Bloodstream Infections in the Intensive Care Unit: a Single-Center Retrospective Bacteriological Analysis Between 2007 and 2019

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Abstract

Hospital-acquired bloodstream infections are a severe worldwide problem associated with significant morbidity and mortality. This retrospective, single-center study aimed to analyze bloodstream infections in patients hospitalized in the intensive care unit of the Military Institute of Medicine, Poland. Data from the years 2007–2019 were analyzed. When the infection was suspected, blood samples were drawn and analyzed microbiologically. When bacterial growth was observed, an antimicrobial susceptibility/resistance analysis was performed. Among 12,619 analyzed samples, 1,509 were positive, and 1,557 pathogens were isolated. In 278/1,509 of the positive cases, a central line catheter infection was confirmed. Gram-negative bacteria were the most frequently (770/1,557) isolated, including Acinetobacter baumannii (312/770), Klebsiella pneumoniae (165/770; 67/165 were the isolates that expressed extended spectrum beta-lactamases (ESBL), 5/165 isolates produced the New Delhi metallo-β-lactamases (NDM), 4/165 isolates expressed Klebsiella pneumoniae carbapenemase (KPC), and 1/165 isolate produced OXA48 carbapenemase), Pseudomonas aeruginosa (111/770; 2/111 isolates produced metallo-β-lactamase (MBL), and Escherichia coli (69/770; 11/69 – ESBL). Most Gram-positive pathogens were staphylococci (545/733), mainly coagulase-negative (368/545). Among 545 isolates of the staphylococci, 58 represented methicillin-resistant Staphylococcus aureus (MRSA). Fungi were isolated from 3.5% of samples. All isolated MRSA and methicillin-resistant coagulase-negative Staphylococcus (MRCNS) strains were susceptible to vancomycin, methicillin-sensitive Staphylococcus aureus (MSSA) isolates – to isoxazolyl penicillins, and vancomycin-resistant Enterococcus (VRE) – to linezolid and tigecycline. However, colistin was the only therapeutic option in some infections caused by A. baumannii and KPC-producing K. pneumoniae. P. aeruginosa was still susceptible to cefepime and ceftazidime. Echinocandins were effective therapeutics in the treatment of fungal infections.

Keywords: central line-associated bloodstream infections, Gram-positive pathogens, Gram-negative pathogens, antimicrobial susceptibility, antimicrobial resistance, intensive care unit

Introduction

Hospital-acquired bloodstream infections (BSI) are a severe care problem worldwide, associated with significant mortality (Massart et al. 2021). According to Watson et al. (2019), hospital-acquired bloodstream infections result in a 1.3- to 4.3-fold increase in the hospitalization duration, 2.8- to 5.3-fold higher hospitalization costs and a 4.3- to 8-fold increase in the percentage of patients who died. Observations from the last few years have shown an increased incidence of bloodstream infections (Salm et al. 2018; Tajima et al. 2021). Moreover, data from Denmark revealed a considerable increase in bacteraemia between 2000 and 2014, although the all-cause 30-day mortality after first-time bacteremia decreased (Holm et al. 2021).

Over 50% of patients admitted to the intensive care unit (ICU) require central vein catheterization (CVC) (Blot et al. 2015). Central lines are necessary for multiple
purposes, including drug infusion, blood sample collection, and hemodynamic monitoring. The presence of a catheter inside a central vein is associated with the risk of central line-associated bloodstream infections (CLABSI). In the USA, five million CVCs are inserted each year, leading to approximately 200,000 cases of CLABSI, and the number of deaths attributable to such infections may be as high as 25,000 (Blot et al. 2015). However, these estimates may be underestimated because some cases of BSI secondary to urinary, respiratory, and gastrointestinal infections may be assigned the International Classification of Disease (ICD) codes for those illnesses (Goto and Al-Hasan 2013).

The objective of this study was to analyze bloodstream infections in patients hospitalized in the intensive care unit of the Military Institute of Medicine between 2009 and 2017 and to determine the changes in the incidence of pathogens and their susceptibility/resistance to antimicrobial agents with particular attention paid to the incidence of CVC infections in the analyzed cohort.

Experimental

Materials and Methods

Study design. It was an observational cohort study. The study protocol was approved by the institutional Bioethical Committee (43/WIM/2020 of August 19, 2020).

Setting. Data were collected in the intensive care unit of the Military Institute of Medicine in Warsaw, Poland, between January 1, 2007, and December 31, 2019. The Military Institute of Medicine is a 1,000-bed university hospital and a regional trauma center. The number of beds in the ICU varied throughout the study period: from 8 (2007–2013), 14 (2014), to 18 beds (2015–2019).

Participants and the procedures when infection was suspected. We analyzed the data of all critically ill patients hospitalized in our ICU during the study period. No other eligibility criteria were applied.

In our center, the physicians always insert central venous catheters, either specialists or residents. Regardless of who performed the CVC insertion, the procedure was the same and was performed aseptically. Trained nurses provided routine care of inserted catheters and venous line connectors. When the infection was suspected, two blood samples were drawn: one sample of peripheral blood and a second one drawn through the CVC; both were submitted to microbiological testing. When a catheter-related bloodstream infection was suspected, the procedure was like that described above. The blood samples were taken from both the catheter and a peripheral vein. The catheter was removed according to clinical guidelines (O’Grady et al. 2011), and the tip of the catheter was microbiologically analyzed. Blood samples were collected by trained nurses under aseptic conditions, according to standard procedures in all cases. Its tip was cut off and microbiologically analyzed whenever the catheter was removed. Catheters were released by physicians, under aseptic conditions, according to standard procedures.

