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Central Line Associated Bloodstream Infections Outside the Intensive Care Unit: A 2-Year Analysis

Catheter Associated Bloodstream Infections Outside Intensive Care Unit

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Abstract:

Objective: There is limited data on the rates of central line associated bloodstream infections (CLABSI) and the characteristics of these infections in units other than intensive care units (ICU). Our aim in this study was to determine the rates and features of CLABSI in non-ICU units.

Method: In our hospital, CLABSI surveillance is performed according to CDC criteria in Internal Medicine Nephrology, Hematology, Oncology, Pediatric Hematology, Oncology and hematopoietic stem cell transplant (HSCT) units other than ICUs. Hospital infections control committee surveillance data is used in this study.

Results: In a total of 70028 patient days and 22358 catheter days, 101 infections were detected in 94 patients. The CLABSI rate was 1.44/1000 patient days, the incidence density was 4.2/1000 catheter days, and the device utilization rate was 0.32. The highest infection rate was observed in the adult HSCT unit (15.18/1000 patient days). 56.4% of the patients were male (n=53) and the mean age of the patients was 32±2.5 years. The mean length of hospitalization was 27.7±2.5 days. Half of the patients (n=47) had permanent and half had transient central lines. When the underlying factors were analyzed, hematologic cancer was found in 54.7% and hemodialysis in 19.2%. Of the 94 infection episodes, 21.8% were polymicrobial. Of the 125 microorganisms isolated, 61.6% were Gram negative, 20.8% were fungi and 17.6% were Gram positive. The most frequently isolated pathogens were *Escherichia coli* (n=17, 13.6%) and *Klebsiella pneumoniae* (n=17, 13.6%), followed by *Staphylococcus aureus* (n=10, 8%) and Candida parapsilosis (n=9, 7.2%). Crude mortality was 36.2% (n=34). Colistin and amikacin were the most effective antibiotics in *E.coli* and *K.pneumoniae*, oxacillin resistance was found as 60% (6/10) in *S. aureus* isolates. In *Candida* species, fluconazole resistance was 15.8% (3/19).

Conclusion: It is important to recognize that CLABSIs can also occur in non-ICU patients, and particularly in the population with hematological cancers, monitoring the rates and identifying risk factors specific to this population are crucial for implementing infection control measures.

Keywords: Central venous catheter, Central line, Infection rate, Non-intensive care unit

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INTRODUCTION

Bloodstream infections are among the most common infections in hospitals (1). Central venous catheter associated bloodstream infection rates vary according to the size of the hospital, the clinic where the patient is hospitalized and the type of catheter (2). Since central venous catheters are the most common cause of infection, central line associated bloodstream infections (CLABSIs) are the most common infections in hospitals today and are particularly important for patients hospitalized in intensive care units (ICUs) due to their high morbidity, mortality, and increased costs (3). Most of the studies on the detection and prevention of CLABSIs have been conducted in ICUs. According to the data of a consortium of developing countries, the rates of CLABSI vary between 1.44 and 20.90/1000 catheter days depending on the type of ICU (4). In Turkey, the Ministry of Health established the national nosocomial infection surveillance system in 2007 and has been collecting data electronically from hospitals across the country since 2008 (5). However, reports from non-ICU settings are very limited and there are no specific recommendations for the prevention of HAIs in these areas (6). The aim of this study was to determine the rates of CLABSI outside the ICUs in our hospital and to identify specific risk factors to shed light on future infection control measures.

METHOD

Patients

In addition to the ICUs in our hospital, CLABSI surveillance is performed in Nephrology, Hematology/Oncology, Pediatric Hematology/Oncology and Hematopoietic Stem Cell Transplantation units. Patients from these units where surveillance was performed in 2015-2016 were included in the study and data were extracted retrospectively from Hospital Infection Control Committee's (HICC) patient follow-up forms. Hospital infections control committee surveillance data is used in this study.

