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Original Article

Bacterial bloodstream infections in level-I trauma intensive care unit in Serbia: incidence, causative agents and outcomes

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Abstract

Introduction: We aimed to describe incidence, outcomes and antimicrobial resistance markers of causative agents of bacterial BSI in the intensive care unit (ICU) in a trauma center in Serbia.

Methodology: Prospective surveillance was conducted from November 2014 to April 2016 in two trauma-surgical ICUs of the Emergency Department of Clinical center of Serbia. Bloodstream infections were diagnosed using the definitions of Center for Disease Control and Prevention.

Results: Out of 406 trauma patients, 57 had at least one episode of BSI (cumulative incidence 14.0%). Overall 62 BSI episodes were diagnosed (incidence rate 11.8/1000 patient/days), of which 43 (69.4%) were primary BSI (13 catheter-related BSI and 30 of unknown origin) and 19 (30.6%) were secondary BSI. The most common isolated pathogen was *Acinetobacter* spp. [n = 24 (34.8%)], followed by *Klebsiella* spp. [n = 17 (24.6%)] and *P. aeruginosa* [n = 8 (1.6%)]. All *S. aureus* [n = 6 (100%)] and CoNS [n = 3 (100%)] isolates were methicillin resistant, while 4 (66%) of Enterococci isolates were vacomycin resistant. All isolates of *Enterobacteriaceae* were resistant to third-generation cephalosporins [n = 22 (100%)] while 7 (87.5%) of *P. aeruginosa* and 23 (95.8%) of *Acinetobacter* spp. isolates were resistant to carbapenems. All-cause mortality and sepsis were significantly higher in trauma patients with BSI compared to those without BSI ($P < 0.001$ each).

Conclusions: BSI is a common healthcare-associated infection in trauma ICU and it is associated with worse outcome. Better adherence to infection control measures and guidelines for prevention of primary BSI must be achieved.

Key words: bloodstream infections; healthcare-associated infections; trauma; outcome; antimicrobial resistance.

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Introduction

Bloodstream infections (BSIs) still represent considerable threat to health care and patient safety. They are the second most common HAI among patients staying more than 48 hours in intensive care unit (ICU) as they affect approximately 4% of all critically ill patients [1]. Despite the decrease of HA-BSI rates in some countries, achieved mainly by reducing the rates of central line-associated bloodstream infections (CLABSI) [2], the incidence and burden of HA-BSI are still substantial worldwide [3]. Moreover, HA-BSI is independently associated with increased risk of both, short and long-term mortality in critically ill patients [4,5].

Trauma patients account for one third of all ICU admissions as the improvement in surgical techniques and life support management of critically injured patients increased survival after the injury. However, exposure to numerous invasive devices, in addition to disrupted barriers and altered immune response, put those who survive initial trauma at particular risk of developing BSI over the course of ICU treatment [6]. Consequently, BSI is two times more frequent in trauma ICU compared to surgical ICU [7] and after VAP it is the second most frequent HAI in trauma patients [8]. In Serbia, "injuries, poisoning and other consequences of external causes" represent sixth among first ten causes of mortality, accounting for 3.2% of all-cause mortality and mortality rate 39.4/100.000 [9]. Despite this, there is no data on incidence, antimicrobial resistance patterns and outcomes of HA-BSI in trauma patients in Serbia and the countries of the Region.

Therefore, this is the first study in South-Eastern European Region which aimed to delineate

epidemiology of bacterial BSI in trauma patients admitted to trauma/surgical ICU of the major referral level I trauma center. This included incidence and causative agents of HA-BSI and their resistance to common antimicrobial markers as well as outcomes associated with occurrence of BSI in trauma patients.

Methodology

Study design, patients, and infection control measures

A prospective surveillance was conducted at two trauma/surgical ICUs of Clinical center of Serbia (CCS) from November 2014 to April 2016. All consecutive adult trauma patients admitted to one of two trauma ICUs and who spent more than 48 hours in ICU were eligible for the study. Exclusion criteria were unspecified injuries, non-traumatic injures (poisoning, drowning, suffocation), hip fractures, late effect of injury, superficial injuries and foreign bodies. Patients with isolated brain injuries caused by low falls due to non-traumatic intracranial hemorrhage were also excluded.