Microbiological analysis. Blood samples (10 ml) were collected into two BactAlert Bottles (bioMérieux, France): a BactAlert FA Plus Bottle to detect the presence of aerobes and fungi and a BactAlert FN Plus Bottle to check for anaerobes. Both blood samples were placed in a BactAlert 3D automatic analyzer (bio-Mérieux, France) and incubated at 37°C either until the growth of the pathogens was observed or until the end of the fifth day of incubation.

When pathogen growth was noted, the samples were inoculated on specific growth media: Columbia agar, McConkey agar, chocolate agar, and Sabouraud agar. When the growth of anaerobic pathogens was observed, the samples were inoculated in a Schaedler agar. The pathogens were incubated in the growth media for 24–48 hours at 37°C under aerobic or anaerobic conditions. After the incubation period, the Gram-stained bacteria morphology was analyzed.

When the growth of a mixed bacterial culture was observed, separating procedures were performed to obtain pure colonies, which were further identified, and antibiotic susceptibility of isolates was assayed. The microorganisms were identified by an automatic VITEK® 2 testing system (bioMérieux, France) using VITEK® ID Cards (VITEK® 2 GN ID Card for the identification of fermenting and non-fermenting Gram-negative bacilli, VITEK® 2 GP ID Cards for Gram-positive bacteria, and VITEK® YST ID Cards of yeast and yeast-like organisms, respectively) following the manufacturer’s instructions. The quality of bacterial identification was assessed with the VITEK® 2 Advanced Expert System. The results were defined as acceptable at a confidence level between 96–99% (excellent identification) or 93–95% (very good quality). Antimicrobial susceptibility testing was performed with the VITEK® 2 system according to the manufacturer’s instructions, using the software 9.02 version and the AST-N 332, AST-P644, AST-643, AST-ST03 cards for Gram-negative bacteria, staphylococci, enterococci, and streptococci, respectively. Between 2007 and 2010, the antimicrobial susceptibility of isolated pathogens was classified according to the Clinical and Laboratory Standard Institute (CLSI 2009; 2010a; 2010b), and since 2011 following the regulations of the European Committee on AntimicrobialSusceptibility Testing (EUCAST 2013; 2017) and the National Reference Centre for Susceptibility Testing in Warsaw, Poland. Control susceptibility tests included reference strains of Pseudomonas aeruginosa.
ATCC 27853, *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *Klebsiella pneumoniae* ATCC 700603, *Klebsiella pneumoniae* ATCC BAA-2814, *Staphylococcus aureus* NCTC 124943, and *Enterococcus faecalis* ATCC 51299.

The microbiological investigation of the catheter was performed using both a semiquantitative Maki et al. (1977) and a quantitative Brun-Buisson et al. (1987) techniques. A central venous line may be a source of blood infection when the growth of the same pathogen identified in a catheter-drawn sample is observed two or more hours earlier in a blood sample drawn from a peripheral vein. In a catheter tip culture, more than 15 CFU colonies of the same pathogen were isolated via the semiquantitative analysis (Maki et al. 1977). More than thousand bacterial species were isolated via the quantitative analysis (Brun-Buisson et al. 1987).

**Study size.** Due to the retrospective nature of this study, its size was not determined before the start of the project.

**Statistical methods.** Collected data were archived and analyzed using the Microsoft Excel software. Descriptive statistics were used for analysis. All figures were prepared with the DataGraph software.

**Results**

The study analyzed data collected between 2007 and 2019. General information regarding the number of patients hospitalized in the ICU, the reasons for their hospitalization, the number of microbiological investigations of blood samples, and the results of these examinations are shown in Tables I and II.

**Study population and blood samples.** Between 2007 and 2019, 3,502 patients were hospitalized in our ICU. Among these, 2,581/3,502 were men (73.7%), and 921/3,502 (26.3%) were women. Among 46,253 microbiological specimens, 12,619 (27.3%) were obtained from blood samples. One thousand five hundred nine (12%) were positive, and 1,557 pathogens were isolated. Among these were 770/1,557 (49.5%) Gram-negative bacteria, 733/1,557 (47.1%) Gram-positive bacteria, and 54/1,557 (3.5%) fungal species. A CVC was inserted into a subclavian vein in 2,588/3,460 cases (98.8%), and the femoral vein in 187/3,460 cases (5.4%). A CVC was implicated in 278/1,509 (18.4%) of positive blood cultures, and the number of infected central vein catheters was 278/632 (44.6%). The pathogens isolated from positive blood cultures are shown in Table II. Among all Gram-negative bacteria, *A. baumannii* was isolated quite often, in 312/770 (40.5%) of cases. It represented 312/1,557 (20%) of all isolated pathogens.

**Isolated pathogens.** Gram-negative bacilli were the most common isolated pathogens in our materials. The most frequently isolated pathogen was *A. baumannii*, followed by *K. pneumoniae*, and *P. aeruginosa*. Among Gram-positive cocci, the most frequent was *MRCNS*, followed by *E. faecalis*. *A. baumannii* was isolated from 312 samples (20% of all isolated pathogens and 40.5% (312/770) of all Gram-negative isolates). *P. aeruginosa* was obtained from 111 blood samples (7.4% (111/1,509)), representing 7.1% of all isolated bacterial species and 14.4% (111/770) of Gram-negative pathogens. Only in two *A. baumannii* isolates with the MBL mechanism of antibiotic resistance were found.

