occurrence of multidrug-resistant bacteria, and provide a basis for rational clinical use of antibiotics, a retrospective analysis was conducted to analyze the clinical distribution and drug resistance of pathogens isolated from CRBSI from 2017 to 2021.

MATERIALS AND METHODS

Study population and design

A single-center retrospective chart review of the electronic medical record of patients in a tertiary care teaching hospital who underwent catheter insertion between January 2017 and December 2021 was performed. We collected data about the characteristics of patients with catheter and CRBSI, including incidence, distribution of departments, characters of pathogens, and drug resistance analysis of pathogens. Suspected contaminating bacteria in blood culture or the duplicate strains in the same patient in the same period were eliminated.

Blood culture and drug sensitivity test

The Bactec-FX200 system and the BacT/ALERT 3D 240 system were used for blood cultures. VITEK 2 Compact automatic microbial analysis system and related ID and AST cards were all products of bioMérieux, France. Agar plates, such as blood agar media, MacConkey media, chocolate agar media, and M-H agar, were all products of OXOID. The standard bacteria strains, including *Staphylococcus aureus* (ATCC 29213 and ATCC 25923), *Enterococcus faecalis* (ATCC 29212), *Escherichia coli* (ATCC 25922), and *Pseudomonas aeruginosa* (ATCC 27853), were used for quality control in the AST. All operations were performed according to the instrument's instructions. The results of AST were judged by referring them to the Clinical and Laboratory Standards Institute (CLSI M100-S33) [6].

Statistical analysis

The drug resistance analysis was performed by WHONET5.6 software.

RESULTS

Information about blood culture for examination

A total of 45,312 blood cultures were examined over the past 5 years, and 2,152 non-repetitive strains were identified with a positive isolation rate of 4.7%, out of which 138 (6.4%) were from CRBSI. From 2017 to 2021, the positive rates of blood cultures were 4.7%, 4.8%, 4.2%, 5.1%, and 5.1%, respectively. The isolation rates of CRBSI were 4.9%, 6.1%, 8.4%, 7.6%, and 5.5%, respectively.

Distribution of CRBSI departments

The major departments in which CRBSI pathogens were isolated during the 5-year period were: Department of Peritoneal Cancer Surgery (86 strains, 62.3%), ICU (Intensive Care Unit) (20 strains, 14.5%), Department of Emergency Medicine (6 strains, 4.3%), and Department of Pulmonary and Critical Care Medicine (6 strains, 4.3%). See Table 1 for details.

The distribution characteristics of CRBSI pathogens

A total of 138 strains of CRBSI pathogens were isolated over the past 5 years, out of which 99 (71.7%) were Gram-positive cocci and 39 (28.3%) strains were Gram-negative bacilli. The top three Gram-positive cocci were coagulase negative *Staphylococcus* (89, 64.5%), *Enterococcus* (6, 4.3%), and *Staphylococcus aureus* (4, 2.9%), respectively. The top three Gram-negative bacilli were *Klebsiella pneumoniae* (17, 12.3%), *Acinetobacter baumannii* (6, 4.3%), and *Burkholderia cepacia* (6, 4.3%). See Table 2 for details.

Antibiotic resistance analysis of major Gram-positive cocci in CRBSI

The results of the analysis using WHONET 5.6 software showed that there were 83 (93.3%) strains of methicillin-resistant coagulase-negative staphylococcus (MRSCoN) among the coagulase-negative *staphylococcus* (CoNS) that occupied the vast majority. No *staphylococci*, neither *Staphylococcus aureus* nor CoNS, were found to be resistant to Vancomycin, Linezolid, Daptomycin, Tigecycline, or Quinupristin/Dalfopristin. The resistance rates of CoNS to Benzylpenicillin, Erythrocin, Ciprofloxacin, Levofloxacin, and TMP were 97.8%, 82%, 65.8%, 67.4%, and 64.7%, respectively, and all were above 60%. The resistance rate of CoNS to Rifampicin was still low, only 4.5%, but it maintained good antibacterial activity. The resistance rates of CoNS to Moxifloxacin, Clindamycin, Gentamicin, and Tetracycline were 42%, 30.3%, 25.8%, and 16.5%, respectively. See Table 3 for details.