Two trauma-surgical ICUs together comprise 25 beds and have approximately 800 admissions annually. Nurse-to-patient ratio is 1:3. Hand hygiene policy includes alcohol-based hand sanitizers placed at each bedside in each ICU room, according to the national recommendations which are adopted from WHO (World Health Organization) hand hygiene guidelines [10,11]. Insertion and maintenance of CVC are done following guidelines of American Society of Anesthesiologists for insertion and maintenance of CVC [12,13]. Placement of the CVC is done in aseptic conditions either by the anesthesiology specialist or by anesthesiology resident under the supervision of a specialist. Hand hygiene (using alcohol-based hand rubs), universal barrier precautions (use of a cap, mask, sterile gown, sterile gloves, and a sterile partial-body drape) and skin preparation (using chlorhexidine) are performed prior and during every CVC insertion. No modification in infection control measures were observed during the study period.

The study was approved by the Ethics Committee of the Clinical Centre of Serbia (No 1358/19) and by the Ethics Committee of the Faculty of Medicine at the University of Belgrade, Serbia (No 29/X-5). Informed consent was obtained from all patients included in the study or patients next to kin.

Surveillance and definitions

On admission, severity of trauma was assessed trough the Injury Severity Score (ISS) which is an anatomical scoring system that provides an overall score for patients with multiple injuries. The Glasgow Coma Scale (GCS), Acute Physiology And Chronic Health Evaluation II score (APACHE II) and Sequential Organ Failure Assessment (SOFA) score are severity-of-disease classification scores and were calculated within 24 hours of admission of a patient in an ICU.

Presence of BSI was prospectively assessed by daily examination of records of patients, clinical course and microbiological results by attending physicians and infection control epidemiologists. BSI was diagnosed using the Centers for Disease and Prevention definitions when clinical symptoms of infection were present 48 hours from admission and laboratory confirmed causative agent was isolated, i.e., recognized pathogen cultured from one or more blood cultures or common skin contaminant cultured from 2 or more blood cultures [14].

BSIs were reported as primary and secondary BSI. Primary BSI was defined as BSI not related to another infection site and for the purpose of the comparability of results with studies which have used European Centre for Disease Prevention and Control (ECDC) criteria, these were divided into catheter-related BSI (CR-BSI) and BSI of unknown origin [15,16]. All other cases of BSI, i.e., those related to another infection site (same organism cultured from bloodstream and primary HAI site, and the organisms exhibit same antibiogram) were considered as secondary BSI [17]. Catheter tips are collected and sent to microbiological laboratory and cultured whenever CVC infection is suspected. Since microbiological proof of a catheter-related infection consider only the same organism isolated from a peripheral blood culture and a catheter blood or a positive semi-quantitative CVC culture (> 15 CFU per catheter segment), CR-BSI are referred to as suspected CR-BSI (s-CR-BSI).

Recurrent CRI was defined as an occurrence of a positive blood culture of identical organism after catheter exchange and three negative blood cultures, or as a persistent positive blood cultures after catheter exchange and positive reinsertion-catheter tip cultures. Therapy was considered inadequate if no effective drug against the isolated pathogen(s) was included in the initial empirical antibiotic treatment within 24 hours of culture collection or the doses and pattern of administration were not in accordance with current medical standards. For patients with polymicrobial BSIs, all pathogens were required to be susceptible to the antimicrobial(s) in the regimen.

Device utilization ratio (DUR) was calculated as the measure of CVC exposure (total number of CVC-

days/total number of patient-days). The presence of multiple CVCs in a single patient on a single day was represented as one CVC-day. Cumulative incidence and incidence rate were used as outcome measures and were expressed as number of BSI episodes per 100 patients and number of BSI episodes per 1000 patient-days, respectively. Catheter-related BSI incidence was calculated as a number of CR-BSI per 1000 CVC-days.

Patients were followed until discharge from the ICU or death. Secondary outcomes comprised sepsis, ICU LOS and ICU mortality. Sepsis was diagnosed at the time of BSI diagnosis according to the American College of Chest Physicians and the Society of Critical Care Medicine Consensus Conference criteria [18].

