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Research paper

Central venous catheter associated blood stream infections (CVC-BSIs) in the non-intensive care settings: Epidemiology, microbiology and outcomes

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KEYWORDS
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Risk factor;
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Abstract *Background:* Most studies have examined central venous catheter associated blood stream infections (CVC-BSIs) in Intensive Care Units (ICUs) but information on CVC-BSIs in non-ICU settings is sparse. This study aimed to determine the burden, microbiologic patterns, and associations of CVC-BSIs in non-ICU settings in a tertiary regional centre, University Hospital Geelong (UHG), Victoria, Australia.
Methods: A retrospective study was conducted in the UHG from October 2016 to April 2018. Based on the National Healthcare Safety Network definition, 23 CVC-BSIs occurred in non-ICU settings. Data analysed using SPSS-v25 with a P value < 0.05 was deemed as significant.
Results: The incidence rate was 1.2 per 10,000 bed-days. The mean age of patients was 57.22 $\pm$ 18 years. 43.5% of patients had Charlson index score of $\geq$5 and 78% received appropriate empiric antibiotics. The 90-day mortality rate was zero. In total, 26 microorganisms were isolated. Gram-negative bacilli were more common than Gram-positive cocci. The mean catheter duration was 45.22 $\pm$ 8.99 days. Hickman lines contributed to 52.2% of BSIs. Within the first two weeks of line insertion, 53.84% of CVC-BSIs occurred with 76.92% of CVC-Gram-negative bacteraemia and 71.4% of BSIs were related to Hickman lines. Also, 69.2% of CVC-BSIs occurred within $\leq$4 weeks of line insertion including 84.6% of CVC-Gram-negative bacteraemia.
Conclusion: CVC-BSIs constitute a significant burden on high risk patients in non-ICU settings, with Gram negative bacilli predominating. A prospective surveillance program for all patients with CVC in the non-ICU setting may improve CVC management processes and influence educational measures.
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Highlights

- CVC-BSIs constitute a burden to high risk patients in non-ICU settings in UHG.
- Outcome; no mortality.
- Tunnelled line-BSIs are dominant CVC-BSIs.
- Gram negative bacilli are predominating isolates.
- First 2 weeks after line insertion a high risk of developing BSI.

Introduction

A variety of intravascular catheters such as short-term CVCs, long-term CVCs, and peripherally inserted central catheters (PICCs) are increasingly used in both the ICU and the non-ICU clinical settings [1]. Patients with CVCs are at risk of bloodstream infections contributing to increased hospital costs, hospital stay and mortality [2—5]. Central line—associated bloodstream infections (CLABSIs) in adult ICUs and neonatal/paediatric ICUs have significantly reduced after the implementation of care bundle [6—10]. Further, PICCs have been used in paediatric intensive care settings as well as among hospitalized adult patients for long-term access and are associated with less blood stream infections [11,12]. Several studies demonstrated that peripheral line-associated bloodstream infections and central line—associated bloodstream infections are also important in non-ICU settings [2,13,14]. Several recent studies indicate that microbiological patterns of CLABSIs have changed after implementation of care bundle [13,15,16].

Following the implementation of a care bundle in the ICU of UHG, the rate of CLABSIs in the ICU at our centre has significantly reduced [6] but information on CVC-BSIs in Non-ICU settings is sparse. We aimed to determine the burden, microbiologic patterns, and associations of CVC-BSIs in non-ICU settings in the UHG, Victoria, Australia.

Methods

Study design and settings

A single centre retrospective cross-sectional study was conducted in UHG, Victoria, Australia. All patients diagnosed with CVC-BSI in non-ICU settings of UHG from October 2016 to April 2018 were included in this study considering inclusion and exclusion criteria. The detailed clinical and laboratory data were collected from patients' medical records and hospital computerized databases and laboratory data. Assessment of patients' survival was based on discharge summary and follow-up visits in outpatient services of UHG. The follow-up period was up to 90 days after the event of CVC-BSIs.

Participants

Inclusion Criteria: All patients in non-ICU settings in UHG who received CVC in UHG and developed CVC-BSIs based on NHSN definition [17] within the 18-month research period were included in this study.

Exclusion Criteria: Patients with positive blood cultures related to an infection at another body site were excluded.