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### Table I
Descriptive statistics of the study population and their primary diagnoses according to ICD10.

| Year | Patients n | Age median | Age minimum | Age maximum | Hospitalization time in ICU (days) median | Hospitalization time in ICU (days) minimum | Hospitalization time in ICU (days) maximum | Q1-Q3 Hospitalization time in ICU (days) | Deaths n (%) |
|------|------------|------------|-------------|-------------|------------------------------------------|-------------------------------------------|------------------------------------------|------------------------------------------|--------------|
| 2007 | 197        | 53         | 18          | 84          | 22                                       | 1                                         | 136                                      | 11–47         | 71 (36%)     |
| 2008 | 182        | 54         | 18          | 86          | 26                                       | 1                                         | 147                                      | 9–48          | 62 (34%)     |
| 2009 | 216        | 60         | 18          | 87          | 16                                       | 1                                         | 124                                      | 7–27          | 68 (31%)     |
| 2010 | 173        | 59         | 21          | 87          | 30                                       | 2                                         | 137                                      | 5–27          | 57 (33%)     |
| 2011 | 224        | 49         | 19          | 82          | 20                                       | 1                                         | 48                                       | 11–58         | 63 (37%)     |
| 2012 | 178        | 43         | 18          | 82          | 23                                       | 1                                         | 107                                      | 5–27          | 40 (33%)     |
| 2013 | 172        | 45         | 18          | 107         | 14                                       | 1                                         | 106                                      | 11–31         | 29 (26%)     |
| 2014 | 186        | 49         | 19          | 91          | 16                                       | 1                                         | 273                                      | 10–36         | 40–67 (39%)  |
| 2015 | 350        | 186        | 18          | 85          | 15                                       | 1                                         | 275                                      | 8–39          | 38–69 (37%)  |
| 2016 | 422        | 350        | 18          | 85          | 14                                       | 1                                         | 205                                      | 8–31          | 37–63 (36%)  |
| 2017 | 422        | 350        | 18          | 87          | 14                                       | 1                                         | 159                                      | 5–36          | 38–69 (37%)  |
| 2018 | 450        | 348        | 19          | 88          | 8                                        | 1                                         | 238                                      | 5–32          | 37–63 (36%)  |
| 2019 | 348        | 348        | 24          | 88          | 8                                        | 1                                         | 24                                       | 24–82         | 36 (43%)     |

Diagnoses were presented in blocks, as on the World Health Organization webpage (https://icd.who.int/browse10/2019/en)

1. Other bacterial diseases [A30–A49]
- including sepsis due to other specified staphylococci (A41.1); sepsis due to aerobes (A41.4); sepsis due to other Gram-negative organisms (A41.5); sepsis, unspecified (A41.9)
2. Malignant neoplasms of lip, oral cavity, and pharynx [C00–C14]
- including malignant neoplasm of other and unspecified parts of the tongue (C02); malignant neoplasm of other and ill-defined sites of the lip, oral cavity, and pharynx (C14)
3. Malignant neoplasms of digestive organs [C15–C26]
- including malignant neoplasm of the stomach (C16); malignant neoplasm of the colon (C18)
4. Malignant neoplasms of respiratory and intrathoracic organs [C30–C39]
- including malignant neoplasm of bronchus and lung (C34)
5. Malignant neoplasms of lymphoid, hematopoietic, and related tissue [C81–C96]
6. Diabetes mellitus [E10–E14]
- including diabetes mellitus with coma (E10.0), ketoacidosis (E10.1), and multiple complications (E10.7)
7. Obesity and other hyperalimentation [E65–E68]
8. Metabolic disorders

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including bacterial meningitis, not elsewhere classified (G00); bacterial meningoencephalitis and meningomyelitis, not elsewhere classified (G04.2); encephalitis, myelitis, and encephalomyelitis in diseases classified elsewhere including motor neuron disease (G12.2);
including status epilepticus (G41); brain stem stroke syndrome (G46.3); cerebellar stroke syndrome (G46.4)
including myasthenia gravis and other myoneural disorders (G70)
including cerebral palsy (G82.3)
including encephalopathy, unspecified (G93.4)
including acute myocardial infarction (I21)
including pulmonary embolism (I26)
including cardia arrest with successful resuscitation (I46.0); other cardiac arrhythmias (I49); heart failure (I50)
including subarachnoid hemorrhage (I60); intracerebral hemorrhage (I61); cerebral infarction (I63); stroke (I64)
including abdominal aortic aneurysm, ruptured (I71.3)
including influenza with pneumonia, seasonal influenza virus identified (J10.0); bacterial pneumonia (J15); pneumonia due to other infectious organisms (J16); pneumonia, organism unspecified (J18)
including other chronic obstructive pulmonary disease (J44); status asthmaticus (J46)
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| Year | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| Lung diseases due to external agents [J60–J70][2]
| 5 | 4 | 5 | 0 | 2 | 2 | 1 | 1 | 3 | 3 | 3 | 4 | 2 |
| Other respiratory diseases principally affecting the interstitium [J80–J84][3]
| 5 | 1 | 5 | 6 | 6 | 4 | 3 | 3 | 5 | 5 | 4 | 3 |
| Suppurative and necrotic conditions of the lower respiratory tract [J85–J86][4]
| 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 0 |
| Other diseases of the respiratory system [J95–J99][5]
| 21 | 10 | 19 | 44 | 38 | 28 | 22 | 19 | 25 | 30 | 28 | 37 | 27 |
| Diseases of esophagus, stomach, and duodenum [K20–K31][6]
| 5 | 4 | 4 | 2 | 2 | 2 | 1 | 0 | 2 | 4 | 5 | 6 | 0 |
| Hernia [K40–K46][7]
| 0 | 0 | 1 | 1 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 2 |
| Other diseases of the intestines [K55–K64][8]
| 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 2 | 3 | 4 | 3 | 1 |
| Diseases of peritoneum [K65–K67][9]
| 5 | 8 | 10 | 11 | 13 | 9 | 11 | 9 | 16 | 16 | 14 | 16 | 10 |
| Diseases of the liver [K70–K77][10]
| 0 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 2 | 2 | 3 | 3 | 0 |
| Disorders of gallbladder, biliary tract, and pancreas [K80–K87][11]
| 13 | 10 | 10 | 13 | 14 | 9 | 8 | 9 | 11 | 9 | 7 | 10 | 6 |
| Other diseases of the digestive system [K90–K93][12]
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 3 | 2 | 0 |
| Infections of the skin and subcutaneous tissue [L00–L08][13]
| 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Systemic connective tissue disorders [M30–M32][14]
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Osteopathies and chondropathies [M80–M94][15]
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |

