




ORIGINAL ARTICLE

Fast and furious: a retrospective study of catheter-associated bloodstream infections with internal jugular nontunneled hemodialysis catheters at a tropical center

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ABSTRACT

Background. Nontunneled hemodialysis catheters (NTHCs) remain the preferred vascular access at hemodialysis (HD) initiation in developing countries. We studied the incidence, risk factors and microbiological spectrum of jugular NTHC-associated bloodstream infections (CABSIs) at a tertiary care center in South Asia.

Methods. In this retrospective cohort study, all adult (≥ 18 years) incident patients who underwent jugular NTHC insertion for HD between January 2016 and June 2017, had no prior history of temporary vascular access insertion and were followed up for ≥ 14 days were included.

Results. A total of 897 patients underwent NTHC insertion during the study period and 169 patients fulfilled the inclusion criteria and contributed 7079 patient days of follow-up. CABSIs incidence was 7.34 episodes per 1000 catheter days and median infection-free survival and time to CABSIs were 96 and 24.5 days, respectively. In multivariate Cox regression analysis, immunosuppressive medication [hazard ratio [HR] 2.87 [95% confidence interval (CI) 1.09–7.55]; $P = 0.033$] and intravenous cefazolin use [HR 0.51 (95% CI 0.28–0.94); $P = 0.031$] was independently associated with CABSIs. The cumulative hazard of CABSIs was 8.3, 13.3, 17.6 and 20.9% at Weeks 1, 2, 3 and 4, respectively. Gram-negative organisms were the most common etiological agents (54.7%) and 40.3% of CABSIs were caused by drug-resistant organisms. Gram-negative and Gram-positive CABSIs were associated with neutrophil left shift and higher procalcitonin compared with coagulase-negative staphylococcal CABSIs.

Conclusions. In South Asia, NTHC-associated CABSIs occur early and are predominantly Gram negative. We hypothesize that poor hygiene practices may play a role in this phenomenon.

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INTRODUCTION

Between 81 and 100% of patients initiating hemodialysis (HD) in the developing world do so with a nontunneled hemodialysis catheter (NTHC) as their vascular access [1–3]. Low socioeconomic status, lack of education and reimbursement options result in delayed referral and emergency dialysis initiation [4]. Because NTHC insertion can be safely carried out under ultrasound guidance without the need for a fluoroscopic facility [5], it is the preferred vascular access for emergency dialysis in resource-poor settings. It is recommended that NTHCs be removed or exchanged over a guidewire within 21 days [6]; however, this is rarely possible due to socioeconomic and logistic constraints. The infection risk associated with this practice in South Asia, with its highly infectious milieu and poor hygiene practices is not known. We studied the incidence, microbiological spectrum and clinical characteristics of catheter-associated bloodstream infections (CABSIs) in incident HD patients with NTHCs at a tertiary referral hospital in southern India.

MATERIALS AND METHODS

In this retrospective cohort study, we included all adult (≥ 18 years) incident HD patients who underwent NTHC insertion (Mahurkar, Covidien AG, Mansfield, MA, USA) in the internal jugular vein between 1 January 2016 and 30 June 2017 and continued dialysis for ≥ 2 weeks at our center. We excluded patients with NTHCs inserted at other centers, femoral NTHCs, central venous catheters inserted for nondialysis indications, NTHCs inserted in intensive care units (ICUs) and patients dialyzed for ≤ 2 weeks at our center after NTHC insertion. The study was approved by the Institutional Review Board and Ethics Committee of our institute.

The aims and objectives of this study were to calculate the incidence rate of CABSIs, calculate the median infection-free survival of NTHCs, calculate the cumulative hazard of developing a CABSIs at various time points after NTHC insertion, determine risk factors for CABSIs, study the microbiological spectrum and antibiotic resistance pattern of organisms causing CABSIs and compare laboratory parameters and complication rates between Gram-positive, Gram-negative and common commensal organisms causing CABSIs.

