Introduction

Bloodstream infections (BSIs) are associated with high morbidity and mortality worldwide, in both developed and developing countries (Tian et al. 2019). They are among the top seven causes of death in Europe and North America, with more than two million episodes each year and a case fatality rate of 13–20%, resulting in 250,000 deaths annually. Approximately 30% of patients with BSI receive ineffective or delayed antimicrobial therapy, which in turn causes increased antimicrobial resistance and mortality (Pfaffer et al. 2020). For this reason, in 2015, the World Health Organization published the Antimicrobial Resistance Global Action Plan to promote awareness and understanding of antimicrobial drug resistance (WHO 2015). In addition, studies conducted in the last decade have associated an increase in the incidence of BSI with a sharp rise in at-risk population numbers (elderly patients, those with chronic diseases or immunosuppression, etc.). These developments are central to the global spread of multiresistant bacteria. Therefore, monitoring changes in the rate of BSI caused by pathogens such as methicillin-resistant Staphylococcus aureus (MRSA) and extended-spectrum β-lactamase (ESBL) or carbapenemase-producing Enterobacteriaceae is key to improving their management and prevention, as well as ensuring the delivery of appropriate healthcare (Diekema et al. 2019; Sader et al. 2019; Martínez Pérez-Crespo et al. 2021).

This study aims to investigate the prevalence of pathogens responsible for BSI, and their antimicrobial susceptibility profiles, in patients at our tertiary care university hospital for 12 years. Understanding the disease burden of BSIs can provide a valuable indicator for healthcare providers.
Experimental

Materials and Methods

This single-center study was conducted at an 880-bed tertiary care university hospital, per the principles of the Declaration of Helsinki. Our hospital was accredited by Joint Commission International two times (2007–2010 and 2012–2015) in the past. Approval was granted by the Ethics Committee (2021–11/6).

This study was a retrospective analysis of all data from blood cultures carried out by the Microbiology Laboratory from January 2008 to December 2019. We evaluated all BSI data without distinguishing between community-onset or hospital-acquired infections because separation in the BD EpiCenter™ data management system (Becton Dickinson, USA) is not very credible. Blood culture specimens from adult (>18 years) patients from hospital wards and intensive care units (ICU) were evaluated. The study was divided into four-time intervals (2008–2010, 2011–2013, 2014–2016, 2017–2019) to track the distribution of microorganisms and changes in antimicrobial resistance and compare between periods during the 12 years. Patient data were obtained from the BD EpiCenter™ data management system. Our study did not include molecular data on resistance profiles. To avoid duplication from the same patient, if the same organism caused persistent BSIs, only one specimen from the first episode within 30 days, was included for each patient in the study. Each infection was considered individually if patients had two or more separate BSIs. Patients below 18 years of age and outpatients were excluded from the study (Zhu et al. 2018).

Guidelines from the Center for Disease Control and Prevention (CDC) were followed to distinguish true BSI agents from contamination. Causative agents for BSIs were considered to be either pathogenic microorganism growth detected in one or more blood cultures or the identical skin microbiota isolates (diphtheroids (Corynebacterium spp. not Corynebacterium diphtheriae), Bacillus spp. (not Bacillus anthracis), coagulase-negative staphylococci (CoNS) including Staphylococcus epidermidis, viridan group streptococci, Aerococcus spp. Micrococcus spp. and Rhodococcus spp.) seen in two or more blood cultures at different times; otherwise, the findings were considered contamination (CDC 2020). The contamination rate was calculated as the ratio of blood culture bottles considered contaminated to the total number of blood cultures collected during the study period (CLSI 2007; Alnami et al. 2015).

Microbiological procedures. All blood cultures throughout the study were monitored using the BACTEC™ 9240 System (Becton Dickinson, USA). Positive bottles were removed, and Gram staining was performed; blood samples were inoculated on 5% sheep blood agar and eosin methylene blue agar and incubated at 37°C for 24–48 hours. Species identification was performed using conventional methods: Phoenix™ 100 System (Becton Dickinson, USA) until 2018, and matrix-assisted laser desorption ionization time-of-flight mass spectrometer (MALDI-TOF MS) (Bruker Daltonics, Germany) in 2019. Antibiotic susceptibility testing was performed using the Phoenix™ 100 System, Kirby-Bauer Disk Diffusion (Oxoid, UK), and gradient diffusion methods (bioMérieux, France). The recommendations of the Clinical and Laboratory Standards Institute (CLSI) until 2014 (CLSI 2013), and European Committee on AntimicrobialSusceptibility Testing (EUCAST) since 2014 (EUCAST 2020) were observed. Isolates were tested for susceptibility to vancomycin and teicoplanin using the gradient diffusion method. According to CDC recommendations, Enterobacteriaceae and Acinetobacter baumannii isolates were defined as carbapenem-resistant when showing resistance to at least one of the following agents: ertapenem, meropenem, imipenem, or doripenem (Goodman et al. 2016). MRSA and ESBL assays from the Phoenix™ 100 System were used to classify MRSA and ESBL-positive samples. ESBL-positive Escherichia coli and Klebsiella pneumoniae isolates were determined according to the Phoenix™ 100 System. S. aureus ATCC® 29213™, E. coli ATCC® 25922™, and Pseudomonas aeruginosa ATCC® 27853™ were quality control strains.