Surveillance

Surveillance in the relevant units is prospective and laboratory-based, and data are recorded on patient tracking forms. The data used include dates of hospitalization, dates of diagnosis and development of infection, underlying diseases, interventional procedures and risk factors, microorganisms grown and susceptibility characteristics. Nosocomial infection diagnoses are made by infection control nurses and physicians according to the Center for Disease Control (CDC) nosocomial infection diagnostic criteria (7).

The number of inpatients, patient days and catheter days were recorded in the surveillance units. CLABSI rate was calculated by dividing the number of infections by patient days and multiplying by 1000, and infection incidence density was calculated by dividing the number of infections by catheter days and multiplying by 1000. Catheter utilization rate was calculated by dividing catheter days by patient days.

Microbiology

Samples obtained from patients for blood culture were inoculated into BACTEC Plus Aerobic/F blood culture bottles (Becton Dickinson Diagnostic Instrument Systems, Sparks, USA) and incubated in the BACTEC FX system (Becton Dickinson, USA) for seven (7) days. Blood culture bottles that showed a positive signal due to growth were passaged onto 5% sheep blood agar, chocolate agar and Eosin Methylene Blue (EMB) agar media. These media were obtained from Biomerieux company. The plates were incubated at 37°C, aerobic and 5% CO2 for 24-48 hours and the microorganisms grown were preliminarily identified by classical microbiological methods such as colony morphology, Gram staining, catalase test, oxidase test and coagulase test. Further identification was performed using Gram Positive (GP), Gram Negative (GN) and Yeast (YST) identification cards in the automated Vitek-2 System (Biomerieux, France). All microorganisms from all episodes are included to the study.

Statistics

The data were transferred to the computer environment with SPSS v20.0 program and descriptive analysis was performed. Data were presented as mean (mean) ± standard deviation (SD), median, lower value (LV), upper value (UV), number (n) and percentage (%).

RESULTS

In a total of 94 patients, 101 CLABSIs were detected in 70,028 patient days and 22,358 catheter days. CLABSI rate was calculated as 1.44/1000 patient days, CLABSI incidence density as 4.2/1000 catheter days, and central venous catheter utilization rate as 0.32 (Table 1). CLABSI rates and incidence densities according to departments are shown in Table 2. The highest infection rate was observed in the adult bone marrow transplantation unit.

Table 1. Central line associated bloodstream infection (CLABSI) rates by years

	Number of patients	Patient day (PD)	Catheter day (CD)	Number of CLABSI	CLABSI * rate / 1000 PD†	CLABSI Incidence density / 1000 CD‡	CVC§ utilization rate
2015	44	34174	11350	49	1.4	3.88	0.33
2016	50	35854	11008	52	1.45	4.54	0.31
Total	94	70028	22358	101	1.44	4.2	0.32

* Central venous catheter-associated bloodstream infection
† patient day
‡ catheter day
§ central venous catheter

Table 2. Rate and incidence densities of central venous catheter-associated bloodstream infections according to departments.

	Patient day	Catheter day	Number of infections	Infection Rate	Incidence density	Utilization rate
Oncology	13038	3143	18	1.38	5.73	0.24
Hematology	12022	2010	12	1	5.97	0.17
Pediatric Oncology	13319	5189	14	1.05	2.7	0.39
Pediatric Hematology	13069	4861	19	1.45	3.91	0.37
Nephrology	13878	4019	15	1.08	3.73	0.29
Adult HSCT*	2019	922	14	6.93	15.18	0.46
Pediatric HSCT*	2683	2214	9	3.35	4.06	0.82
Total	70028	22358	101	1.44	4.2	0.32

* Hematopoietic stem cell transplant

56.4% of the patients were male (n=53), the mean age was 32±2.5 years, and the median age was 31 (0-90).

The mean length of hospitalization was 27.7±2.5 and the median length of stay was 20 (4-148) days. Half of the patients (n=47) had permanent and half had transient catheter-related bloodstream infections. When the risk factors of the patients were analyzed, hematologic cancer was found in 54.7%, hemodialysis in 19.2% and other possible risk factors are summarized in Table 3.

