Evaluation of Risk Factors in Central Venous Catheter Related Bloodstream Infection in A Critical Care Unit Patients

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ABSTRACT

Background: Critically ill individuals hospitalized to intensive care units require the use of central venous catheters (CVCs), which are crucial medical devices.

Objective: To investigate multiple aspects of blood stream infection in ICU patients with central venous catheters.

Subjects and methods; This was an observational study on 208 patients admitted to ICU and prepared to CVC insertion with the use of central line bundle and the length of stay was ≥ 72 h. Patients were followed up for any signs of infection. If systemic catheter related infection with or without local infection was suspected, microbiological evaluation was done on monitoring signs of infection.

Result: We found a statistically significant relation between catheter-related bloodstream infections (CRBSIs) incidence and comorbidities, total parenteral nutrition (TPN) use, number of CVCs, and longer CVC duration. CRBSI incidence was also significantly related to increased blood transfusion and mechanical ventilation duration. There was a significant relation between CRBSI incidence and outcome, with lower survival in CRBSI patients; 73 patients (61.3%) than non-CRBSI patients; 81 patients (91%). A significant association between development of CRBSI and prolonged ICU and hospital lengths of stay was noticed. Catheter site and ultrasound guidance were not significantly related to CRBSI risk.

Conclusion: our study indicated a high incidence of CRBSIs in the ICU setting, with 57.2% of patients developing CRBSI. The study identified several risk factors associated with CRBSI, including TPN, the number of CVCs, CVC duration, blood transfusion, and duration of mechanical ventilation.

Key words: Central Venous Catheter, Bloodstream Infection, Critical Ill Unit, CRBSI.

INTRODUCTION

ICU-acquired catheter-related bloodstream infections (CRBSIs) are prevalent and significantly impact mortality, morbidity, and healthcare expenditures [1].

Critical care unit patients with sepsis, characterized as potentially fatal organ dysfunction due to an uncontrolled immune response to infection, are at increased risk for CRBSIs [2].

On the other hand, there is a dearth of solid evidence demonstrating that the signs used to diagnose suspected sepsis can also detect CRBSI when the diagnosis is suspected but not yet proven. Furthermore, the relative risk of death from CRBSI is still not known and is within the range of -12.24% to 25.96%. Decisions about the management method for central venous catheters in patients suspected of having CRBSIs are influenced by death rates [3].

Although knowing the CRBSI related death rate is crucial, a systematic review found no strong evidence to help choose a care strategy for patients suspected of having a CRBSI [1, 4].

This study aimed to investigate multiple aspects of blood stream infection in ICU patients with central venous catheters. In the first place, it aimed to find out how often bloodstream infections occur. The second objective was to better understand the factors that put intensive care unit patients at risk for infections caused by central venous catheters.

PATIENTS AND METHODS

This cross-sectional study was conducted in the Intensive Care Unit at Zagazig University Hospitals from December 2021 to December 2022. The study sample consisted of 208 patients, either males or females, selected from the surgical ICU using systematic random sampling.

Inclusion criteria:
1) Patients aging from 18 and 70 years old.
2) Recently admitted to participating ICU with length of stay ≥ 72 h.
3) CVC insertion in the ICU.
4) Same type of CVC.
5) Application of CVC care bundle.
6) Anesthetist applied after training for application under supervision of senior staff for at least 10 cases.
7) BMI range 18.5-35.

Exclusion criteria:
1) Patients with open wound, burn, sepsis or infection at site of CVC insertion.
2) Femoral vein for central venous access.
3) CVC insertion outside ICU.
4) Length of stay less than 72h.

Operational design:

The 208 patients who were undergoing CVC insertion under complete aseptic conditions according to protocol of the Institute for Healthcare Improvement's central catheter bundle as follows: Proper hand hygiene involves rinsing hands with water and antibacterial soap or an alcohol-based wash.

A broad sterile drape should be used to cover the patient's insertion site. Before starting to implant the catheter, let the chlorhexidine skin antisepsis air-dry for about 2 minutes. Adults should avoid inserting catheters into their femoral veins, when possible, to ensure proper central venous access. Thoroughly evaluate the central line's requirement and promptly remove any extraneous lines [5].