Protocol for diagnosis and management of CABSIs

The protocols for catheter insertion, manipulation and HD at our center are given in the Supplementary material. In all patients with clinical features suggestive of CABSIs (see definition below), paired blood cultures (10 mL each from the peripheral blood and venous catheter hub) were obtained under sterile conditions, inoculated in culture media (BACT/ALERT SA, bioMérieux, Durham, NC, USA) and immediately transported to the microbiology laboratory. Peripheral blood cultures were obtained from the median cubital vein (if symptoms occurred apart from an HD session) or from the dialysis circuit (if symptoms occurred during HD). Plasma and serum samples for total and differential white cell count and serum procalcitonin were also sent simultaneously. The empirical antibiotic policy for the management of CABSIs at our center is vancomycin 1 g intravenous (IV) stat and piperacillin/tazobactam 4.5 g IV stat followed

by 2.25 g IV every 8 hours. The antibiotic regime was modified where indicated based on blood culture results. The NTHC was removed once a CABSIs was confirmed. We did not attempt catheter salvage.

Microbiological methods

After microbial growth was detected by an automated system (BACT/ALERT 3D, bioMérieux), Gram stain was performed and growth subcultured onto blood agar and MacConkey agar as indicated for species identification and typing. Antibiotic susceptibility testing was carried out using Kirby–Bauer's disc diffusion technique (HiMedia Laboratories, Mumbai, India).

Definitions

We followed the Centers for Disease Control and Prevention (CDC) guidelines [7] for diagnosis of central line-associated bloodstream infections. CABSIs was defined as bacteremia associated with intravascular catheter with all of the following elements:

1. in the case of common commensals like coagulase-negative staphylococcus (CoNS), both catheter and peripheral blood cultures growing the same organism; in the case of all other organisms, at least one positive blood culture (catheter hub or peripheral blood or both);
2. Clinical manifestations of infection (one or more of the following: fever $>38^{\circ}\text{C}$, chills or hypotension);
3. no other apparent source for the bloodstream infection and
4. catheter in use within 48 h of the CABSIs.

Organisms causing CABSIs were classified as Gram positive, Gram negative and common commensals, the latter defined as those belonging to the list of common commensals in the National Health Safety Network organisms list [7]. Drug resistance patterns for cultured organisms were defined as per the International Expert Proposal for Interim Standard Definitions for Acquired Resistance [8].

For patients who developed a CABSIs, the patient days at risk (catheter days) were defined as the number of days from catheter insertion to the date paired blood cultures were sent (the patient was deemed to have developed the CABSIs at that time point even though the NTHC was usually removed 48 h later). For patients who did not develop a CABSIs, it was defined as the number of days from NTHC insertion to NTHC removal or the date the patient left our center. The incidence of CABSIs was calculated for the first CABSIs episode only and subsequent NTHC insertions in the same patient were not considered for analysis. Broad-spectrum antibiotic use was defined as the use of third- and fourth-generation cephalosporins, carbapenems, β -lactamase inhibitors, fluoroquinolones, aminoglycosides, trimethoprim–sulfamethoxazole or anaerobic antimicrobials (metronidazole, clindamycin, tigecycline, etc.) for >24 h. IV cefazolin use was defined as 1 g (single dose) administered as a surgical antibiotic prophylaxis prior to arteriovenous fistula (AVF) surgery. Neutrophil left shift was defined as the presence of neutrophil band forms on peripheral smear. Serum procalcitonin was measured by the time-resolved amplified cryptate emission technique (BRAHMS Kryptor PCT-sensitive assay, Thermo Fisher Scientific, Waltham, MA, USA).

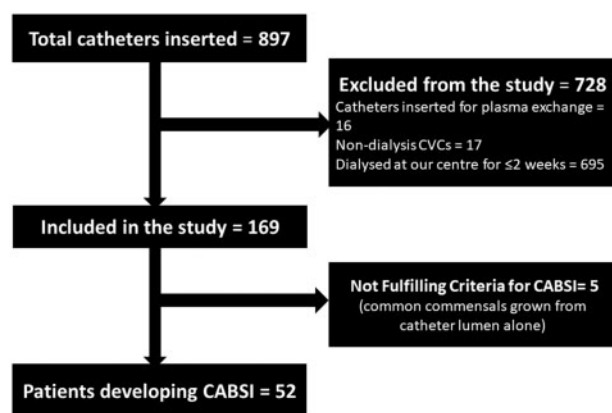


FIGURE 1: Study flow diagram.

Data sources

Demographic, clinical and laboratory parameters were retrieved from the hospital information system. Data regarding HD characteristics, including date of catheter insertion, HD frequency, date of catheter removal and last HD at our center, were retrieved from the HD facility records.

