Central line-associated bloodstream infections at the multidisciplinary intensive care unit of Universitas Academic Hospital, Bloemfontein, South Africa

E Glover,[1] MB ChB, FCP (SA), MMed (Int), Dip (HIV); **A Abrahamson,**[2] **J Adams,**[2] **S R Poken,**[2] **S-L Hainsworth,**[2] **A Lamprecht,**[2] **T Delport,**[2] **T Keulder,**[2] **T Olivier,**[2] **S D Maasdorp,**[3] MB ChB, FCP(SA), MMed (Int), Cert Pulm (SA) Phys

[1] *Division of Infectious Diseases, Department of Internal Medicine, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa*

[2] *Medical students, Department of Internal Medicine, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa*

[3] *Division of Pulmonology and Critical Care, Department of Internal Medicine, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa*

Corresponding author: S Maasdorp (maasdorpsd1@ufs.ac.za)

Background. Central line-associated bloodstream infections (CLABSIs) are frequently encountered device-related healthcare-associated infections in critically ill patients, causing substantial morbidity, mortality and prolonged hospitalisation.

Objectives. To determine the incidence of CLABSI, median catheter dwell-time prior to developing CLABSI, as well as the causative microorganisms of CLABSI among patients admitted to the multidisciplinary intensive care unit (MICU) at Universitas Academic Hospital, Bloemfontein.

Methods. We conducted a retrospective review of medical and laboratory records of all MICU patients who had a central line placed between January and December 2018.

Results. A total of 377 patients were admitted to the MICU in 2018, of which 182 met the inclusion criteria for the present study. From the cohort of 182 patients, 16.5% (*n*=30) of patients presented with 32 CLABSI episodes, with two patients having had two independent episodes each. A total of 1 215 central line days were recorded, yielding a CLABSI rate of 26.3/1 000-line days. Laboratory analysis identified microorganisms in 38 blood cultures, with Gram-negative organisms (55.3%; *n*=21) being predominant over Gram-positive organisms (39.5%; *n*=15) and fungi (5.3%; *n*=2).

Conclusion. The incidence of CLABSI at the MICU at Universitas Academic Hospital is high. Urgent intervention with strict compliance to prevention bundles is required to reduce the high incidence of CLABSI.

Keywords. central line-associated bloodstream infections; intensive care; line days.

A central line is defined as 'an intravascular catheter that terminates at or close to the heart, or in one of the great vessels that is used for infusion, withdrawal of blood, or haemodynamic monitoring.'[1] Central lines are frequently inserted and have become an established part of routine patient management in the intensive care unit (ICU).[2] Common sites for central line insertion include the subclavian, internal jugular and femoral veins.[2] Bloodstream infections (BSIs) may arise following central line placement, either due to breaches in sterility at the time of insertion or during catheter maintenance.[3]

The Centers for Disease Control and Prevention's (CDC) surveillance definition for central line-associated bloodstream infection (CLABSI) is a laboratory-confirmed BSI that is unrelated to an infection at another site in a patient with a central line *in situ* for at least two consecutive days.[1] According to the International Nosocomial Infection Control Consortium report conducted in 45 countries between 2012 and 2017, the rate of CLABSI was found to be 5.05/1 000 central line days.[4] CLABSI is associated with prolonged hospital stays, increased cost of medical care and increased mortality.[5,6]

The National Healthcare Safety Network of the CDC is currently the most authoritative organisation receiving, collating and reporting on data obtained concerning CLABSI in the USA.[7] The 2011 - 2014 report on antimicrobial-resistant pathogens describes the recent epidemiology of pathogens causing BSIs and associated antimicrobial resistance. Causative pathogens associated with CLABSI include Gram-positive bacteria (*Coagulase-negative Staphylococci* (16.4%), *Staphylococcus aureus* (13.2%), *Enterococcus faecalis* (8.4%)), Gram-negative bacteria (*Klebsiella pneumoniae* (8.4%), *Escherichia coli* (5.4%), *Enterobacter* (4.4%), *Pseudomonas aeruginosa* (4%)), fungi (*Candida albicans* (6.0%)) and other pathogens (14.6%).[7] Geldenhuys *et al.*[8] found a predominance of Gram-negative organisms as the cause of CLABSI within a South African (SA) neonatal ICU. It is worth noting that the profile of BSI and CLABSI pathogens in developed countries is very different to that in developing countries, where Gram-negative pathogens predominate.