Definitions

- Blood stream infection (BSI) refers to the recovery of a microbial pathogen in blood culture by feature of infection, not specimen contamination
- A positive blood culture was labelled a BSI if it met the NHSN [17] laboratory-confirmed bloodstream infection (LCBI) definitions (criteria 1, 2 or 3)
- A central venous catheter (CVC) such as short-term CVCs and PICCs is a catheter whose tip resides in a central vein
- A short-term central venous catheter (ST-CVC) is intended for temporary use and it is neither tunnelled subcutaneously nor fully implanted
- A peripherally inserted central catheter (PICC) is also considered a central venous catheter
- Central venous catheter associated blood stream infection (CVC—BSI) refers to a bloodstream infection that appears in the presence of a central venous catheter or within 48 h of removal of a central venous catheter and which cannot be attributed to an infection unrelated to the catheter.
- Charlson Comorbidity Index (CCI): CCI predicts 10-year survival in patients with multiple comorbidities. It was calculated by using MDCalc.
- Pitt Bacteraemia Score (PBS): PBS predicts mortality among patients with bloodstream infection and was calculated based on temperature (35.1—36 °C or 39.0—39.9 °C: 1 point, $\leq$35 or $\geq$40 °C: 2 points), blood pressure (hypotension: 2 points), mental status (disorientation: 1 point, stupor: 2 points, coma: 4 points), respiratory status (mechanical ventilation: 2 points) and cardiac status (cardiac arrest: 4 points).
- Appropriate empiric antimicrobial therapy means the receipt of an antimicrobial agent after the index blood culture was drawn and was considered appropriate if it included antimicrobials to which the specific isolate (s) displayed susceptibility in vitro.

Statistical analysis

Data were analysed by IBM SPSS Statistics V25 (SPSS-v25) with using descriptive analysis and chi-square test for

associations. A P value < 0.05 was considered as significant. Incidence rate of CVC-BSIs was calculated per bed-days as below:

$$\frac{\textit{Number of CVC_BSIs Patients during the period covered by the research in non_ICU beds}}{\textit{Number of Non ICU beds} \times \textit{period covered by the research (days)}}$$

Results

23 patients were diagnosed with CVC-BSIs outside the ICU, 15 male patients (65.2%) and eight female patients (34.8%). The incidence rate of CVC-BSIs in non-ICU settings was 1.2 per 10,000 bed-days while during the same period, two CVC-BSIs occurred in the ICU of UHG with an incidence rate of 1.5 per 10,000 bed-days. The mean age of patients ± Standard Deviation was 57.22 ± 18 years (3–81 years). All CVCs were removed after the diagnosis of CVC-BSIs as part of their management. All patients survived beyond 90 days following a CVC-BSI event. 43.5% (10/23) of CVC-BSIs occurred in patients with Charlson Comorbidity Index (CCI) of 5 and higher. There was a significant association between CCI and Pitt bacteraemia score ($P < 0.05$) whereas there was no significant association between CCI and isolated microorganisms. There was a significant association between CCI and abnormal serum creatinine level in patients ($P < 0.05$). However, there was not a significant association between CCI of patients and previous surgery, between CCI of patients and receiving antibiotics during 30 days preceding the CVC-BSI or between CCI of patients and immune suppressive therapy (Table 1).

Hickman lines were used for 12 patients (52.2%), followed by short term CVCs and PICCs in seven (30.4%) and Permacath in four (17.4%) patients. There was no significant association between the type of CVC and CCI or the type of CVC and Pitt bacteraemia score or between the type of CVC and isolated microorganisms. There was a significant association between the type of CVC and abnormal serum creatinine level ($P < 0.0001$).

The mean duration of inserted catheters ± Standard Deviation was 45.22 ± 8.99 days with shortest period of 4 days and a longest period of 365 days. There was a significant association between the duration of the CVC and immune suppressive therapy ($P < 0.05$). Within the first two weeks of line insertion, 14 (53.8%) CVC-BSIs occurred with 10 (76.9%) of CVC-Gram-negative bacteraemia. Moreover, eighteen (69.2%) CVC-BSIs occurred within ≤4 weeks of line insertion including 11 (84.6%) of CVC-Gram-negative bacteraemia (Table 2).

Within the first 2 weeks of catheter insertion, 71.4% (10/14) of BSIs were related to Hickman lines while 28.57% (4/14) of BSIs had short term CVCs or PICCs (Fig. 1). *Enterococcus faecalis* was isolated in two patients after 24 weeks of line insertion. There was a significant association between the type of CVC and its duration ($P < 0.05$).

A total of 26 microorganisms were isolated from 23 patients with CVC-BSIs including gram-negative bacilli (13/26), gram-positive cocci (11/26), gram-positive bacilli (1/26) and *C.albicans* (1/26). There was no significant association between CCI and isolated organisms (Table 3).

Discussion

Over the 18-month study period, 23 patients were categorised as CVC-BSIs in non-ICU settings with an incidence rate of 1.2 per 10,000 bed days versus two CVC-BSIs in the ICU of UHG with an incidence rate of 1.5 per 10,000 bed-day. In spite of a reduction in the rate of CLABSIs after the implementation of a care bundle in the ICU of UHG [6] with all initiatives directed towards the rate of zero [18–20], CVC-BSIs in non-ICU settings in UHG remain a concern. Furthermore, a one-day prevalence survey of CVCs among inpatient adults demonstrated that 70% of all CVCs were used for patients in non- ICU settings [21] however ICU patients have a higher risk factors to develop CVC-BSIs in some studies [22,23] which support our findings of higher incidence rate in the ICU setting.