Microbiological assessment

Isolation and identification of bacterial strains were done following standard microbiological procedures. Antimicrobial susceptibility was estimated using the Kirby-Bauer disk diffusion method and a Vitek2 compact semiautomated system (bioMérieux, Marcy-I'Etoile, France). Zone diameter was measured and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines until end of December 2015 and European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendation from January 2016 onwards [19,20]. Strains that showed intermediate susceptibility and resistance to the specific antibiotic were considered resistant. Antimicrobial resistance was presented trough the AMR markers as follows:

- for *S. aureus*: markers of methicillin (oxacilline, cefoxitin or methicillin) resistance - MRSA,
- for *Enterococci*: markers of glycopeptides (vancomycin) resistance - VRE,
- for *Enterobacteriaceae:* 3rd generation cephalosporins (ceftriaxone, cefotaxime or ceftazidime) and carbapenems (imipenem, meropenem or doripenem, ertapenem) resistance,
- for gram negative rods (*Pseudomonas* spp. and *Acinetobacter* spp.): antipseudomonal carbapenems (imipenem or meropenem) resistance.

Table 1. Characteristics and outcomes of trauma patients with and without BSI.

	Bloodstream infection		
Characteristic	**Yes (n = 57)**	**No (n = 349)**	**P value**
General characteristics			
Age	52 (37)	48 (34)	0.525
Male gender	44 (77.2)	268 (76.8)	0.947
Comorbidities	23 (40.4)	142 (40.7)	1.000
Clinical characteristics at admission			
Emergency surgery	23 (40.4)	93 (26.6)	0.034
Glasgow coma score	12 (6)	14 (5)	0.001
APACHE II score	12 (9)	8 (9)	< 0.001
SOFA score	6 (4)	3 (3)	< 0.001
Injury characteristics			
Type of injury			
Blunt	53 (93.0)	334 (95.7)	0.322
Penetrating	4 (7.0)	15 (4.3)	
ISS	24.1 ± 8.3	19.3 ± 8.4	< 0.001
Mild (< 9)	0 (0.0)	25 (7.2)	0.002
Moderate (9-15)	7 (12.3)	87 (24.9)	
Severe (16-24)	24 (42.1)	151 (43.3)	
Critical (25-75)	26 (45.6)	86 (24.6)	
Device exposure			
CVC-days, median	16 (24)	6 (8)	< 0.001
CVC-days > 7 days	50 (87.7)	147 (42.1)	< 0.001
MV-days, median	13 (14)	2 (5)	< 0.001
Outcomes			
Sepsis	38 (66.7)	27 (7.7)	< 0.001
ICU mortality	26 (45.6)	63 (18.1)	< 0.001
ICU LOS*	21 (5-131)	8 (2-77)	< 0.001

Values are number (%), mean ± SD or median (IQR); APACHE II score: Acute Physiology and Chronic Health Evaluation II Score; SOFA score: Sequential Organ Failure Assessment score; ISS: Injury severity score; CVC: central venous catheter; MV: mechanical ventilation.

Statistical analysis

For continuous variables, the Kolmogorov-Smirnov test was used to assess the assumption of normality. Continuous data are presented as the mean ± standard deviation or median (interquartile range, IQR) and categorical data are presented as numbers (percentages). Comparison of continuous data between groups of patients with and without BSI for was done by using Student t test or Mann-Whitney U test, and for categorical data Pearson's Chi-square test or Fisher's exact test were used. A Cox proportional hazards method was used to assess survival probability, adjusted for age, hypotension, comorbidities, injury severity and severity of disease). All statistical tests were two-sided and were performed at a 5% significance level. Statistical analyses were performed using SPSS version 20.0 software (IBM-SPSS Inc, Armonk, NY, USA).

