AMLS Archives of Medical Laboratory Sciences

Original Article

Central Catheter Infection in Patients on Acute and Chronic Hemodialysis: A Cross Sectional Study

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Received: August 21, 2022; Accepted: November 6, 2022

Abstract

Background and Aim: The most common complication of central venous catheter (CVC) in hemodialysis (HD) is infection. Identifying CVC- related infection (CVC-RI) risk factors and causative micro - organisms is essential for setting prevention policies. This study aims to determine the prevalence of CVCRIs and identify any associated risk factors among these patients.

Methods: We conducted a cross-sectional study from 2017 to 2018 to determine the prevalence of central catheter - related infections among all adult patients on both acute and chronic hemodialysis who had central catheters in place at a tertiary care hospital in Qazvin City. Data on demographics, comorbidities, dialysis duration, catheter - related complications, catheter removal, dialysis details (frequency, duration), catheter insertion site, and any history of central catheter - related infections were collected from medical records. A central catheter - related infection is defined as a positive blood culture obtained from a central venous catheter tip or any other related site (e.g., tunnel, exit site) with clinical signs of infection such as fever, chills, or localized pain and tenderness. Micro - organisms isolated from cultures of CVC, catheter tips, and blood cultures were identified. Chi-square and t-test were performed to compare demographic and clinical variables. $P < 0.05$ was considered statistically significant.

Results: 171 patients (214 hospital admissions) enrolled in the study. Of these hospital admissions, 91 (42.5%) had CVC-RI. There was no significant relationship between CVC-RI and age, gender, body mass index (BMI), marital status, education, residency, comorbidities, addiction, and etiology of kidney failure. Variables such as smoking ($p = 0.012$), catheter type ($p = 0.031$), CVC location ($p = 0.026$), emergency catheter placement ($p = 0.005$), previous catheter history ($p = 0.004$), and number of previous catheter ($p = 0.006$), previous catheter infection history ($p = 0.002$), and antibiotic use in the recent month ($p = 0.001$) were associated with an increased CVC-RI. Of the positive blood cultures, the majority were gram - positive bacteria.

Conclusion: CVC-RI in HD is high and smoking, CVC location, number of previous catheters and their infection history, and antibiotic use in the recent month are risk factors related to CVC-RI. Education on proper hygiene for the prevention of CVC-RI is essential for patients that had no previous intravascular line. *Staphylococcus aureus* must be taken into account for empirical therapy.

Keywords: Catheter-Related Infections; Hemodialysis; Comorbidity; Risk factors

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Please cite this article as: Akhavan L, Najjari H, Bijani B, Kordi A, Allami A. Central Catheter Infection in Patients on Acute and Chronic Hemodialysis: A Cross Sectional Study. Arch Med Lab Sci. 2023;9:1-11 (e5). https://doi.org/10.22037/amls.v9.39205

Introduction

Patients on hemodialysis (HD) require a vascular-access site for blood removal and replacement during dialysis. Patients with acute and chronic renal failure undergoing HD are known to be at increased risk of central venous catheter (CVC) related infection (1). Bloodstream infection (BSI) is a major cause of morbidity and mortality in patients on HD, particularly those dependent on central venous catheters for

vascular access. Among the various HD access routes, tunneled, cuffed catheters (TCCs) have the highest risk of infection compared with arteriovenous fistulae (AVFs) (2). Since the artery- vein fistula (AVF) has the longest survival rate and the least complication frequency, it should, whenever it is possible, be the first choice for vascular approaches (3).

Temporary (non - tunneled, non - cuffed) catheters are designed for short - term use in patients on HD who do not have permanent access to dialysis, when urgent HD is indicated at the time of maturation of AVF and in patients in whom all other vascular approaches have been exhausted (4).

Despite the prioritization of AVF, nearly 80% of those patients start treatment with dialysis catheters (5), which are associated with significant morbidity and mortality due to infections in patients on HD. (6).