Limited publications on CLABSI in adult patients from Free State Province, SA, are available. The aim of the present study was to determine the incidence of CLABSI, the median catheter dwell-time prior to developing CLABSI, as well as the causative microorganisms of CLABSI among patients admitted to the multidisciplinary ICU (MICU) of a tertiary hospital in Free State Province, SA.

Methods

This was a retrospective descriptive study of adult patients (≥18 years) who were admitted to the MICU at Universitas Academic Hospital between 1 January 2018 and 31 December 2018. Patients were included in the study if they had a central line *in situ* ≥48 hours, irrespective of whether the line was placed within or outside the ICU. Patients admitted to the MICU for <48 hours or who had a central line *in situ* for <48 hours were excluded from the study.

Universitas Academic Hospital is a 616-bed public sector tertiary hospital in Bloemfontein. The MICU functions as a closed ICU and has a total of eight beds, although only up to five patients can be cared for at any given time due to nursing staff shortages. Nurses working in the ICU are generally full-time employees, although not all are necessarily ICU qualified. Agency staff are required to assist infrequently. The nurse-to-patient ratio is typically 1:2. Approximately 350 patients/annum from both medical and surgical disciplines are managed in this unit. There are no full-time medical officers or fellows working in the ICU, and registrars rotating from various clinical disciplines and variable levels of experience are usually tasked to insert central lines. Ultrasound was unavailable at the time that the present study was conducted and therefore not used for line insertion. The standard central venous line that was placed was an Arrow three-lumen central venous catheter with blue flextip.

Indications for placing central lines included medication infusion, fluid, and electrolyte replacement therapy, as well as total parenteral nutrition. Parental nutrition was administered through a dedicated lumen of the central venous catheter. All patients admitted to the ICU also routinely had arterial lines inserted. The standard procedure for central or arterial line insertion is by using a sterile technique, donning a sterile gown and gloves, sterilising the skin with 0.5% chlorhexidine gluconate in 70% alcohol solution, and extensive draping of the patient with sterile linen with only the site of line insertion exposed before puncturing the skin. A sterile transparent Tegaderm dressing is placed over the insertion site and line after completing the procedure.

There is no formal protocol for insertion, maintenance, handling of extensions or hubs and removal of central venous catheters. However, the daily care of central lines includes inspecting the insertion site, replacing dressings if wet or soiled, performing hand hygiene before attending the infusion sets and replacing infusion sets every 72 hours. Central venous lines are replaced if there is a suspicion of line sepsis and not according to a predetermined schedule. The tips of central lines are routinely sent for semi-quantitative culture if CLABSI is suspected. Paired quantitative blood samples are not routinely requested. The lines are also routinely removed if no longer required or replaced with peripheral lines when the patients are transferred out of the ICU. As this was a retrospective study and the exact procedure of line insertion was not documented in the patient records, it is not possible to determine if strict sterile techniques were adhered to at all times.

Hospital files with clinical notes from the ICU clinicians and nursing personnel, Universitas Academic Hospital's electronic medical record system (MEDITECH), as well as the National Health Laboratory System's LABTRACK results portal were all used to collect information on clinical and microbiological data required for the present study.

The CDC surveillance definition, stating that CLABSI is a laboratory-confirmed BSI unrelated to an infection at another site in a patient with a central line *in situ* for at least two consecutive days, was used to define CLABSI.[1] This is opposed to a catheter-related bloodstream infection (CRBSI), defined as a BSI occurring 48 hours before or after catheter removal and a positive blood culture of ≥10³ colony forming units (CFU)/mL or >15 CFU on a semi-quantitative culture of the same microorganism of blood drawn from the catheter, or differential time to positivity of blood culture from the catheter two hours or more before a peripheral blood culture.[9] CRBSI was not evaluated in the current study. Patients were deemed to have CLABSI if the CDC definition for CLABSI was fulfilled and treating clinicians indicated a diagnosis or treatment for CLABSI in the clinical notes, or if no other site of infection could be inferred from the clinical records.

A data sheet was designed to collect data on patient characteristics, admitting discipline, catheter dwell-time before CLABSI diagnosis, the venue where the central line was inserted, respiratory support, concomitant infectious conditions and outcomes, microorganisms cultured, as well as the antimicrobial susceptibility profile. Data on adherence to strict aseptic technique during line insertion, as well as line insertion site, were not well documented and therefore not collected.

Data from the data sheets were transcoded onto a Microsoft Excel spreadsheet and analysed by the Department of Biostatistics, Faculty of Health Sciences, University of the Free State, using statistical analyses software, version 9.4 (SAS Institute, USA). Medians and percentiles were calculated for continuous data. Frequencies and percentages were calculated for categorical data.

