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The pathogens of blood stream infection in the patients who applied to emergency medicine service: a three year retrospective analysis of a university hospital

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Abstract

Blood stream infection (BSI) is a critical clinic situation that requires immediate diagnosis and treatment. In this study, we aimed to determine the BSI pathogens among the patients who admitted to emergency medicine clinic (EC). A retrospective surveillance study was conducted to evaluate the results of blood culture of the emergency patients in a university hospital between January 2015 and December 2017. Total 4569 blood culture were performed between the study period, and 802 (17.5%) of them yielded positive result, of which 14 (1.7%) were fungi, and remaining 788 (98.3%) were bacteria. Except the coagulase-negative staphylococci (CNSs) which was the major contaminant of blood cultures; *Escherichia coli* (n: 170; 21.2%) was the most frequently isolated organisms in this survey, and this was followed by *Klebsiella* spp. (n: 55; 6.8%) and *Staphylococcus aureus* (n: 54; 6.7%). The frequency of extended spectrum beta-lactamases (ESBLs) among the members of Enterobacteriaceae was measured as 38.2%, and the methicillin resistance of *S. aureus* was 7.4%. The common community acquired bacteremia agents were detected as relatively less, in such an order as *Streptococcus pneumoniae* (n: 14; 1.7%), beta-hemolytic streptococci (n: 11; 1.3%), and *Brucella* spp. (n: 7; 0.8%). This study indicates that gram negative enteric bacteria are the most frequent pathogens of BSI, and the high antimicrobial resistance mediated by ESBL resistance poses a substantial therapeutic problem in our region. The results also suggest that *S. pneumoniae* seems to be circulating in the community despite the vaccination campaigns. Emergency departments are critical units to diagnose community-acquired bacteremia and to commence appropriate antimicrobial chemotherapy for the patients with BSI.

Keywords: Bloodstream infection, *Escherichia coli*, *Staphylococcus aureus*, sepsis

Introduction

Bloodstream infections (BSIs) are one of the leading life-threatening infections not only for the hospitalized patients but also for the patients in the community. Though there is no global analysis about the statistics for this illness, it is estimated that population burden of the disease is about 149-240/100 000; and annual 26 million persons are effected by sepsis all over the world [1]. Blood stream infections are classified at three stages in terms of the severity of the illness, and the mortality rate of BSI is significantly depended on these stages, as 17 to 30% for sepsis, 50% for severe sepsis, and about 80% for septic shock [2].

Blood stream infections are critical diseases that require timely onset of the appropriate antimicrobial treatment. In a prospective study that enrolled 263 patients with BSI in the emergency clinic (EC), the authors reported that rapid diagnosis, and commencing the early goal-directed therapy could reduce the patients' mortality as 40% [3]. However, a wide spectrum of bacteria and fungus

can cause BSI, and each pathogen may require specific targeted antimicrobial treatment. Therefore, knowing the frequent pathogens of BSI at national or regional level is important for regulation of the appropriate empirical treatment.

Clinical symptoms of the patients with BSI generally include high fever (or hypothermia), confusion, skin rashes, vomiting, and sometimes coma [4]. Due to severity of the associated symptoms, more that 66% of the patients with BSI generally apply to medical aid in the emergency service rather than the outpatient clinics [5]. Therefore, emergency clinics (ECs) are the most important units of the hospitals for timely diagnosis of the community-acquired BSI. However, up to date, there is very limited data of the BSI pathogens from the patients in ECs in our country. In this study, we aimed evaluate the pathogens of BSIs and their important antimicrobial drug resistance features from the patients who applied to EC of our hospital, for a three year period.

Material and Methods

Study Setting

A retrospective surveillance study was conducted in Turgut Ozal Medical Center, a 1300-bed regional tertiary care hospital. The data of the patients at ≥ 18 years old who applied to adult emergency

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department between 1 January 2015 to 17 December 2017 were screened from the medical database of the hospital, and the patients associated with septic symptoms, who were taken clinical specimen for blood culture were included in this study. The patient with multiple admissions due to same episode of infection was accepted as single case.