Statistics analysis

Independent t-test and Mann–Whitney *U* test were used to compare means between two groups and one-way analysis of variance or Kruskal–Wallis *H* test was used to compare means between more than two groups, as applicable. For categorical variables, the chi-squared test was used to compare proportions. Kaplan–Meier analysis and survival curves were used to estimate the median infection-free survival, log-rank test was used to compare the equity of survivors among categories and the Cox proportional hazards model was used to determine risk factors for CABSIs. All variables that reached 20% significance in univariate analysis were included in the multivariate analysis along with the variables ‘age’ and ‘gender’. The cumulative hazard of CABSIs was assessed using the Nelson–Aalen estimate. A 5% level of significance was considered significant. Statistical analysis was carried out using Stata version 13.1 (StataCorp, College Station, TX, USA).

RESULTS

Figure 1 shows the study flow diagram. A total of 897 patients underwent NTHC insertion during the study period and were potentially eligible, of which 728 patients did not meet inclusion criteria. Thus 169 patients were confirmed eligible and included in the study and contributed 7079 patient days of follow-up.

All patients had emergency HD initiation, the most common indication being CKD Stage G5 (94.6%), while the remainder had acute kidney injury, acute kidney injury superimposed on chronic kidney disease or rapidly progressive renal failure. The right internal jugular vein was the site of insertion for 167 of 169 catheters.

CABSIs incidence rate, infection-free survival and cumulative hazard of CABSIs

A total of 52 CABSIs occurred in the study population, an incidence rate of 7.34 episodes per 1000 patient days at risk. The median catheter days for the study population as a whole and

the non-CABSIs group were 36 and 43 days, respectively. The median time to CABSIs was 24.5 days in the CABSIs group.

Tables 1 and 2 compare the demographic and clinical characteristics of the CABSIs and non-CABSIs groups. Table 3 shows the results of the log rank, univariate and multivariate analysis of risk factors for CABSIs. In multivariate Cox regression analysis, immunosuppressive medication {hazard ratio [HR] 2.87 [95% confidence interval (CI) 1.09–7.55]; $P=0.033$ } and IV cefazolin use [HR 0.51 (95% CI 0.28–0.94); $P=0.031$] were independently associated with CABSIs.

The median infection-free survival for the study population using the Kaplan–Meier estimate was 13.7 weeks (Figure 2). The Nelson–Aalen estimate showed that the cumulative hazard for CABSIs was 8.3, 13.3, 17.6 and 20.9% at 1, 2, 3 and 4 weeks, respectively, after NTHC insertion (Table 4).

Microbiological spectrum and resistance pattern of organisms causing CABSIs

A total of 53 organisms were cultured from 52 patients. Organisms were cultured from peripheral blood alone in 3 patients, catheter hub alone in 13 patients and both peripheral blood and catheter hub in 36 patients. The most common organisms causing CABSIs were Gram-negative bacilli (Table 5). CoNS were the only common commensals identified. Oxacillin resistance was seen in 56.2% of CoNS and 14.3% of *Staphylococcus aureus* isolates (Table 6). Among Gram-negative bacilli, 37.9% were drug resistant (Table 7)—four isolates were extended spectrum β -lactamase producing strains, six isolates were multidrug resistant and one isolate was extensively drug resistant. Thus 40.3% of CABSIs were caused by drug-resistant organisms. Neither antibiotic exposure nor hospitalization were associated with drug-resistant CABSIs ($P=0.602$ and 0.235, respectively).

Clinical and laboratory features of CABSIs and association with the organism cultured

The most common symptoms at presentation were fever with chills (92.4%) and septic shock (5.7%) and the remaining presented with chills. Gram-positive and Gram-negative organisms were found to have a significantly higher prevalence of left shift on peripheral smear and higher procalcitonin levels compared with CoNS ($P<0.001$ for both; Table 8). Hospitalization, intensive care unit (ICU) admission, metastatic complications (septic arthritis, 1; septic pulmonary emboli, 1) and mortality rates were 11.5, 3.8, 3.8 and 3.8%, respectively, for the study population. The latter three complications occurred exclusively in Gram-negative CABSIs, although the number did not reach statistical significance. Patients who developed CABSIs due to CoNS, Gram-positive or Gram-negative organisms did not differ in their demographic or clinical characteristics, including broad-spectrum antibiotic ($P=0.86$) and cefazolin ($P=0.48$) exposure (analysis not shown).