The incidence of bacteremia is 15 times more with indwelling catheters than with either fistulas or synthetic grafts (7). Also, because of frequent infections and the need for antimicrobial therapy, resistance to antimicrobials (particularly vancomycin) is high in HD patients. Determining CVC - related infection (CVC-RI) risk factors and causative pathogens may help in its prevention and improve patient quality of life and survival, hence it is imperative to identify and mitigate infection risk in End-Stage Renal Disease (ESRD) patients on HD (8). The microorganisms most frequently isolated during catheter-related bacteremia in HD are staphylococci and other Gram-positive cocci. According to US data, coagulase - negative staphylococci (CoNS) are found in 32-45% of cases, *Staphylococcus aureus* in 22-29%, and Enterococci in 9-13% of cases. Gram-negative bacteria have been isolated in 21-30% of cases (9). However, a majority of the patients in Iran are initiated on hemodialysis via a catheter and there were no data regarding CVC-RI in HD in Qazvin province by culture methods. There are two major and five minor dialysis centers in the province of Qazvin.

In this cross-sectional study, we aimed to determine the frequency of HD CVC-RI, causative pathogens, and their predisposing factors at the two major dialysis centers in the province. In order to assess risk factors for CVC-RI, epidemiological data of all hospitalized patients on HD were collected and then the patients with and without CVC-RI were compared.

Methods

Study design

This is a cross- sectional study which was performed in two university hospitals of Qazvin University of Medical Sciences HD wards.

Ethical considerations were in accordance with the ethical standards of the Helsinki Declaration (1964, amendment of 2008). A participant information sheet containing the particulars of the study was provided to all the patients and written informed consent was taken from all the patients. Participant information sheets and informed consent were available in Persian. The details of the reports were kept completely confidential.

Study population

All adult patients on acute and chronic HD with a central venous catheter were admitted to Qazvin University hospitals and were evaluated for an infection related to vascular access and suspected CVC-RI (November 2017 to April 2018). In all cases, consults from nephrologists, infectious disease specialists, microbiologists, and vascular surgeons were requested. Finally, 214 admissions have been evaluated. HD nurses screened patients for vascular access-related infection as part of standard procedure during each HD session. The study protocol was implemented when the patient displayed signs or symptoms suspicious of CVC-RI before or during the HD session, which included fever (38.0°C before dialysis and 37.7°C during dialysis), chills, rigors, hypotension, and new unexplained malaise, especially with concurrent exclusion of catheter - unrelated infectious foci (determined by the nurse with or without evaluation by the rounding physician). When a patient became symptomatic during HD, HD was stopped for as long as necessary to obtain blood samples from both catheter hubs. Patients gave consent for peripheral vein blood cultures and catheter tips to determine CVC-RI, and written informed consent to participate in the study. We used standardized definitions for central venous catheter endpoints (8). A physician confirmed the diagnosis of CVC-RI. The patients with clinical or laboratory evidence of another focus of infection were classified into the non - infected catheter group. In the first step, patients were divided into three groups “catheter infected”, “possible catheter infected” (purulent discharge from catheter site, erythema, or tenderness over exit site + negative blood culture + the absence of any other focus of infection) and “non - catheter infection” and finally, two primary groups were considered as CVC-RI.

Laboratory tests

Blood culture sets consisting of an aerobic adult blood culture bottle (10 ml blood each) from the venous central catheter, and a peripheral vein were obtained using an antiseptic technique. All the catheters withdrawn were referred for cultures under proper conditions. The decision to remove a catheter within the study period was made independently by the physician in charge of each patient when the catheter was no longer needed (in cases of recovery or death), or new access was required (where there was suspicion of catheter - related infection or catheter dysfunction). Blood samples were drawn from a peripheral vein at the time of removal if there was any suspicion of catheter - related infection. After bedside inoculation, the blood culture bottles were delivered to and processed at the Bou Ali Sina and Velayat Hospital Microbiology Laboratories as per routine microbiology laboratory procedures. The in - center dialysis physician also monitored the blood-drawing process.

Cultures of blood were incubated aerobically at 37 ºC for periods of up to seven days. They were subcultured when turbid or after seven days onto blood agar and incubated aerobically at 37 ºC. All isolates were again speciated and typed as described. The pour plates were incubated aerobically for 48 hrs, and colony counts were performed.

To identify the Gram-positive cocci (such as Staphylococcus spp., Streptococcus spp., and Enterococcus spp.) the following biochemical tests were performed after cultural growth on mannitol salt agar, the production of catalase, coagulase, DNase, indole, methyl red, citrate utilization, urease production, optochin sensitivity, bacitracin sensitivity, camp, bile esculin hydrolysis, nitrate broth, starch hydrolysis, growth in 6.5% NaCl, and motility agar (10). To identify the gram - negative bacilli (such as Enterobacteriaceae, and non - fermentative bacilli), the samples were cultured on blood and MacConkey agar plates. The plates were incubated in aerobic conditions for 24 hours at 37°C. Following the incubation, some bacteria were collected from colonies, and subsequently, gram staining and oxidase tests were performed. Oxidase - negative samples were evaluated by deferential biochemical tests such as citrate, urea, indole, and movement test, and they were identified precisely (11). When cultures were sent for suspected HCRI, then immediately initiated empiric antibiotics therapy which included vancomycin and ceftazidime. Since some patients experienced multiple infections at different catheter positions, each new infection of the placed catheter was analyzed separately.