Blood Culture, Identification, and Susceptibility

A set of 5 to 10 ml blood samples were aseptically obtained from the venipuncture, and were inoculated to aerobic blood culture bottles (Bio-Mérieux, France). The specimens were sent to microbiology laboratory of the hospital, immediately. The bottles were incubated in Bac/TAlert automatized blood culture system (Bio-Mérieux, France) until the positive signal was obtained, which was indicating a growth of microorganism occurred.

Subcultures from the positive bottles were done on the tripticase soy agar with 5 to 7 % blood, Eosine Methylene Blue agar, and chocolate agar mediums (Oxoid, UK), and incubated at 35 °C for 18-24 hours. The growing microorganisms were identified by classical bacteriologic methods, and with Vitek MS (matrix assisted laser desorption/ionization time of flight) mass spectrometry device (Bio Mérieux, France).

The antimicrobial susceptibility of the bacterial strains was done with disk diffusion method according to European Committee on Antimicrobial Susceptibility (EUCAST) criteria [6]. Extended spectrum beta-lactamase production of the gram negative bacilli from Enterobacteriaceae was studied with double disk synergy test, and the methicillin resistance of *Staphylococcus aureus* isolates was investigated with cefoxitin disk susceptibility [6].

Data Analysis

Demographic data of the patients including age and gender, and the data belonging to frequency of the isolated strains were expressed as number (n) and percentage (%). The measured frequencies were compared with chi square test, and $p < 0.05$ was accepted as statistically significant.

Results

Within about three year of study period, a total of 4569 patients between 18 to 93 years old were included in this study, of which 1867 (41%) were female and 2702 (59%) were male. Of these, 802 (17.6%) blood culture samples were found positive for any microorganism including bacteria or fungi, and 3767 (82.4%) resulted as negative.

Isolated strains were divided under two characters, as the blood culture contaminants and the real BSI pathogens. Total 338 (42.15%) isolates were accepted as blood culture contaminants as follows: Coagulase negative staphylococci (CNS) 289 (36%), *Micrococcus* spp. and 20 (2.4%), and *Corynebacterium* spp. 17 (2.1%). The distribution of the contaminant bacteria is showed in the Figure 1.

Total 464 (57.85%) isolates were accepted as the exact BSI pathogens, of which 21 showed polymicrobial growth (more than one pathogen), and remaining 443 samples yielded single pathogen growth. Statistical analysis showed that gram-negative bacterial isolates (n:310) were significantly higher than the gram positives

(n:128) among BSI pathogens (38.6% vs 15.9%, $p < 0.05$). On the other hand, a total 14 samples yielded fungal growth of which 13 were *Candida* spp., and one was *Aspergillus* spp. The top five common pathogens found in this study as follows: *E. coli* (n:170; 21.1%), *Klebsiella* spp. (n:55; 6.8%), *S. aureus* (n:54; 6.7%), *Streptococcus* spp. (n:39; 4.8%), and *Enterococcus* spp. (n:32; 4%). The distribution of the BSI pathogens according to study years is showed in the Table 1.

For *E. coli* and *Klebsiella pneumoniae* strains, the frequency of ESBL production were found as 39.4% and 34.5%, orderly, and the methicillin resistance among *S. aureus* strains was measured as 7.4%.

