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# Epidemiology of Bloodstream Infections by Single-Center Retrospective Study

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#### Abstract

Worldwide, bloodstream infections (BSIs) have a high morbidity rate of 1 to 4 and an estimated 15% to 30% crude death rate. 1, 5-7 Antimicrobial resistance (AMR) is a severe issue, especially for Enterobacteriaceae that are carbapenem-resistant and produce extended-spectrum beta lactamases (ESBLs), such as Escherichia coli and Klebsiella species1,7 (CRE). Only 2 reports on the epidemiology of BSIs have been published in Japan, but neither one includes information on patient comorbidities, microbiologic tests, or BSI severity.

**Keywords:** Bloodstream infection; Mortality; Epidemiology; Antimicrobial resistance; Surveillance

#### Introduction

According to a prior study, ESBL-producing E coli and Klebsiella species were more common in Japanese university hospitals between 2008 and 2012. 1 It is crucial to have a thorough understanding of BSIs in Japan in order to effectively treat them as well as conduct antimicrobial stewardship programmes aimed to describe the epidemiology of BSIs, highlighting AMR's participation and the influence it has on patient prognosis.

#### Methods

#### Study Design and Data Collection

This single-center, retrospective analysis involved all of the patients with positive blood culture results throughout a 5-year period from January 1, 2012, to December 31, 2016, at the Showa University Hospital, a tertiary teaching hospital in Japan with 1,014 beds. Infection source (e.g., catheter-related blood stream infection [CRBSI] or urinary tract infection), isolated microorganisms, and AMR data were extracted from patient medical records. Patient age, sex, place of onset (hospital-acquired or community-acquired infection) [1], length of stay, mortality, Charlson Comorbidity Index (CCI), quick sepmisrelated organ failure assessment (qSOFA), and sequential organ failure assessment (SOFA) In the absence of blood gas analysis, SOFA values were estimated as SpO2/FiO2.14. The patients were categorised based on the results were divided into two groups: those who survived for at least 30 days (the survival group) and those who passed away within 30 days (the death group). All other patients were classed as community-acquired infections. A hospital acquired infection was defined as a positive blood culture at two days following hospital admission [2]. 15 A single BSE episode was defined as a polymicrobial infection when more than one microbial species was isolated.

# **Microbiologic Results of Blood Culture**

The isolation of the organism from one or more positive blood cultures was used to define BSIs. Other than sputum and urine, the following blood cultures were acceptable sources of skin-resident or environmental bacteria: two or more blood cultures, blood cultures combined with intravascular catheter, cerebrospinal fluid, bile, or abscess samples. Only the first BSI episode was taken into consideration for individuals with repeated positive blood cultures within a year (including readmission instances) [3]. Using the BD BACTEC FX System, blood cultures were taken (Becton, Dickinson and Company, strains.

Franklin Lakes, NJ). MicroScan WalkAway was used to check all

## **AMR Definition**

Staphylococcus aureus, E. coli, Klebsiella species, Enterobacter species, Serratia species, Pseudomonas species, and Acinetobacter species were the seven bacteria evaluated for AMR. Proteus species were left out of the analysis because ESBL-producing isolates were only found in 1 case [4]. The clinical breakpoints of the Clinical and Laboratory Standards Institute were utilised to define AMR. At least three of the following antimicrobials were ineffective against multidrug-resistant Pseudomonas aeruginosa strains: piperacillin and tazobactam, ceftazidime, fluoroquinolones (ciprofloxacin or levofloxacin), aminoglycosides (gentamicin or amikacin), and carbapenems (imipenem or meropenem) [5]. Acinetobacter species that were multi-drug resistant were also resistant to carbapenems, aminoglycosides, and fluoroquinolones. The broth microdilution method was used to screen for oxacillin and cefoxitin resistance in S aureus. The double disc synergy experiment was used to quantify ESBL production. Ceftazidime and cefotaxime-containing discs were placed next to discs containing amoxicillin and clavulunic acid [6]. 20 The synthesis of metallo-beta-lactamase (MBL) was assessed using a disc coated with sodium mercaptoacetic acid with a disc containing ceftazidime and imipenem. the Japanese standards, which include the isolation and identification of Enterobacteriaceae as well as a minimum inhibitory concentration of meropenem of 2 mg/mL or minimal inhibitory concentrations of imipenem of 2 mg/mL and cefmetazole of 64 mg/mL. 22 Methicillin-resistant S aureus (MRSA), ESBLproducing bacteria, carbapenem-resistant P aeruginosa, CRE, and MBL-producing bacteria were the five antimicrobial-resistant diseases whose 30-day death rates were compared with those of the comparable non-AMR infections [7].