Drug resistance analysis of major CRBSI Gram-negative bacteria

The drug resistance rates of *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Burkholderia cepacia* detected in CRBSI were high, and most drug resistance

Table 1. Distribution of CRBSI-causing isolates from 2017 to 2021 according to department.

Wards	Isolates	Ratio (%)
Department of Peritoneal Cancer Surgery	86	62.3
Intensive Care Unit	20	14.5
Department of Emergency Medicine	6	4.3
Department of Pulmonary and Critical Care Medicine	6	4.3
Department of Nephrology	5	3.6
Department of Gynecology	5	3.6
Others	10	7.2
Total	138	100

Table 2. Distribution and constituent ratio of pathogens in CRBSI from 2017 to 2021.

Pathogen	n	Ratio (%)
Gram-positive cocci	99	71.7
Coagulase-negative *Staphylococci*	89	64.5
Enterococci	6	4.3
Staphylococcus aureus	4	2.9
Gram-negative bacilli	39	28.3
Klebsiella pneumoniae ssp pneumoniae	17	12.3
Acinetobacter baumannii	6	4.3
Burkholderia cepacia	6	4.3
Pseudomonas aeruginosa	4	2.9
Other Gram-negative bacilli	6	4.3
Total	138	100

rates were ≥ 50%, according to the WHONET 5.6 analysis result (Table 4).

DISCUSSION

With the development of medical technology, PICC has been widely applied in clinical practice as a safe and effective therapeutic pathway [7]. It is widely used for the administration of parenteral nutrition, prolonged antimicrobial therapy, or chemotherapy [8,9]. The major departments in which CRBSI pathogens were isolated in our study were the Department of Peritoneal Cancer Surgery and the ICU. Infection is a complication that occurs in patients with malignant tumors. According to the analysis, 62.3% of the patients with CRBSI in our hospital came from the Department of Abdominal Cancer Surgery. Most patients have lower immunity, severe damage to blood vessels caused by chemotherapy, and long-term retention of PICC in veins, which become the main causes of infection. Parenteral nutrition (PN) is a valuable and life-saving treatment for patients in the Department of Peritoneal Cancer Surgery and ICU. And PN is an independent risk factor for intravenous catheter-related blood stream infection (CRBSI) [10]. Professionalized PICC placement care can effectively prevent the occurrence of catheter-associated bloodstream infections and enhance nurses' professional skills [11].

Among the pathogens of patients with CRBSI in our hospital from the past 5 years, Gram-positive cocci were significantly higher than Gram-negative bacilli, among which coagulase-negative staphylococci had the highest isolation rate, which was consistent with previous results [12,13]. Coagulase-negative staphylococci are opportunistic pathogens that widely exist in nature, the skin surface of the human body, and pipelines communicating with the outside world. They can invade along the surface of the catheter through the puncture point and migrate to the tip of the catheter to cause CRBSI [14]. With the extensive use of clinical antibiotics, the increase of interventional therapy, and the decline of body immunity, coagulase-negative staphylococcus can cause bloodstream infection, wound infection, and other clinical manifestations, and coagulase-

Table 3. Resistance of important Gram-positive cocci to commonly used antibiotics from 2017 to 2021.

