

Original Research Article

Clinical and microbiological spectrum of catheter-related bloodstream infections in non-tunneled and tunneled internal jugular vein hemodialysis catheters at a tertiary care hospital in Uttarakhand

Sharon Kandari¹, Rohit Puri^{1*}, Sandeep Saini¹, Mahendra Singh², Anshuman Biswal¹, Arshdeep Singh¹, Parul Ahlawat¹, Anil Cheriyan¹, Sandeep Kaur¹, Abhay Gangdev¹

¹Department of Nephrology, All India Institute of Medical Science, Rishikesh, Uttarakhand, India

²Department of CFM, All India Institute of Medical Science, Rishikesh, Uttarakhand, India

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*Correspondence:

Dr. Rohit Puri,
E-mail: Rpuri90@gmail.com

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ABSTRACT

Background: Catheter-related bloodstream infection (CRBSI) is a significant cause of morbidity and mortality in patients undergoing hemodialysis. In this prospective cohort study, we studied the incidence rate of CRBSI as well as the clinical and microbiological profile in non-tunneled and tunneled hemodialysis catheters.

Methods: Patients were recruited as per inclusion/exclusion criteria. Patients with non-tunneled internal jugular catheters were followed for 1 month and tunneled internal jugular were followed for 3 months. Patients with clinical signs and symptoms suggestive of CRBSI were admitted. We followed the centers for disease control and prevention (CDC) guidelines for the diagnosis of catheter-associated bloodstream infections microbiological methods-blood samples were inoculated on an automated BACTEC system for 5 days. If microbial growth was detected by the automated system, Gram staining was performed and growth was sub-cultured on culture media.

Results: The 202 patients underwent internal jugular vein hemodialysis catheter insertion. The 21 patients were excluded from the study. Total 181 patients were confirmed eligible. The 16.0% of the participants (29 patients) developed CRBSI during follow up. Incidence of CRBSI in our study was 3.73 episodes per 1000 catheter days. Diabetes mellitus and low BMI were risk factors for CRBSI. Most of the CRBSI were caused by gram negative organism. Overall, 65.5% of CRBSI were caused by multidrug resistant organisms.

Conclusions: Incidence of CRBSI was high in non-tunneled catheters as compared to tunneled catheters.

Keywords: Catheter related blood-stream infection, Internal jugular vein, Tunneled cuffed catheter, Hemodialysis, Multi-drug resistance

INTRODUCTION

The most common modality of renal replacement therapy for end-stage renal disease (ESRD) patients in India is hemodialysis.¹ According to various studies, in 81 to 100% of patients in the developing world hemodialysis is initiated through non-tunneled catheters.²

Infection is an important cause of hospitalization and the second most common cause of death among ESRD

patients undergoing hemodialysis.³ CRBSI is a significant cause of morbidity and mortality in patients undergoing hemodialysis.⁴ The cumulative risk within three months for catheter-related bacteremia has been documented to be around 35%.⁵

The factors which affect the prevalence of CRBSI includes patient related factors, type of catheter, frequency of catheter manipulation.⁶ The major organisms responsible for such infections are gram-positive organisms, the most

important of which are coagulase-negative *Staphylococcal* (CoNS) and *Staphylococcus aureus*.

In general, non-tunneled catheters have a higher rate of infection, 3.8 to 6.6 episodes/1,000 days, compared with tunneled catheters, which vary from 1.6 to 5.5 episodes/1,000 days.⁷

A Varun et al in a retrospective cohort study of 18-month duration included a total of 897 patients (>18 years) with no past history of HD catheter insertion. Incidence of CRBSI was 7.34 episodes per 1000 catheter days.²

Only a few studies had reported about the clinical and microbiological profile of CRBSI from north India. In this prospective cohort study, we studied the incidence rate of CRBSI as well as the clinical and microbiological profile in non-tunneled and tunneled hemodialysis catheters.

