Prevalence of Catheter-related Bloodstream Infection and Distribution of Multidrug Resistance Microorganisms among the Hospitalized Patients

Oltiana Petri[1,2,3]*, Klotilda Vrenjo[2], Alda Angjeli[1], Erjona Abazaj[4] , Blerta Kika[4], Andi Koraqi[3], Albana Daka[1]

[1]Department of Microbiology, American Hospital, Tirana, Albania; [2]Department of Education and Health, Sports University, Tirana, Albania; [3]Department of Microbiology, University of Medicine, Tirana, Albania; [4]National References Laboratory, Institute of Public Health, Tirana, Albania

Abstract

BACKGROUND: Central venous catheter (VC)-related bloodstream infection (CRBSI) is associated with high rates of morbidity and mortality in critically ill patients over the world.

AIM: The aims study is to evaluate the prevalence of CRBSI and to identify some of the factors.

METHODS: This was a retrospective, observational study carried out in the tertiary care hospital "Mother Theresa," Tirana and American Hospital, Tirana, over a period of 3 years from January 2016 to December 2018. Data were collected retrospectively from various electronic sources shared by the hospitals and linked using patients' unique medical record numbers. A total of 170 patients with indwelling VC were included in the study. The catheters were cultured using the standard procedure. Statistical analysis version SPSS-20 software was used for calculation of data.

RESULTS: Overall 170 patients analyzed in this study, the prevalence of CRBSI results 58.8%. The positivity from the University Hospital Center (UHC) "Mother Theresa" resulted 65.1% (82/126 cases) and the positivity from American Hospitals (AH) resulted 40.91% (18/44 cases). Patients from UHC Mother Theresa were (odds ratio) 2.69 times higher in risk for CRBSI compared to patients from AH, for confidence interval 95% (1.33–5.44) p value resulted to be with strong association = 0.005. The average age resulted 59.68 ± 14.26, with minimum age 9 years old and maximum age 83 years old. The most infected age groups resulted patients with age 61–70 years old. Central VC had a higher positivity compared to other catheters types. Regarding the spectrum of bacteria implicated in CRBSI infections, Gram positive bacteria (67%) were the most predominant compared to Gram-negative bacteria (33%), but regarding the antimicrobial resistance, the Gram-negative bacteria resulted majority of multidrug resistance.

CONCLUSION: The overall prevalence of CRBSI was 58.8%. Patients from Mother Theresa Hospital have the highest prevalence compared to patients of American Hospital. Men patients were the most predominant sex; age groups 61–70 years old presented the highest positive cases with CRBSI. *Staphylococcus* spp.*, Acinetobacter* spp.*, Proteus* spp., etc., were the most common isolate. We found antimicrobial resistance almost in all bacteria, but Gram-negative bacteria resulted majority of multidrug resistance.

Introduction

Nowadays, the medical science has made great progress in perfecting of case management treatment protocols as well as in medical equipment and diagnostic methods. Modernization of medical sciences is increasingly providing and implementing a large number of medical devices which have increased the quality of life of the patient, through the increasing efficiency of intravenous administration of medical drugs and fluids as well as helping to improve the results of conditions of certain medical [1], [2], [3]. The use of venous catheters (VCs) has become quite common in medical practices, where in most cases, they are considered quite appropriate in many of the life-saving situations [4]. However, on the other hand, the implementation of those medical devices, especially VC in the patient's body, in addition to the benefits it brings to their good performance, shows some complications such as vascular, cardiac, and pulmonary complications, complications during their placement.

Last but not least are the various infections that patients can get when manipulating VCs. Marcos *et al*. mentioned in their paper that bloodstream infections are a significant cause of morbidity and increased mortality in health-care facilities as a consequence of central VC-related bloodstream infection (CRBSI) [5]. They attributed to an increased length of stay and increased costs [6]. The use of a VC plays a significant risk factor for circulatory infections [7]. The range of infections encountered in 5 million catheters installed within a year in the United States of America (USA) ranges from 250,000 to 400,000 cases. Bacteria, molds, and yeasts are the most common infections in these catheters installed [3], [8], [9].