Statistical analysis. Statistical analysis was performed using IBM SPSS 23.0 (IBM SPSS Statistics, USA). The categorical descriptive data were presented as frequency distribution and percentages (%). Long-term trends in the distribution of agents and resistance rates isolated from both wards and ICUs were evaluated using linear regression. The incidence of bacteremia was expressed as the ratio of cases per 10,000 hospital/unit bed days and per 1,000 hospital/unit admissions, with information obtained from the hospital management database. Changes in annual incidence rates (per unit and total), were analyzed with Spearman correlation analysis, in which the strength of the relationship increases as it approaches ±1 and decreases as it approaches 0. Antibiotic resistance patterns against ceftriaxone, cefotaxime, cefepime, imipenem, meropenem, ertapenem, pipercillin-tazobactam, amikacin, gentamicin, colistin, and ciprofloxacin as treatment for E. coli, K. pneumoniae, A. baumannii, and P. aeruginosa in hospital wards and ICUs were compared using the chi-square method. The same method was also used to compare antibiotic resistance against daptomycin, oxacillin, vancomycin, teicoplanin, and linezolid for S. aureus, CoNS, and vancomycin, teicoplanin, linezolid, penicillin, and high-level gentamicin for Enterococ-
**Results**

In our hospital, from 2008 to 2019, a total of 136,030 blood cultures were processed for 34,782 patients from wards and ICUs. Of these, 11,542 isolates identified in 10,584 blood culture bottles from 7,096 patients were included in this study, while 11,443 isolates identified in 10,232 blood culture bottles from 4,460 patients were deemed contaminated according to CDC criteria and therefore were excluded from the study. Our contamination rate (10,232/136,030) was calculated to be 7.5%.

In our study, 8,891 BSI episodes occurred among 7,096 (4,016 – 56.6% male and 3,080 – 43.3% female) patients. Proportions of species are shown in Table I. 80.4% of samples were collected from wards, and 19.6% from ICUs. The overall rate of polymicrobial episodes was 19.4%, with significantly higher numbers in ICUs (27.7%) compared to hospital wards (17.3%) (chi-square; p < 0.001).

In the analysis of monomicrobial growths, *E. coli* was the most commonly seen Gram-negative (11.6%) and CoNS the most common Gram-positive (10.1%) agent. The most commonly found fungi were *Candida parapsilosis* (2.7%) and *Candida albicans* (2.5%). In polymicrobial growth analysis, although *E. coli* was the most common accompanying agent in the wards and overall, *A. baumannii* was the most frequent in ICU patients. When we evaluated polymicrobial and monomicrobial growth together, CoNS (12%) emerged as the most common pathogen, followed by *E. coli* (11.8%), *K. pneumoniae* (8.9%), *S. aureus* (8.6%), *A. baumannii* (7.6%), and *P. aeruginosa* (5%).

Fig. 1 and 2 show the frequency of microorganisms within all positive blood cultures. There was a significant decrease in the overall frequency of polymicrobial and CoNS isolates over the study period; the frequency of *K. pneumoniae* isolates increased significantly on the

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**Table I**

Distribution of microorganisms in bloodstream infections in the wards and intensive care units.

| Bloodstream infection episodes | Wards n (%) | Intensive care units n (%) | Overall n (%) |
|-------------------------------|-------------|----------------------------|---------------|
| **Gram-negative**             |             |                            |               |
| *Escherichia coli*            | 3,065 (42.8%) | 710 (40.9%)               | 3,775 (42.5%) |
| *Klebsiella pneumoniae*       | 529 (7.4%)   | 146 (8.4%)                | 675 (7.6%)    |
| *Acinetobacter baumannii*     | 261 (3.6%)   | 186 (10.7%)               | 447 (5.0%)    |
| *Pseudomonas aeruginosa*      | 275 (3.8%)   | 65 (3.7%)                 | 340 (3.8%)    |
| **Gram-positive**             |             |                            |               |
| *Coagulase-negative staphylococci* | 717 (10%) | 184 (10.6%)               | 901 (10.1%)   |
| *Staphylococcus aureus*       | 717 (10%)    | 96 (5.5%)                 | 813 (9.1%)    |
| *Enterococcus faecalis*       | 188 (2.6%)   | 57 (3.3%)                 | 245 (2.8%)    |
| *Enterococcus faecium*        | 191 (2.7%)   | 38 (2.2%)                 | 229 (2.6%)    |
| **Fungi**                     |             |                            |               |
| *Monomicrobial (Total)*       | 5,913 (82.7%)| 1,257 (72.3%)             | 7,170 (80.6%) |
| **Polymicrobial**             | 1,240 (17.3%)| 481 (27.7%)               | 1,721 (19.4%) |
| **Total**                     | 7,153 (100%) | 1,738 (100%)              | 8,891 (100%)  |
wards and in ICUs, whereas the frequency of *S. aureus* isolates decreased significantly in ICUs (Fig. 1).