METHODS

This prospective cohort study was conducted from November 2022 to February 2024 in department of nephrology, All India institute of medical sciences, Rishikesh. Patients were recruited as per inclusion/exclusion criteria. Patients with non-tunneled internal jugular catheters were followed for 1 month and tunneled internal jugular were followed for 3 months. Patients with clinical signs and symptoms suggestive of CRBSI were admitted and a detailed history, clinical examination, and relevant laboratory investigations, as part of their management per se were sent. Paired blood cultures (10 ml each from a peripheral vein and central venous catheter) were obtained under sterile conditions, inoculated in culture media and immediately sent to the microbiology lab. Samples for CBC and serum procalcitonin with all routine investigations like LFT, KFT, and urine culture (wherever required) were also sent. Antibiotics were started empirically (injection of Vancomycin and ceftriaxone in renal modified doses) and modified according to culture results. They were provided standard treatment including dialysis as per indication.

Microbiological methods-blood samples were inoculated on an automated BACTEC system for 5 days. If microbial growth was detected by the automated system, Gram staining was performed and growth was subcultured on culture media.

If there was any growth on the media, colony identification and antibiotic susceptibility test was carried out.

Definitions used in the study

Standard definition/criteria

We followed the centers for disease control and prevention (CDC) guidelines for the diagnosis of catheter-associated bloodstream infections.⁸ CRBSI is defined as bacteremia associated with an 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 C, chills or hypotension); 3. No other apparent source for the bloodstream infection and 4. Catheter in use within 48 h of the CRBSI.

Multidrug-resistance organisms were defined as resistance to one or more classes of antimicrobial agents.⁹

Outcome measures

Primary endpoint

Incidence rate=Number of CRBSI events/ Number of catheter days×1000

Secondary endpoint

Clinical profile of patients with CRBSI, Microbiological profile of patients with CRBSI and laboratory profile of patients with CRBSI

Statistical methods

Data were coded and recorded in MS excel spreadsheet program. SPSS v23 (IBM Corp.) was used for data analysis. Descriptive statistics were elaborated in the form of means/standard deviations and medians/IQRs for continuous variables, and frequencies and percentages for categorical variables. Group comparisons for continuously distributed data were made using independent sample 't' test when comparing two groups. If data were found to be non-normally distributed, appropriate non-parametric tests in the form of Wilcoxon test were used. Chi-squared test was used for group comparisons for categorical data. In case the expected frequency in the contingency tables was found to be <5 for >20% of the cells, Fisher's Exact test was used instead. Linear correlation between two continuous variables was explored using Pearson's correlation (if the data were normally distributed) and Spearman's correlation (for non-normally distributed data). Statistical significance was kept at p<0.05.

RESULTS

The 202 patients of more than or equal to 18 years of age fulfilling inclusion criteria underwent internal jugular vein hemodialysis catheter insertion. The 21 patients were excluded from the study. Total 181 patients were confirmed eligible.

Demography and baseline lab parameters

The mean age (in years) was 44.06±15.34.124 (68.5%) of the participants were male. The 160 (88.4%) of the participants had hypertension. The 67 (37.0%) of the

participants had diabetes mellitus. The mean BMI (kg/m²) was 21.88±2.65.12 (6.9%) of the participants had BMI <18.5 kg/m² and 24 (13.7%) of the participants had BMI >25.0 kg/m² (Table 1).

Outcomes

Patients with non-tunneled internal jugular vein hemodialysis catheters were followed for 1 month and tunneled internal jugular vein hemodialysis catheters were followed for 3 months and contributed total 7770 catheter days (4539 for tunneled catheters and 3231 for non-tunneled catheters).

The 16.0% of the participants (29 patients) developed CRBSI during follow up.

Incidence of CRBSI in study was as following (Table 2).