Seeing the major problems related to infections encountered in the installation of central VCs, we have

undertaken this study to evaluate the prevalence, risk factors, and outcomes of blood infections associated with central VC, in patients hospitalized at the University Hospital Center "Mother Teresa" (UHCMTH) and American Hospital, Tirana, over a period of 3 years from January 2016 to December 2018.

Methods

A retrospective study was performed for hospitalized cases at the UHCMTH and American Hospitals (AH) who have been treated for infections caused by VC during the period 2016–2018. In this paper, we have included 170 suspected cases for CRBSI, 126 (74.1%) cases were involved by the microbiological laboratory of UHC, while 44 (25.9%) cases were involved by the microbiological laboratory of the AH. Inclusion criteria were all patients (women and men) hospitalized at the UHCMTH and American Hospital during the period 2016–2018, for various problems, and after the use of VCs, they are suspected for CRBSI infection. All individuals aged 18 ± 75 years, who have been monitored for VC infections. Patients suspected and tested in respective microbiological laboratories (UHCMT and AH) for other infection are excluded by this study.

UHC serves as a tertiary public center which deals with the treatment of acute cases and patients who have vital health problems. American Hospital with three hospitals private center offers a private service to patients with a wide range of treatments from the simplest to the most complicated. Many of the patients treated at UHCMTH, Tirana, and those treated at the AH, had the necessity of their treatment with CRBSI. We analyzed all patients hospitalized near these two large diagnostic centers who were suspected as cases bloodstream infections caused by VCs.

In terms of record files information of each of patients with CRBSI regarding their individual data were obtained from database systems of two hospital centers that are included in this study. Sociodemographic data such as age and gender was requested. Furthermore, we were obtained data about the ward where they were hospitalized, the type of catheter used, and the problems they had encountered with these patients. Regarding the result of microbiological testing findings, the data for each patient is were obtained from the Laboratory of Microbiology at UHC and AH. For positive cases, it is seen which pathogen caused this infection and if they performed the antimicrobial resistance. Statistical analysis for all data was performed using the Statistical Package for the Social Sciences version 20.0 (Chicago, IL, USA). Age, in the data analysis, was considered as continuous quantitative variable. Gender, in the data analysis, was considered as a binary variable (female/male). Descriptive analyses were performed: Mean, frequency, and percentage are given for each data. Categorical variables were compared by the χ^2 test or Fisher's exact test (if expected cell counts were <5) and continuous variables were compared by Student's *t*-test. The data were presented by tables and figures accompanied by the relevant explanation. Values <0.05 are considered statistically significant and logistic regression for odds ratio 95% confidence interval (CI) is used to determine the relationship between risk factors and CRBIs.

Results

The prevalence of central VC-related blood infections for the 170 cases included in this study was 58.8% (100/170 cases). In Table 1, we have presented the baseline patient characteristics of suspected CRBSI cases for both laboratories (UHC and AH) and positivity within each category of variables.

Table 1: Baseline patient characteristics and catheters profile among the suspected cases for CRBSI in UHC and AH

Variables	Total number of cases	Negative	Positive
Hospital centers	170	70	100
UHC "Mother Theresa"	126 (74.1%)	44 (34.9%)	82 (65.1%)
American Hospital	44 (25.9%)	26 (59.09%)	18 (40.91%)
Gender			
Female	60 (35.3%)	23 (38.4%)	37 (61.6%)
Male	110 (64.7%)	47 (42.7%)	63 (57.3%)
Age groups			
<30 years old	7 (4.1%)	5 (71.4%)	2 (28.6%)
30–40 years old	21 (12.3%)	14 (66.7%)	7 (33.3%)
41–50 years old	26 (15.3%)	11 (42.3%)	15 (57.7%)
51–60 years old	42 (24.7%)	18 (42.9%)	24 (57.1%)
61–70 years old	51 (30%)	17 (33.3%)	34 (66.7%)
>71 years old	23 (13.5%)	5 (61.6%)	18 (21.7%)
Catheters profile			
Femoral venous catheters	21 (12.3%)	11 (52.4%)	10 (47.6%)
Jugular venous catheters	42 (24.7%)	19 (45.3%)	23 (54.7%)
Subclavian central catheters	29 (17%)	12 (41.4%)	17 (58.6%)
Intravascular catheters	25 (14.7%)	15 (60%)	10 (40%)
Central venous catheters	74 (43.5%)	24 (32.4%)	50 (67.6%)