Fig. 2 shows the frequency of resistant strains within all positive blood cultures. Vancomycin-resistant enterococcus (VRE) rates in both wards and ICUs have remained unchanged over the 12 years, while the rate of MRSA in ICUs has decreased significantly. Overall, ESBL-positive *E. coli* and *K. pneumoniae*, carbapenem-resistant *E. coli* and *K. pneumoniae*, and colistin-resistant *K. pneumoniae* and *A. baumannii* have all increased significantly over the years.

Tables II and III show the resistance rates of the most common bacteria at different points during the 12 years. In *E. coli*, we found that resistance against...
Fig. 2. Frequency of microorganisms within all positive blood cultures over the 12 years.

VRE – vancomycin-resistant enterococci, MRSA – methicillin-resistant S. aureus, ESBL – extended-spectrum β-lactamase

VRE

| Year     | Overall | Wards | Intensive Care Units |
|----------|---------|-------|----------------------|
| 2008-2010| 0.6     | 0.5   | 0.8                  |
| 2011-2013| 1.6     | 1.6   | 1.5                  |
| 2014-2016| 1       | 1.1   | 0.5                  |
| 2017-2019| 0.4     | 0.4   | 0.6                  |

MRSA

| Year     | Overall | Wards | Intensive Care Units |
|----------|---------|-------|----------------------|
| 2008-2010| 2.3     | 1.8   | 3.2                  |
| 2011-2013| 1.5     | 1.2   | 2.7                  |
| 2014-2016| 1.2     | 1.3   | 0.9                  |
| 2017-2019| 1.7     | 1.9   | 0.8                  |

ESBL-positive *Escherichia coli*

| Year     | Overall | Wards | Intensive Care Units |
|----------|---------|-------|----------------------|
| 2008-2010| 3.7     | 4.4   | 2.1                  |
| 2011-2013| 4.5     | 5.3   | 1.7                  |
| 2014-2016| 4.2     | 4.9   | 1.1                  |
| 2017-2019| 5.2     | 5.8   | 2.2                  |

ESBL-positive *Klebsiella pneumoniae*

| Year     | Overall | Wards | Intensive Care Units |
|----------|---------|-------|----------------------|
| 2008-2010| 2.2     | 2.2   | 2.2                  |
| 2011-2013| 2.2     | 2.1   | 2.7                  |
| 2014-2016| 5.2     | 4.2   | 9.4                  |
| 2017-2019| 7       | 7.9   | 12.2                 |

Carbapenem-resistant *Escherichia coli*

| Year     | Overall | Wards | Intensive Care Units |
|----------|---------|-------|----------------------|
| 2008-2010| 0.1     | 0.1   | 0                    |
| 2011-2013| 0.1     | 0.1   | 0.2                  |
| 2014-2016| 0.3     | 0.4   | 0.2                  |
| 2017-2019| 1.1     | 1.2   | 0.6                  |

Carbapenem-resistant *Klebsiella pneumoniae*

| Year     | Overall | Wards | Intensive Care Units |
|----------|---------|-------|----------------------|
| 2008-2010| 0.6     | 0.3   | 1.1                  |
| 2011-2013| 1.5     | 0.9   | 3.7                  |
| 2014-2016| 4.6     | 2.9   | 11.8                 |
| 2017-2019| 6.6     | 5.7   | 11.2                 |

Carbapenem-resistant *Acinetobacter baumannii*

| Year     | Overall | Wards | Intensive Care Units |
|----------|---------|-------|----------------------|
| 2008-2010| 6.4     | 3.6   | 12.3                 |
| 2011-2013| 7.8     | 4.8   | 18.8                 |
| 2014-2016| 7.1     | 4.6   | 17.5                 |
| 2017-2019| 6.7     | 4.7   | 16.2                 |

Colistin-resistant *Acinetobacter baumannii*

| Year     | Overall | Wards | Intensive Care Units |
|----------|---------|-------|----------------------|
| 2008-2010| 0.0     | 0.0   | 0.0                  |
| 2011-2013| 0.1     | 0.1   | 0.0                  |
| 2014-2016| 0.4     | 0.3   | 0.0                  |
| 2017-2019| 1.2     | 1.2   | 1.2                  |