After catheter insertion:

Apply sterile dressings using transparent, semi-permeable dressings. The clear dressings should be changed every 5-7 days, or if they become dirty, loose, or wet, and a chlorhexidine-based antiseptic should be applied to the site. Taking care of the catheter's hub, cap, and pipeline If an administrative set, including any attachments, becomes dirty or looks like it might be infected, you should replace it no more than once every 72 hours. Within 24 hours of starting infusion, replace tubing that is used to give lipids, blood products, or blood. According to protocol, CVCs should be changed every 7 days or whenever there are indications of infection, sepsis, or unintentional removal: The following symptoms should be present in order to confirm a systemic catheter-related infection: temperature of 38.3°C or higher, chills, rigors or hypotension upon flushing the catheter, and biological indicators of inflammation; and there is no known clinical source of infection:

A. No local signs of infection (erythema, induration/tenderness, pus at exit site):

After deciding to remove the catheter, the next step is to take a culture of the catheter and the new insertion site; depending on the results, empirical treatment may or may not be administered. Empirical treatment plus: no clinical decision to remove catheter After the guidewire exchange, a blood culture and culture catheter are performed.

If the results are negative, the therapy can be stopped. On the other hand, if the results are positive, the catheter and the new site of insertion can be removed. Please remove the catheter and the new site of insertion if the quantitative blood culture is greater than or equal to 5:1, and continue treatment if the qualitative blood culture is less than or equal to 5:1.

B. Local signs of infection (erythema, induration/tenderness, pus at exit site): After deciding to remove the catheter, the next step is to swab the exit site, culture the catheter and the new site of insertion, and then start empirical treatment; if the culture comes back positive, the treatment can be adjusted; if it comes back negative, treatment can be stopped. Without a clinical decision to remove the catheter, we will swab the exit site and implement empirical treatment; if the results are positive, we will remove the catheter immediately and adjust the treatment accordingly; if the results are negative, we will not remove the catheter and will continue the treatment as before [6].

Microbiological evaluation on monitoring of signs of infection:

As (CDC) recommendations for (CRBSI): It is important to establish whether an infection is likely to be related to the CVC or is incidental. The CVC was removed aseptically, the distal 5 cm of the catheter is amputated and processed as described in previous research [7]: In order to culture the catheter segment quantitatively, one must first flush it with broth, vortex it, or sonicate it in broth. Then, one must serially dilute the broth and surface plate it on sheep blood agar. The number of colonies is determined once the incubation period has elapsed. The presence of a colony count that is five to ten times higher in CVC blood than in peripheral vein blood is indicative of a bloodstream infection that had originated via the catheter. Every sample will be tested for its ability to withstand certain antibiotics.

Patients were classified according to blood cultures into two groups:

Group A: included CRBSI cases.

Group B: included CVCs without CRBSI.