The positivity from the UHC "Mother Theresa" resulted 65.1% (82/126 cases) and the positivity from AH resulted 40.91% (18/44 cases). Patients from UHC Mother Theresa were (odds ratio) 2.69 times higher in risk for CRBSI compared to patients from AH, for CI 95% (1.33–5.44) p value resulted to be with strong association = 0.005.

Overall, 170 patient's female and male in our study, the positivity of CRBSI for female resulted 37% and 63%, respectively. If we compared the positivity within each gender, female has the higher positivity versus male. Hence, the positivity resulted 61.6% (37/60) for female and 57.3% (63/110) for male. We did not found an association for the positivity and gender. p value resulted >0.05. Patients <30 years old presented only 4.1% of all analyzed cases.

The most predominant age groups resulted patients 61–70 years old and 51–60 years old with 30% and 24.7%, respectively. We have calculated the positivity within each category of age. As it shown in

Table 1, the age groups 61–70 years have the higher positivity 66.7%. Related to the age groups, 41–50 years old and 51–60 years old can be mention that they presented almost the same prevalence of positivity 57.7% and 57.1%, respectively. The age groups more than 71 years old present the lowest positivity within the group. We have analyzed the types of catheters used for each patient that was introduced in this study. The most predominant type of catheters was central VCs in 43.5% of all analyzed cases. We have used the same calculated positivity for each of catheter types. The positivity within each type is as follows. Patients to whom a central VC has been applied had a higher positivity compared to other catheters types. Hence, the positivity of patients with CVS is 67.6% of cases, patients with subclavian central catheters are 58.6%, patients with jugular VCs are 54.7%, patients with femoral VCs are 47.6%, and the last one is the patients with intravascular catheters with positivity 40%. Figure 1 presents the distribution of positive and negative all catheters profile among our analyzed patients.
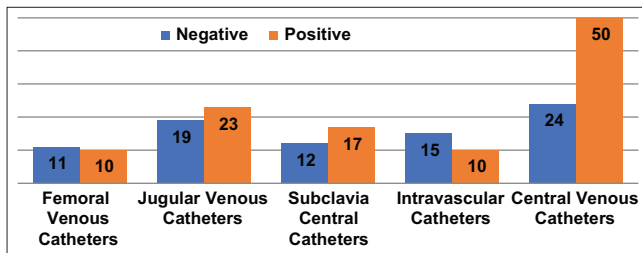

Figure 1: The number of negative/positive cases divided by catheter profile

Table 2 presents the types of bacteria that have been encountered in CRBSI-suspected patients for two hospital centers (UHC and AH). As Gram-negative bacteria, the species that were encountered in hospitalized patients at UHC are: *Acinetobacter* spp. in a total resulted 8.6% (*Acinetobacter baumannii* one case), *Enterobacter* spp. 1.2%, *Enterococcus faecium* 1.2% and *Enterococcus faecalis* 3.6%, *Klebsiella pneumoniae* 1.2%, *Pantoea agglomerans* 1.2%, *Proteus* spp. 3.6% in total (*Proteus mirabilis* two cases), *Pseudomonas aeruginosa* 6.2%, and *Serratia odorifera* 1.2%. The genus *Staphylococcus* spp. (63.4%) was identified as a Gram-positive bacterium and the most encountered species were *Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus haemolyticus,* etc.

Regarding the distribution of microorganisms in patients hospitalized at AH, we found *A. baumannii* 16.6% and *Pseudomonas* spp. (11.1%), the most common Gram-negative bacteria encountered in these patients, while other Gram-negative species such as *P. mirabilis*; *Enterobacter* spp.*;* and *Cronobacter* spp. resulted in 5.6%, respectively. On the other hand, Gram-positive bacteria resulted as below; *Staphylococcus epidermidis* 33.2%; *S. aureus* 11.1%*;* and *Kocuria kristinae* and *E. faecalis* in 5.6%, respectively.