Results

Out of 848 patients admitted to ICU over year and a half period, 662 were adult patients who were hospitalized for more than 48 hours. Of, these, 31 patients were excluded due to non-traumatic mechanisms of injury (poisoning, drowning and suffocation) and 36 were excluded due to late effect of injuries, superficial injuries or foreign bodies. Additionally, 74 patients were excluded due to diagnosis of burns, hip fractures or isolated brain injuries caused by non-traumatic injury, such as spontaneous intracranial bleeding. From 115 patients/relatives informed consent was not obtained which led to the sample of 406 trauma patients included in the final analysis.

406 trauma patients (312 males and 94 females) were followed for 5258 ICU days. Of these, 57 patients had at least one episode of BSI (cumulative incidence 14.0%). Overall, 62 BSI episodes were diagnosed in 57 patients with the incidence rate of 11.8/1000 patient/days. The average time from admission to ICU until BSI was 13 ± 11.2 days, ranging from 2 to 75 days (median (IQR): 10 (11)). CVC utilization ratio was 82 per 100 patient-days. Median length of stay was 9 days (range, 2-131).

Comparison of demographic characteristics, underlying conditions and data about severity of the disease at the admission, between patient with and without BSI is provided in Table 1. There was no significant difference in demographics and comorbidities in patients with BSI and those without BSI. However, patients with BSI in higher percent had emergency surgery (P = 0.034) and had lower median GCS on admission (P = 0.001). Overall, patients with BSI evinced more severe medical condition on admission considering higher median APACHE II and SOFA score in BSI group (P < 0.001 for both). Blunt trauma was more common type of injury in both groups of patients. Patients with BSI had overall more severe injuries according to higher ISS (24.1 ± 8.3 *vs*. 19.3 ± 8.4, P < 0.001) and significantly higher percent of critically severe injuries (45.6% *vs.* 24.6%, P = 0.002). Regarding the exposure to invasive devices over the course of ICU treatment, median number of days spent with CVC in place or on mechanical ventilation was significantly higher in patients who acquired BSI compared to those who did not (P < 0.001 for both). Among 57 patients with bloodstream infections, 17 (29.8%) received inadequate initial empiric antimicrobial treatment. The crude ICU all-cause mortality was 21.9% and it was two and a half times higher in patients who developed BSI (45.6% *vs*. 18.1%, P < 0.001). Sepsis developed 66.7% of patient with BSI and 7.7% of patients without BSI (P < 0.001). Median ICU stay was significantly longer in patients with BSI compared to those without BSI (21 days *vs.* 8 days, P < 0.001).

Despite the significant difference in all-cause ICU mortality between patients with BSI and patients without BSI, Kaplan-Meier survival analysis showed that there is no significant difference in mean time to death between two groups of patients (40.9 days *vs*. 34.4 days, log-rank P = 0.084) (Figure 1). There was no

Figure 1. Adjusted (for age, hypotension, comorbidity score, GCS, ISS, APACHE II and SOFA score) survival probability from ICU admission to death, stratified according to presence of BSI.

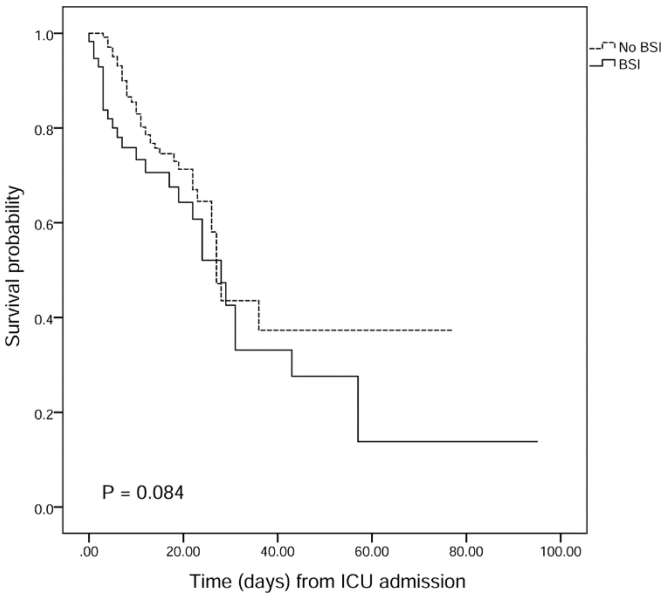

Table 2 Distribution of causative agents by type of BSI.