Table 3. Risk factors of 94 patients with central venous catheter-associated bloodstream infections

Risk factors	N	%
Transfusion	75	79.8
Hematologic malignancy	54	57.4
Indwelling catheter (port or Hickman)	50	53.2
Temporary central venous catheter	48	51.1
Urinary catheter	36	38.3
H2 receptor blocker	35	37.2
Neutropenia	29	30.9
Malignant solid tumor	20	21.3
Hemodialysis	18	19.2
Total parenteral nutrition	17	18.1
Hypertension	6	6.4
Chronic kidney disease	6	6.4
Infection on admission	4	4.3
Autoimmune diseases	4	4.3
Peripheral arterial catheter	3	3.2
Diabetes mellitus	1	1.1

Of the 94 infection episodes, 21.8% were polymicrobial. Of the 125 microorganisms isolated, 62.4% were Gram negative, 20% were fungi and 17.6% were Gram positive. The most frequently isolated pathogens were *Escherichia coli* (n=17, 13.6%) and *Klebsiella pneumoniae* (n=17, 13.6%). These were followed by *Staphylococcus aureus* (N=10, 8%) and *Candida parapsilosis* (N=9, 7.2%) (table 4). Crude mortality was 36.2% (n=34).

While colistin and amikacin were the most effective antibiotics in *E.coli* and *K.pneumoniae*, amikacin and ciprofloxacin were found in P.aeruginosa. High resistance rates were observed in *A.baumannii.* Resistance rates were low in *S.maltophilia* (Table 5). In Gram positive microorganisms, *Staphylococcus aureus* was the most common agent and oxacillin resistance was found to be 60% (6/10). Resistance to fusidic acid and ciprofloxacin was not detected (0/6 and 0/8, respectively) and 10% (1/10) to clindamycin. Fluconazole resistance in *Candida* species was 15.8% (3/19), one of the resistant fungi was *C.krusei* and 2 were *C.parapsilosis.*

DISCUSSION

"The Institute for Health Care Improvement" conducts the "Save 5 million lives" campaign by optimizing infection control, but this campaign only targets patients hospitalized in the ICU (8). Is it really possible to reduce CLABSI rates by targeting only ICU patients? In a survey study investigating the rate at which patients use central venous catheters, it was found that 55% of patients hospitalized in intensive care used central venous catheters (CVCs), while this rate was 24% in other clinics. However, considering that the majority of patients were hospitalized outside intensive care units (70%), it is understood that the majority of CVCs in this study were used in non-ICU clinics (9). In addition, there are also data indicating that catheters stayed longer in units other than intensive care units. In one study, the median catheter length of stay was reported to be 6 days in internal units, 8 days in surgical units and 3 days in ICU (10). An article published in 2004 also recommended that surveillance should be carried beyond intensive care units (11).

Table 4. Distribution of causative microorganisms.

		N	within group %	Total %
Gram positive	*Staphylococcus aureus*	10	45.5	8.0
	CNS	8	10.3	6.4
	Staphylococcus epidermidis	6	27.3	4.8
	Staphylococcus hominis	1	4.5	0.8
	Staphylococcus haemolyticus	1	4.5	0.8
	Enteroccus faecium	2	9.1	1.6
	Enterococus avium	1	4.5	0.8
	Streptococus spp.	1	4.5	0.8
	Subtotal	22	100.0	17.6
Gram Negative	*Escherichia coli*	17	21.8	13.6
	Klebsiella pneumoniae	17	21.8	13.6
	Acinetobacter baumannii	8	10.3	6.4
	Pseudomonas aeruginosa	8	10.3	6.4
	Stenotrophomonas malthophilia	8	10.3	6.4
	Enterobacter cloacea	4	5.1	3.2
	Acinetobacter lwoffi	3	3.8	2.4
	Acinetobacter junii	2	2.6	1.6
	Serratia marcescens	2	2.6	1.6
	Aeromonas sobria	2	2.6	1.6
	Acinetobacter ursingi	1	1.3	0.8
	Citrobacter koseri	1	1.3	0.8
	Enterobacter aerogenes	1	1.3	0.8
	Klebsiella oxytoca	1	1.3	0.8
	Pseudomonas stutzeri	1	1.3	0.8
	Rhizobium radiobacter	1	1.3	0.8
	Delftia acidovorans	1	1.3	0.8
	Subtotal	78	100.0	62.4
Fungus	*Candida parapslosis*	9	36.0	7.2
	Candida albicans	6	24.0	4.8
	Candida famata	4	16.0	3.2
	Candida krusei	4	16.0	3.2
	Candida tropicalis	1	4.0	0.8
	Candida guilliermondii	1	4.0	0.8
	Subtotal	25	100,0	20
Total		125		100