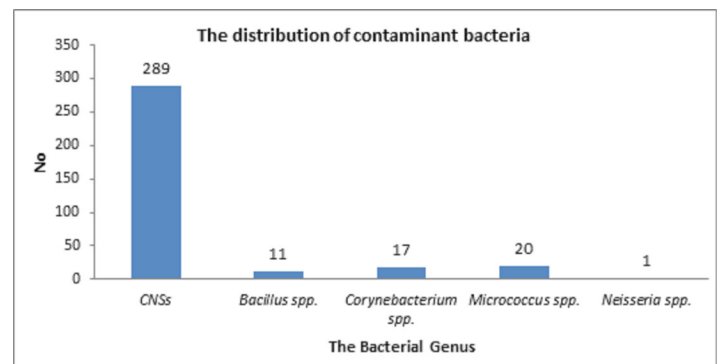


Figure 1. Blood culture contaminant that originated from the skin flora. CNSs are the most frequently detected strains

Table 1. Pathogen distribution of BSI according to study years

Pathogens	No of 2015	Pathogens by 2016	Years 2017
Gram Negative Bacteria			
<i>E. coli</i>	35	50	85
<i>Klebsiella</i> spp.	12	20	23
<i>Pseudomonas aeruginosa</i>	8	10	7
<i>Acinetobacter baumannii</i>	5	9	11
<i>Brucella</i> spp.	2	3	3
<i>Enterobacter</i> spp.	4	2	7
<i>Citrobacter</i> spp.	1	1	3
<i>Proteus</i> spp.	1	1	0
<i>Stenotrophomonas maltophilia</i>	0	0	1
<i>Salmonella</i> spp.	0	0	1
<i>Moraxella</i> spp.	0	1	0
<i>Aeromonas</i> spp.	0	0	1
Gram Positive Bacteria			
<i>S. aureus</i>	19	14	17
<i>Streptococcus</i> spp.	6	12	21
<i>Actinomyces</i> spp.	1	0	0
Fungi			
<i>Candida</i> spp.	3	3	5
<i>Aspergillus</i> spp.	1	0	0

Discussion

In this study, we retrospectively evaluated the bloodstream pathogens of the patients who admitted to emergency department of a university hospital for a three year period. Emergency clinics are likely to be the most appropriate departments for such a study, because of the fact that the patients with BSI represent severe clinical symptoms which require immediate medical interventions. On the other hand, to evaluate such patients, and to manage their empirical treatments appropriately, the emergency physicians should know the common pathogenic agents and their antimicrobial susceptibility trends in their region. However, according to our knowledge, there is less data about this subject in the scientific literature, and very limited information is available from our country. Therefore, we think that this study will provide important knowledge not only for emergency residents but also for the other medical disciplines related with the critical care.

A number symptom from a febrile disease to fatal shock can be seen in a patient with BSI, depending on the characteristics of the organisms and the immune response of the host. It is reported that gram-negative pathogens can cause more severe symptoms than the gram-positives, because of the frequent endotoxemia caused by the lipopolysaccharide content of the gram-negative cell wall [7,8]. Additionally, storming immune response of the host can trigger anaphylotoxic effects which can result with hypotension and circulatory collapse [9]. Consequently, a patient with BSI can admit to EC with fever or hypothermia, low blood pressure, dysregulation on tissue perfusion, loose of the consciousness, blood clotting abnormalities, metastatic skin lesions, organ failures (especially in kidney), and gastrointestinal symptoms such as vomiting or paralytic ileus [10]. Therefore, immediate treatment of BSI is lifesaving for many patients, and an aggressive treatment approach is needed, which focus not only the antimicrobial therapy but also for the regulation of other life-threatening complications [11]. In this point, the determination of the infecting pathogen is critical since the clinical situation can vary according to its virulence factors.

Bloodstream infections generally develop as a result of the penetration of the pathogen from the host's body floras to the blood- or lymphatic stream. It is particularly very common when a local infection exist in a certain body area [12]. The sepsis guideline which was published by National Guideline Center indicated that BSI usually emerge as a secondary infection from a primary source in respiratory tract, urinary tract, abdominal organs, skin, and pelvis [13]. Therefore, the pathogens that cause BSI generally include the common pathogens that are the frequent causes of the infections in these areas.