Colistin-resistant *Klebsiella pneumoniae*

| Year     | Overall | Wards | Intensive Care Units |
|----------|---------|-------|----------------------|
| 2008-2010| 0.0     | 0.0   | 0.0                  |
| 2011-2013| 0.3     | 0.3   | 0.5                  |
| 2014-2016| 2.6     | 1.7   | 6.8                  |
| 2017-2019| 6.8     | 6.8   | 6.8                  |
|                | Escherichia coli (%) (n = 1,360) | p     | Klebsiella pneumoniae (%) (n = 1,031) | p     | Acinetobacter baumannii (%) (n = 864) | p     | Pseudomonas aeruginosa (%) (n = 580) | p     |
|----------------|----------------------------------|-------|--------------------------------------|-------|--------------------------------------|-------|-------------------------------------|-------|
|                | Wards | ICU | Overall                              |       | Wards | ICU | Overall                              |       | Wards | ICU | Overall                              |       |
| Ceftriaxone    | 25.7   | 23.8 | 25.6                                 | 0.664 | 38    | 50.4 | 41.1                                 | <0.001| 38.2  | 28.5 | 33.4                                 | 0.002 |
| Cefotaxime     | 11.3   | 23.8 | 12.3                                 | <0.001| 10.7  | 20.2 | 13.1                                 | <0.001| 32.6  | 43.5 | 38.0                                 | 0.001 |
| Cefepime       | 36.9   | 49.5 | 37.9                                 | 0.010 | 46.8  | 67.2 | 52.0                                 | <0.001| 47.7  | 62.5 | 55.0                                 | <0.001|
| Imipenem       | 1.4    | 1    | 1.3                                  | 0.589 | 25.1  | 48.9 | 31.1                                 | <0.001| 74.9  | 88.7 | 81.7                                 | <0.001|
| Meropenem      | 0.9    | 1    | 0.9                                  | 0.620 | 24.7  | 48.9 | 30.8                                 | <0.001| 74.7  | 90.7 | 82.6                                 | <0.001|
| Ertapenem      | 2.9    | 4.8  | 3.1                                  | 0.219 | 25.6  | 46.6 | 30.9                                 | <0.001| 76    | 74.3 | 75.2                                 | 0.558 |
| Piperacillin-Tazobactam | 23.8   | 25.7 | 24                                  | 0.663 | 50.5  | 72.5 | 56.1                                 | <0.001| 50    | 66.7 | 58.2                                 | <0.001|
| Amikacin       | 1.4    | 1.9  | 1.4                                  | 0.438 | 5.6   | 21   | 9.5                                  | <0.001| 70.4  | 76.2 | 73.2                                 | 0.053 |
| Gentamicin     | 26.1   | 36.2 | 26.8                                 | 0.024 | 23.3  | 42.7 | 28.2                                 | <0.001| 62.2  | 75.2 | 68.6                                 | <0.001|
| Colistin       | 0.2    | 1    | 0.3                                  | 0.275 | 6     | 14.1 | 8.1                                  | <0.001| 2.3   | 1.4  | 1.8                                  | 0.477 |
| Fosfomycin     | 0      | 0    | 0                                   | –     | 0.8   | 1.1  | 0.9                                  | 0.411 | 1.6   | 0.9  | 1.3                                  | 0.570 |
| Ciprofloxacin  | 44.6   | 44.8 | 44.6                                 | 0.978 | 37.2  | 69.8 | 45.5                                 | <0.001| 81.2  | 96.8 | 88.9                                 | <0.001|
| ESBL           | 36.6   | 43.8 | 37.1                                 | 0.086 | 45.9  | 56.9 | 48.7                                 | 0.001 | –     | –    | –                                  | –     |
| Carbapenem-resistant | 3.3    | 4.8  | 3.5                                  | 0.294 | 29.8  | 58.4 | 37.1                                 | <0.001| 90.5  | 93.8 | 92.1                                 | 0.080 |

ESBL – extended-spectrum β-lactamase, – – not tested
cesfotaxime, cefepime, and gentamicin was significantly more common in the isolates from ICU patients than in the wards (Table II). ESBL-positive *E. coli* bacteraemia rate was 37.1%, and there was no statistically significant difference between ICU and non-ICU settings. In patients with *K. pneumoniae* infection, resistance rates for all antibiotics were found to be significantly higher in ICU patients. ESBL-positive *K. pneumoniae* bacteraemia rate was 48.7% and carbapenem-resistant *K. pneumoniae* bacteraemia rate was 37.1%. The resistance rate was significantly higher in the ICU setting. *A. baumannii*, resistance to cefotaxime, cefepime, imipenem, meropenem, pipacillin-tazobactam, gentamicin, and ciprofloxacin was significantly higher in ICU patients. Regarding *P. aeruginosa*, resistance to ceftazidine, cefepime, imipenem, meropenem, pipacillin-tazobactam, gentamicin, and ciprofloxacin was also found to be significantly higher in ICU patients than in the wards (Table II).

When we investigated Gram-positive bacteraemia, daptomycin, vancomycin, and linezolid-resistant *S. aureus* were not detected. However, oxacillin-resistant *S. aureus* (an indicator of MRSA) was significantly higher in ICU patients. While daptomycin and vancomycin resistance was not detected in CoNS, oxacillin resistance (indicating MRCoNS) was also found to be significantly higher in ICU patients. In the *E. faecalis* and *E. faecium* isolates, penicillin resistance was found to be significantly higher in non-ICU patients (Table III).

