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RESEARCH ARTICLE

Epidemiology of Hospital-acquired Primary Bloodstream Infections: 5-Year Experience

Yeşim Alpay Çağlar[1], Pınar Korkmaz[2], Nevil Aykın[3], Figen Çevik[3], Hülya Bilgili[3]

[1]Department of Infectious Diseases and Clinical Microbiology, Balıkesir University Faculty of Medicine, Balıkesir, Türkiye
[2]Department of Infectious Diseases and Clinical Microbiology, Dumlupınar University Faculty of Medicine, Kütahya, Türkiye
[3]Department of Infectious Diseases and Clinical Microbiology, Yunus Emre State Hospital, Eskişehir, Türkiye

ABSTRACT

Objective: Bacterial bloodstream infections (BSI) are among the most common causes of healthcare-associated infections. In this study, the patients diagnosed with primary BSI were evaluated, risk factors and the distribution profiles of the pathogenic microorganisms were identified.

Materials and Methods: Culture-confirmed 206 nosocomial primary bacteremic episodes were evaluated regarding age, gender, underlying disease, presence of a catheter, distribution of pathogenic microorganisms, and status of their antimicrobial resistance.

Results: 206 episodes of bacteremia were identified in 183 patients diagnosed with nosocomial primary BSI during a period of 5 years among the patients evaluated with active surveillance. The most common underlying disease was diabetes mellitus. There was an intravascular catheter in 55% of the patients. The most commonly isolated microorganisms were *A.baumannii*, coagulase-negative staphylococci and *E.coli*.

Conclusion: In recent years, the bacterial profile of the causative agents of BSI has changed from gram-positive to gram-negative microorganisms. Antibiotic resistance rates have also increased significantly. In the selection of empirical treatment, it is important to know the complicating factors, the causative pathogen profile of the region and hospital, and the antibiotic susceptibility and resistance rates for appropriate treatment.

Keywords: Antimicrobial susceptibility, hospital-acquired bloodstream infections, microorganism, primary bacteremia

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INTRODUCTION

Bacterial BSI are major infectious complications in critical patients and the most common causes of healthcare-associated infections.[1,2] Diagnostic and therapeutic interventions applied to patients play a role as a predisposing factor for infection. Higher severity scores and durations of intensive care unit (ICU) stays and catheterization are well-established risk factors for catheter-related BSI.[3] It is observed more frequently in ICU due to more invasive procedures such as increased use of invasive medical devices, increase in aggressive medical treatments, and invasive procedures and the presence of other complicating factors in this group patients.[4]

Prolonged use and inappropriate care of intravascular catheters are important risk factors for the development of hospital-acquired BSI.[5] Primary BSI are those with no other focus of infection and intravascular catheter-related BSI.[6] Intravenous catheters are the most common cause of primary bloodstream infections and it is also defined as catheter-related bacteremia.[7,8] Hospital-acquired BSI are generally among the three leading infections observed in the ICU.[9,10] Previously-isolated nosocomial microorganisms and antimicrobial susceptibility should be considered when selecting empiric antibiotic therapy.[11] In this study, we aimed to evaluate the clinical, epidemiological, microbiological profiles of the patients diagnosed with primary BSI.

Address for Correspondence: Yeşim Alpay Çağlar, Department of Infectious Diseases and Clinical Microbiology, Balıkesir University Faculty of Medicine, Balıkesir, Türkiye
E-mail: yesim.alpay@hotmail.com **ORCID ID:** 0000-0003-2298-7531

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MATERIALS and METHODS

This study was conducted in a 700-bed research hospital in Türkiye. Patients diagnosed during a period of 5 years were evaluated. BSI and surveillance data were classified according to CDC (Centers for Disease Control and Prevention) criteria. Secondary BSI and pediatric age groups were excluded. Patients with primary BSI and isolates from bacteremic episodes that developed at different times in the same patient were included in the study. The ethics committee of the hospital approved the study protocol (Yunus Emre State Hospital Ethics Committee (56761182-900-1228 /14.11.2014). The study was performed in accordance with the principles of the Declaration of Helsinki.

Patients were evaluated in terms of age, gender, underlying disease and presence of catheter, distribution of pathogenic microorganisms and antimicrobial resistance.

Blood samples were collected from at least two different veins after the skin was first disinfected with 70% isopropyl alcohol and then povidone iodine. The cultures were incubated in a Bactec 9120 (Becton Dickinson, USA) blood culture system at 37°C.

The cultures were incubated in a Bactec 9120 (Becton Dickinson, USA) blood culture system at 37°C. The cultures were inoculated on blood agar, eosin methylene blue (EMB) agar, chocolate agar and Sabouraud dextrose agar (SDA). Identification and antibiograms were performed using VITEK 2 ID-AST (BioMerieux, France) automated system.

Statistical Analysis

Statistical analyses were performed using the SPSS Statistics program (version 19.0, SPSS Inc., Chicago, Ill., USA). All data are presented as median, mean±standard deviation. Chi-square and student T test were used for comparison of independent variables. The analyses of this research assumed a statistical significance threshold of $p<0.05$.