Outcome measures

The primary outcome measure for this study is the prevalence of central catheter-related infections among patients undergoing both acute and chronic hemodialysis. Secondary outcomes include identifying risk factors associated with the development of these infections: data on demographics, comorbidities (cerebrovascular accident, cardiovascular, diabetes mellitus, HTN, collagen vascular disease, and neoplastic disease), catheter (type, insertion site, duration of placement and inserter), urgent catheter, catheter age, previous catheter (number, type, duration), catheter - related complications, and catheter removal, dialysis details (frequency, duration), and any history of central catheter-related infections, recent antibiotic therapy, infection signs, admission reason, number of previous admissions (especially recent), admission duration, and outcome of line. The risk factors for CVC-RI were compared between the examined group and the control group of patients with no infections in the course of the research period.

Statistical analysis

Frequency (percentages) were computed to present categorical variables such as catheter-related infection, causative micro-organisms, gender, history of catheter-related infection, causes of ESRD, and blood C/S. The chi-square test (or Fisher's exact probability test) was performed to compare categorical demographic and clinical variables (such as gender, comorbidities, duration of CVC, and insertion site) between the groups of patients with and without CVC-RI.

We found that the distribution of some continuous variables such as patient's age, BMI, and previous line duration deviated significantly from a normal distribution using the one-way Kolmogorov - Smirnov test ($P < 0.05$). The data appeared to be skewed, indicating that nonparametric tests should be used for analysis. Hence, these variables were expressed as the median values with their interquartile ranges (IQR) and differences were evaluated for significance by the Mann-Whitney U-test. Other continuous variables had normal distribution and hence mean±standard deviation (SD) was calculated and the student's t-test was used to compare these variables between two groups. Statistical significance was considered as $p<0.05$. All data analysis was performed using the SPSS version 25.0 for the Windows statistical package (SPSS Inc., Chicago, IL, USA).

Results

The present study was a cross-sectional study on 171 patients (214 hospital admissions) with acute or chronic renal failure who underwent HD using a catheter during 1 year in two university hospitals (Velayat and BuoAli Sina hospitals in Qazvin province). Of these hospital admissions, 91 (42.5%) were diagnosed as CVC-RI and 123 hospital admissions (57.5%) as non - CVC-RI. Demographic data and the underlying issues related to catheter infections are shown in table 1. Table 2 outlines the characteristics of the central venous catheters of the study population at the time of suspected catheter-related hospital admissions demographics.

Table1. Baseline characteristics and possible underlying condition of Catheterized patients with suspected infection at the time of suspected catheter - related hospital admissions (N = 214 hospital admissions)