Certain risk factors (variables) assessed in each group to detect CRBSI rate in the participating ICU and variables related were age, sex, BMI, indications of admission (trauma, postoperative, COPD…), catheter insertion site either subclavian or internal jugular, sonar guided insertion, APACHE II score on admission, comorbidity like (diabetes mellitus, asthma, cardiac diseases, and malignancy), mechanically ventilated or not and duration of ventilation, Ryle feeding, total parental nutrition, administration of blood products, urinary catheterization, number of CVCS inserted, duration of catheterization, duration of hospitalization, and clinical outcome.
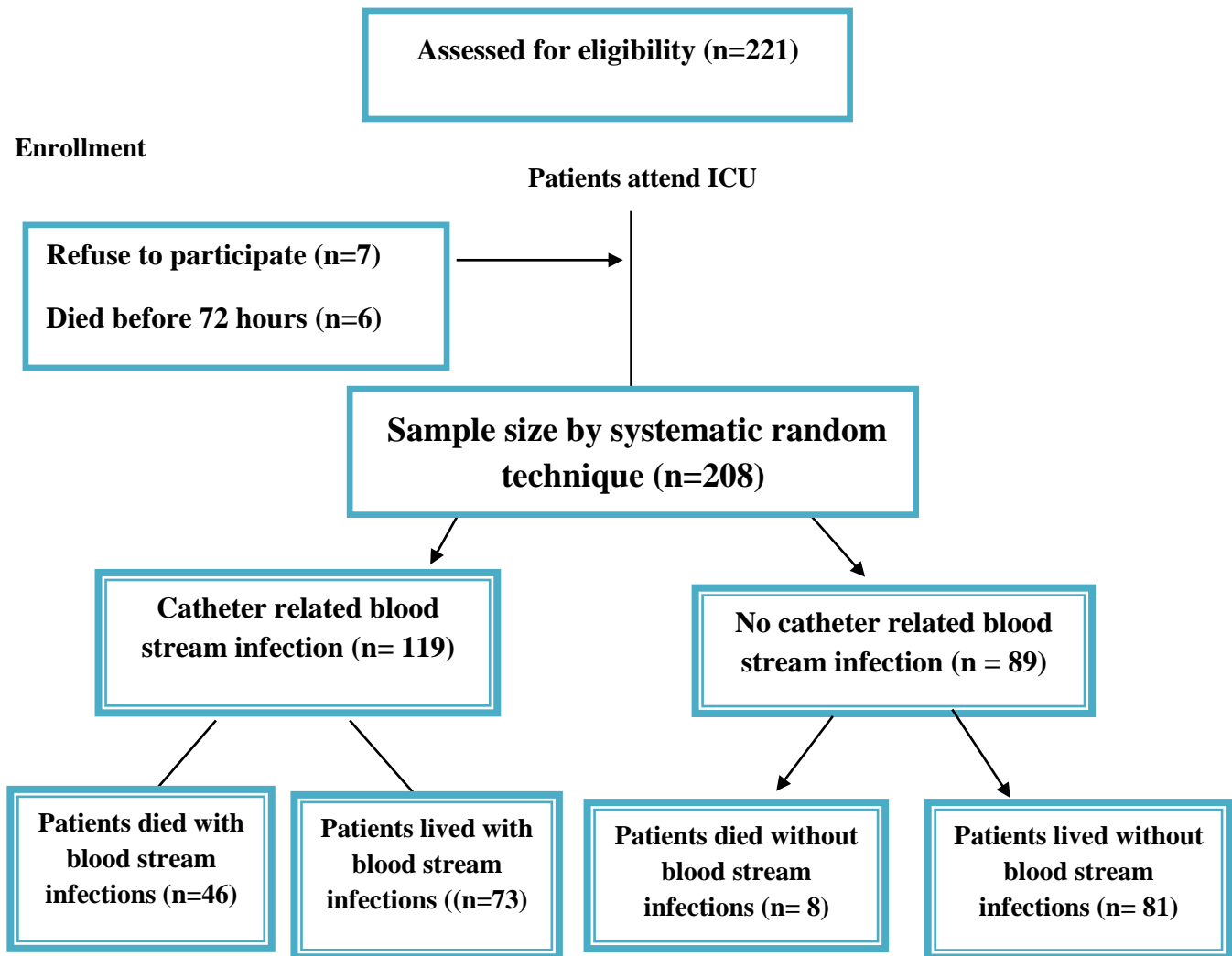
Assessed for eligibility (n=221)

Enrollment

Patients attend ICU

Refuse to participate (n=7)

Died before 72 hours (n=6)

Sample size by systematic random technique (n=208)

Catheter related blood stream infection (n= 119)

No catheter related blood stream infection (n = 89)

Patients died with blood stream infections (n=46)

Patients lived with blood stream infections ((n=73)

Patients died without blood stream infections (n= 8)

Patients lived without blood stream infections (n= 81)

Figure (1): Flow chart

Ethical approval:

The study was approved by the Ethics Committee of the Faculty of Medicine at Zagazig University. A detailed description of the study's objectives was given to each participant before they completed an informed consent form. The Helsinki Declaration was adhered to at every stage of the investigation.

Statistical analysis

Using SPSS 27.0 software, all data were collected, tabulated, and statistically analyzed. The Shapiro-Wilk test was used to check if the data was normally distributed. Presentation of categorical data was done using relative percentages and frequencies.

When appropriate, we used chi-square test, Monte Carlo test, or Fisher's exact test to see whether there were differences between the qualitative variables. When reporting quantitative non-parametric data, data were analyzed using the median and interquartile range. The Mann-Whitney U test was used to compare the two groups based on quantitative characteristics. P value < 0.05 was considered significant.

RESULTS
Table (1) shows that 119 patients (57.2%) developed catheter-related blood stream infections.

Table (1): Distribution of studied patients according to catheter related blood infection:

	N=208	%
-Catheter related blood stream infection:		
Yes	119	57.2%
No	89	42.8%

Table (2) shows that 35.3% and 13.4% of patients with blood stream infection had diabetes or diabetes with cardiac disease respectively. Comorbidity was found to be statistically associated to the occurrence of catheter-related blood stream infections.