Table 2: Organisms isolated from catheter-related bloodstream infection (CRBSI)

Types of bacteria	UHC (n/%)	AH
Total no. of Gram negative and Gram positive	82/126	18/44
Gram-negative bacteria		
Acinetobacter spp. (*Acinetobacter baumannii*)	7 (8.6%)	3 (16.6%)
Enterobacter spp.	1 (1.2%)	1 (5.6%)
Klebsiella pneumoniae	1 (1.2%)	0 (0%)
Pantoea agglomerans	1 (1.2%)	0 (0%)
Proteus spp. (*Proteus mirabilis*)	3 (3.6%)	1 (5.6%)
Pseudomonas aeruginosa	5 (6.2%)	2 (11.1%)
Serratia odorifera	1 (1.2%)	0 (0%)
Cronobacter spp.	0 (0%)	1 (5.6%)
Gram-negative bacteria (without specification)	6 (7.3%)	
Gram-positive bacteria		
Staphylococcus spp.	18 (22.0%)	0 (0%)
Staphylococcus lugdunensis	1 (1.2%)	0 (0%)
Staphylococcus aureus	11 (13.4%)	2 (11.1%)
Staphylococcus epidermidis	18 (22.0%)	6 (33.2%)
Staphylococcus haemolyticus	4 (4.9%)	0 (0%)
Enterococcus faecium	1 (1.2%)	0 (0%)
Enterococcus faecalis	3 (3.6%)	1 (5.6%)
Streptococcus spp.	1 (1.2%)	0 (0%)
Kocuria kristinae	0 (0%)	1 (5.6%)

All cases resulted as positive for CRBSI to the microbiological laboratory have undergone antimicrobial resistances test. The range of antibiotics used for each patient confirmed for the presence of bacteria is relatively high and ranges from 18 to 27 antibiotics for each. In Table 3, we have presented the susceptible, intermediate susceptibility, and resistant for each antibiotic used.

Table 3: Distribution of antimicrobial resistance for positive cases

Antibiotics	Total number	Susceptible	Intermediate susceptibility	Resistant
Doxycycline	16	5	5	6
Cefixime	13	2	1	10
Cefoxitin	8	2		6
Imipenem	15	3	3	9
Clindamycin	8	2		6
Ceftazidime	13	1	5	7
Ertapenem	7	2		5
Nalidixic acid	17	2	2	13
Tobramycin	12	3	1	8
Moxifloxacin	18	11	7	
Meropenem	17	4	4	9
Vancomycin	15	2	7	6
Cefazolin	11	3	1	7
Rifampicin	18	10	4	4
Ofloxacin	5	3		2
Azithromycin	14	1	1	12
Cefotaxime	9	4		5
Cefuroxime	17	4	1	12
Amoxycillin	15	2	2	11
Levofloxacin	17	5	2	10
Ceftriaxone	17	6		11
Gentamycin	18	8	2	8
Clarithromycin	7	1	2	4
Piperacillin/tazobactam	16	5	3	8
Norfloxacin	17	5	1	11
Cefepime	10	3		7
Ciprofloxacin	16	5	2	9
Doripenem	8	1	1	6
Amikacin	7	2	4	1
Cefaclor	5	1	1	3
Nitrofurantoin	8	5	1	2
Amoxicillin	1			1
Ticarcillin	1			1
Bactrim	2	1		1
Ampicillin	4	1		3
Aztreonam	1		1	
Co-trimoxazole	1	1		
Colistin	1		1	
Cefpodoxime	1		1	
Ofloxacin	1			1
Gatifloxacin	1			1
Ticarcillin	1			1
Novobiocin	1	1		
Cephalexin	1	1		
Augmentin	1			1
Cefprozil	1			1
Teicoplanin	1	1		
Ticarcillin/clavulanic acid	2	1	1	