The first non-ICU surveillance data was published by the German nosocomial surveillance system in 2006 (12). In this study, data from 42 university and state hospitals were generated using CDC nosocomial infection diagnostic criteria. After at least 3 months of surveillance, the rate of non-ICU vehicle use was found to be 4.6%, which is considerably lower than the rate of vehicle use determined in our study (32%) and the rate found in the survey study by Climo and colleagues (24.4%) (8). The high rate in our study was attributed to the high-risk group of patients with cancer and receiving long-term chemotherapy.

Table 5. Resistance characteristics of the main Gram negative agents (n/%).

	E.coli		*K.pneumoniae* (n=15)		*P.aeruginosa* (n=8)		*A.baumannii* (n=8)		*S.maltophilia* (n=8)	
	(n=17)	%	n	%	n	%	n	%	n	%
Amikacin	3/15	20	6/15	40	0/7	0	3/8	37.5		
Ciprofloxacin	8/15	53.3	8/16	50	0/7	0	7/8	87.5		
Levofloxacin	1/1	100	0/1	0					1/5	20
Cefepime	9/15	60	13/16	81.3	2/7	28.6	4/4	100		
Ceftazidime	9/13	69.2	10/13	76.9	2/8	25			0/1	0
Meropenem	5/14	35.7	7/16	43.8	2/7	28.6	7/8	87.5		
TMP-SMZ*	8/15	53.3	13/16	81.3					1/8	12.5
Tigecyclin	0/10	0	4/7	57.1			4/8	50	0/1	0
Colistin	0/13	0	2/15	13.2	0/7	0	0/8	0	0/1	0
ESBL†	11/17	64.7	10/17	58.8						

* Trimethoprim sulfamethoxazole

† Extended spectrum beta lactamase

If we look at the incidence densities of CLABSI, Vonberg et al. found an infection rate of 4.3 infections/1000 catheter days in various internal and surgical clinics, while Marschall et al. found 5.7 infections/1000 catheter days in four general internal medicine clinics. These rates are similar to the 4.2 infections/1000 catheter days found in our study. In another recent study examining patient-related risk factors contributing to CLABSI, the infection rate was 0.35 infections / 1000 patient days, which is lower than the rate of 1.44 infections / 1000 patient days in our study. This was attributed to the fact that underlying diseases such as hematologic malignancy and neutropenia, which were also identified as risk factors in this study, were more common in our patient group.

If we look at the CLABSI rates in intensive care units throughout Turkey, we see that they vary between 0.0/1000 and 9.1/1000 catheter days in various intensive care units according to the 2019 National Healthcare Associated Infections Surveillance Network summary report. This shows that the CLABSI rates we detected in our study are comparable to intensive care rates and supports the idea of moving surveillance beyond intensive care units (13).