Ethical approval to conduct the study was obtained from the University of the Free State Health Sciences Research Ethics Committee (ref. no. UFS-HSD2019/0357/2506), as well as from the Free State Department of Health. The requirement for individual informed consent was waived because this was a retrospective study.

Results

A total of 377 patients were admitted to the MICU in 2018, of whom 182 patients met the inclusion criteria and were enrolled in the present study. A total of 32 CLABSI episodes were identified in 16.5% of patients (*n*=30/182), with two patients having had two independent episodes of CLABSI. A total of 227 central lines were inserted in the 182 patients during the 12 months' study period, and a total of 1 215 central line days were recorded. The 32 CLABSI episodes yielded a CLABSI rate of 26.3/1 000 line days. The median (interquartile range (IQR)) catheter dwell-time for all 182 patients was 5 (3 - 8) days, with a range of 2 - 44 days. For the 30 patients with CLABSI, the median (IQR) catheter dwell-time was 9.5 (6 - 19) days, with a range of 3 - 44 days.

The characteristics of the patients who developed CLABSI are presented in Table 1. The median (IQR) age was 42.5 (24 - 62) years, with a range of 16 - 76 years. Almost half (46.7%; *n*=14) of the patients were medical patients, followed by neurosurgery (26.7%; *n*=8) patients. Central line placements were primarily performed in the MICU (43.3%; *n*=13), followed by in theatre (36.7%; *n*=11).

Most of the patients (68.8%; *n*=22) had a central line *in situ* for 3 - 8 days. Central lines were removed in 53.3% (*n*=16) of episodes of infection. The site of catheter insertion at the time of bacteraemia or fungaemia was not recorded. Data on whether catheter tips were sent for analysis or paired quantitative blood samples submitted were not

Table 1. General characteristics of the study population who developed CLABSIs

Characteristics	*n* (%)
Sex (*n*=30)	
Male	23 (76.7)
Female	7 (23.3)
Discipline (*n*=30)	
Medical	14 (46.7)
Surgery	5 (16.7)
Neurosurgery	8 (26.7)
Gynaecology	2 (6.7)
Other	1 (3.3)
Number of line days (*n*=32)	
<3 days	5 (15.6)
3 - 8 days	22 (68.8)
>8 days	5 (15.6)
Insertion venue (*n*=30)	
MICU	13 (43.3)
Theatre	11 (36.7)
Ward	6 (20.0)
Other sites of infection (*n*=30)	
Pneumonia	11 (36.7)
Urinary tract infection	3 (10.0)
Meningitis	1 (3.3)
Abdominal disease	1 (3.3)
Unknown	14 (46.7)
Respiratory support (*n*=30)	29 (96.7)
Outcome (death) (*n*=30)	14 (46.7)

CLABSI = central line-associated bloodstream infection;
MICU = multidisciplinary intensive care unit.

Table 2. Microorganisms cultured (*n*=38) from 30 patients with CLABSI

Organisms	*n* (%)
Gram-positive organisms	15 (39.5)
Staphylococcus aureus	7 (18.4)
Enterococcus faecalis	7 (18.4)
Enterococcus faecium	1 (2.6)
Gram-negative organisms	21 (55.3)
Klebsiella pneumoniae	6 (15.8)
Acinetobacter baumannii	12 (31.6)
Escherichia coli	1 (2.6)
Providencia stuartii	1 (2.6)
Pseudomonas aeruginosa	1 (2.6)
Fungi	
Candida albicans	2 (5.3)

CLABSI = central line-associated bloodstream infection.

Discussion

We found the incidence of CLABSI to be 26.3/1 000-line days at the MICU, the only incidence statistic currently available for the MICU at Universitas Academic Hospital. Therefore, this CLABSI incidence rate cannot be compared with historical data. The CLABSI rate in our present study is much higher than the 5.05/1 000 line days reported by Rosenthal *et al*.[4] We postulate that poor compliance with the CLABSI protocol and bundle-care programme, which is intended to limit and prevent the occurrence of CLABSI, most likely played a role, although this was not specifically assessed. Valencia *et al*.[10] found that poor adherence to CLABSI guidelines in developing countries has a significant effect on the CLABSI rate. Other sites of infection included pneumonia (36.7%), urinary tract infection (10.0%) and meningitis (3.3%). Bacteraemia may have resulted from any of these sites and could have potentially influenced the results if treating clinicians incorrectly classified an infection as CLABSI when it may instead have originated at a different site other than the central line.