		Study Groups			
		Catheter infection N = 57	**Possible catheter infection N = 34**	**Non - Catheter infection N = 123**	**Total N = 214**
Age (years) (Median [IQR])		63 [52-70]	62 [37-72]	61 [51-71]	61 [51-71]
Gender (N [%])	Female	31 (54.4)	18 (52.9)	64 (52.0)	113 (52.8)
	Male	26 (45.6)	16 (47.1)	59 (48.0)	101 (47.2)
BMI (Kg/m^2) (Median [IQR])		23.8 [21.8-25.9]	24.5 [21.3-28.1]	24.1 [21.6-27.7]	24.1 [21.5-27.4]
Marital (N [%])	Single or divorced	5 (8.8)	4 (11.8)	12 (9.8)	21 (9.8)
	Married	52 (91.2)	30 (88.2)	111 (90.2)	193 (90.2)
Residency (N [%])	Urban	54 (94.7)	29 (85.3)	104 (84.6)	187 (87.4)
	Rural	3 (5.3)	5 (14.7)	19 (15.4)	27 (12.6)
Smoker (N [%])		10 (17.5)	1 (2.9)	4 (3.3)	15 (7.0)
Addict (N [%])		3 (5.3)	0	5 (4.1)	8 (3.7)
Underlying (N [%])		51 (89.5)	33 (97.1)	115 (93.5)	199 (93.0)
Cardiovascular (N [%])		21 (36.8)	10 (29.4)	34 (27.6)	65 (30.4)
Cerebrovascular (N [%])		6 (10.5)	3 (8.8)	8 (6.5)	17 (7.9)
DM (N [%])		29 (50.9)	15 (44.1)	67 (54.5)	111 (51.9)
HTN (N [%])		43 (75.4)	26 (76.5)	91 (74.0)	160 (74.8)
Collagen vascular (N [%])		0	0	3 (2.4)	3 (1.4)
Neoplasia (N [%])		6 (10.5)	2 (5.9)	5 (4.1)	13 (6.1)
CRF reason (N [%])	DM	31 (54.4)	17 (50.0)	70 (56.9)	118 (55.1)
	HTN	15 (26.3)	11 (32.4)	24 (19.5)	50 (23.4)
	collagen vascular	0	0	1 (0.8)	1 (0.5)
	UTI	8 (14.0)	4 (11.8)	7 (5.7)	19 (8.9)
	GN	1 (1.8)	1 (2.9)	4 (3.3)	6 (2.8)
	ADPKD	1 (1.8)	0	4 (3.3)	5 (2.3)
	AKI	1 (1.8)	1 (2.9)	13 (10.6)	15 (7.0)
Recent Antibiotic therapy (N [%])		16 (28.1)	13 (38.2)	14 (11.4)	43 (20.1)

BMI: Body mass index, DM: Diabetes mellitus, HTN: Hypertension, UTI: Urinary tract infection, GN: Glomerulonephritis, ADPKD: Autosomal dominant polycystic kidney disease, AKI: Acute kidney injury, CVC: Central venous catheter, GI: Gastrointestinal, RTI: Respiratory infection.

Table 2. Characteristics of the central venous catheters at the time of suspected catheter-related hospital admissions (N = 214 hospital admissions)