DISCUSSION

In South Asia, emergency dialysis initiation with a jugular NTHC is the norm [1, 2]. Thereafter patients defer AVF construction for financial and logistic reasons, with <50% having a functional AVF even 4 months after HD initiation. As a result, the mean duration of NTHC use is as long as 77 days [1].

Our CABSIs incidence rate of 7.4 episodes per 1000 catheter days is higher than studies from North America, Europe and

Table 1. Baseline characteristics of the study population with comparison between the CABSIs and non-CABSIs groups

Variables	Overall (n = 169)	No CABSIs (n = 117)	CABSIs (n = 52)	P-value
Age (years), mean ± SD	47.2 ± 14.2	47.4 ± 13.0	46.6 ± 16.6	0.359
Male, %	64.5	63.2	67.3	0.611
Diabetes, %	40.8	42.7	36.5	0.449
BMI (kg/m ²), mean ± SD	23.2 ± 4.8	22.7 ± 4.2	24.2 ± 5.9	0.969
Serum albumin (g/dL), mean ± SD	3.5 ± 0.7	3.5 ± 0.7	3.4 ± 0.7	0.326
Serum ferritin (ng/mL), mean (95% CI) ^a	358.4 (195.6–660.6)	364.2 (183.5–711.0)	355.7 (202.5–621.5)	0.811
Charlson's comorbidity index, mean ± SD	3.6 ± 1.8	3.6 ± 1.7	3.8 ± 1.9	0.766
eGFR (mL/min/1.73 m ²) at HD initiation ^a	5.1 (3.4–6.7)	5.1 (3.5–6.5)	5.1 (3.4–7.2)	0.654
Current immunosuppression, %	7.1	5.9	9.6	0.396
Season of NTHC insertion, n (%)				0.438
Summer	77 (45.5)	57 (48.7)	20 (38.4)	
Monsoon	25 (14.8)	17 (14.5)	8 (15.4)	
Winter	67 (39.6)	43 (36.7)	24 (46.1)	

^aExpressed as median (25–75th percentile).

BMI, body mass index; eGFR, estimated GFR by Chronic Kidney Disease Epidemiology Collaboration creatinine formula.

Table 2. Clinical details of the study population during the follow-up period with comparison between the CABSIs and non-CABSIs groups

Variables	Overall (n = 169)	No CABSIs (n = 117)	CABSIs (n = 52)	P-value
HD frequency, thrice weekly, %	97.6	98.3	96.1	0.398
Broad-spectrum antibiotic use during the follow-up period, %	36.7	36.7	36.5	0.979
IV cefazolin use during the follow-up period, %	47.9	52.9	36.5	0.048 ^a
Hospitalization during the follow-up period, n (%)				
Elective procedure (AV fistula/biopsy)	81 (68.6)	62 (72.9)	19 (57.6)	0.106 ^b
Nonelective admission	37 (21.9)	23 (19.6)	14 (26.9)	
Emergency dialysis initiation		16 (18.8)	11 (33.3)	
Non-CABSIs infection		1 (1.2)	2 (6.1)	
Emergency surgery		5 (5.9)	1 (3.0)	
Cardiovascular event		1 (1.2)	0 (0)	

^ap < 0.05.

^bBetween elective and nonelective admission.

Africa that have reported jugular NTHC CABSIs incidence rates ranging from 1.67 to 5.6/1000 catheter days [9–13]. We used the CDC definition of CABSIs rather than the more stringent Infectious disease Society of America (IDSA) criteria for definite catheter-related bloodstream infection or CRBSIs [14]. The latter has been criticized for being labor intensive, expensive and impractical and has a low sensitivity and accuracy for the diagnosis of HD catheter-related infections [15, 16]. CRBSIs rates using these criteria are up to 18% lower than CABSIs rates using the CDC definition [9, 17]. This is illustrated by the fact that among the studies alluded to earlier, the highest incidence rate was reported by a study from The Netherlands [10] that used the same CABSIs definition we did.

Similar to Hoen et al. [18], we too found concomitant immunosuppression to be independently associated with an increased risk of CABSIs. Almost half the study population received a single dose of IV cefazolin as surgical antibiotic prophylaxis prior to AVF construction during the follow-up period. We found IV cefazolin to be protective against CABSIs, probably because of its action against Gram-positive organisms, which are the most common cause of CABSIs worldwide [6, 9, 10].