The incidence of BSI episodes per year and over 12 years was calculated as a ratio of 10,000 hospital bed days and 1,000 hospital admissions. The incidence of BSI in our hospital over the 12 years was 20.8/10,000 bed days, and 10.2/1,000 admissions. An inverse correlation was demonstrated for MRSA isolates in 10,000 bed days (r = −0.978, p = 0.022) and 1,000 admissions (r = −0.977, p = 0.023) when calculating annual incidence rates. In other resistant strains, no significant correlation (direct or inverse) was found per 10,000 hospital/unit bed days or 1,000 hospital/unit admissions.

### Discussion

Our study is important for highlighting changes and trends in the frequency of bacteraemia isolates and their antibiotic resistance detected in our hospital over a long period. CLSI guidelines advocate a target of < 3% contamination rate in blood cultures (CLSI 2007). However, in studies from different geographical regions and countries with diverse socioeconomic levels, a higher rate of 3.8–10.4% has been reported, which is similar to our results of 7.5% (Chukwuemeka and Samuel 2014; Abu-Saleh et al. 2018). A German study reported a 2.8% contamination rate in blood cultures (Schönweck et al. 2021).

Our hospital is a tertiary care hospital with low staffing levels, a heavy workload, and an increasing frequency of invasive procedures. All these contribute to the cross-infection with microorganisms from patient to patient. It may account for our high contamination rate (7.5%). However, we found a significant decrease in the overall frequency of CoNS isolates in samples, related to the contamination rate.

*S. aureus* is the leading cause of Gram-positive bacteraemia worldwide, while *E. coli* is the most significant cause of Gram-negative bacteraemia (Hattori et al. 2018; Tian et al. 2019; Pfaller et al. 2020). In a study conducted in Iran, CoNS was found to be the most common Gram-positive pathogen while the most common Gram-negative bacteria was *P. aeruginosa* (Keihanian et al. 2018). In two other studies conducted in our country, the most common Gram-positive pathogen were *E. faecalis* (Satılım and Aşgın 2019) and *S. epidermidis*.
patients (Ham et al. 2020). In our study, CoNS was found frequently in Gram-positive bacteria, a result of our high contamination rate. Meanwhile, similar to the literature, E. coli was the most common Gram-negative bacterium.

The prevalence of polymicrobial infection in BSI episodes is reported to vary between 8–32% (Yo et al. 2019). Similarly, in our study, this rate was 19.4%. According to the international EUROBACT study, which examined BSIs in 162 ICUs; monomicrobial growth was reported in 88% of the patients (58.3% Gram-negative, 32.8% Gram-positive, 7.8% fungal, 1.2% anaerobic), while polymicrobial growth was reported in 12% (Tabah et al. 2012). Similar to these results and those of other studies, we found Gram-negative bacteria to be the most common etiological agents for BSI in the ICUs, and Gram-positive bacteria emerged as the second most common cause (Tabah et al. 2012; Chaturvedi et al. 2021; Kallel et al. 2021).

Changing trends in the prevalence of pathogens caused by BSI have also been recorded. The SENTRY study group and two other studies have described an increase in the prevalence of K. pneumoniae in BSIs over time (Li et al. 2020; Pfaffer et al. 2020; Tsuzuki et al. 2021). A study from Greece, our neighboring country, noted using data from WHONET that although the prevalence of K. pneumoniae in hospital wards has decreased in past years, it has increased in ICUs (Polemis et al. 2020). In contrast, in our study, we saw a significant increase in the prevalence of K. pneumoniae – overall in hospital wards and ICUs. One SENTRY study (Pfaffer et al. 2020) found the prevalence of MRSA to be decreasing over time, while another SENTRY study (Diekema et al. 2019) noted an increase in ESBL-positive E. coli and K. pneumoniae, and carbapenem-resistant Enterobacteriaceae. Studies conducted in China reported the increasing incidence of carbapenem-resistant K. pneumoniae (Tian et al. 2019; Mineau et al. 2018) and MRSA in hospital wards (Tian et al. 2019), but a decrease in MRSA and ESBL-positive K. pneumoniae in ICUs (Tian et al. 2019). Meanwhile, ESBL-positive E. coli has increased in ICUs in Toronto (Mineau et al. 2018), while the prevalence of MRSA has decreased in Spain (Martínez Pérez-Crespo et al. 2021). In our study, we noted a significant decrease in the prevalence of MRSA in our ICUs over the study period, while overall, the prevalence of all other phenotypically resistant Gram-negative bacteria increased significantly.

According to the SENTRY study, BSIs caused by MRSA were seen among patients in the non-ICU setting, while VRE, ESBL-positive Klebsiella sp., carbapenem-resistant Klebsiella sp., and E. coli were more common among patients in ICUs (Pfaffer et al. 2020). In the US, the prevalence of MRSA was higher in ICU patients (Ham et al. 2020). In our study, there was no statistically significant difference in the prevalence of VRE, although MRSA was significantly more common in ICUs than in the hospital wards. Our study found the rate of antibiotic-resistant isolates to be generally higher in ICUs than in hospital wards. ICUs are units where resistant infectious species and critical patients are monitored and treated; furthermore, these dedicated areas frequently require invasive interventions. Therefore, the likelihood of encountering resistant bacteria here is higher than in other hospital wards.