	Study Groups

		Catheter infection N = 57	Possible catheter infection N = 34	Non-Catheter infection N = 123	Total N = 214
Catheter type (N [%])	Shaldon	34 (59.6)	15 (44.1)	84 (68.3)	133 (62.1)
	Permanent CVC	23 (40.4)	19 (55.9)	39 (31.7)	81 (37.9)
Catheter site (N [%])	Femoral	21 (36.8)	8 (23.5)	57 (46.3)	86 (40.2)
	Subclavian	9 (15.8)	15 (44.1)	33 (26.8)	57 (26.6)
	Jugular	27 (47.4)	11 (32.4)	33 (26.8)	71 (33.2)
Inserter (N [%])	General surgeon	1 (1.8)	2 (5.9)	4 (3.3)	7 (3.3)
	Vascular subspecialist	22 (38.6)	21 (61.8)	41 (33.3)	84 (39.3)
	Emergency specialist	0	0	7 (5.7)	7 (3.3)
	Surgery resident junior	34 (59.6)	11 (32.4)	71 (57.7)	116 (54.2)
Urgent catheter (N [%])		28 (49.1)	6 (17.6)	72 (58.5)	106 (49.5)
Catheter age (days) (Median [IQR])		40 [23-90]	44.5 [14-180]	11 [5-90]	30 [7-90]
Previous catheter (N [%])		25 (43.9)	20 (58.8)	41 (33.3)	86 (40.2)
Previous line type (N [%])	No catheter	31 (54.4)	13 (38.2)	83 (67.5)	127 (59.3)
	Shaldon	21 (36.8)	17 (50.0)	34 (27.6)	72 (33.6)
	Permanent CVC	3 (5.3)	3 (8.8)	5 (4.1)	11 (5.1)
	AVF	2 (3.5)	1 (2.9)	1 (0.8)	4 (1.9)
Previous line duration(days) (Median [IQR])		0 [0-30]	10 [0-30]	0 [0-17]	0 [0-26]
Previous catheter number (N [%])		0 [0-1]	1 [0-3]	0 [0-1]	0 [0-1]
Previous catheter infection (N [%])		16 (28.1)	12 (35.3)	18 (14.8)	46 (21.6)
Catheter replace history (N [%])		23 (40.4)	20 (58.8)	40 (32.5)	83 (38.8)
Recent Antibiotic therapy (N [%])		16 (28.1)	13 (38.2)	14 (11.4)	43 (20.1)
Infection signs (N [%])	Without infection sign	1 (1.8)	4 (11.8)	117 (95.9)	122 (57.3)
	Tenderness	4 (7.0)	0	0	4 (1.9)
	Fever	51 (89.5)	30 (88.2)	5 (4.1)	86 (40.4)
	Induration & pus	1 (1.8)	0	0	1 (0.5)
Admission reason (N [%])	Unknown final diagnosis	0	0	40 (32.5)	40 (18.6)
	Catheter infection	52 (91.2)	29 (85.3)	3 (2.4)	84 (39.3)
	GI infection	1 (1.8)	0 (0.0)	8 (6.5)	9 (4.2)
	UTI	1 (1.8)	1 (2.9)	8 (6.5)	10 (4.7)
	RTI	0	0	5 (4.1)	5 (2.3)
	Uremia	3 (5.3)	4 (11.8)	54 (43.9)	61 (28.5)
	Catheter dysfunction or hemorrhage	0	0	3 (2.4)	3 (1.4)
	Uncontrolled Blood Sugar	0	0	2 (1.6)	2 (0.9)
Readmission (N [%])		14 (24.6)	9 (26.5)	13 (10.6)	36 (16.8)
Admission (N [%])	1	46 (80.7)	29 (85.3)	109 (88.6)	184 (86.0)
	2	9 (15.8)	4 (11.8)	12 (9.8)	25 (11.7)
	3-4	2 (3.6)	1 (2.9)	2 (1.6)	5 (2.4)
Admission duration (days) (Median [IQR])		5 [4-7]	6 [4-10]	4 [0-7]	5 [2-7]
Duration of placement(days) (Median [IQR])		36 [19-90]	68 [15-215]	0	0 [0-32]
Outcome of line (N [%])	No intervention	0	4 (11.8)	67 (54.5)	71 (33.2)
	Spontaneous exit	0	1 (2.9)	0	1 (0.5)
	Fistula establishment	1 (1.8)	0	13 (10.6)	14 (6.5)
	Catheter dysfunction	1 (1.8)	0	4 (3.3)	5 (2.3)
	Catheter infection resolved	28 (49.1)	19 (55.9)	6 (4.9)	53 (24.8)
	Renal transplant	1 (1.8)	0	0	1 (0.5)
	Renal recovery	0	0	5 (4.1)	5 (2.3)
	Replacement Shaldon	20 (35.1)	3 (8.8)	15 (12.2)	38 (17.8)
	Permanent CVC establishment	3 (5.3)	4 (11.8)	3 (2.4)	10 (4.7)
	After death	3 (5.3)	3 (8.8)	10 (8.1)	16 (7.5)

UTI: Urinary tract infection, GI: Gastrointestinal, RTI: Respiratory infection

e 3, the patients with clinical or laboratory evidence of another infection focus were classified into the non-infected catheter group, and two groups of "catheter infected" and "possible catheter infected" were identified as CVC-RI. Finally, demographic and underlying variables were compared between infected

and non - infected catheter groups. The mean age of patients in the infected catheter group was 59.3 years and in the non - infected catheter group was 59.9 years respectively (no significant differences between the two groups). Eleven (12.1%) of the infected catheters and four (3.3%) non - infected catheters were smokers and a significant difference was observed between the two study groups (p=0.012). Considering the comorbidities, hypertension and diabetes were observed in 160 (74.8%) and 111 (51.9%) patients respectively, and there was no significant difference between the two groups. The most common reasons for chronic renal failure were diabetes, and hypertension as the reason for renal failure was diabetes in 118 (55.1%) and hypertension in 50 (23.4%), respectively.

The differences in other demographic variables (gender, BMI, marital status, residency, and addiction), and underlying disease (cardiovascular, cerebrovascular, diabetes mellites (DM), hypertension (HTN), collagen vascular, and neoplasia) were not statically significant between two study groups. 133 (62.1%) of studied hospital admissions had Shaldon catheters that 49 hospital admissions (53.8%) had CVC-RI. Catheter infections were more common in patients with permanent hemodialysis catheters. Out of the infected catheters, 42 (46.2%) were found to be permanent CVC, while among the non-infected catheters, 39 (31.7%) were discovered to be permanent CVC. The statistical analysis revealed a significant difference between the two groups with p = 0.031. The difference in incidence of catheter infection between the three types of catheters was significant (P = 0.026) as the incidence was 40.2%, 26.6%, and 33.2% in femoral, subclavian and jugular catheters respectively. Insertion of the catheter in an emergent situation had a lower risk of infection, as 35 (38.5%) of the infected catheter were inserted in an emergent situation but in the non - infected group, 71 (57.7%) were emergent catheters (P = 0.005). 47 (51.6%) of infected catheter cases had a history of previous catheter insertion but only 39 (32.2%) non - infected group had a previous catheter (p=0.004).