Table (2): Relation between catheter related blood stream infection and comorbidity among studied patients:

	Catheter related blood stream infection	No catheter related blood stream infection	Test	P
	N=119 (%)	**N=89 (%)**		
No	36 (30.3%)	35 (40.4%)		
Cardiac	0 (0%)	16 (18%)		
Diabetes	42 (35.3%)	14 (15.7%)		
Asthmatics	9 (7.6%)	7 (7.9%)		
Malignancy	9 (7.6%)	7 (7.9%)	MC	<0.001**
DM, cardiac	16 (13.4%)	8 (9%)		
DM, malignancy	4 (3.4%)	0 (0%)		
DM, cardiac, malignancy	3 (2.5%)	1 (1.1%)		

DM (diabetes mellitus); MC: Monte Carlo test; **: highly significant

Table (3) shows that there was statistically significant relation between incidence of catheter related blood stream infection and TPN, blood transfusion, and MV duration.

Table (3): Relation between catheter related blood stream infection and admission-related data among studied patients:

	Catheter related blood stream infection	No catheter related blood stream infection	χ^2	p
	N=119 (%)	**N=89 (%)**		
MV				
Yes	104 (87.4%)	69 (77.5%)	3.542	0.06
No	15 (12.6%)	20 (22.5%)		
Transfusion				
Blood	40 (33.6%)	56 (62.9%)		
Plasma	0 (0%)	4 (4.5%)	MC	<0.001**
Both	8 (6.7%)	8 (9%)		
No	71 (59.7%)	21 (23.6%)		
TPN:				
Yes	32 (26.9%)	4 (4.5%)	Fisher	<0.001**
No	87 (73.1%)	85 (95.5%)		
	Median (IQR)	**Median (IQR)**	**Z**	**p**
MV duration (days)	8 (2 – 15)	3 (1 – 6)	-5.543	<0.001**

MV (mechanical ventilation); TPN (total parenteral nutrition); χ^2: Chi square test; Z: Mann Whitney test; IQR: interquartile range; **: highly significant\.

Table (4) shows that there was statistically significant relation between incidence of catheter related blood stream infection and number of CVC and CVC duration.

Table (4): Relation between catheter related blood stream infection and catheter-related data among studied patients:

	Catheter related blood stream infection	No catheter related blood stream infection	χ^2	p
	N=119 (%)	N=89 (%)		
Catheter site:				
Subclavian	45 (37.8%)	39 (43.8%)	0.763	0.382
Internal jugular	74 (62.2%)	50 (56.2%)		
Sonar guided:				
Yes	55 (46.2%)	44 (49.4%)	0.212	0.645
No	64 (53.8%)	45 (50.6%)		
Number of CVC				
1	41 (34.5%)	83 (93.3%)		
2	54 (45.4%)	6 (6.7%)	73.835	<0.001**
3	20 (16.8%)	0 (0%)		
4	4 (3.4%)	0 (0%)		
	Median (IQR)	**Median (IQR)**	**Z**	**p**
CVC duration (days)	14 (3.5 – 18)	8 (7 – 9)	-8.454	<0.001**

χ^2: Chi square test; Z: Mann Whitney test; IQR: interquartile range; **: highly significant

Table (5) illustrates that the duration of stay in the hospital and intensive care unit was significantly correlated with the rate of blood stream infections caused by catheters.

Table (5): Relation between catheter related blood stream infection and length of hospital stay among studied patients:

	Catheter related blood stream infection	No catheter related blood stream infection	Z	p
	Median (IQR)	Median (IQR)		
ICU LOS (days)	14 (9 – 19)	8 (7 – 10)	-8.064	<0.001**
Hospital LOS (days)	15 (11 – 22)	10 (8 – 12)	-8.208	<0.001**

ICU (intensive care unit); LOS (length of stay); Z: Mann Whitney test; **: highly significant

Table (6) shows that bloodstream infections caused by catheters were found to be significantly correlated with the study's results. Specifically, 61.3% of participants with these infections survived until the end of the trial, compared to 91% without.

Table (6): Relation between catheter related blood stream infection and outcome among studied patients:

	Catheter related blood stream infection	No catheter related blood stream infection	χ^2	p
	N=119 (%)	N=89 (%)		
Outcome:				
Alive	73 (61.3%)	81 (91%)	23.314	<0.001**
Dead	46 (38.7%)	8 (9%)		

χ^2: Chi square test; **: highly significant

DISCUSSION

Intravenous drug-related bloodstream infections (BSIs) are a major cause of illness, death, and healthcare expenditures, particularly in the intensive care unit. Central venous catheters are the most common source of bloodstream infections (BSIs) encountered in hospitals. Our study's overarching goal was to examine several facets of bloodstream infection in intensive care unit (ICU) patients with central venous catheters, since CRBSI rates are affected by both patient- and catheter-related factors, including the severity of illness [6].