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- Including pneumonitis due to food and vomit (J69.0)
- Including adult respiratory distress syndrome (J80); other interstitial pulmonary diseases (J84)
- Including abscess of the mediastinum (J85.3)
- Including postprocedural respiratory disorders (J85.4); respiratory failure (J96)
- Including perforation of the esophagus (K22.3); duodenal ulcer, acute with hemorrhage (K26.0), acute with hemorrhage and perforation (K26.2); gastrojejunal ulcer with hemorrhage (K28.0), hemorrhage and perforation (K28.2); acute hemorrhagic gastritis (K29)
- Including ventral hernia (K43)
- Including paralytic ileus and intestinal obstruction without hernia (K56)
- Including peritonitis (K65)
- Including toxic liver disease (K71); hepatic failure (K72)
- Including cholecystitis (K81); obstruction of the bile duct (K83.1); acute pancreatitis (K85)
- Including gastrointestinal hemorrhage, unspecified (K92.2)
- Including other local infections of the skin and subcutaneous tissue (L08)
- Including systemic lupus erythematosus (M32)
- Including osteomyelitis (M86)
Table I. Continued.

|                              | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|------------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| Injuries to the head [S00–S09]\(^a\) | 5    | 5    | 7    | 9    | 2    | 8    | 11   | 9    | 27   | 23   | 23   | 24   | 16   |
| Injuries to the neck [S10–S19]\(^b\) | 0    | 0    | 0    | 4    | 0    | 2    | 3    | 0    | 2    | 0    | 0    | 2    | 0    |
| Injuries to the thorax [S20–S29]\(^c\) | 4    | 3    | 3    | 2    | 0    | 2    | 0    | 4    | 7    | 3    | 8    | 4    | 2    |
| Injuries to the abdomen, lower back, lumbar spine, and pelvis [S30–S39]\(^d\) | 2    | 3    | 3    | 4    | 2    | 0    | 2    | 10   | 17   | 23   | 17   | 9    |
| Injuries to the shoulder and upper arm [S40–S49]\(^e\) | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
| Injuries to the hip and thigh [S70–S79]\(^f\) | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 2    | 2    | 0    | 0    | 2    |
| Injuries to the knee and lower leg [S80–S89]\(^g\) | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 2    | 0    | 1    | 0    |
| Injuries involving multiple body regions [T00–T07]\(^h\) | 44   | 45   | 53   | 21   | 32   | 41   | 48   | 57   | 101  | 142  | 145  | 141  | 134  |
| Burns and corrosions [T20–T32]\(^i\) | 4    | 9    | 6    | 9    | 16   | 10   | 11   | 11   | 19   | 31   | 29   | 35   | 26   |
| Poisoning by drugs, medicaments, and biological substances [T36–T50]\(^j\) | 0    | 2    | 1    | 1    | 2    | 2    | 0    | 2    | 1    | 3    | 2    | 1    | 0    |
| Other and unspecified effects of external causes [T66–T78]\(^k\) | 0    | 1    | 0    | 0    | 1    | 0    | 0    | 1    | 1    | 0    | 0    | 1    |      |

Diagnoses were presented in blocks, as on the World Health Organization webpage (https://icd.who.int/browse10/2019/en)

\(^a\) including fracture of the skull and facial bones (S02); intracranial injury (S06); other and unspecified injuries of the head (S09)

\(^b\) including open wound of the neck (S11); fracture of the neck (S12); injury of nerves and spinal cord at neck level (S14); injury of blood vessels at neck level (S15)

\(^c\) including fracture of rib(s), sternum, and thoracic spine (S22); injury of blood vessels of the thorax (S25); injury of other and unspecified intrathoracic organs (S27); crushing injury of the thorax and traumatic amputation of part of thorax (S28)

\(^d\) including fracture of lumbar spine and pelvis (S32); injury of blood vessels at abdomen, lower back, and pelvis level (S35); injury of intra-abdominal organs (S36)

\(^e\) including traumatic amputation of shoulder and upper arm (S48)

\(^f\) including fracture of the femur (S72); crushing injury of hip and thigh (S77)

\(^g\) including crushing injury of the lower leg (S87); traumatic amputation of the lower leg (S88)

\(^h\) including fractures involving multiple body regions (T02); crushing injuries involving multiple body regions (T04); other injuries involving multiple body regions (T06); multiple unspecified injuries (T07)

\(^i\) including burn and corrosion of head and neck (T20); burn and corrosion of trunk (T21); burn and corrosion of respiratory tract (T27); burn and corrosion of other internal organs (T28); burns and corrosions of multiple body regions (T29); burns classified according to the extent of body surface involved (T31)

\(^j\) including poisoning by narcotics and psycholyphatics (hallucinogens) (T40)

\(^k\) including hypothermia (T68); drowning and nonfatal submersion (T75.1); effect of electric current (T75.8); anaphylactic shock (T78.2)
Table II
The number of microbiological analyses, with their results, performed between 2007 and 2019.