Microbiological profile of organisms causing CRBSI

The 13 different organisms were cultured from 29 patients. The 26 patients showed growth on cultures sent from catheter hub, 14 on peripheral blood. The 11 patients had growth on both catheter hub and peripheral blood while 3 had growth on peripheral blood alone (Figure 1-3).

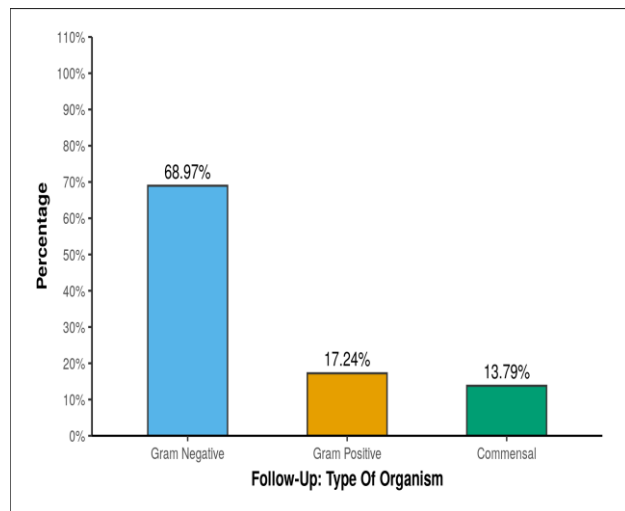


Figure 1: Distribution of type of organism causing CRBSI.

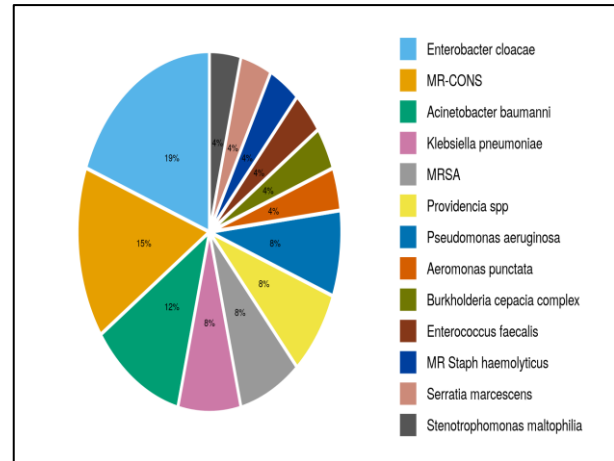


Figure 2: Distribution of organism on central line.

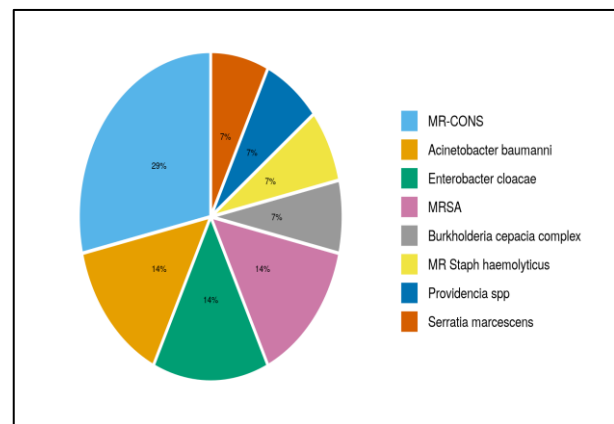


Figure 3: Distribution of follow-up: organism on peripheral line.

Antibiotic resistance

The 50% of the gram-negative isolates were resistant to at least one class of antibiotics while all gram-positive isolates showed drug resistance. Overall, 65.5% of CRBSI were caused by multidrug resistant organisms (Table 3).

Risk factors for CRBSI

Diabetes mellitus and low BMI were identified as risk factors for CRBSI among study population (Table 4).

Table 1: Demography and baseline lab parameters.