Pathogen	Primary BSI n = 43		Secondary BSI n = 19	Total
	CR-BSI n = 13	Unknown source n = 30		
S. aureus	2 (15.4)	2 (6.1)	2 (8.7)	6 (8.7)
Enterococci	0 (0.0)	5 (15.1)	1 (4.3)	6 (8.7)
Klebsiella spp.	1 (7.7)	8 (24.2)	8 (34.7)	17 (24.6)
E. coli	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Proteus spp.	0 (0.0)	1 (3.0)	0 (0.0)	1 (1.5)
Serratia spp.	0 (0.0)	1 (3.0)	0 (0.0)	1 (1.5)
Providencia spp.	0 (0.0)	2 (6.1)	1 (4.3)	3 (4.3)
Acinetobacter spp.	5 (38.5)	9 (27.3)	10 (43.5)	24 (34.8)
Pseudomonas spp.	4 (30.8)	3 (9.1)	1 (4.3)	8 (11.6)
CoNS	1 (7.7)	2 (6.1)	0 (0.0)	3 (4.3)
Total	**13 (100)**	**33 (100)**	**23 (100)**	**69 (100)**

CR-BSI: Catheter-related BSI; CoNS: Coagulase-negative staphylococci.

significant difference in mortality between patient with primary and patients with secondary BSI [17 (44.7%) *vs*. 9 (47.4%)]. However, mortality was significantly higher in patients who received inadequate empiric therapy [12 (70.6%) *vs.* 14 (37.8%)].

Out of 62 BSI episodes, 13 (21%) was suspected-catheter-related BSI (s-CR-BSI). There were 4295 catheter-days during the study period, resulting in an incidence rate of 3.0/1000 CVC-days. For 30 BSI episodes (48.4%) no source of infection could be identified and together with CLABSI they comprised primary BSI (69.4%; IR = 10.0/1000 CVC days). For 19 (30.6%) BSI episodes infection cite was identified and those were considered as secondary BSI. Sources of 19 secondary BSI were as follows: 13 (68.4%) respiratory tract, 3 (15.8%) SSI and 3 (15.8%) UTI.

Sixty-nine pathogens were obtained from 62 BSI episodes, of which 6 were polymicrobial (5 of them with 2 bacteria and 1 with 3 bacteria). Distribution of causative agents of BSI is summarized in Table 2. The most common pathogens recovered were Gram-negative bacteria (*Acinetobacter* spp., *Klebsiella* spp. and *Pseudomonas* spp.) accounting for 71% of all isolates. For all three types of BSI (primary s-CR-BSI, primary-unknown source and secondary BSI) *Acinetobacter* spp. was the most frequent pathogen recovered. Gram-positive bacteria (*S. aureus*, coagulase-negative staphylococci-CoNS, *Enterococci*) were obtained from 20.8% of positive blood stream isolates (8.7%, 8.7% and 4.3%, respectively).

Antimicrobial resistance markers in causative pathogens of BSI are presented in Table 3. While all isolates of *S. aureus* and CoNS were methicillin resistant, 66% of Enterococci were resistant to vancomicin. Regarding *Enterobacteriaceae,* all isolates of *Klebsiella* spp., *Proteus* spp*., Serratia* spp. and

Table 3. Antimicrobial resistance markers in causative pathogens of BSI.

Microorganism	AMR marker	n	n (%) R
Gram-positive cocci			
S. aureus	MRSA	6	6 (100)
CoNS	MRCoNS	3	3 (100)
Enterococci	VRE	6	4 (66.7)
Enterobacteriaceae			
Klebsiella spp.	3GC-NS	17	17 (100)
	CAR-NS	17	13 (76.5)
Proteus spp.	3GC-NS	1	1 (100)
	CAR-NS	1	0 (0.0)
Serratia spp.	3GC-NS	1	1 (100)
	CAR-NS	1	0 (0.0)
Providencia spp.	3GC-NS	3	3 (100)
	CAR-NS	3	2 (66.7)
Other gram-negative bacteria			
Pseudomonas spp.	CAR-NS	8	7 (87.5)
Acinetobacter spp.	CAR-NS	24	23 (95.8)

MRSA: methicillin-resistant *S. aureus*; CoNS: Coagulase-negative staphylococci; MRCoNS: Methicillin-resistant coagulase-negative staphylococci; VRE: Vancomycin-resistant enterococci; VAN: vancomycin; 3GC: Third-generation cephalosporin; CAR: carbapenem.