|                              | 2007  | 2008  | 2009  | 2010  | 2011  | 2012  | 2013  | 2014  | 2015  | 2016  | 2017  | 2018  | 2019  |
|------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Beds in ICU (n)              | 8     | 8     | 8     | 8     | 8     | 8     | 14    | 18    | 18    | 18    | 18    | 18    | 18    |
| Hospitalizations (n)         | 179   | 182   | 216   | 173   | 224   | 178   | 172   | 186   | 350   | 422   | 422   | 450   | 348   |
| Microbiological analyses (n) | 2,361 | 2,349 | 2,710 | 2,454 | 3,123 | 2,796 | 2,797 | 2,811 | 4,093 | 5,376 | 5,030 | 5,089 | 5,264 |
| Microbiological analyses of blood samples (n) | 670 | 613 | 785 | 641 | 1,245 | 1,016 | 944 | 831 | 1,219 | 1,326 | 988 | 1,161 | 1,180 |
| Blood microbiological analyses, negative results (n) | 548 | 473 | 632 | 534 | 1,130 | 889 | 809 | 690 | 1,064 | 1,140 | 858 | 1,023 | 994 |
| Blood microbiological analyses, positive results (n) | 107 | 120 | 135 | 97 | 104 | 99 | 106 | 112 | 120 | 154 | 104 | 106 | 145 |
| Blood microbiological analyses, contaminated samples (n) | 15 | 20 | 18 | 10 | 11 | 28 | 29 | 29 | 35 | 32 | 26 | 32 | 41 |
| Microbiological analyses of the tip of the catheter (n) | 30 | 23 | 28 | 18 | 39 | 29 | 45 | 53 | 70 | 70 | 76 | 77 | 65 |
| Microbiological analyses of the tip of the catheter, positive results (n) | 13 | 11 | 17 | 12 | 21 | 11 | 31 | 30 | 20 | 29 | 31 | 26 | 26 |

resistance to antimicrobial agents. In such cases, colistin was virtually the only therapeutic choice. In the last two years of the period analyzed, all *P. aeruginosa* isolates were susceptible to ceftazidime, cefepime, and gentamycin.

The most frequently isolated species of Enterobacteriales were *K. pneumoniae* (165 isolates) and *E. coli* (69 isolates). More than 40% (67/165) of *K. pneumoniae* strains and more than 16% (*E. coli* 11/69) exhibited an ESBL mechanism of resistance. Fortunately, all these pathogens were susceptible to meropenem, and only six of these isolates produced carbapenemases.

We had a broad spectrum of therapeutic options for fungal infection treatment. *Candida albicans* isolates...
**Table III**
The number of pathogens isolated from blood samples between 2007 and 2019.

| Pathogen (mechanism of antibiotic resistance) | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | Total |
|-----------------------------------------------|------|------|------|------|------|------|------|------|------|------|------|------|-------|
| *Acinetobacter baumannii*                     | 33   | 24   | 22   | 19   | 38   | 26   | 25   | 29   | 18   | 26   | 20   | 18   | 14    | 312   |
| *Pseudomonas aeruginosa*                      | 12   | 9    | 12   | 7    | 5    | 7    | 6    | 8    | 8    | 9    | 6    | 11   | 109   |
| *Pseudomonas aeruginosa* (MBL)                | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 1    | 0    | 0    | 2     |
| *Stenotrophomonas maltophilia*                | 0    | 0    | 4    | 0    | 1    | 1    | 2    | 2    | 4    | 7    | 4    | 0    | 1     | 26    |
| *Klebsiella pneumoniae*                       | 4    | 8    | 5    | 2    | 4    | 2    | 4    | 9    | 7    | 14   | 6    | 8    | 13    | 88    |
| *Klebsiella pneumoniae* (ESBL)                | 11   | 8    | 3    | 3    | 2    | 4    | 1    | 10   | 7    | 7    | 4    | 5    | 2     | 67    |
| *Klebsiella pneumoniae* (NDM)                 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 4     |
| *Klebsiella pneumoniae* (KPC)                 | 0    | 4    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 4     |
| *Escherichia coli*                            | 1    | 3    | 2    | 0    | 3    | 3    | 4    | 6    | 4    | 9    | 7    | 11   | 5     | 58    |
| *Enterobacter cloacae*                        | 1    | 0    | 1    | 0    | 1    | 1    | 3    | 3    | 2    | 5    | 5    | 7    | 5     | 34    |
| *Enterobacter cloacae* (ESBL)                 | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 1    | 0    | 2    | 0    | 2    | 0     | 7     |
| *Proteus mirabilis*                           | 0    | 1    | 0    | 0    | 0    | 2    | 2    | 2    | 1    | 3    | 3    | 3     | 4     | 21    |
| *Proteus mirabilis* (ESBL)                    | 4    | 3    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 2    | 2    | 0     | 6     |
| *Morganella morganii*                         | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 2    | 0    | 2     | 8     |
| *Serratia marcescens*                         | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 2    | 2    | 0    | 2     | 8     |
| *Staphylococcus aureus*                       | 1    | 5    | 1    | 3    | 7    | 3    | 3    | 3    | 4    | 4    | 4    | 9    | 18    | 65    |
| *Staphylococcus aureus* (MRSA)                | 3    | 7    | 15   | 3    | 5    | 4    | 2    | 3    | 7    | 3    | 2    | 4    | 0     | 58    |
| *Coagulase-negative Staphylococcus (CNS)*     | 2    | 2    | 5    | 3    | 2    | 2    | 6    | 4    | 6    | 12   | 5    | 1     | 4     | 54    |
| *Coagulase-negative Staphylococcus (MRCNS)*   | 31   | 25   | 34   | 35   | 22   | 34   | 35   | 23   | 38   | 28   | 18   | 15    | 30    | 368   |
| *Enterococcus faecalis*                       | 5    | 8    | 15   | 5    | 5    | 5    | 4    | 5    | 6    | 16   | 2    | 6    | 13    | 95    |
| *Enterococcus faecalis* (HLAR)                | 0    | 3    | 9    | 0    | 2    | 3    | 0    | 0    | 0    | 0    | 1    | 2    | 0     | 20    |
| *Enterococcus faecium*                        | 1    | 2    | 9    | 5    | 1    | 2    | 1    | 0    | 4    | 3    | 0    | 2    | 7     | 37    |
| *Enterococcus faecium* (VRE)                  | 0    | 1    | 0    | 1    | 0    | 0    | 0    | 1    | 1    | 0    | 1    | 2    | 3     | 11    |
| *Enterococcus faecium* (HLAR)                 | 1    | 1    | 1    | 6    | 1    | 2    | 1    | 1    | 1    | 0    | 3    | 2    | 21    |
| *Streptococcus pneumoniae*                    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1     | 3     |
| *Neisseria meningitidis*                      | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1     |
| *Candida albicans*                            | 5    | 3    | 4    | 5    | 2    | 4    | 1    | 1    | 2    | 1    | 2    | 1     | 3     | 34    |
| *Candida glabrata*                            | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 1     | 4     |
| *Candida krusei*                              | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0     | 1     |
| *Candida tropicalis*                          | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0     | 1     |
| *Candida parapsilosis*                        | 0    | 2    | 0    | 0    | 0    | 2    | 1    | 1    | 3    | 1    | 1    | 0    | 3     | 14    |
| **Total**                                     | 115  | 125  | 141  | 103  | 104  | 103  | 107  | 112  | 124  | 159  | 107  | 109  | 148   | 1,557 |