In this study, all CVCs were removed after the diagnosis of CVC-BSIs and no death occurred within 90 days' follow-up. The 30-day mortality in Saliba et al. study [24] was 14% which defined death from any cause within 30 days of vascular catheter related blood stream infections among 546 non-ICU patients during 10-year Cohort study. Also, Tedja et al. [25] reported a hospital mortality rate of 23% among patients with central line associated blood stream infections in non-ICU settings. Moreover, Lin et al. [15] identified a delay in catheter removal was as a significant factor associated with mortality in patients with central line-associated bloodstream infections in ICU patients. The limitations of our study such as small sample size and follow-up measures might explain the low mortality rate.

The CVC-BSIs in current research were mainly attributed to tunnelled catheters. Tunnelled catheter -related blood stream infections were reported by other studies [26,27] in patients with tunnelled catheters. Also, Gram-negative organisms were highlighted as the predominate cause of Hickman line-related infection in Chee et al. study [27] that supports our findings.

Within the first 2 weeks of line insertion, 54% of CVC-BSIs occurred with 77% of CVC-Gram-negative bacteraemia and 71.4% of BSIs were related to Hickman lines. Gram-negative bacteraemia was more frequent than Gram-positive bacteraemia in the current study (50% vs 46.13%). A high rate of gram positive bacteraemia attributed to CVCs were reported in certain studies [7,10,28,29] ranging from 40% to 60.5% whereas gram negative bacteraemia in some studies ranged from 32% to 77.8% [14,16,30,31]. It seems the number of CVC- Gram-negative bacteraemia is increasing.

The present study shows 33.3% of CVC-BSIs were attributed to non-tunnelled catheters (ST-CVCs and PICCs). Peripherally inserted central venous catheters (PICCs) are

Table 1 Baseline characteristic associated with CVC-BSIs, non-ICU settings, the UHG, Victoria, Australia, October 2016—April 2018.

Variables	Number	Percentage (%)
Co-morbidities	22/23	95.7
• Haematologic cancer	11/23	47.8
• Solid tumour	1/23	4.3
• Diabetes Mellitus	4/23	17.4
• Chronic kidney Diseases	7/23	30.4
• Chronic Heart Failure	6/23	26
• Chronic Lung Disease	2/23	8.7
• others	2/23	8.7
Hospitalization in the previous 12 months	20/23	87
On immune-suppressive therapy	15/23	65.2
Surgery in the previous 30 days	3/23	13
Antibiotics during 30 days preceding onset	12/23	52.2
Bacterial infection in the previous 3 months	8/23	34.8
Previous MDRO bacteraemia	1/23	4.3
Mean Serum Albumin level ± Standard Deviation, mg	30.17 ± 4.9 Min 19, Max 40	
Low serum Albumin level	17/23	73.9
Mean Serum Creatinine level ± Standard Deviation, mg	231.43 ± 257 Min 24, Max 921	
High serum Creatinine	8/23	34.8
Peripheral WBC count categories ($10^3/\mu L$)		
• 0—5	11/23 (M: 10, F:1)	47.8
• 5-15	9/23 (M: 3, F:6)	39.1
• 15—20	2/23 (M: 2, F: 0)	8.7
• >20	1/23 (M: 0, F:1)	4.3
Survived	23/23	100
Mean Charlson index score ± Standard Deviation	4.5 ± 1.99 Min 1, Max 8	
Pitt bacteraemia score		
• 0—1	14/23	60.9
• 2	5/23	21.7
• 3	2/23	8.7
• 4 and more	2/23	8.7
Empiric antimicrobial treatment		
• Appropriate	18/23	78.3
• Inappropriate	5/23	21.7

Table 2 The distribution of CVC-BSIs based on the catheter duration and isolated organisms, non-ICU settings, the UHG, Victoria, Australia, October 2016—April 2018.