	n	Resistance rate (%)	n	Resistance rate (%)	n	Resistance rate (%)
Benzylpenicillin	89	97.8	4	75	6	16.7
Oxacillin	89	93.3	4	25	-	-
Erythrocin	89	82	4	50	6	83.3
Ciprofloxacin	79	65.8	4	25	6	66.7
Levofloxacin	89	67.4	4	0	6	66.7
SMZ/TMP	85	64.7	4	25	-	-
Moxifloxacin	81	42	3	0	-	-
Clindamycin	89	30.3	4	25	-	-
Gentamicin	89	25.8	4	25	6	0
Tetracycline	79	16.5	4	0	6	83.3
Rifampicin	89	4.5	4	0	-	-
Vancomycin	89	0	4	0	6	0
Linezolid	89	0	4	0	6	0
Daptomycin	23	0	1	0	-	-
Tigecycline	68	0	2	0	6	0
Quinupristin/Dalfopristin	79	0	4	0	1	0

"-" indicates that this resistance test was not done.

Table 4. Resistance of important Gram-negative bacilli to commonly used antibiotics from 2017 to 2021.

Antibiotics	Klebsiella pneumoniae spp pneumoniae (n = 17)		Acinetobacter baumannii (n = 6)		Burkholderia cepacia (n = 6)	
	n	Resistance rate (%)	n	Resistance rate (%)	n	Resistance rate (%)
Cefazolin	15	100	-	-	-	-
Ampicillin/Sulbactam	17	94.1	5	80	-	-
Ceftriaxone	17	94.1	5	80	-	-
Gentamicin	17	94.1	5	60	-	-
Piperacillin/Tazobactam	17	88.2	1	100	-	-
Aztreonam	17	88.2	-	-	-	-
Meropenem	17	88.2	5	100	4	75
Ciprofloxacin	17	88.2	6	83.3	-	-
Tobramycin	17	82.4	6	66.7	-	-
Ceftazidime	17	76.5	6	83.3	6	0
Cefepime	17	76.5	6	66.7	-	-
Levofloxacin	17	76.5	6	50	6	100
Imipenem	17	76.5	6	83.3	-	-
SMZ/TMP	17	64.7	6	16.7	6	83.3
Minocycline	17	52.9	6	100	6	83.3
Amikacin	17	52.9	-	-	-	-
Cefotetan	17	47.1	-	-	-	-

"-" indicates that this resistance test was not done; SMZ/TMP: sulfamethoxazole and trimethoprim.

negative staphylococcus has become a common bacterium in hospital infection monitoring.

This study indicated that the resistance of coagulase-negative *staphylococcus* to Penicillin, Oxacillin, and Erythromycin was at a high level. No bacteria resistant to Linezolid and Vancomycin were found in the study, but *staphylococci* with Linezolid resistance mediated by 23s rRNA gene mutation, ribosomal protein L3 mutation, and *cfr*, *fexA*, and *optrA* genes have been reported in China [15-17]. Therefore, clinical management of antibiotic use should be strengthened to prevent the emergence of drug-resistant strains. For patients with coagulase-negative staphylococcal infection, the degree of infection should be selected according to the clinical drug sensitivity results in the laboratory. In view of the high drug resistance rate of coagulase-negative *staphylococcus* in our hospital, Vancomycin and Linezolid can be used as the first choice of antibiotics. This study showed that the sensitivity rate of *staphylococci* to Quinupristin/Dalfopristin was 100%, suggesting that Quinupristin/Dalfopristin could be used as the drug of choice for the treatment of staphylococcal infection. As a common opportunistic pathogen, *Enterococci* is an important pathogen of nosocomial infections. Opportunistic infections occur in immunocompromised hosts and lead to infection of multiple sites, such as the urinary tract, wound, biliary tract, blood, abdominal cavity, and endocardial tract, among which bloodstream infections are particularly serious [18]. Due to the continuous rise of vancomycin-resistant *enterococci*, ampicillin-resistant strains, and gentamicin-resistant strains, clinical treatment of severe infections caused by *enterococci* has faced great challenges in recent years. In this research, the proportion of *enterococci* isolated from CRBSI in our hospital was 4.3%, its sensitivity to Vancomycin, Linezolid, and Quinupristin/Dalfopristin was 100%, to Penicillin, it was 16.7%, and the rates to Erythromycin, Tetracycline, and Quinolone drugs were all higher than 60%. In order to avoid the occurrence of drug-resistant strains, antibiotics should be used rationally according to the actual situation of patients and the drug sensitivity results issued by the laboratory to provide timely and effective treatment for patients.