were completely susceptible to fluconazole and *non-albicans Candida* species were susceptible to echinocandins and amphotericin.

**Discussion**

Bloodstream infections may lead to metastatic infections, severe sepsis, and multiorgan failure. The prevalence of bloodstream infections is estimated at 174–204/100,000 in North America and 166–189/100,000 in Europe, corresponding to 73,349–84,823 cases in the USA and 157,750–276,318 in Europe (Goto and Al-Hasan 2013). CVCs may be related to BSIs in 90% of cases (Polderman and Girbes 2002).

Possible reasons for this strong correlation include lack of asepsis upon catheter insertion and use, skin changes (e.g., burn-related), the biofilm formation on the catheter’s inner and outer surfaces, and the development of central vein thrombosis at the site of the catheter insertion. The only way to decrease the number of CLABSI cases is to ensure rigorous asepsis when the
Table IV
Resistance of Gram-negative pathogens to antimicrobial agents.

| Antimicrobial agent | Pseudomonas aeruginosa | Acinetobacter baumannii | Stenotrophomonas maltophilia | ESBL-negative Enterobacterales | ESBL-positive Enterobacterales | KPC-producing Klebsiella pneumoniae |
|---------------------|------------------------|-------------------------|-----------------------------|-------------------------------|-------------------------------|----------------------------------|
|                     | 2007 n = 9             | 2008 n = 12             | 2009 n = 9                  | 2010 n = 12                   | 2011 n = 7                    | 2012 n = 6                      |
| Ceftazidime         | 2                      | 4                       | 3                           | 0                             | 0                             | 1                                |
| Cefepime            | 0                      | 3                       | 0                           | 0                             | 0                             | 1                                |
| Piperacillin/tazobactam | 1               | 1                       | 5                           | 0                             | 0                             | 1                               |
| Gentamycin          | 5                      | 4                       | 5                           | 1                             | 3                             | 2                               |
| Ciprofloxacin       | 6                      | 3                       | 5                           | 0                             | 2                             | 2                               |
| Imipenem            | 3                      | 2                       | 4                           | 4                             | 2                             | 1                               |
| Meropenem           | 3                      | 0                       | 4                           | 3                             | 2                             | 1                               |
|                     |                        |                         |                             | 1                             | 2                             | 0                               |
|                     |                        |                         |                             | 1                             | 4                             | 4                               |
|                     |                        |                         |                             | 4                             | 3                             | 7                               |
| Gentamycin          | 30                     | 22                      | 7                           | 11                            | 29                            | 24                               |
| Ciprofloxacin       | 32                     | 24                      | 21                          | 19                            | 34                            | 25                               |
| Imipenem            | 11                     | 6                       | 10                          | 11                            | 31                            | 23                               |
| Meropenem           | 6                      | 6                       | 8                           | 11                            | 31                            | 23                               |
| Trimethoprim-sulfamethoxazole | 20                  | 18                      | 16                          | 19                            | 36                            | 24                               |
| Ampicillin/sulbactam | 12                  | 12                      | 8                           | 12                            | 19                            | 3                               |
| Colistin            | –                      | –                       | –                           | –                             | –                             | 0                               |
|                     |                        |                         |                             | 0                             | 0                             | 0                               |
|                     |                        |                         |                             | 0                             | 0                             | –                               |
| Gentamycin          | 30                     | 22                      | 7                           | 11                            | 29                            | 24                               |
| Ciprofloxacin       | 32                     | 24                      | 21                          | 19                            | 34                            | 25                               |
| Imipenem            | 11                     | 6                       | 10                          | 11                            | 31                            | 23                               |
| Meropenem           | 6                      | 6                       | 8                           | 11                            | 31                            | 23                               |
| Trimethoprim-sulfamethoxazole | 20                  | 18                      | 16                          | 19                            | 36                            | 24                               |
| Ampicillin/sulbactam | 12                  | 12                      | 8                           | 12                            | 19                            | 3                               |
| Colistin            | –                      | –                       | –                           | –                             | –                             | 0                               |
|                     |                        |                         |                             | 0                             | 0                             | 0                               |
|                     |                        |                         |                             | 0                             | 1                             | 0                               |
|                     |                        |                         |                             | 3                             | 4                             | 2                               |
| Amoxicillin/clavulanate | 12                 | 9                       | 3                           | 4                             | 2                             | 4                               |
| Gentamycin          | 10                     | 9                       | 3                           | 4                             | 2                             | 4                               |
| Ciprofloxacin       | 13                     | 11                      | 4                           | 4                             | 2                             | 4                               |
| Imipenem            | 4                      | 3                       | 0                           | 0                             | 0                             | 0                               |
| Meropenem           | 0                      | 0                       | 0                           | 0                             | 0                             | 0                               |
| Trimethoprim-sulfamethoxazole | 13                  | 9                       | 2                           | 3                             | 1                             | 3                               |
| Amikacin            | –                      | 0                       | –                           | –                             | –                             | –                               |
| Gentamicin          | –                      | 0                       | –                           | –                             | –                             | –                               |
| Tigecycline         | –                      | 2                       | –                           | –                             | –                             | –                               |
| Trimethoprim-sulfamethoxazole | –                  | 4                       | –                           | –                             | –                             | –                               |
| Colistin            | –                      | 0                       | –                           | –                             | –                             | –                               |
Table IV. Continued.