In a study conducted in the USA, the incidence of MRSA per 10,000 bed days was reported to have decreased (Jernigan et al. 2020). In a study from China, the incidence of Gram-positive microorganisms in BSI per 1,000 admissions had decreased (Zhu et al. 2018). In another study from China, a detected increase in the incidence of Gram-negative microorganisms was not considered statistically significant (Zhu et al. 2021). The incidence density increased linearly in a medical-surgical intensive care unit during 2005–2007 in Turkey (from 3.57 to 9.60 per 1,000 patient-days) (Erdem et al. 2009). The incidence of BSI in our hospital over the 12 years was 20.8/10,000 bed days and 10.2/1,000 admissions. In our study, the correlation of phenotypically resistant bacteria with 10,000 hospital bed days and 1,000 hospital admissions was examined, and an inverse correlation was found in MRSA isolates only for both 10,000 bed days and 1,000 admissions.

In conclusion, although our study was conducted at only one healthcare center, our hospital is a tertiary hospital and the largest in the South Marmara region of Turkey. While our contamination rate is high, the prevalence of polymicrobial growth and CoNS has decreased significantly over the years. However, although the frequency of S. aureus and MRSA has decreased significantly in ICUs, the prevalence of K. pneumoniae increased. The most important finding of this study was the dramatic increase in carbapenem and colistin resistance in recent years. Our infection control committee has been operating since 1995. We have blood culture collection procedures, and we use regular educational interventions for proper blood culture specimen collection for physicians, nurses, and phlebotomists. We have a hand hygiene policy, infection control education and procedures, and antimicrobial stewardship policies (restriction for broad-spectrum antibiotics, cumulative antibiogram, following usage of antibiotics by defined daily doses, de-escalation, and stop order).

In order to prevent the spread of K. pneumoniae and other resistant bacteria, we are trying to increase hand hygiene compliance rates by constantly repeating hand hygiene training. Physicians can use broad-spectrum antibiotics (such as carbapenems and polymyxins) only with the approval of infectious diseases and clinical microbiologists (restriction policy). We believe we need...
to re-evaluate our hospital's hand hygiene policy, infection control procedures, and antimicrobial stewardship. On the other hand, physicians should be aware of the increasing drug resistance, such as ESBL and carbapenem resistance, and choose their empiric treatment according to susceptibility patterns. We believe that monitoring the distribution of pathogens and antibiotic susceptibility profiles at regular intervals, especially in ICUs, will contribute to our understanding of the increase of resistant microorganisms and help prevent their spread with antimicrobial stewardship and infection control policies.

**Declartions**

This manuscript was presented at the National Turkish Society of Microbiology Congress as an oral presentation (Evaluation of Blood Culture Growth Between 2007–2019) on 25–27 December 2020.

**Author contributions**

All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by all of the authors. The first draft of the manuscript was written by NUT and all authors commented on previous versions of the manuscript. Writing – review and editing were performed by CO, BE, and HA. All authors read and approved the final 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.

**Literature**

Abu-Saleh R, Nitzan O, Saliba W, Colodner R, Keness Y, Yanovskay A, Edelstein H, Schwartz N, Chazan B. Bloodstream infections caused by contaminans: Epidemiology and risk factors: A 10-year surveillance. Isr Med Assoc J. 2018 Jul;20(7):433–437.

Alnami AY, Aljasser AA, Almousa RM, Torczyan AA, BinSaeed AA, Al-Hazmi AM, Somily AM. Rate of blood culture contamination in a teaching hospital: A single center study. J Taibah Univ Medical Sci. 2015 Dec;10(4):432–436. https://doi.org/10.1016/j.jtumed.2015.08.002

Bıçak İ, Varışlı AN, Peker SA. [Distribution and antibiotic susceptibility of agents was isolated from blood cultures: Our four-years data] (in Turkish). Cerrahi Ameliyathane Sterilizasyon Enfeksiyon Kontrol Hemsirjeliği Dergisi. 2020;1(1):8–19.

CDC. Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and Non-central Line Associated Bloodstream Infection) [Internet]. Atlanta (USA): Centers for Disease Control and Prevention; 2020 [cited 2022 May 01]. Available from https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc_clabscurrent.pdf

Chaturvedi P, Lamba M, Sharma D, Mamoria VP. Bloodstream infections and antibiotic sensitivity pattern in intensive care unit. Trop Doct. 2021 Jan;51(1):44–48. https://doi.org/10.1177/0049475520977043

Chukwuemeka I, Samuel Y. Quality assurance in blood culture: A retrospective study of blood culture contamination rate in a tertiary hospital in Nigeria. Niger Med J. 2014;55(3):201–203. https://doi.org/10.4103/0300-1652.132038

CLSI. Performance standards for antimicrobial susceptibility testing. 23rd ed. CLSI supplement M100. Wayne (USA): Clinical and Laboratory Standards Institute; 2013.