Basic clinical details	Mean±SD, Median (IQR), Min-Max OR
Age	44.06±15.34, 44.00 (32.00-56.00), 18.00-83.00
Age (in years)	
18-30	40 (22.1%)
31-40	40 (22.1%)
41-50	40 (22.1%)
51-60	31 (17.1%)
61-70	24 (13.3%)
71-80	3 (1.7%)
81-90	3 (1.7%)

Continued.

Basic clinical details	Mean±SD, Median (IQR), Min-Max OR
Gender	
Male	124 (68.5%)
Female	57 (31.5%)
Hypertension (Yes)	160 (88.4%)
Diabetes mellitus (Yes)	67 (37.0%)
BMI (kg/m ²)	21.88±2.65, 21.40 (19.90-23.50), 17.00-29.80
Diagnosis	
CKD 5D	165 (91.2%)
RPRF	9 (5.0%)
AKD	7 (3.9%)
Previous treatment	
None	91 (50.3%)
Antibiotics	90 (49.7%)
Site	
Right	161 (89.0%)
Left	20 (11.0%)
Catheter type	
Non tunneled	119 (65.7%)
Tunneled	62 (34.3%)
Season of catheter insertion	
Winter	106 (58.9%)
Summer	61 (33.9%)
Monsoon	13 (7.2%)
Catheter days	42.93±29.08, 30.00 (30.00-90.00), 2.00-90.00
Frequency of HD	
Twice	3 (1.7%)
Thrice	178 (98.3%)
Broad spectrum antibiotic use (Yes)	3 (1.7%)
Hospitalization (Yes)	2 (1.1%)
Elective procedure (Yes)	62 (34.3%)
Non CRBSI infection (Yes)	2 (1.1%)
Emergency surgery (Yes)	0 (0.0%)
Cardiovascular events (Yes)	1 (0.6%)
Investigations	Mean±SD Median (IQR) Min-Max
Hemoglobin (g/dL)	8.29±1.29 8.20 (7.50-9.10) 4.8-11.4
TLC (/mm ³)	7.64±3.01 7.30 (5.40-9.08) 2.2-24.0
Creatinine (mg/dL)	9.10±4.58 8.10 (6.31-11.00) 1.9-42.0
Albumin (g/dL)	2.97±0.59 3.05 (2.60-3.32) 1.0-4.3

Table 2: incidence of CRBSI.

Catheter type	Catheter days	CRBSI episodes	Incidence
Overall	7770	29	3.73
Non tunneled	3231	16	4.95
Tunneled	4539	13	2.86

Table 3: Antibiotic resistance pattern for organisms causing CRBSI.

Antibiotics	MRCoNS, (n=4)	MRSA, (n=3)	Methicillin resistant <i>Staphylococcus hemolyticus</i> (n=1)	<i>Enterococcus faecium</i> (n=1)
Erythromycin	100	100	100	100
Ciprofloxacin	100	33.3	100	0
Levofloxacin	100	33.3	100	0
Penicillin	100	100	100	0
Clindamycin	75	33.3	100	0
Tetracycline	50	0	0	100
Cotrimoxazole	50	33.3	0	0

Continued.

Antibiotics	<i>Enterobacter cloacae</i> (n=5)	<i>Acinetobacter baumannii</i> (n=3)	<i>Klebsiella pneumoniae</i> (n=2)	<i>Aeromonas punctata</i> (n=1)	<i>Providencia</i> spp. (n=2)
Piperacillin tazobactam	20	25	0	100	0
Ampicillin	0	0	100	0	0
Amoxycillin-clavulanate	40	0	0	0	0
Cefuroxime	40	0	100	100	0
Cefixime	0	0	100	0	50
Cefepime	20	0	100	0	0
Ceftazidime	20	0	0	100	100
Cotrimoxazole	50	0	100	100	0
Tetracycline	75	0	100	0	0
Levofloxacin	20	0	100	100	100
Ciprofloxacin	60	0	0	100	100
Meropenem	0	0	0	100	0
Imipenem	0	0	0	100	0
Aztreonam	20	0	0	0	100

Table 4: Association between CRBSI and various parameters.