Discussion

VCs are the most commonly used medical devices in hospitalized patient's settings. They have become indispensable tools for the successful treatment of patients with chronic or life-threatening illnesses. The establishment of VCs provides a secure access to the central circulation for infusion of therapies, nutritional support, hemodynamic monitoring, hemodialysis, etc. Although the benefits we receive from using VCs, in most cases, the problems encountered by them outweigh the benefits gained, especially when a long-term approach to the central venous system is needed. VC patients pose a risk of developing local complications and systemic infectious complications. The most serious complications are bacteremia, sepsis, and mortality [7], [10], [11], [12]. The problem of circulatory infections related to the use of VCs has been gaining increasing attention in recent years [10]. This is because VCs cause a lot of morbidity and mortality, which increase the costs of health care [6], [13]. All over the world, diagnostic tests for CRBSI are recommended/ performed in those patients who are clinically suspected of having CRBSI (i.e., present with unspecified signs such as fever, hypotension, tremor, leukocytosis, and no other obvious focus of infection) [10].

The prevalence of catheter-related blood infections in 170 patients analyzed in this study during the periods 2016–2018, for public and private hospital center was 58.8%. This prevalence is higher than other study conducted by Negi *et al*. (2019) who were the prevalence of CRBSI resulted 24.4%, and Curtis (2009), the prevalence of CRBSI resulted 22.7%. Nidhi *et al*. [14] and Curtis [15], but our prevalence was lower than another study conducted by Gahlot *et al*., 2013, were found in their study, the CRBSI prevalence was 62.5% [16]. We have analyzed data from two different hospitals which represent two different services public and private. In 126 patients admitted to UHC, 34.9% (44/126) tested negative and 65.1% (82/126) tested positive for CRBSI. Related to the hospitalized patients at the American Hospital (44 patients in total), the positivity for CRBSI resulted 40.9% (18/44) was positive and negative 59.1% (26/44). If we compare the positivity founded between the cases analyzed by UHC and those by AH, it is clear that the number of patients and also the prevalence is higher for UHC. Hence, patients from UHC are 2.69 times more likely to have problems with catheter-induced infections compared to AH patients (odds ratio 2.69); CI 95% (1.33–5.44) p value resulted in 0.005.

The exact mechanisms by which gender may influence the risk for CRBSI infection are unclear, but may be related to changes in skin colonization or unknown anatomical differences between men and women. Findings regarding CRBSI are consistent throughout the literature [17], [18], [19], [20]. According to Bevin Cohen *et al*., no study has found significantly higher rates of infection in women if we compare them with men [21].

In our study, the positivity of CRBSI for female resulted 37% and for male 63%. If we compared the positivity within each gender, female has the higher positivity versus male. Hence, the positivity resulted 61.6% (37/60) for female and 57.3% (63/110) for male. We did not find an association for the positivity and gender. The p value resulted >0.05. Patients <30 years old presented only 4.1% of all analyzed cases.

Some studies were not found an association between the age and higher risk for bacteremia in VC types [22], [23], [24], [25] whereas other studies reported higher risk of hospitalized septicemia in older patients [26], [27]. Regarding our data, the mean age results 59.68 ± 14.26, with minimum age 9 years old and maximum age 83 years old. In this category of variables, we have calculated the positivity within each age group to seen which of them has the higher positivity. After the calculated of data, age groups 61–70 years have the higher positivity 66.7%, and the age groups 41–50 years old and 51–60 years old presented almost the same prevalence of positivity 57.7% and 57.1%, respectively, meanwhile, the age groups more than 71 years old present the lowest positivity within the group.

All types of catheters are associated with catheter-related bloodstream infection (CRBSI). CVADs are associated with a higher rate of CRBSI than peripheral IV catheters, therefore, interventions to reduce the rate of CRBSI are especially important for their management and care [8]. Elsewhere CRBSI is also referred to as central line-associated bacteremia and catheter-related infection [28]. In our study, we found a strong significant correlation which was observed in terms of positivity and catheter placement location for χ^2 = 2.3 CI 95% p = 0. 007.