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#### **Statistical Analysis**

The categorical variables were compared using Pearson's chisquare or Fisher's exact tests, and the continuous variables were compared using the Student test. The significance level for all 2-tailed statistical tests was P .05. The yearly BSI mortality rates were compared using the Bonferroni correction. The level of significance was chosen at P .0125 [8]. Multiple logistic regression analysis was carried out to find variables significantly related to 30-day death from all causes. All variables in the\sunivariate analyses were included in a multivariate analysis of indepen-\sdent association with 30-day mortality with the calculation of adjusted\sodds ratios (ORs) (ORs). The degree of multicollinearity was evaluated using Spearman's rank correlation analysis. SPSS statistics version 24.0 was used for the statistical analysis [9].

# Results

The bacteria that were recovered from the BSI patients. The most common pathogens were E coli, S aureus, and Streptococcus species. Carbapenem- and fluoroquinolone-resistant Pseudomonas species, MRSA, ESBL, and fluoroquinolone-resistant E coli were the most frequently isolated AMR pathogens. Patients with yeast infections and other multi-microbial infections have a significant mortality risk. the findings of a 30-day mortality analysis using multivariate logistic regression [10]. Age 65 years, hospital acquired infection, qSOFA, SOFA score, CCI, CRBSI, urinary tract infection, BSI-caused Streptococcus species, E coli or yeasts, and surgery were all substantially linked to 30-day mortality, according to multivariate analysis [11].

#### Discussion

This is the first study that, to our knowledge, describes the epidemiology of BSIs in Japan, including the participation of AMR bacteria, patient comorbidities, and severity of illness scores (eg, CCI, qSOFA, and SOFA score). According to estimates, the 30-day and in-hospital death rates were 15.2% and 22.6%, respectively. Hospitalacquired BSIs have a 30-day death rate of 19.3%, according to earlier studies. 9 In Japan, the projected overall crude mortality rate for nosocomial BSIs is 24.5%. 1 Because severity of sickness scores and AMR testing were not taken into account in prior investigations, comparisons are challenging. In Japan, coordinated, widespread BSI surveillance is required for the comparison of clinical markers. Global in-hospital mortality has been estimated to be 15.3% in Ireland5, 40.0% in Brazil23, and 28.9% in Vietnam [12]. Mortality rates vary by nation. The variations in death rates could be brought on by variations in pathogen dispersion and healthcare services. In comparison to other nations, Brazil23 and Vietnam7 had a greater prevalence of AMR in Enterobacteriaceae, and some findings indicated that fungal BSIs contributed significantly to death. Fungal BSIs were found to be independently linked with 30-day mortality in this study's multivariate analysis. For immunocompromised and critically ill patients, such as those with malignancies, continuous cancer chemotherapy, and organ transplants, fungal BSIs pose a life-threatening risk. The incidence of fungal BSIs is also increased by the use of intravenous catheters. Antifungal therapy must be started right away for these individuals, although early diagnosis is challenging due to the lengthy time it takes to detect fungal growth in blood cultures. These elements might contribute to the explanation of the elevated mortality risk in fungal BSIs. The analysis included episodes of BSI where coagulasenegative staphylococci, Bacillus species, Corynebacterium species, and Cutibacterium species were strongly suspected to be the cause. Patients who had intravenous catheters or hematologic malignancies were most frequently affected by BSIs linked to those microorganisms.

# Conclusion

Due to the difficulty in separating infectious from contaminating microorganisms, BSIs with culture isolates of skin-resident and environmental bacteria were eliminated from several earlier researches. Comparisons between BSI studies that did not include such bacteria and those that did should be done with caution due to potential influences on incidence and fatality estimates. Community-acquired BSIs in this study had a low mortality risk, which is consistent with other studies indicating the majority of BSIs caused by E coli happened in the community and weren't life-threatening cases. BSIs brought on by Klebsiella and E. coli species ESBL-producing isolates were linked to considerably higher 30-day mortality, whereas isolates without ESBLs had relatively low 30-day mortality. Furthermore, gram-negative bacteria with carbapenem resistance had a significant 30-day death rate. In particular, compared to what was shown in other nations, we found a high incidence of carbapenem-resistant Pseudomonas species. The findings indicate that AMR has a bad prognosis in BSIs, however there were insufficiently many antimicrobial-resistant isolates to determine the relevance of any prognostic impact of AMR. It is necessary to conduct more research to determine how AMR affects patient prognosis. The retrospective design and conduct of the study at a single institution in Tokyo are some of its drawbacks. The outcomes might not be applicable to other parts of Japan where AMR is distributed differently. However, there are no aggregated national data in Japan. As a pilot research for national surveillance and possibly international data comparison, this examination offers useful information. Second, our institution does not offer quick diagnostic tests, such as matrixassisted laser desorption/ionization time-of-flight mass spectrometry. Prognosis is impacted by pathogen identification quickly; however few institutions in Japan have access to these tools. Finally, some AMR data were collected through screening tests (such as the double disc synergy test) therefore they contain resistance brought about by other carbapenemases, AmpC beta-lactamases, and other sources.

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