CLSI. Principles and Procedures for Blood Cultures; Approved Guideline. CLSI document M47-A. Wayne (USA): Clinical and Laboratory Standards Institute; 2007.

Dickema DJ, Hseuh PR, Mendes RE, Pfaller MA, Rolston KV, Sader HS, Jones RN. The microbiology of bloodstream infection: 20-year trends from the SENTRY antimicrobial surveillance program. Antimicrob Agents Chemother. 2019 Jul;63(7):e00355-19. https://doi.org/10.1128/AAC.00355-19

Erdem I, Ozugultekin A, Inan AS, Engin DO, Akcay SS, Turan G, Dincer E, Oguzoğlu N, Goktas P. Bloodstream infections in a medical-surgical intensive care unit: Incidence, aetiology, antimicrobial resistance patterns of Gram-positive and Gram-negative bacteria. Clin Microbiol Infect. 2009 Oct;15(10):943–946. https://doi.org/10.1111/j.1469-0691.2009.02863.x

EUCAST. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 10.0. Basel (Switzerland): The European Committee on Antimicrobial Susceptibility Testing; 2020.

Goodman KE, Simner PJ, Tamma PD, Milstone AM. Infection control implications of heterogeneous resistance mechanisms in carbapenem-resistant Enterobacteriaceae (CRE). Expert Rev Anti Infect Ther. 2016 Jan 02;14(1):95–108. https://doi.org/10.1586/14787210.2016.1106940

Ham DC, See J, Nosovad S, Crist M, Mahon G, Fike L, Spicer K, Talley P, Finchum A, Kainer M, et al. Investigation of hospital-onset merihcillin-resistant Staphylococcus aureus bloodstream infections at eight high burden acute care facilities in the USA, 2016. J Hosp Infect. 2020;105(3): 502 – 508. https://doi.org/10.1016/j.jhin.2020.04.007

Hattori H, Maeda M, Nagatomo Y, Takuma T, Niki Y, Naito Y, Sasaki T, Ishino K. Epidemiology and risk factors for mortality in bloodstream infections: A single-center retrospective study in Japan. Am J Infect Control. 2018 Dec;46(12):e75–e79. https://doi.org/10.1016/j.ajic.2018.06.019

Jernigan JA, Hatfield KM, Woldorf H, Nelson RE, Olubajo B, Reddy SC, McCarthy N, Paul P, McDonald LC, Kallen A, et al. Multidrug-resistant bacterial infections in U.S. hospitalized patients, 2012–2017. N Engl J Med. 2020 Apr 02;382(14):1309–1319. https://doi.org/10.1056/NEJMoa1914433

Kallel H, Houcke S, Resiere D, Roy M, Mayence C, Mathien C, Mootien J, Demar M, Hommel D, Djossou F. Investigation of hospital-onset methicillin-resistant Staphylococcus aureus bloodstream infections on 25–27 December 2020. Trop Doct. 2021 Jan;51(1):44–48. https://doi.org/10.1177/0049475520977043

Keihanian F, Saeidinia A, Abbasi K, Keihanian F. Multidrug-resistant Enterobacteriaceae: Current status and future challenges. Am J Infect Control. 2018 Dec;46(12):e75–e79. https://doi.org/10.1016/j.ajic.2018.06.019

Jernigan JA, Hatfield KM, Woldorf H, Nelson RE, Olubajo B, Reddy SC, McCarthy N, Paul P, McDonald LC, Kallen A, et al. Multidrug-resistant bacterial infections in U.S. hospitalized patients, 2012–2017. N Engl J Med. 2020 Apr 02;382(14):1309–1319. https://doi.org/10.1056/NEJMoa1914433

Kallel H, Houcke S, Resiere D, Roy M, Mayence C, Mathien C, Mootien J, Demar M, Hommel D, Djossou F. Investigation of hospital-onset methicillin-resistant Staphylococcus aureus bloodstream infections on 25–27 December 2020. Trop Doct. 2021 Jan;51(1):44–48. https://doi.org/10.1177/0049475520977043

Keihanian F, Saeidinia A, Abbas K, Keihanian F. Epidemiology of antibiotic resistance of blood culture in educational hospitals in Rasht, North of Iran. Infect Drug Resist. 2018 Oct;11:1723–1728. https://doi.org/10.2147/IDR.S169176

Li Y, Li J, Hu T, Hu J, Song N, Zhang Y, Chen Y. Five-year change of prevalence and risk factors for infection and mortality of carbapenem-resistant Klebsiella pneumoniae bloodstream infection in a tertiary hospital in North China. Antimicrob Resist Infect Control. 2020 Dec;9(1):79. https://doi.org/10.1186/s13756-020-00728-3
Martínez Pérez-Crespo PM, López-Cortés LE, Retamar-Gentil P, García JFL, Vinuesa García D, León E, Calvo JMS, Galán-Sánchez F, Natera Kindelan C, del Arco Jiménez A, et al.; PROBAC REIPI/GEIH-SEIMC/SAEI Group. Epidemiologic changes in bloodstream infections in Andalucía (Spain) during the last decade. Clin Microbiol Infect. 2021 Feb;27(2):283.e9–283.e16. https://doi.org/10.1016/j.cmi.2020.05.015