The majority of CABSIs in our study were Gram-negative. This phenomenon has also been reported from other centers in

South Asia [19, 20], while the rest of the world [6, 9, 10, 12, 13, 17, 21–23] encounters predominantly Gram-positive CABSIs. Patients who developed a CABSIs did so at a median of 24.5 days after NTHC insertion, while the median duration of catheter use for the non-CABSIs group was 43 days. Also, the cumulative hazard of CABSIs was found to increase early and was far higher than that reported from the developed world [6, 17]. Since bacteremia occurs between 5 and 26 days after colonization [24], this indicates that in susceptible patients, colonization of the catheter lumen occurred early. Gram-negative organisms are predominantly fecal in origin, and we therefore hypothesize that the high incidence of CABSIs, and Gram-negative CABSIs in particular, may be related to poor hygiene practices.

The CDC has highlighted specific interventions that play a crucial role in reducing the risk of CABSIs, including hand hygiene, catheter and exit site care protocols, the use of antibiotic lock solutions, antiseptic impregnated dressings and catheters, dialysis station disinfection protocols and staff and patient education programs [25]. Although not a part of this study, a subsequent hand hygiene audit in our dialysis unit confirmed that compliance with hand hygiene among dialysis nurses and technicians was only 52 and 66% before and after patient contact, respectively. Poor patient hygiene [13] and inadequate adherence

Table 3. Cox regression analysis for risk factors of CABSIs

Variable	Events	Time to CABSIs (weeks)		Univariate analysis		Multivariate analysis	
		Mean (95% CI)	Log rank P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age	–	–	–	0.99 (0.97–1.01)	0.674	0.99 (0.97–1.02)	0.756
Gender (female)	17/60	10.65 (9.19–12.12)	0.503	1.21 (0.68–2.18)	0.505	1.59 (0.81–3.12)	0.172
Diabetes (yes)	19/69	10.92 (9.64–12.21)	0.128	0.64 (0.36–1.14)	0.132	0.77 (0.37–1.59)	0.485
BMI	–	–	–	1.04 (0.98–1.10)	0.135	1.05 (0.99–1.12)	0.089
eGFR at HD initiation	–	–	–	1.04 (0.94–1.16)	0.371	–	–
CCI	–	–	–	1.00 (0.86–1.16)	0.919	–	–
Serum albumin	–	–	–	1.04 (0.68–1.59)	0.837	–	–
Broad-spectrum antibiotic use (yes)	19/62	10.47 (9.25–11.68)	0.350	0.76 (0.43–1.34)	0.352	–	–
IV cefazolin use (yes)	19/81	11.05 (9.95–12.15)	0.016	0.50 (0.28–0.89)	0.019	0.51 (0.28–0.94)	0.031 ^a
Nonelective hospitalization (yes)	14/37	9.67 (7.94–11.40)	0.210	1.55 (0.77–3.11)	0.214	–	–
Immunosuppression (yes)	5/12	4.84 (3.29–6.39)	0.024	2.80 (1.09–7.19)	0.032	2.87 (1.09–7.55)	0.033 ^a

^ap < 0.05.

BMI, body mass index; eGFR, estimated GFR by the Chronic Kidney Disease Epidemiology Collaboration formula; CCI, Charlson's comorbidity index.

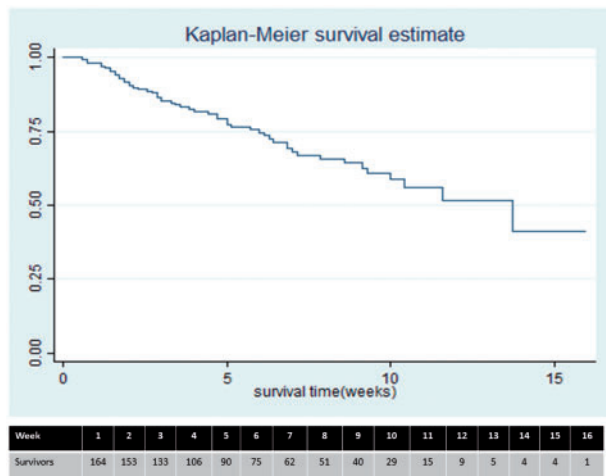


FIGURE 2: The Kaplan–Meier infection-free survival curve for jugular NTHCs. The median infection-free survival was 13.7 weeks. (x-axis: catheter days or patient days at risk in weeks).