Parameters	CRBSI status		P value
	Yes CRBSI (n=29)	No CRBSI (n=152)	
Age (in years)	44.72±13.20	43.93±15.75	0.775 ¹
18-30	4 (13.8%)	36 (23.7%)	0.427 ²
31-40	6 (20.7%)	34 (22.4%)	
41-50	9 (31.0%)	31 (20.4%)	
51-60	8 (27.6%)	23 (15.1%)	
61-70	2 (6.9%)	22 (14.5%)	
71-80	0 (0.0%)	3 (2.0%)	
81-90	0 (0.0%)	3 (2.0%)	
Gender			
Male	18 (62.1%)	106 (69.7%)	0.415 ³
Female	11 (37.9%)	46 (30.3%)	
Hypertension (Yes)	25 (86.2%)	135 (88.8%)	0.751 ²
Diabetes mellitus (Yes)***	16 (55.2%)	51 (33.6%)	0.027 ³
BMI (kg/m²)	20.92±1.51	22.06±2.78	0.088 ⁴
BMI (kg/m²)***			
<18.5	2 (6.9%)	10 (6.8%)	0.021 ²
18.5-22.9	24 (82.8%)	84 (57.5%)	
23.0-24.9	3 (10.3%)	28 (19.2%)	
25.0-29.9	0 (0.0%)	24 (16.4%)	
Hemoglobin (g/dl)	8.24±1.17	8.30±1.32	0.783 ¹
TLC (/mm³)	6.99±2.65	7.76±3.07	0.210 ⁴
PLT (Lacs)	1.85±0.88	5.66±27.43	0.880 ⁴
Creatinine (mg/dl)	8.85±3.39	9.15±4.78	0.750 ⁴
Albumin (g/dl)	3.04±0.68	2.96±0.57	0.358 ⁴
Previous treatment			
None	15 (51.7%)	76 (50.0%)	0.865 ³
Antibiotics	14 (48.3%)	76 (50.0%)	
Site			
Right	24 (82.8%)	137 (90.1%)	0.327 ²
Left	5 (17.2%)	15 (9.9%)	
Catheter type			
Non tunneled	16 (55.2%)	103 (67.8%)	0.190 ³
Tunneled	13 (44.8%)	49 (32.2%)	

Continued.

Parameters	CRBSI status		P value
	Yes CRBSI (n=29)	No CRBSI (n=152)	
Season of catheter insertion			
Winter	15 (51.7%)	91 (60.3%)	0.332 ³
Summer	13 (44.8%)	48 (31.8%)	
Monsoon	1 (3.4%)	12 (7.9%)	
Catheter days***	22.41±12.98	46.84±29.67	<0.001 ⁴
Frequency of HD			
Twice	0 (0.0%)	3 (2.0%)	1.000 ²
Thrice	29 (100.0%)	149 (98.0%)	
Broad spectrum antibiotic use (Yes)	0 (0.0%)	3 (2.0%)	1.000 ²
Hospitalization (Yes)	0 (0.0%)	2 (1.3%)	1.000 ²
Elective procedure (Yes)	8 (27.6%)	54 (35.5%)	0.409 ³
Non CRBSI infection (Yes)	0 (0.0%)	2 (1.3%)	1.000 ²
Emergency surgery (Yes)	0 (0.0%)	0 (0.0%)	1.000 ³
Cardiovascular events (Yes)	0 (0.0%)	1 (0.7%)	1.000 ²
Follow-up: immunosuppression (Yes)	2 (100.0%)	6 (85.7%)	1.000 ²

***Significant at p<0.05, 1: t-test, 2: Fisher's Exact Test, 3: Chi-Squared Test, 4: Wilcoxon-Mann-Whitney U Test

DISCUSSION

Demography and clinical characteristics of study population

The mean age (in years) of our study population was 44.06±15.34. It was same as in study done by Agrawal et al. The patients in were relatively older in study by Gupta et al and Weijmer et al 68.5% of patients in our study population were male. It was almost similar in study of Viswanath (68.2% male). A south Indian study conducted by Gupta et al had 66% male participants. The mean BMI (kg/m²) was 21.88±2.65 in our study population. 6.9% of the participants had BMI<18.5 kg/m². Our results showed that patients with low BMI were prone to develop CRBSI.