The duration of inserted line (week)	NO of Patients	Percentage of Patients (%)	Gram positive isolates	Gram negative isolates	Candida albicans
<2	12/23	52.2	4/12	10/13	0/1
2—4	4/23	17.4	2/12	1/13	1/1
4—6	1/23	4.3	1/12	0/13	0/1
6—8	3/23	13	2/12	2/13	0/1
8—12	0/23	0	0/12	0/13	0/1
12—24	1/23	4.3	1/12	0/13	0/1
>24	2/23	8.7	2/12	0/13	0/1
Total	23	100	12	13	1

now commonly used for patients in the Hospital in the Home (HITH) services. In a non-randomized study on long-stay surgical ICU patients, the incidence of PICC-BSIs (0.22%) was less than that of antiseptic coated CVCs (0.6%) [32]. A prospective study of high-risk hospitalized patients indicated that the rate of PICC-BSIs and

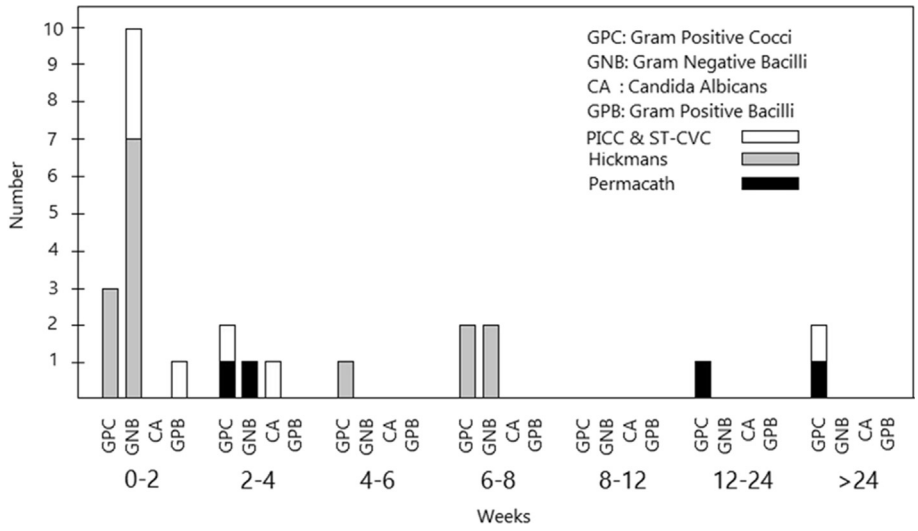

Figure 1 The distribution of common isolates based on the CVC type and the line duration in patients with CVC-BSIs, non-ICU settings, the UHG, Victoria, Australia, October 2016—April 2018.

Table 3 Common organism isolated in patients with CVC-BSIs, non-ICU settings, the UHG, Victoria, Australia, October 2016—April 2018.

Organism	Number	Percentage (%)
Gram-positive cocci(GPC)		
Staphylococcus aureus	5/26	19.23
Staphylococcus hominis	2/26	7.69
Staphylococcus epidermidis	1/26	3.84
Streptococcus mitis	1/26	3.84
Enterococcus faecalis	2/26	7.69
Gram-negative bacilli(GNB)		
Escherichia coli	3/26	11.54
Pseudomonas aeruginosa	3/26	11.54
Enterobacter aerogenes	1/26	3.84
Enterobacter cloacae	1/26	3.84
Klebsiella pneumoniae	1/26	3.84
Klebsiella oxytoca	1/26	3.84
Stenotrophomonas maltophilia	1/26	3.84
Chryseobacterium indologenes	1/26	3.84
Moraxella lacunata	1/26	3.84
Candida albicans	1/26	3.84
Gram-positive Bacilli (GPB)		
Bacillus cereus	1/26	3.84
Total	26	100

conventional CVC-BSIs were similar (2—5 per 1000 catheters-days) but this rate declined among outpatients (0.4 per 1000 catheters-days) [12]. A systematic review showed a lower risk of PICC-BSIs in outpatients but this risk among hospitalized patients was similar to that of other CVCs [33]. PICCs used in children has led to less blood-stream infection compared with central venous catheters and are now considered an alternative to a CVC in the paediatric ICU [11]. The risk of BSIs increases during the two weeks after PICC insertion and then remain high until PICC removal [34]. More research is required to evaluate whether PICCs are associated with less infection than other CVCs and also to determine potential risk factors of PICC-BSIs.

Limitations of the study

We recognize the study limitations including retrospective study design and small sample size. We could not have recorded the incidence rate of CVC-BSIs per line days due to lack of required data.

Conclusion and suggestions

This study demonstrates that CVC-BSIs constitute a significant burden on high risk patients in non-ICU settings with Gram negative bacilli predominating. A prospective CVC-BSI surveillance program in the non-ICU settings would identify increasing rate of non-ICU CVC-BSIs. This may facilitate targeted interventions of preventive measures to reduce the risk CVC-BSIs in the non-ICU settings.

Ethics

This project was approved by the Human Research Ethics Committee of Barwon Health (Reference No: 18/91 and HREA 176596).

Authorship statement

All authors read and approved the submitted manuscript and accept responsibility for the paper. ZA; study design, data collection and statistical analysis and manuscript drafting. PS; data collection and manuscript reviewing. EA; planning the study and manuscript reviewing.

Conflict of interest

The authors declare no conflict of interest.

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Provenance and peer review

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