to catheter care protocols by dialysis unit staff are associated with an increased risk for Gram-negative CABSIs [12]. A high rate of Gram-negative CABSIs has also been reported among undocumented immigrants in the USA undergoing emergent HD [26], pointing to socioeconomic factors as risk multipliers. Although IV cefazolin could have promoted the overgrowth of Gram-negative organisms, we did not find an association between cefazolin use and the type of organism cultured. Dialyzer reuse and contaminated water are other risk factors associated with outbreaks of Gram-negative bloodstream infections [27]; however, we did not reuse dialyzers and endotoxin levels and

Table 4. Nelson–Aalen estimate of the cumulative hazard of CABSIs for every week of NTHC use (n = 169)

Duration of NTHC use (weeks)	Patients at risk	Cumulative hazard of CABSIs (%)	SE	95% CI
1	164	8.3	0.021	0.050–0.137
2	153	13.3	0.026	0.090–0.196
3	133	17.6	0.030	0.124–0.245
4	106	20.9	0.033	0.152–0.283
5	90	24.6	0.036	0.182–0.327
6	75	30.9	0.041	0.236–0.399
7	62	34.5	0.044	0.266–0.439
8	51	35.9	0.045	0.278–0.456
9	40	39.5	0.049	0.306–0.500
10	29	44.8	0.057	0.344–0.567
11	15	49.2	0.067	0.369–0.631
12	9	49.2	0.067	0.369–0.631

SE, standard error.

microbiological cultures of water samples throughout the study period met the Association for the Advancement of Medical Instrumentation (AAMI) criteria. Staff training, periodic assessment of competency in catheter care and aseptic technique and audits of hand hygiene and vascular access care have been shown to reduce blood stream infection (BSI) rates by up to 54% [28] and, coupled with patient education initiatives, would be the most appropriate interventions to reduce the CABSIs rate in the subcontinent.

Despite this being an incident cohort, 40% of CABSIs were caused by drug-resistant organisms. Since prior antibiotic

exposure or hospitalization was not associated with drug-resistant CABSIs, it is likely that these organisms were acquired either from the community or the dialysis unit. Community-acquired drug-resistant infections are a growing menace in South Asia, driven by a high infectious disease burden, rising incomes and the availability of cheap generic over-the-counter antibiotics and their rampant misuse by physicians, the general public and agri-industries [29]. The high prevalence of infections by nonfermenting Gram-negative bacilli is also noteworthy. At the time of this study, our institution did not have matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) or gene sequencing to further speciate these isolates; however, we can speculate, based on data from other centers, that they were most likely *Burkholderia* species, *Pseudomonas fluorescens* or *stutzeri*, *Acinetobacter lwoffii*, *Stenotrophomonas maltophilia*, *Alkaligenes fecalis* or *Sphingobacterium* species [30].

Table 5. Spectrum of organisms causing CABSIs

Organism	Number of isolates (n = 53)
Gram-negative organisms (54.7%)	
NFGNB, not typed	1
<i>Escherichia coli</i>	3
<i>Pseudomonas aeruginosa</i>	6
<i>Enterobacter cloacae</i>	2
<i>Acinetobacter baumannii</i>	1
<i>Burkholderia cepacia</i>	1
<i>Sphingobacterium multivorum</i>	1
<i>Citrobacter diversus</i>	1
<i>Aeromonas</i>	1
Gram-positive organisms (15.1%)	
<i>Staphylococcus aureus</i>	7
<i>Enterococcus faecium</i>	1
Coagulase-negative staphylococci (30.2%)	16

NFGNB, nonfermenting Gram-negative bacteria.

Table 6. Antibiotic resistance pattern for CoNS and Gram-positive organisms causing CABSIs

Antibiotic	CoNS (n = 16), %	<i>Staphylococcus aureus</i> (n = 7), %	<i>Enterococcus faecium</i> (n = 1), %
Rifampicin	12.5	0	0
Oxacillin	56.2	14.3	0
Teicoplanin	0	0	0
Linezolid	0	0	0
Vancomycin	0	0	0

Table 7. Antibiotic resistance pattern of Gram-negative organisms causing CABSIs

Antibiotic	NFGNB (n = 15), %	<i>Escherichia coli</i> (n = 3), %	<i>Pseudomonas aeruginosa</i> (n = 6), %	<i>Enterobacter cloacae</i> (n = 2), %	<i>Acinetobacter baumannii</i> (n = 1), %
Piperacillin-tazobactam	0	0	0	0	100
Meropenem	40	0	0	0	100
Cefepime	20	0	0	0	100
Amikacin	46.6	0	0	0	100
Ceftazidime	26.6	0	0	0	100
Levofloxacin	6.6	0	0	0	100

NFGNB, nonfermenting Gram-negative bacteria: not typed, 13; *Sphingobacterium multivorum*, 1 and *Burkholderia cepacia*, 1.