Providencia spp. were resistant to third-generation cephalosporins. Considering carbapenem resistance of these bacteria, majority of isolates of *Klebsiella* spp. (76.5%) and *Providencia* spp. (66.7%) were denoted as carbapenem-resistant. Gram-negative rods, *Pseudomonas* spp. and *Acinetobacter* spp. were highly resistant to carbapenems as 87.5% and 95.8% of their isolates, respectively, were not susceptible to this antibiotic.

Discussion

In our study cumulative incidence of BSI in trauma ICU was 14% and the incidence rate was 11.8/1000 patient/days. Similar to these findings, cumulative incidence in studies which reported BSI as primary outcome in trauma patients was 15.2% in American trauma ICU [21] while in India ranged from 10.6% in level-1 trauma center [22] to 21% in trauma-surgical ICU [23]. Diverse results were reported from studies that analyzed BSI as a fraction of all HAIs in critically ill ICU patients. In USA, BSI was the third most common HAI accounting for 9.1%-14% of all HAIs [24,25], the second most common in Brazilian ICU (19% of all HAIs) [26] and fifth most common HAI in Canada (5% of all HAIs) [27]. There is no data on incidence of BSI or HAI in trauma patients in Serbia, however, according to the last national point prevalence study of HAI conducted in 2011 in Serbian acute care hospitals, BSI was the third most prevalent HAI in ICU, after surgical site infections and urinary tract infections [28].

Primary BSI in our study comprised 69.4% of all BSI with IR 10.0/1000 CVC-days. Of these, 21% were considered as suspected CR-BSI (IR 3.0/1000 CVC-days) and 48.4% were reported as BSI of unknown origin. Rates of BSI associated with CVC use in ICU vary depending on infection control practices and definition used to diagnose this infection. Thus, the rate of CLABSI in limited-resource countries with poor compliance to infection control programs range from 1.6 in adult ICU to 44.6 cases per 1000 CVC-days in pediatric ICU [29] while in Finland BSI rate range between 0.4 and 0.9/1000 patient-days [30]. Second referrers to definition used to diagnose BSI related to vascular catheters, i.e., some studies report CLABSI while others report CR-BSI, which are diagnosed following different criteria. While CLABSI is term used by CDC/NHSN, defined as primary infection developed in patient with a CVC in place for more than 48 hours before the onset of BSI that is not related to infection at another site and does not require catheter tip culture or peripheral blood culture as a criterion, CR-BSI requires specific laboratory tests such as catheter tip culture and different time to positivity as a condition to be diagnosed. Consequently, incidence of BSI associated with CVC use can be rather over- or underestimated [31], which could be the case in our study if considering only overall primary BSI or CR-BSI, respectively. Despite the fact that only third of the primary BSI were microbiologically ascertained as s-CR-BSI in our study, 95.3% of patients with primary BSI were exposed to CVC for more than two days preceding BSI (data not shown) and would have been considered as CLABSI according to CDC/NHSN definitions. Regardless of the definition used, predominance of primary BSI in our study over secondary BSI (69.4% *vs*. 30.6%) is important information as it stresses necessity for more thorough search and prevention of infections of primary cites and better adherence to hand hygiene and CVC guidelines as possible reasons for such a BSI distribution.

Changing epidemiology of causative agents of BSI, from Gram-negative to Gram-positive, has been reported by previous studies [30]. On contrary, study conducted previously in combined medical-surgical ICU in Serbia (in which the third of the patients were trauma inpatients) showed that Gram-positive microorganisms were slightly more frequent than Gram-negative bacilli and CoNS was the most frequent cause of BSI followed by *S. aureus* [32]. In our study, however, *Acinetobacter* spp. was the most common cause of all three types of BSI, followed by *Klebsiella* spp. and *Pseudomonas* spp. This is in line with data from Indian trauma center and ICU of University Greek Hospital [22,33] as well as from invasive isolates recovered in Serbian ICUs reported to Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR) network in 2016 [34], which suggests reverse trend in causative agents of BSI in ICU and trauma patients in Serbia, from Gram-positive to Gram-negative, possibly due to dissemination of resistant clones of Gram-negative rods in ICU.