The risk of CLABSI is directly related to catheter dwell-time.[11] Among 4 011 patients at the University of Maryland Medical Centre with a CLABSI rate of 2.33/1 000 line days, the median catheter dwell-time after which patients developed CLABSI was found to be 5.5 days.[12] Mer *et al*.[13] conducted one of the largest studies related to CLABSI at a Johannesburg hospital in SA and found that central lines can safely be left *in situ* for up to 14 days when the necessary infection control measures are adhered to. The median catheter dwell-time of 9.5 days in patients with CLABSI v. 5 days in the whole study population in our present study may point to a delay in removing central lines that are no longer required or even undue delay in recognising the central line as a source of infection and replacing it timeously.

Despite central lines having become indispensable for the care of patients in ICUs, complications from central lines such as CLABSI can significantly prolong the length of stay in the ICU, increase healthcare-associated cost,[14] and is also associated with an increased risk of death.[15] Risk factors associated with CLABSI include the duration of central lines, the use of central lines to draw blood, peripherally inserted rather than tunnelled lines, and if femoral sites are used for line insertion.[16,17] In recognition of CLABSI as an important preventable hospital-acquired infection, the 'Best Care Always!'

collected. Almost all the patients (96.7%; *n*=29) required respiratory support in the form of invasive mechanical ventilation. The mortality rate for all 377 patients admitted to the ICU in 2018 was 22.5% (*n*=85), as opposed to 46.7% (*n*=14) of the patients with CLABSI.

Microorganisms were cultured in 38 of the submitted blood culture specimens and are shown in Table 2. Of the 32 CLABSI episodes, 15.6% (*n*=5) were polymicrobial, and in 84.3% (*n*=27) of episodes, only one organism was identified.

The most common organisms isolated from peripheral and central line blood cultures were *Acinetobacter baumannii* (31.6%; *n*=12), *Enterococcus faecalis* (18.4%; *n*=7), *Staphylococcus aureus* (18.4%; *n*=7) and *Klebsiella pneumoniae* (15.8%; *n*=6).

Antimicrobial susceptibility and sensitivity testing was done for all Gram-positive and Gram-negative bacteria and is shown in Table 3. Gram-negative bacteria exhibited high rates of antimicrobial resistance. Among *Klebsiella pneumoniae* organisms, extended-spectrum β-lactamases (33.3%; *n*=2) and carbapenem resistance (33.3%; *n*=2) were common. *Acinetobacter baumannii* organisms were uniformly multidrug-resistant. The *Providencia stuartii* isolate, although only one, was an AmpC β-lactamase producer. This organism was resistant to most of the β-lactam antibiotics but retained susceptibility to cefepime. The Gram-positive organism, *Enterococcus faecium*, had a single positive culture characterised as vancomycin resistant.

Table 3. Susceptibility profile of microorganisms

Antimicrobial agent	Rate of susceptibility n (%)							
	S. aureus 7 (18.4)	E. faecalis 7 (18.4)	E. faecium 1 (2.6)	A. baumanii 12 (31.6)	P. aeruginosa 1 (2.6)	K. pneumoniae* 6 (15.8)	E. coli 1 (2.6)	P. stuartii† 1 (2.6)
Amikacin	-	-	-	1 (8.3)	1 (100.0)	6 (100.0)	1 (100.0)	
Gentamycin	-	-	-	-	-	-	-	-
Ampicillin	4 (57.1)	7 (100.0)	0	-	0	-	0	0
Amoxicillin-clavulanic acid	-	-	-	-	-	2 (33.3)	0	0
Cefepime	-	-	-	-	1 (100.0)	2 (33.3)	1 (100.0)	1 (100.0)
Cefuroxime	-	-	-	-	-	2 (33.3)	1 (100.0)	0
Cefotaxime Ceftriaxone	-	-	-	-	0	2 (33.3)	1 (100.0)	0
Cefoxitin	-	-	-	-	0	2 (33.3)	1 (100.0)	-
Ceftazidime		-	-	-	1 (100.0)	2 (33.3)	1 (100.0)	0
Ciprofloxacin	-	5 (71.4)	0	0	1 (100.0)	3 (50.0)		1 (100.0)
Clindamycin	4 (57.1)							
Cloxacillin	4 (57.1)	-	-	-	-	-	--	
Ertapenem	-	-	-	0	-	4 (66.7)	1 (100.0)	1 (100.0)
Erythromycin	4 (57.1)	0	0	-	-	-	-	-
Imipenem	-	-	-	0 (0)	1 (100.0)	4 (66.7)	1 (100.0)	1 (100.0)
Linezolid	7 (100.0)	7 (100.0)	1 (100.0)	-	-	-	-	-
Meropenem	-	-	-	0	1 (100.0)	4 (66.7)	1 (100.0)	1 (100.0)
Piperacillin-tazobactam	-	-	-	0	1 (100.0)	2 (33.3)	1 (100.0)	-
Trimethoprim-sulfamethoxazole	6 (85.7)	-	-	-	-	-	0	1 (100.0)
Vancomycin	7 (100.0)	7 (100.0)	0	-	-	-	-	
Tigecycline	-	-	-	10 (83.3)	-	5 (83.3)	-	0
Rifampin	5 (71.4)	-	-	-	-	-	-	-