The most common comorbidity among our study population was hypertension. The 88.4% of the participants were hypertensive. The 37.0% of the participants had diabetes mellitus. Diabetes mellitus was also associated with increased risk of CRBSI in our study.

Incidence of CRBSI

Incidence of CRBSI in our study was 3.73 episodes per 1000 catheter days. Overall CRBSI incidence in our study is lower than various Indian studies done previously.^{2,10-14} Varun et al reported overall CRBSI incidence rate of 7.34 episodes per 1000 catheter days.² It was a retrospective study and they included only non-tunneled IJV catheters in their study. Parameswaran et al also reported higher CRBSI rate. CRBSI rate was 8.75 episodes per 1000 catheter days in their study. They included patients in whom catheters were inserted for other indications than hemodialysis. Majority of patients who developed CRBSI in their study had femoral HD catheters.¹⁰ Behra et al and Bhojaraja et al also reported higher CRBSI rates. Behra et al in their prospective study found CRBSI rate of 6.12

episodes per 1000 catheter days. The incidence of CRBSI was 13.39 episodes per 1000 catheter days.

The possible cause for overall lower incidence of CRBSI in our study is a shorter follow-up duration. Follow-up was 1 month for non-tunneled and 3 months for tunneled catheters.

We found that incidence of CRBSI was high in non-tunneled catheters as compared to tunneled catheters. It was 2.86 per 1000 catheter days among tunneled catheters and 4.95 per 1000 catheter days in non-tunneled catheters. The same has been established by various studies done previously in different part of world.⁶ Weijmer et al found incidence rate of 2.9 episodes among tunneled catheters and 12.8 episodes per 1000 catheter days among non-tunneled catheter patients.¹⁵

Some recent Indian studies also reported a lower incidence rate of CRBSI than our study had more tunneled catheters in study population.¹⁶⁻¹⁸ Patil et al reported incidence rate of 1.3 episodes per 1000 catheter days. Their entire study population had tunneled catheters.¹⁹ Shah et al studied incidence of CRBSI in a retrospective Indian study. 80% of study population had tunneled catheters. CRBSI incidence was 0.36 episodes per 1000 catheter days.¹⁶

Microbiology

Most of the CRBSI in our study were caused by gram negative organism. *Enterobacter cloacae* was the most common organism isolated. 68.97% of CRBSI were caused by gram-negative organisms. The same trend has been seen in other Indian studies and developing countries.^{2,11,19-21} Studies from developed countries and some Indian centres found gram-positive predominance.^{10,11,13,15,16,22}

Most of the participants of our study population were having low socio-economic status and taking haemodialysis from outside centres. As gram-negative infections are predominantly transmitted through water and organisms are fecal in origin. Patients developed CRBSI after discharge from our hospital, we hypothesized that gram-negative predominance in our study may be related to poor hygiene practices.

Antibiotic resistance

We found that 65.5% of CRBSI were caused by multidrug resistant organisms. Overall antibiotic resistance was high in our study. Drug resistance was significantly lower in study from south India conducted by Gupta et al they reported 21% of organisms were multidrug resistant in their study.¹² All gram-positive isolates were resistant to more than one class of antibiotics in our study. Our study showed that all gram-positive isolates were sensitive to vancomycin and linezolid. The 50% of the gram-negative isolates were resistant to at least one class of antibiotics. We also found that none of the isolates of *Pseudomonas*, *Stenotrophomonas maltophilia*, *Serratia marcescens*, *Burkholderia cepacia* were drug resistant.