RESULTS

Over a 5-year period, 206 episodes of bacteremia were identified in 183 patients diagnosed with hospital-acquired primary BSI. 52% of the patients were male. The mean age was 66 (18–91) years. The mean duration of hospitalization was 27 days. 73% of the patients were followed up in intensive care units. Demographic features are shown in Table 1.

The most common underlying disease was diabetes mellitus (DM) and it was determined to increase length of stay in hospital significantly ($p=0.040$). There was an intravascular catheter in 55% (100) of the patients and presence of catheter was found to be associated with length of stay in day hospital ($p<0.001$). The most commonly isolated microorganisms were determined to be *Acinetobacter baumannii, coagulase-negative staphylococci* (CoNS) and *Escherichia coli*.

Distribution of pathogen microorganisms and antimicrobial resistance rates are shown in Tables 2-4.

DISCUSSION

BSI is associated with significant health costs.[10] Identification of the source of infection and microorganism is important for the implementation of preventive measures. Determination of antimicrobial resistance and susceptibility is necessary for the selection of the optimal treatment.[11]

Table 1. Demographic features

Total patient (n)	183
Age (years)	66 (18-91)
Gender, %	
Female	48
Male	52
Total bacteremic episod (n)	206
Intravascular Catheter (%)	55
Duration of hospitalization (days)	27
Follow-up in intensive care unit (%)	73

Table 2. Distribution of hospital-acquired primary bloodstream infections and most frequently isolated pathogens

Microorganism	Frequency (%)
*Acinetobacter baumannii**	40 (19.4)
Coagulase-negative *Staphylococci* (CoNS)**	32 (15.5)
*Escherichia coli****	30 (14.5)
Enterococcus spp	27 (13.1)
Klebsiella pneumoniae	20 (9.7)
Pseudomonas aeruginosa	18 (8.7)
Staphylococcus aureus	17 (8.3)
Enterobacter spp	9 (4.4)
Candida spp	8 (3.9)
Serratia marcescens	3 (1.5)
Streptococcus spp	2 (1)
Total	206 (100)

*: Meropenem resistance in *Acinetobacter* species is 45%; **: Methicillin resistance in *S. aureus* species is 54%, methicillin resistance in Coagulase-Negative staphylococci is 36%; ***: ESBL rate in *E.coli* species is 52%, ESBL rate in *Klebsiella species* is 50%. ESBL: Extended spectrum beta lactamase

Table 3. Antimicrobial resistance rates of gram-negative microorganisms

	E. coli (%)	*A. baumannii* (%)	*P. aeruginosa* (%)	*K. pneumoniae* (%)
Amox/clavula	69	88	100	44
Cefepime	43	45	59	32
Cefoxitin	30	100	100	47
Cefuroxime	63	75	100	32
Ceftazidime	60	51	63	39
Ceftriaxone	40	87	80	36
Ciprofloxacin	42	39	50	14
Levofloxacin	55	42	50	31
Imipenem	23	54	40	42
Meropenem	20	45	33	50
Gentamicin	47	40	33	21
Amikacin	23	48	16	32
TMP/SMZ	47	74	–	35
Pip-tazobactam	33	52	39	26
Colistin	10	9	11	–
Tigecycline	10	20	–	42

ESBL rate in E.coli species is 52%, ESBL rate in Klebsiella species is 50%. TMP/SMZ: Trimethoprim/sulfamethoxazole; ESBL: Extended spectrum beta lactamase

Increases in BSI due to gram-negative bacteria have been reported in recent years.[12–15] Similarly in our study, gram-negative bacteria were the most common pathogens in BSI. A total of 3747 articles were screened and 11 observational studies, and 5 investigating risk factors for persistent gram-negative BSI, conducted between 2002 and 2020 were included. The presence of end-stage renal disease, central venous catheter, infections due to extended-spectrum β-lactamase-producing strains, resistance to empirical treatment and unfavorable response at 48 hours emerged as independent risk factors for persistent bacteremia.[16]

The most frequently observed gram-negative pathogens among hospital-acquired BSI are *Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae* and *Enterobacter* species.[17,18] In our study, *A. baumannii* and *E. coli* were the most commonly seen gram-negative bacteria and *coagulase-negative staphylococci* (CoNS) were the most frequently observed gram-positive bacteria. Other studies have reported that *E. coli* was frequently observed as a pathogenic microorganism.[19,20]

Over the years, changes have been observed in the pathogen profile of BSI. In recent years, better infection prevention and control programs for catheterization have led to decreased rates of BSI due to gram-positive microorganisms.[21,3] Decreases in rates of BSI due to MRSA have also been reported.[22] However, the prevalence rate of *Acineto-*

Table 4. Antimicrobial resistance rates of gram-positive microorganisms

	S. aureus (%)	CoNS (%)	*Enterococ* spp (%)
Oxacillin	54	36	–
Erythromycin	50	48	44
Gentamicin	60	57	44
Imipenem	56	25	68
Clindamycin	43	52	38
Levofloxacin	35	33	–
Linezolid	0	0	0
Ciprofloxacin	40	34	33
Teicoplanin	0	0	0
Tetracycline	40	40	41
Tigecycline	50	81	75
TMP/SMZ	41	70	30
Vancomycin	0	0	0