Determination of the BSI pathogens and their antibiotic resistance properties are very important since such data can significantly vary according to many socio-economic and ethnic factors of the human populations in different geographic areas. One of the most important factors related with the pathogen distribution of BSI is the antimicrobial resistance frequency of the bacteria in the community. About 20 years ago, gram positive bacteria, such as *S. aureus*, *S. pneumoniae*, and other *Streptococcus* species were found as the most common agents in community-acquired BSIs [14]. However, after the antimicrobial resistance dramatically increased in gram negative organisms from the late 90s [15], the

proportion of these pathogens significantly increased in BSI, since the primary infection in respiratory tract or other body sites due to the gram positives could be treated [16].

In this study, we determined that almost 60% of the BSI pathogens were gram negative bacteria. Among these, the members of Enterobacteriaceae (including *E. coli*, *Klebsiella* spp., *Enterobacter* spp, and *Citrobacter* spp.) was the largest group that constitutes 77% of all gram negative agents detected in this study. We found that *E. coli* and *Klebsiella* spp. were the leading pathogens among our patients. On the other hand, we determined that gram positive cocci including *S. aureus*, *Streptococcus* spp., and *Enterococcus* spp. were constituting more than 95% of all gram positive bacteria those were found as the BSI pathogens in this study, among these *S. aureus* was the leading pathogen. These findings were in accordance with the data from the countries in Europe and North America. Buetti et al [17] reported that *E. coli* was the first and *S. aureus* was the second most frequent BSI pathogens among 42800 patients from Switzerland, for a six year period between 2008 and 2014. In another study, Esel et al [18] reported that %40 of the BSI pathogens was gram negative and *E. coli* was the first frequent pathogen in our country. We observed that nonfermentative gram negative bacteria, such as *Acinetobacter* spp., and *Pseudomonas* spp., were also frequent in our strains as each was 5.5% of all BSI pathogens. This was also an important concern for our community because of these agents generally associated with high mortality due to their high antimicrobial resistance [19]. Additionally, we observed that two fungus, *Candida* spp, and *Aspergillus* spp. were about 3.3% of our all the BSI pathogens of our patients, of which candida was the predominant agent (Table 1). In a study that carried out by Hoenigl et al [20] in Austria, it was reported that no fungal pathogen was detected in community-acquired BSIs. Therefore, we thought that some of the hospitalized patients in immunosuppressive situation could re-admit to EC department in the study period.

We also determined that the most common BSI pathogens, such as *S. pneumoniae*, beta-haemolytic streptococcus, and *Haemophilus influenzae* were relatively low in this study. This is most possibly due to the vaccination practices against to pneumococcus in children, which has been performed since 2010 in our country. Nevertheless, it seems that adults are still under exposure of this pathogen in our community. Additionally, in this survey, we detected only one *H. influenzae* that was the most important pathogen of infants. This was most likely due to the patient characteristics in this study, which was consisting the only adult patients. Furthermore, we observed that *Brucella* spp. was the BSI pathogen of 7 patients. This was also another concern for our population, which indicates the zoonotic transfer of some pathogens is still ongoing in our region.

Extended spectrum of beta-lactamases are important antimicrobial resistance mechanisms for gram negative enteric bacilli. In this study, we observed that almost 40% of the *E. coli* and *Klebsiella* spp. were found as the ESBL-producers. Though this resistance is frequent in healthcare associated infections in our country, as much as 44% [21], the results of this study has showed that this resistance is also frequent in our community. On the other hand, though the methicillin resistance is very high in the nosocomial isolates of *S. aureus* in our country, as much as 72% [21], we found

relatively low frequency of this resistance among our blood culture isolates of *S. aureus* strains, as 7.4%.

Conclusion

In this study, we studied the BSI pathogens of the patients who applied to EC of our hospital for three years, and we found that gram-negative bacilli were the most frequent pathogens in our region. Regarding the high antimicrobial resistance with these bacterial strains, it seems that emergency physicians should keep in mind these agents when they evaluate the patients suspected for having BSI.

Competing interests

The authors declare that they have no competing interest.

Financial Disclosure

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