In this study, *Klebsiella pneumoniae* was the main Gram-negative bacterium causing CRBSI in the hospital, followed by *Acinetobacter baumannii* and *Burkholderia cepacia*. Patients with critical illness, extremely low immunity, long-term bed rest, repeated use of interventional operations, and multiple antibiotics were the main reasons for *Klebsiella pneumoniae* and *Acinetobacter baumannii* isolated from CRBSI in the hospital to show multidrug resistance. Carbapenem drugs used to be effective drugs for the treatment of *Klebsiella pneumoniae* infections. Due to their widespread use, carbapenem resistant *Klebsiella pneumoniae* appeared, which brought great difficulties to clinical treatment. The common resistance mechanism of *Klebsiella pneumoniae* to carbapenem antibiotics is mainly to produce KPC, NDM, IMP, VIM, and other metal enzymes for now. Moreover, there is loss of outer membrane porin (OMP) or abnormal overexpression of the efflux pump system, accompanied by high expression of β-lactamases such as AmpC and ESBL [19].

The correlation research indicated that the risk factor affecting the bloodstream infection of carbapenem-resistant *Klebsiella pneumoniae* is the retention of CVC [20]. Sulbactam-containing agents, such as cefoperazone and sulbactam, can be used empirically for the treatment of carbapenem-resistant *Klebsiella pneumoniae* and *Acinetobacter baumannii*. *Burkholderia cepacia* is naturally resistant to a variety of antibiotics, and its resistance mechanism is complex [21]. *Burkholderia cepacia* has poor cell membrane permeability, and it is difficult for antibacterial drugs to enter the bacterial cells through the outer membrane [22]. It has an outer membrane lipoprotein similar to the pumping system of *Pseudomonas aeruginosa*, which can pump antibacterial drugs into the bacteria out of the body, showing high resistance to quinolone antibacterial drugs and chloramphenicol [23], and can be induced to produce enzymes that inactivate antibiotics, such as β-lactamase and metallo β-lactamase. Metallo β-lactamase is the main cause of resistance for *Burkholderia cepacia* to broad-spectrum cephalosporins, including imipenem [24]. This study showed that the resistance of *Burkholderia cepacia* from CRBSI to Quinolones, SMZ/TMP, Minocycline, and Meropenem was above 75%, but their sensitivity to Ceftazidime was 100%, indicating that Ceftazidime can be used for treatment in clinical practice.

CONCLUSION

In summary, relevant medical staff should be regularly trained to strengthen awareness of aseptic operation, standardize the catheter maintenance process of nursing staff, and conduct health education for patients and their families to effectively prevent CRBSI in hospitals. When CRBSI occurs, clinical attention should be paid to monitor the changes in the condition, combined with the results of drug sensitivity test, standardized medication, and active and effective treatment. The emergence of multidrug-resistant strains has brought great difficulties and challenges to clinical treatment. The Nosocomial Infection Department should formulate strict prevention and control procedures, and medical staff should strictly implement relevant preventive measures and work together to prevent the occurrence of multidrug-resistance.

Ethical Approval and Consent to Participate:

The study was approved by the Ethics Committee of the Beijing Shijitan Hospital. The informed consent was waived, because this study is a retrospective study with a review of related data through electronic medical records. The authors declare that this study is in accordance with the Helsinki Declaration and the relevant

national laws and policies, and the authors will never disclose the information of all patients.

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Declaration of Interest:
There is no conflict of interest between the authors of this study and the authors are responsible for the authenticity of its content.

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