Mineau S, Kozak R, Kissmon M, Paterson A, Oppedisano A, Douri F, Gogan K, Willey BM, McGeer A, Poutanen SM. Emerging antimicrobial resistance among Escherichia coli strains in bloodstream infections in Toronto, 2006–2016: A retrospective cohort study. CMAJ Open. 2018 Oct;6(4):E580–E586. https://doi.org/10.9778/cma jo.20180039

Pfaller MA, Carvalhaes CG, Smith CJ, Diekema DJ, Castanheira M. Bacterial and fungal pathogens isolated from patients with bloodstream infection: frequency of occurrence and antimicrobial susceptibility patterns from the SENTRY Antimicrobial Surveillance Program (2012–2017). Diagn Microbiol Infect Dis. 2020 Jun;97(2):115016. https://doi.org/10.1016/j.diag microbio.2020.115016

Polemis M, Tryfinopoulou K, Giakkoupi P, Vatopoulos A; WHO-NET-Greece study group. Eight-year trends in the relative isolation frequency and antimicrobial susceptibility among bloodstream isolates from Greek hospitals: data from the Greek Electronic System for the Surveillance of Antimicrobial Resistance – WHONET-Greece, 2010 to 2017. Euro Surveill. 2020 Aug 27;25(34):1900516. https://doi.org/10.2807/1560-7917.ES.2020.25.34.1900516

Sader HS, Castanheira M, Streit JM, Flamm RK. Frequency of occurrence and antimicrobial susceptibility of bacteria isolated from patients hospitalized with bloodstream infections in United States medical centers (2015–2017). Diagn Microbiol Infect Dis. 2019 Nov;95(3):114850. https://doi.org/10.1016/j.diagmicrobio.2019.06.002

Satlimiş Ş, Aşgin N. [Distribution of antibiotic susceptibility profiles of bacteria frequently isolated in blood cultures by years] (in Turkish). ANKEM Derg. 2019;33(3):95–101. https://doi.org/10.5222/ankem.2019.095

Schöneweck F, Schmitz RPH, Rißner F, Scherag A, Löfler B, Pletz MW, Weis S, Brunkhorst FM, Hagel S. The epidemiology of bloodstream infections and antimicrobial susceptibility patterns in Thuringia, Germany: a five-year prospective, state-wide surveillance study (AlertsNet). Antimicrob Resist Infect Control. 2021 Dec;10(1):132. https://doi.org/10.1186/s13756-021-00997-6

Tabah A, Koulenti D, Laupland K, Misset B, Valles J, Bruzzi de Carvalho F, Paiva JA, Çakar N, Ma X, Eggimann P, et al. Characteristics and determinants of outcome of hospital-acquired bloodstream infections in intensive care units: the EUROBACT International Cohort Study. Intensive Care Med. 2012 Dec;38(12):1930–1945. https://doi.org/10.1007/s00134-012-2695-9

Tian L, Zhang Z, Sun Z. Antimicrobial resistance trends in bloodstream infections at a large teaching hospital in China: a 20-year surveillance study (1998–2017). Antimicrob Resist Infect Control. 2019 Dec;8(1):86. https://doi.org/10.1186/s13756-019-0545-z

T Suzuki S, Matsumaga N, Yahara K, Shibayama K, Sugai M, Ohnagari N. Disease burden of bloodstream infections caused by antimicrobial-resistant bacteria: A population-level study, Japan, 2015–2018. Int J Infect Dis. 2021 Jul;108:119–124. https://doi.org/10.1016/j.ijid.2021.05.018

WHO. Global action plan on antimicrobial resistance [Internet]. Geneva (Switzerland): World Health Organization; 2015 [cited 2022 May 01]. Available from https://apps.who.int/iris/rest/bitstreams/864486/retrieve

Yo CH, Hsein YC, Wu YL, Hsu WT, Ma MMH, Tsai CH, Chen SC, Lee CC. Clinical predictors and outcome impact of community-onset polymicrobial bloodstream infection. Int J Antimicrob Agents. 2019 Dec;54(6):716–722. https://doi.org/10.1016/j.ijantimicag.2019.09.015

Zhu Q, Yue Y, Zhu L, Cui J, Zhu M, Chen L, Yang Z, Liang Z. Epidemiology and microbiology of Gram-positive bloodstream infections in a tertiary-care hospital in Beijing, China: a 6-year retrospective study. Antimicrob Resist Infect Control. 2018 Dec;7(1):107. https://doi.org/10.1186/s13756-018-0398-x

Zhu Q, Zhu M, Li C, Li L, Guo M, Yang Z, Zhang Z, Liang Z. Epidemiology and microbiology of Gram-negative bloodstream infections in a tertiary-care hospital in Beijing, China: a 9-year retrospective study. Expert Rev Anti Infect Ther. 2021 Jun 03;19(6):769–776. https://doi.org/10.1080/14787210.2021.1848544