| Antimicrobial agent | NDM-producing *Klebsiella pneumoniae* | OXA48-producing *Klebsiella pneumoniae* |
|---------------------|-------------------------------------|---------------------------------------|
|                     | 2007 n = 0 2008 n = 0 2009 n = 0 2010 n = 0 2011 n = 0 2012 n = 0 2013 n = 0 2014 n = 0 2015 n = 0 2016 n = 0 2017 n = 0 2018 n = 1 2019 n = 2 |
| Amikacin            |                      | – – – – – – – – – – – – 2 1 2 |
| Gentamicin          |                      | – – – – – – – – – – 1 1 1 |
| Tigecycline         |                      | – – – – – – – – – – 2 1 0 |
| Trimethoprim-sulfamethoxazole |          | – – – – – – – – – – 1 1 1 |
| Colistin            |                      | – – – – – – – – – – 0 0 0 |

![Graphs](image.png)

Fig. 2. Gram-positive alert pathogens with mechanisms of resistance, isolated between 2009 and 2019.

Our work has been one of the most extensive single-center analyses performed in Poland in recent years. The study was conducted over a long period in a multidisciplinary ICU, with most of the cases being surgical and trauma patients. Some of them may be immunocompromised; in such patients, the transfer of pathogens from the site of infection to the lumen of the catheter via different connectors may be reasonably easy, resulting in more facile development and progression of a disease.

The data suggest that one in 20 ICU patients develop bloodstream infections. The longer the period of central vein catheterization, the higher the incidence of catheter is placed and used (Ling et al. 2016; Bell and O’Grady 2017; Ielapi et al. 2020).
catheter infection (Gunst et al. 2011). We found that the incidence of positive microbiological results in blood samples was 12.8%. Those values are relatively low compared to the results of other studies which report positive results in 18.9% to 31.3% of cases (Rani et al. 2012; Musicha et al. 2017; Rani et al. 2017). This discrepancy may be due to the procedures at our center, where patient blood samples are analyzed microbiologically every time the patient’s body temperature exceeds 38°C. Some studies from ICUs in southern Poland report a lower incidence of BSI (Wałaszek et al. 2018). However, the spectrum of pathogens isolated from blood samples was similar to our results, including *A. baumannii*, coagulase-negative staphylococci, *E. coli*, *P. aeruginosa*, *K. pneumoniae*, and *C. albicans* (Kolpa et al. 2018; Wałaszek et al. 2018).

The etiology of bloodstream infection depends on the geographical localization of the hospital. For example, in Malawi (Africa), the most common BSI pathogens are *Salmonella* Typhi and *Streptococcus pneumoniae* (Musicha et al. 2017). The Surveillance Network data from Korea collected from 2006 to 2017 showed that the most common pathogens were *E. coli* and *S. aureus*. In Japan, *E. coli*, *S. aureus*, and *K. pneumoniae* are the most common isolates (Rani et al. 2017; Lee et al. 2018).

Data from the European Antimicrobial Resistance Surveillance Network study performed in 22 countries between 2000 and 2009 indicated that *E. coli* and *S. aureus* were the most common BSI pathogens (Gagliotti et al. 2011). The results of a EUROBACT study spanning 162 ICUs in 24 European countries and Turkey, Brazil, and China showed that in 53%, 32%, 7.8%, and 1.2% of cases, bacteremia was caused by Gram-negative bacteria, Gram-positive pathogens, fungi, and anaerobic bacteria, respectively. Multidrug-resistant pathogens were isolated in 47.8% of cases (Tabah et al. 2012). Our results were similar, although there were some differences in the exact numbers of...
isolated pathogens (49.5% Gram-negative strains, 47.1% Gram-positive strains, and 3.5% fungi).

Gram-positive pathogens were responsible for half of all bloodstream infections. Most of them were staphylococci. Their resistance to methicillin ranges from 40 to 60%. Of importance is that MRCNS are a more likely etiological factor in infection than MRSA (Gunst et al. 2011; Louzi et al. 2016; Tian et al. 2019; Tomaszewski et al. 2019). Our results supported this observation. Moreover, MRCNS exhibit greater resistance to antimicrobials, except against vancomycin. We also noted the difference in resistance to gentamycin and trimethoprim/sulfamethoxazole. Such differences may result from the different proportions of branched-chain and straight-chain fatty acids in the membrane lipids of bacteria (Tiwari et al. 2020). However, susceptibility to sulphonamide is significant clinically because the drug can be administered orally, which may be necessary in patients who suffer from staphylococcal bone infections and require proper therapy for an extended time.

In many studies, Gram-negative pathogens responsible for more than half of bloodstream infections pose a greater therapeutic challenge than Gram-positive bacteria, partially due to their increasing antibiotic resistance. Enterobacteriales produce ESBL and CPE mechanisms of resistance. Both Acinetobacter spp. and Pseudomonas spp. exhibit mechanisms of resistance that are multidirectional and difficult to treat.