Infections are thought to arise through contamination from commensal skin flora and may be introduced during insertion or subsequent care. The catheter insertion site itself provides the most direct route of entry for the pathogen and this is the most common cause of CRBSI. These infections are caused mainly by Gram-positive bacteria, in particular *S. aureus* and coagulase-negative staphylococci such as *S. epidermidis*, which is the most common [14]. However, infections can be caused by a wide range of microorganisms including *Enterococci, Candida* spp.*, Acinetobacter* spp.*, Pseudomonas* spp.*,* and *Klebsiella* spp. It is likely that specific pathogens vary depending on different wards of hospitals and the individual colonization profile of the patient. In long-term catheters, the hub of the catheter is the main area for colonization and portal of infection and it is suggested that increasing length of catheterization is linked with a greater risk of developing a catheter-related infection [29], [30], [31].

Regarding the spectrum of bacteria implicated in CRBSI infections (100 positivity/170 patients in total) in both hospitalized patients (private and public), the most predominant bacteria resulted Gram positive in 67% (67/100) compared to Gram negative 33% (33/100).

In UHC (82 positive cases), our study shows that most 69.5% (57/82) of the patients were caused by Gram-positive organisms as compared with 30.5% (25/82) of those caused by Gram-negative organisms. Related to CRBSI infections in AH (18 positive cases), our study shows that most 55.5% (10/18) of the cases were caused by Gram-positive organisms as compared with 44.5% (8/18) of those caused by Gram-negative organisms.

In majority for both hospitals, bacteremia was caused from Gram-positive bacteria. In patients with CRBSIs, only 4 (30.7%) out of 13 of the total *S. aureus* isolates were methicillin-resistant and 3 (21.4%) out of 14 Gram-negative bacterial isolates were extended-spectrum beta-lactamase-producing organisms (such as *Enterobacter* spp.; *K. pneumoniae*; *P. mirabilis;* and *P. aeruginosa*). A total of 5 (29.4%) out of 17 isolates were multidrug resistance including five isolates of *Acinetobacter* spp. and three isolates of *P. aeruginosa*.

Our study shows that Gram-positive bacteria were the most predominant compared to Gram-negative bacteria but regarding the antimicrobial resistance, the Gram-negative bacteria resulted majority of multidrug resistance.

All samples that were analyzed in microbiological laboratory of both hospitals (UHC and AH), for the presence of infection, have undergone to antibiogram test after a positive result. A wide range of antibiotics [8], [19], [20], [21], [22], [23], [24], [25], [26], [27] were used for each patient that is confirmed for the presence of bacteria. Antibiotics such as moxifloxacin, rifampicin, and gentamycin show the highest susceptibility test in almost of positive cases, while other antibiotics such as doxycycline, cefixime, ceftazidime, nalidixic acid, tobramycin, and meropenem show the highest number of antimicrobial resistances.

Conclusion

The overall prevalence of CRBSI in our study was 58.8%. Patients from Mother Theresa Hospital have the highest prevalence compared to patients of American Hospital. Men patients were the most predominant sex; age groups 61–70 years old presented the highest positive cases with CRBSI. *Staphylococcus* spp.*, Acinetobacter* spp.*, Proteus* spp.*,* etc., were the most common isolate. Our study shows that Gram-positive bacteria were the most predominant compared to Gram-negative bacteria. We

found antimicrobial resistance almost in all bacteria, but Gram-negative bacteria resulted majority of multidrug resistance. These complications are often related to the technique that the medical staff uses while performing the procedure. Furthermore, it is important to recognize and manage these complexities of immediate that may occur, because they can often become life threatening to the patient.

Recommendation

An early diagnosis of cases with CRBSI infection is recommended because this will avoid morbidity and mortality related to CRBSI.

The final diagnosis of catheter infection can be made using a combination of symptoms and clinical signs along with quantitative culture techniques.

Always should be taken care in determining a suspect case with CRBSI, because there is a salient difficulty among the medical staff to make distinguishing infection from contamination.

Infection of CRBSI is completely preventable if we apply strict hygiene measures, all medical staffs are training and a high standard individual care must be offer.

Sterile barrier precautions and skin asepsis reduce contamination from commensal organisms, and it is widely believed that routine change of catheters decreases colonization levels.

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