Clinical presentation of patients with CRBSI

We found that majority of patients who developed CRBSI had fever and chills during or after hemodialysis. Few patients (5.9%) had shock. Median catheter days were 20 days in CRBSI group and 30 days in non-CRBSI group ($p < 0.001$) in our study. Median time for CRBSI was 20 days in our study. Our findings were similar to study of Agrawal et al and Viswanath et al.^{2,20}

We found significant differences in clinical presentation according to type of organism causing CRBSI. Two patients had shock on presentation, both had gram-negative organism on culture out of which one was *pseudomonas* and other was *Enterococcus cloacae*. The 95% of patients who had gram-negative infection were hospitalised. The percentage of patients who required hospitalisation in gram-positive and commensals was 60% and 75% respectively. But this was not statistically significant ($p = 0.076$). The duration of hospital stay was also more in gram negative infections ($p = 0.931$, statistically insignificant). One patient required ICU admission who died at 16th day of hospital admission. It was also caused by gram-negative organism. We found that TLC was more in gram-negative infections ($p = 0.036$). Procalcitonin levels were significantly high in gram-negative infections at the time of hospitalisation ($p = 0.006$). The same trend was also observed in various earlier studies. Farrington et al found that duration of hospital stay, ICU requirement and metastatic complications were more in gram-negative infections.²² Shahar et al reported that gram-negative organisms have poor outcomes.¹⁷

From above findings we can conclude that gram negative infections are generally more severe and they should be treated aggressively.

Outcomes of CRBSI

In our study catheter was removed in 69% of patients with CRBSI, catheters were salvaged in 27.6% patients. One patient was expired. Overall mortality was 3.4%. The patient who expired was 45-year-old diabetic male with gram negative infection. His serum procalcitonin levels were elevated and had leucocytosis and neutrophilia. He had tunneled catheter in right IJV.

Mortality was low in our study in comparison with other studies from developing world but higher than developed countries. It was almost similar to study by Agrawal et al they reported mortality rate of 3.8%.² It was 10% in an Indian retrospective study done by Shah et al.¹⁶ Bhojaraja et al found mortality rate of 6.6%.¹⁴ Overall mortality was 1.1% in study of Shahar S et al, both patients expired had gram-negative infection.¹⁷

The possible causes of lower mortality rate in our study are lower sample size being a time bound study, lower follow up duration.

Risk factors for CRBSI

Multivariate analysis showed that diabetes mellitus and low BMI were risk factors for CRBSI in our study. Patients with BMI $< 18.5 \text{ kg/m}^2$ were at risk for developing CRBSI ($p = 0.021$). They were more prone because malnutrition is associated with lower immunity.²³ CRBSI rate was also more in diabetics ($p = 0.027$). Diabetes mellitus was also a risk factor for CRBSI in some other studies.^{12,13} It was statistically significant in studies of Behra et al, Gupta et al 76.5% of patients who developed CRBSI were diabetics in study conducted by Viswanath et al.^{13,20}

CONCLUSION

This study was conducted to study CRBSIs in internal jugular non-tunneled and tunneled hemodialysis catheters at a tertiary care hospital in Uttarakhand. This study and analysis of previous published studies indicate that incidence of CRBSI was high in non-tunneled catheters as compared to tunneled catheters. Majority of CRBSI in North India were caused by gram-negative organisms. Low BMI and diabetes were risk factors for CRBSI. Gram-negative infections were characterised by high procalcitonin and high TLC as compared to gram-positive and commensal organisms. Gram-negative infections had longer duration of hospital stay.

A notable strength of this study was its prospective and observational design, which is in contrast to the predominantly retrospective nature of existing Indian studies. However, a drawback of the study was its restricted follow-up period till one month for non-tunneled

catheters and three months for tunneled catheters as the study was time bound. Hence further research is needed on the follow-up of these patients to determine the long-term outcome and risk factors for developing CRBSI.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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