Our study showed that neutrophil left shift and high procalcitonin distinguished Gram-positive and Gram-negative infections from those by CoNS. It is well known that CoNS species cause less virulent infection [31], and these two laboratory tests can guide empirical antibiotic therapy pending the results of blood cultures: IV cloxacillin and a third- or fourth-generation cephalosporin for a patient with neutrophil left shift and high procalcitonin and IV vancomycin for a patient with low procalcitonin and absence of neutrophil left shift.

This study has many limitations. First, we acknowledge that the incidence rate reported in this study may be biased, as data were obtained from a retrospective cohort. Many patients had to be excluded from the analysis because they left our center to follow-up elsewhere. However, we deliberately kept our exclusion criteria stringent to enrich our study population with subjects who would have a long enough follow-up period to get an accurate estimate of CABSIs incidence and risk over time. We did not use the Infectious Diseases Society of America definition for CRBSI because we believe it is not practical in resource-poor settings, where immediate catheter removal for tip culture is not possible and laboratories do not report differential time to positivity or quantitative cultures. We could not report the exit site infection rate for jugular NTHCs, which is itself a risk factor for CABSIs [6], because this was not documented in the dialysis records. We did not have information on patients' education background and financial status, which are surrogates for personal hygiene. The microbiological spectrum associated with CABSIs in our cohort may differ from that encountered in other centers. This highlights the need for each center to audit its CABSIs microbiological spectrum and tailor the choice of empirical antibiotic(s) accordingly. Patient and dialysis staff hand hygiene audits were not included in the design of this study and hence our conclusion that the high CABSIs incidence was related to poor hygiene practices remains hypothesis generating. Lastly, while IV cefazolin was found to be protective against CABSIs, a retrospective study design does not provide evidence to support the use of cefazolin to prevent CABSIs in patients who wish to delay construction of a permanent vascular access.

The strengths of this study are that it reports for the first time the incidence and cumulative hazard of CABSIs associated with the long-term use of jugular NTHCs in South Asia. Clinicians can now provide patients with data regarding the risk of CABSIs over time and counsel them to construct an AVF early given the high cost of treating Gram-negative or drug-resistant CABSIs.

In conclusion, jugular NTHCs are associated with an unacceptably high risk for CABSIs in South Asia as early as the second week following insertion. Concomitant immunosuppression is a risk factor, while IV cefazolin administered as antibiotic prophylaxis for AVF surgery is protective against CABSIs. Most

Table 8. Clinical presentation of CABSIs by type of organism

Variables	CoNS (n = 16)	Gram-positive (n = 8)	Gram-negative (n = 28)	P-value
Laboratory parameters				
Neutrophil left shift, %	31.2	100	100	<0.0001
Neutrophils on peripheral smear (%), mean \pm SD	80.0 \pm 7.4	87.3 \pm 4.9	90.5 \pm 5.0	0.174
Total leukocyte count (cells/mm ³) ^a	10 100 (8000–11 550)	12 800 (7500–20 600)	10 400 (7900–17 450)	0.620
Procalcitonin ^a (ng/mL)	1.9 (0.9–3.4)	61.2 (0.9–145)	21.2 (4.3–114)	<0.001
Complications, %				
Hospitalization	6.25	12.5	14.3	0.728
ICU admission	0	0	7.1	0.899
Metastatic complications	0	0	7.1	0.637
Mortality	0	0	7.1	0.355

^aExpressed as median (25–75th centile).

infections are Gram negative and we hypothesize that poor adherence to hand hygiene by patients and/or dialysis staff may be contributory. Compared with CoNS species, Gram-negative and Gram-positive CABSIs are associated with neutrophil left shift and high procalcitonin.

SUPPLEMENTARY DATA

Supplementary data are available at ckj online.

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CONFLICT OF INTEREST STATEMENT

None declared. The results presented in this article have not been published previously in whole or part, except in abstract format.

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