Considering AMR markers in causative pathogens of BSI, we found alarmingly high rates of *Enterobacteriaceae* strains resistant to third-generation cephalosporins (100% of strains) and carbapanems (66.7%-85.7%) as well as high percentage of *Pseudomonas* spp. and *Acinetobacter* spp. resistant to carbapenems (87.5% and 95.8% of non-susceptible strains, respectively). Alarmingly high resistance of invasive strains of *Klebsiella* spp. to third-generation cephalosporins and *Pseudomonas* spp. and *Acinetobacter* spp. strains to carbapenems has been previously reported in Serbia in prospective

surveillance study within Clinical Centre of Serbia [35] and from CEASAR in 2016 [34]. In contrary, surveillance networks in USA, National Healthcare Safety Network (NHSN) and International Nosocomial Infection Control Consortiu (INNIC) [36,37] and high-income countries of European Antimicrobial Resistance Surveillance Network (EARS-Net) [38] reported considerably lower rates of isolates resistant to common AMR markers, reflecting the differences in measures of primary BSI prevention and control. Although, there is no data available on resistance to common AMR markers of pathogens causing BSI in trauma patients from countries close to Serbia, our results are similar to AMR data of invasive isolates in acute care hospitals in countries of South-Eastern European Region [34]. At clinical level, this data is highly important since the choice of empirical therapy of BSI/CLABSI and its duration depend on understanding the distribution and resistance patterns of their causative agents in specific setting or patient population. At national level, this imposes the necessity for implementation of measures for antibiotic consumption restriction together with general and pathogen-specific measures for disruption of transmission of resistant clones.

As earlier studies suggests, BSI contributes significantly to increased mortality, LOS and costs of medical treatment [4,8]. In trauma patients with BSI who develop sepsis mortality ranges from 21.2% in USA up to 75% in India [8,22]. Our study demonstrated similar results, with all-cause ICU mortality in patients with BSI being 45.6% which is 8.7 times higher than mortality in non-BSI group (18.1%). In addition, rates of sepsis and ICU LOS in our sample were, 2.5 and 2.6 times higher in patients with BSI, respectively. Of note is the fact that in our sample 66.7% of BSI was sepsis-associated. It, thus, remains uncertain in which way BSI is implicated in increased risk of mortality, i.e., whether it is a factor leading to sepsis and consequent death or it is just a marker of sepsis severity and organ dysfunction. Nevertheless, it has been shown that primary bacteremia is associated with higher mortality in critically ill patients compared with pulmonary and abdominal sources of sepsis [39], which, together with results of our study, highlights the importance of BSI prevention in critically injured patients.

Several limitations of the study should be addressed. We did not asses CVC number and type, as well as the insertion sites, since the CVC-associated BSI was not the primary outcome of our study and the risk factors for such a BSI have been subject of numerous earlier reports. Also, we did not have data on previous antibiotic consumption due to the urgent type of referral. However, this is the first study to outline epidemiology and characteristics of patients with bacterial laboratory-confirmed BSI in population of trauma patients in tertiary referral trauma center in Serbia. Prospective design allowed us to record numerous clinical and disease severity variables as well as to track infections and the exposure to risk factors with reduced possibility of information bias and misclassification.

Conclusions

BSI is a common HAI in trauma ICU affecting 14% of all inpatients and resulting in higher rates of sepsis, ICU LOS and mortality, compared to trauma patients without BSI. Predominance of primary BSI (CR-BSI and unknown origin) as well as predominance of *Acinetobacter spp.* and *Klebsiella* spp. and their high resistance to commonly used antibiotics, stress necessity for striker overall and CVC-specific infection control measures in critically ill trauma patients.

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