S. aureus = Staphylococcus aureus; E. faecalis = Enterococcus faecalis; E. faecium = Enterococcus faecium; A. baumanii = Acinetobacter baumanii; P. aeruginosa = Pseudomonas aeruginosa; K. pneumoniae = Klebsiella pneumoniae; P. stuartii = Providencia stuartii.

*n=2 Klebsiella pneumoniae organisms were extended spectrum β-lactamase strains and n=2 were carbapenem-resistant OXA-48 strains.

†Providencia was an Amp-C strain.

(BCA) campaign was launched to focus the efforts of healthcare workers on preventative measures in the form of bundles of care.[18] In one of the longest-running intervention studies related to CLABSI in SA, Richards et al.[19] evaluated the impact of improved compliance to a CLABSI prevention bundle on the CLABSI rate in a private hospital group. The study was conducted in 49 hospitals comprising 1 207 ICU and 493 high-care beds. During the first phase, buy-in was ensured from hospital managers and infection prevention and control (IPC) nurses were trained on the CLABSI bundle checklists and measurement of central line days. In the second phase, training was expanded regionally for IPC nurses and unit managers. Phase 3 comprised continued audits, benchmarking, and quality improvement. At the end of the study, 1 119 558 central-line days were captured, compliance with CLABSI prevention bundles improved from 73.1 - 90.5%, and the CLABSI rate decreased from 3.55/1 000 to 0.13/1 000 central line days.[19]

We observed a higher percentage of Gram-negative (55.3%) than Gram-positive organisms (39.5%) (Table 2). This observation is consistent with previous studies.[8,20] Acinetobacter baumannii (31.6%) was the most frequent Gram-negative organism cultured. A. baumannii is frequently found as a coloniser in hospitalised patients but can also result in nosocomial infections. Evidence suggests an increased incidence of multidrug-resistant strains globally.[21] A. baumannii is common among individuals who are immunocompromised and those with a prolonged hospital stay >90 days.[22] All 12 isolates identified in this present study were designated multidrug-resistant after sensitivity testing.

A third (33.3%; n=2) of the K. pneumoniae isolates were extended-spectrum β-lactamase producers. These isolates are therefore resistant to commonly used antibiotics such as penicillin and cephalosporins.[23] Furthermore, 33.3% (n=2) of K. pneumoniae isolates were carbapenem-resistant. Both patients with carbapenem-resistant infections died. Candida albicans was cultured in two CLABSI episodes and was sensitive to fluconazole. According to the Infectious Diseases Society of America's guidelines, this is important because fluconazole prophylaxis is appropriate if the Candida score is used in high-risk patients.[24]

Study limitations

This was a retrospective study, and hospital records were inadequate to consistently identify information on the anatomical site and venue of central line insertion. Multiple anatomical insertion sites per patient made it difficult to determine where the primary source and concomitant infection resulted from. Comorbid conditions

complicated the CLABSI significance we observed in this present study. It has been previously demonstrated that comorbid conditions serve as important risk factors for the development of CLABSI.[25] Many patients presented to the MICU with underlying conditions and developed a CLABSI. However, drawing inference between the comorbid condition causing the CLABSI or the inverse was not possible in the current study.

Conclusion

Our study found a high CLABSI incidence of 26.3/1 000-line days at the MICU of Universitas Academic Hospital. Most of the pathogens cultured were multidrug-resistant organisms. Continued education to ensure compliance with the CLABSI bundle is required. Furthermore, well-designed prospective studies are recommended to determine the incidence of CLABSI, adherence to CLABSI bundles, association between the anatomical site of the central line, morbidity, mortality and length of ICU stay associated with CLABSI. This may inform future protocols with regards to preventing CLABSI in the ICU setting.

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