In our study, 119 (57.2%) developed catheter related blood stream infection and 54 (26%) from the total patients died by the end of study.

In agreement with a multicentric study by **Rosenthal et al.** [8], including eight countries. Our density-based CRBSI incidence of 12 per 1000 catheter days was far lower than that. Later, the International Nosocomial Infection Control

Consortium published an updated version of this conclusion based on a multicentric study that included 36 nations. With a density incidence of approximately 6 per 1000 catheter days, CRBSI rates have been declining [9].

This also agrees with **Zhong et al.** [10] whose CRBSI incidence, risk factors, and mortality in that patient population were the primary outcomes of the study. They included 686 patients with 795 putative CRBSI episodes; 19.2% of those episodes were certified as CRBSIs; and 17.4% of patients died within 30 days, which contradicts our findings.

In our study, comorbidity was found to be statistically associated to the occurrence of catheter-related blood stream infections.

In a study conducted by **Singer et al.** [11], it was found that individuals with arterial hypotension (MAP < 70 mmHg) had a considerably increased relative risk of CRBSI compared to those without hypotension. This finding is in slight agreement with that study. Moreover, diabetes was not found to be a risk factor for CRBSI.

On the other hand, **Zhong et al.** [10] reported that individuals diagnosed with diabetes mellitus exhibited a comparatively reduced incidence of CRBSIs. Several factors may contribute to this discrepancy, including variations in the study populations, differences in healthcare settings, and potential confounding variables.

In our study, between 26.9% of patients with a catheter-related blood stream infection and 4.5% of patients without such an infection, a statistically significant correlation was found between the two variables.

Our findings are in agreement with **Garnacho-Montero et al.** [12] who reported that in the univariate analysis, there was a greater incidence of CRBSI related with the usage of TPN. In addition, a large body of research has linked TPN to an increased likelihood of CRBSI. A connection between TPN and the risk of CRBSI has been established in the guidelines of both ASPEN and the CDC. The reason behind this is that dextrose is a preferred food item for bacteria [13,14].

Consistent with this, another investigation confirmed that CRBSI was linked to hypoalbuminemia and malnutrition (OR 3.13; 95% CI 1.38-5.24, p<0.05) [15].

Furthermore, it is extremely important for healthcare providers to handle venous devices and TPN with the utmost care and sterile barriers to prevent the worsening of CRBSI symptoms [11]. **Chopra et al.** [16] came to a different conclusion about the relationship between the two variables.

We found a statistically significant correlation between the number of central venous catheters (CVCs) implanted and the occurrence of catheter-related blood stream infections (34.5 percent of patients with CRS-related infections vs 93.3 percent of patients without CRS-related infections who received a single CVC).

While there is a lack of data from previous studies to draw any firm conclusions about the pros and cons of this clinical practice, a systematic review did find that CVC removal and reinsertion could cause significant pain, serious complications, and treatment delays or interruptions in critically ill patients. Hence, further studies are needed to confirm the probable cause of the higher mortality rate in patients who had CVCs reinserted.

Multilumen catheters were identified as an individual risk factor for CRBSI, which is related to the number of lumens of the venous devices [10]. The results align with the guideline from the CDC (category IB) to use implanted devices with the fewest lumens possible. This is because bacteria can enter the catheter through the connections, and the risk is increased with devices with more entrances [13].

We found a statistically significant correlation between the length of time a catheter was in place and the frequency of catheter-related blood stream infections; the former group had a substantially greater CVC duration.

Excessive heterogeneity in the outcomes was observed in the studies pertaining to the number of days of catheterization. Since the CDC has determined that central device replacement is not required on a regular basis (category IB) [17, 18], the degradation and dysfunctionality that venous devices undergo from repeated manipulations [19], over time might be the true cause of infection. Previous studies have shown that the colonization of catheters is heavily influenced by the quality of care and management provided, as thrombosis and intraluminal and extraluminal fibrin foster microbial development [20].

Our findings corroborate those of **Bretón et al.** [21] who found that the length of time a catheter was left in the body increased the likelihood of CRBSI. Furthermore, **Singer et al.** [11] found that the duration of catheterization increases the incidence of CRBSI in their systematic review and meta-analysis.