TMP/SMZ: Trimethoprim/sulfamethoxazole

bacter species has increased, particularly in recent years and currently it is identified in 3%–20% of intensive care and hospital-acquired infections.[23,24]

In a study, the distribution of pathogens in nosocomial BSI was found as follows: 20% *P. aeruginosa*, 20% *S. aureus*, 20.2% CoNS, 13.3% *E. coli*, 13.3%, *Klebsiella pneumonia* and 13.3% *C. albicans*.[25] In another study conducted in intensive care units, the pathogens in primary BSI were as follows; 42.9% *S. aureus*, 22.5% CoNS, 4.1% *Enterococcus* spp., 16.3% *Acinetobacter* and 14.3% other pathogens. In the same study, it was reported that extended spectrum beta lactamase (ESBL) positivity was detected in 70% of *E. coli* species and 93.7% of *Klebsiella* species and oxacillin resistance was detected in 81.7% of *S. aureus* and 81.8% of CoNS.[26] In our study, ESBL was found 52% in *E. coli* species and 50% in *Klebsiella* species, while methicillin resistance was found 54% in *S. aureus* species and 36% in CoNS. In a study, the rates of ESBL in *E.coli* and *Klebsiella* species were reported to be 81.8% and 91.3%, respectively. It was reported that the antimicrobial resistance rates among non-fermenting gram-negative bacteria were higher and the most susceptible group was carbapenems.[27] Other studies found that the most susceptible antibiotics against *P. aeruginosa* were piperacillin-tazobactam, ceftazidime, cefepime, amikacin, levofloxacin and imipenem, while the most susceptible antibiotics against *Acinetobacter* species were determined to be colistin, tigecycline, imipenem and meropenem.[27–31] Our study obtained similar results.

In our study, effective antibiotics for *E.coli* and *Klebsiella* species were carbapenems, piperacillin/tazobactam, quinolones and amikacin.

In a study investigating *E.coli* resistance in European countries, the resistance rates to third-generation cephalosporin, aminoglycoside, and aminopenicillins were determined to be 49%, 20–38%, and higher than 70%, respectively.[32] The results in our study are similar. Vancomycin, teicoplanin and linezolid were the most effective antibiotics against Gram-positive bacteria. Similarly, vancomycin, teicoplanin and linezolid were found to be the most effective antibiotics in a study evaluating BSI due to *S. Aureus*.[33]

It is observed that the frequency of hospital-acquired bloodstream infections and the antibiotic resistance rates of the bacteria causing these infections are increasing.[34,35] Inappropriate antibiotic selection leads to infection with antibiotic-resistant strains. Exposure of bloodstream infections to various and prolonged parenteral antibiotics is associated with the emergence of resistant strains.[36] 73% of the patient group included in our study were followed up in ICUs. The prevalence of resistant strains is high in ICUs due to long-term and multiple antibiotic use. Michalopoulos et al.[19] reported long-term antibiotic use as an important independent risk factor for the development of nosocomial multidrug-resistant gram-negative bloodstream infections. In another study by the same author, DM was observed as a risk factor for catheter-associated gram-negative bloodstream infections.[19] It was also reported as an important predisposing factor in other studies.[37] In our study, DM was the most common comorbidity. Catheters have been reported to be responsible for 27–87% of primary bloodstream infections.[19,37,38] Although gram-positive microorganisms are frequently seen in catheter-associated bloodstream infections, gram-negative members of Enterobacteriaceae and non-fermentative gram-negative bacteria can also be causative agents and have increased in recent years.[39] In our study, 55% of the patients were catheterized.

Blot et al.[15] reported in their study that; especially gram-negative are common in hospital-acquired bloodstream infections in critically ill patients. To improve outcomes, efforts to prevent hospital-acquired bloodstream infections and optimize their management through adequate resource control and antibiotic therapy need to be intensified.

Primary BSI frequently occurs in ICUs cohorts and has a poor impact on outcomes. Surveillance for BSI among patients admitted to ICUs is essential to inform healthcare delivery, planning preventive approaches, monitoring resistance, and detecting emerging pathogens.[3]

CONCLUSION

Primary bloodstream infections are important among hospital-acquired infections. Prolonged hospitalization is associated with increased mortality, costs and surveillance studies and infection control policies are important in preventing these and selecting appropriate treatment. With the widespread use of interventional procedures and the increase in resistant microorganisms, changes in the agent profile and parallel increases in antibiotic resistance rates are observed. Therefore, until culture and antibiogram results are obtained, empirical antibiotic choices should be made by examining patient risk factors and hospital surveillance data, evaluating the agent profile and antibiotic resistance rates.

Disclosures

Ethics Committee Approval: The study was approved by the Yunus Emre State Hospital Ethics Committee (No: 56761182-900-1228, Date: 14/11/2014).

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