In our study, Gram-negative bacteria were isolated in 49.5% of cases. The most frequently isolated was A. baumannii (40.5%), followed by K. pneumoniae (21.4%), P. aeruginosa (14.1%), and E. coli (9%). These results differ significantly from those found in an analysis of 9,334 strains of A. baumannii performed between 1994 and 2011 (Munoz-Price et al. 2013), during which time this pathogen was responsible for 11% of blood infections. This situation is alarming because the only effective antimicrobial against this pathogen is colistin.

Among the Gram-negative bacteria, 30.4% were K. pneumoniae or E. coli. The ESBL mechanism of resistance was found in 40.6% of K. pneumoniae and 16% of E. coli. These results are similar to those found by other researchers. According to the literature, the ESBL mechanism of resistance is present in 34–75% of K. pneumoniae and is increasingly common (Gunst et al. 2011; Louzi et al. 2016; Tian et al. 2019). Fortunately, we found this pathogen to be entirely susceptible to meropenem. Moreover, only a small number of the isolated K. pneumoniae exhibited a KPC resistance mechanism.

There are a few significant limitations to our study. The first group of constraints is related to other observational studies with routinely collected electronic data. They include missing data, potential bias, and possible misclassification or inconsistencies in medical coding. The second one is related to the indication for blood sample collection. In our center, blood samples were collected when the infection was suspected clinically. It cannot be ruled out that some patients’ pathogens were present in their bloodstream with no clinical and bacteriological signs and symptoms of infection. The third one is related to the setting of this study: our analysis is connected to only one hospital, although a large one. Finally, assessing the results with some differences in patient-level factors, such as the severity of illness, may have influenced the conclusions.

Despite the limitations mentioned earlier, we believe that our results may be informative and exciting for those interested in the epidemiology of BSI. Our study estimated bloodstream infections in a large tertiary university hospital and trauma center for 13 years, as incidence rates and pathogens’ distribution, and their susceptibility/resistance to antimicrobial agents. The presented data may constitute material for further analyses assessing the microbiological situation in Poland and the region to improve the quality of care and outcome in critically ill patients.

Conclusions

Our 13-year study shows that among 12,619 microbiologically analyzed blood samples, 12% (1,509/12,619) were positive. In 278/1,509 (18.4%) of cases, a central line catheter infection was confirmed, and 1,557 pathogens were isolated.

The most frequently (770/1,557; 49.5%) isolated species were Gram-negative bacteria. Among the Gram-negative bacteria, the most frequently isolated were A. baumannii (312/770; 40.5%), K. pneumoniae (165/770 (24.1%); 67/165 (40.6%) of them produced ESBL, 5/165 (3%) – produced NDM, 4/165 (3.4%) – expressed KPC, 1/165 (0.6%) – produced OXA48), P. aeruginosa (111/770 (14.4%); 2/111 (1.8%) strains produced MBL), and E. coli (69/770 (9%); 11/69 (15.9%) strains expressed ESBL).

Gram-positive pathogens were isolated in 733/1,557 (47.1%) cases. The majority were staphylococci (545/733; 74.4%), mainly coagulase-negative (368/545; 67.5%). MRSA species represented 58/545 (10.6%) of all staphylococci. Fungi were isolated from 3.5% of samples.

Using these data to improve clinical practice, one can say that the MRSA and MRCNS species are susceptible to vancomycin, MSSA is susceptible to isoxazolyl penicillins, and VRE is susceptible to linezolid and tigecycline. However, colistin remains the only therapeutic option in some infections caused by A. baumannii and KPC-producing K. pneumoniae. P. aeruginosa is still susceptible to cefepime and ceftazidime. Echinocandins are effective therapeutics in treating fungal infections caused by C. albicans and non-albicans Candida species.
The bacteriological situation in our department, assessed by the incidence of infections, is similar to other ICUs in Poland and Eastern Europe. However, the number of *A. baumannii* and *P. aeruginosa* among the isolated pathogens is disturbing. We implemented and followed the infection control procedures. They include the decontamination of the patient environment, prevention of secondary contamination, personnel training, compliance control, hand hygiene, and clothing policy. We also follow the central catheter procedures. They emphasize full aseptic, and the additional connections are reduced to a minimum. A separate catheter lumen is reserved for parenteral nutrition, and the administration of drugs takes place after the disinfection of the connectors.

The applied infection reduction procedures follow the existing recommendations (Hryniewicz et al. 2013). In addition to the guidelines, it is essential to be aware of the infections, severity of the problem, prevention methods, and the real benefits of compliance with the recommendations that translate into a reduction in the frequency of infections in intensive care units.

**List of abbreviations**

| Abbreviation | Description |
|--------------|-------------|
| BSI          | bloodstream infection |
| CLABSI       | central line-associated bloodstream infections |
| CVC          | central venous catheter |
| ESBL         | extended-spectrum beta-lactamases |
| HLR          | high-level aminoglycoside resistance |
| ICD          | International Classification of the Diseases |
| ICU          | intensive care unit |
| KPC          | *Klebsiella pneumoniae* carbapenemase |
| MBL          | metallo-β-lactamases |
| MRSA         | methicillin-resistant *Staphylococcus aureus* |
| MRCS         | methicillin-resistant coagulase-negative *Staphylococcus* |
| MSSA         | methicillin-susceptible *Staphylococcus aureus* |
| NDM          | New Delhi metallo-β-lactamase |
| VRE          | vancomycin-resistant enterococci |

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**Ethical statement**

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Military Institute of Medicine, Warsaw, Poland (43/WIM/2020 of August 19, 2020).

**Author contributions**

Conceptualization, AG, ZR, and DT; methodology, AG; formal analysis, AG and DT; investigation, AG; data curation, A.W.-K.; writing-original draft preparation, AG, ZR, and DT; writing-review and editing, AG, ZR, A.W.-K, and DT; visualization, DT; project administration, AG, ZR, DT, and A.W.-K. All authors have read and agreed to the published version of the manuscript.

**Conflict of interest**

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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