In our study, the incidence of catheter-related blood stream infections and the catheter site did not show a statistically significant relationship.

We found the same incidence of CRBSI at all three locations, which is consistent with the findings of **Garnacho-Montero et al.** [12]. More important factors in the occurrence of CR-BSIs than the anatomic site may be the adoption of rigorous sterile insertion precautions, the standardization of continuous catheter care, and the duration of catheterization. Contrary to our findings, jugular vein catheters are thought to be more likely to produce CRBSI than other sites of CVC placement [22]. **Hajjej et al.** [23] reported that, CRBSI and catheter colonization (CC) were more common when the catheter was placed in the jugular vein or femoral vein rather than the subclavian location.

Multivariate study failed to corroborate this finding. It should be noted that adults should not have central venous access through the femoral vein but should instead use a subclavian site or a jugular site [13]. Patients whose insertion sites were located subclavian had a reduced risk of CRBSI, according to clinical evidence [24].

The correlation between sonar-guided CVC insertion and catheter-related blood stream infections was not statistically significant in our study.

That agrees with what **Imataki et al.** [25] discovered; they also discovered that CRBSI rates did not go down when central venous catheters were placed using ultrasound guidance. In contrast, **Takeshita et al.** [26] examined the effectiveness of ultrasound guidance in preventing catheter-related bloodstream infections and found that; ultrasound-guided central venous catheterization was associated with a slightly lower incidence of these infections.

Transfusions of blood and blood products were performed by 66.4% of patients with catheter-related blood stream infections compared to 14.6% of patients without such infections, indicating a statistically significant association between the two.

This is consistent with the goals of **Erbay et al.** [27], who sought to determine variables that increase the likelihood of CRBSIs occurring again after a catheter has been inserted. According to their findings, patients who received blood product transfusions had a higher risk of CRBSI recurrence (p = 0.049).

Patients with catheter-related blood stream infections had MVs for longer periods of time, and **Yamin et al.** [28] found that MVs can raise the risk of CRBSIs.

The incidence of catheter-related blood stream infections was significantly correlated with the result in our investigation. Specifically, 61.3% of patients with these infections survived till the end of the study, compared to 91% without these infections.

Consistent with findings from the 75-country Extended Prevalence of Infection in Intensive Care (EPIC II) study, ICU patients infected with Gram-negative pathogens had a higher mortality rate [29].

Contrary to what **Hajjej et al.** [23] found, there was no significant difference in the number of patients who died within each group. This was true for group A, which consisted of patients with CRBSI, and group B, which included patients with catheter colonization. The corresponding p-values were 0.314, 22.4 and 13.03, respectively. For group C, which included patients without CRBSI or catheter colonization, the corresponding p-values were 0.054 and 0.422, respectively. Hence, CRBSI was probably the cause of death in the CRBSI group.

Zhong et al. [10] found no statistically significant difference in mortality rates between patients with and without CRBSIs who had central venous catheters removed for suspected CRBSIs, therefore this also contradicts their findings. In addition, there is a discrepancy between these findings and those of a previous cohort study that looked at the mortality rates of patients with CRBSIs and other infections acquired in the intensive care unit but found no differences [30]. Another cohort study by **Lorente et al.** [31] found that patients with CRBSIs had reduced mortality rates compared to those with other illnesses, which contradicts this.

Longer time in the intensive care unit and overall hospital stay were significantly associated with the development of CRBSI, according to our study.

Comparing clinical data from 43 pediatric cancer patients with bloodstream infections to 43 similarly matched control patients without BSIs was also done in a cohort study. According to **Biwersi et al.** [32], the duration of hospitalization is prolonged due to CRBSI. **Rosado et al.** [5] found that longer hospital stays were related with an increased risk of CRBSI, hence our findings are in line with theirs.

CONCLUSION

Our study indicated a high incidence of CRBSIs in the ICU setting, with 57.2% of patients developing CRBSI. The study identified several risk factors associated with CRBSI, including TPN, the number of CVCs, CVC duration, blood transfusion, prolonged use of mechanical ventilation (MV) and a high APACHE II scoring. There was no statistically significant correlation between CRBSI and co-morbidities, the location of catheter insertion, or the use of sonar-guided procedures in the study. Moreover, the study showed that CRBSI was significantly associated with negative outcomes, such as an increased death rate, longer ICU stays, and hospital lengths of stay.

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