In a 10-year study from Spain investigating CLABSI mortality risk factors in non-ICU patients, the infection rate was found to be 0.23/1000 patient days and the causative agents were Gram-positive cocci (70.1% cases), Gram-negative bacilli (31.1%) and Candida species (1%) (14). In our study, a very low infection rate and different agents are noteworthy. The low infection rate was attributed to the fact that almost half of the catheters in the study were peripheral catheters with low infection risk and the risky patient population in our study. Looking at the details of our study, the highest infection rate was observed in the adult bone marrow transplantation unit. Again, the reason why gram-negative bacteria and fungi were more common as causative agents was thought to be the high number of immunosuppressed patients in our study. In another study, 23 non-ICU CLABSIs occurred. The incidence rate was 1.2 per 10,000 bed days. When we interpret this rate, which is considerably lower than our study, we attribute it to the fact that the number of immunosuppressed patients in this study was only half of the total patients. In this study, a total of 26 microorganisms were isolated and similar to our study, Gram-negative bacilli were found to be more common than Gram-positive cocci (15).

A recent, 3-year case-control study examining the incidence and risk factors for CLABSI in hematologic and oncologic patients included a total of 610 patients, with 10.6 cases per 1,000 CVC days. Multiple CVC use per case, CVC implantation for stem cell transplantation, acute myeloid leukemia, leukocytopenia (≤ 1000/μL), carbapenem therapy and pulmonary diseases were found to be independent risk factors (16). This rate is much higher than our study and the causative agents were Gram-positive with 94.6%, again very different from our study. In another study examining the causative agents in oncologic and hematologic patients, it was shown that the epidemiology of CLABSI has changed: The proportion of Gram-negative bacteria increased over time (from 11.9% to 29.4%; p<0.001), and the absolute number and proportion of multidrug-resistant Gram-negative bacteria also increased (from 9.5% to 40.0%; p=0.039). *Pseudomonas aeruginosa* increased and constituted up to 40% of all Gram-negative bacteria (17). In our study, the most common microorganism was *Acinetobacter baumannii*, which attracted attention with its high resistance rate. This difference was attributed to the fact that it constituted the flora of our hospital as the most common agent in almost all units.

In a study examining the changing epidemiology in cancer patients, a previous cohort (cohort 1) of similar cancer patients who had BSI at the same institution between September 1999 and November 2000 was compared with the current cohort (cohort 2). When the 2 cohorts were compared, it was observed that the frequency of gram-negative organisms as the etiologic agent of CLABSI increased significantly from 24% in cohort 1 to 52% in cohort 2 (P < 0.0001) (18).

According to a study from Israel, there has also been a linear shift towards the predominance of Gram-negative bacilli (p<0.001 for trend). In 1996, 68% (68/100) of CLABSIs were caused by Gram-positive cocci, while in 2012, 77.8% (28/26) were caused by Gram-negative bacilli. The shift towards Gram-negative CLABSIs and the associated mortality necessitates that empirical treatment for CRBSIs should be guided by local epidemiology (19).

Limitations of the study

The limitations of our study are that it included data from a single center and mortality and risk factor analysis could not be performed due to lack of data.

CONCLUSION

In conclusion, we observe that catheter-associated bloodstream infection rates are comparable to those in intensive care units, especially in non-ICU clinics where immunosuppressed patients are followed. Although the idea that CLABSI rates in non-ICU clinics should be monitored is not new, there is no sufficient data on this subject to date. It is important to monitor CLABSI rates in units with high catheter utilization rates even if they are not intensive care units. Due to inter-institutional patient population and practice differences, CLABSI mortality and infection risk factors should be studied in each institution and necessary infection control measures should be taken.

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Conflict of Interest

On behalf of all authors, I, as the corresponding author, accept and declare that; we have NO affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Support Resources

No financial support was used by authors during this study.

Ethical Declaration

Ethical permission was obtained from the Medical Faculty Clinical / Human Research Ethics Committee for this study with date 17/04/2017 and number 63/3 and Helsinki Declaration rules were followed to conduct this study.

Authorship Contributions

Concept: AC, YT Design: AC, Supervising: BK, FK, YT, Data collection and entry: AC, DE, FK, Analysis and interpretation: MK, HD, FK, BK Literature search: AC, ASI, BK, Writing: AC, Critical review: AC, BK, FK, SK, FK, DE, ASİ, YT.

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