A history of previous intravascular line, number of previous catheters, previous catheter infection history, and history of catheter replacement was significantly more prevalent in the infected catheter group (p=0.004, 0.006, 0.002, and 0.006, respectively). Consumption of antibiotics in the recent month was more prevalent in the infected catheter group. Among 91 infected catheters, 28 (30.8) had a recent history of antibiotic consumption, but among 123 non-infected catheters, only 15 (12.2%) had that history (p=0.001). In other characteristics, no significant difference was found between the two groups.

Microorganisms Cultivated

The majority of blood cultures had no bacterial growth after 5 days of cultivation. Of the positive blood cultures, the majority were gram - positive bacteria and skin flora (Table 4). Bacteria detected in contaminated cultures are excluded from the breakdown of bacterial growth.

Table 3. Comparison of demographic and main variables in study events (N = 214)

Variables		Infectious catheter (N = 91)	Non - infectious catheter (N = 123)	P-Value
Age (years)		59.3 ± 16.3	59.9 ± 17.5	0.828
Gender (female)		49 (53.8)	64 (52.0)	0.793
BMI		24.3 ± 4.5	24.8 ± 4.6	0.417
Marital status	Single Married divorced	6 (6.6) 82 (90.1) 3 (3.3)	8 (6.5) 111 (90.2) 4 (3.3)	0.999
Housing status (village)		9 (9.9)	18 (14.6)	0.301
Education (illiterate)		13 (14.3)	14 (11.4)	0.527
Smoking		11 (12.1)	4 (3.3)	0.012*
Inhalation Substance Abuse		3 (3.3)	5 (4.1)	1,000
Brain Vascular Disease		7 (7.7)	10 (8.1)	0.907
Heart disease - cardiovascular		28 (30.8)	37 (30.1)	0.914
Diabetes		43 (47.3)	68 (55.3)	0.245
Blood pressure		69 (75.8)	92 (74.0)	0.759
Collagen vascular disease		0 (0.0)	3 (2.4)	0.263

Variables		Infectious catheter (N = 91)	Non - infectious catheter (N = 123)	P-Value
Neoplastic disease		7 (7.7)	6 (4.9)	0.394
Cause of Kidney Failure	Diabetes	47 (51.6)	71 (57.7)	0.126
	blood pressure	27 (29.7)	23 (18.7)	
	Vascular disease	0 (0.0)	1 (0.8)	
	UTI	11 (12.1)	8 (6.5)	
	GN	2 (2.2)	4 (3.3)	
	ADPKD	1 (1.1)	4 (3.3)	
	AKI	3 (3.3)	12 (9.8)	
Type of catheter	Shaldon	49 (53.8)	84 (68.3)	0.031*
	Permanent CVC	42 (46.2)	39 (31.7)	
CVC location	Femoral	29 (31.9)	57 (46.3)	0.026*
	Subclavian	23 (25.3)	34 (27.6)	
	Jugular	39 (42.9)	32 (26.0)	
Catheter inserter	General surgeon	3 (3.3)	4 (3.3)	0.118
	Vascular Surgeon	43 (47.3)	41 (33.3)	
	Emergency medicine specialist	1 (1.1)	6 (4.9)	
	Resident of Surgery	44 (48.4)	72 (58.5)	
Dialysis weekly		2.9 ± 0.3	2.9 ± 0.4	0.630
Emergency catheter		35 (38.5)	71 (57.7)	0.005
Catheter age		112.4 ± 160.8	75.4 ± 134.2	0.071
Previous catheter		47 (51.6)	39 (32.2)	0.004*
Previous intravascular line	None	36 (39.6)	75 (61.0)	0.004*
	Shaldon	38 (41.8)	34 (27.6)	
	Permanent CVC	7 (7.7)	4 (3.3)	
Previous catheter duration		41.6 ± 120.9	26.7 ± 81.2	0.301
Number of previous catheters		1.4 ± 2.1	0.6 ± 1.3	0.006*
Previous catheter infection history		29 (31.9)	17 (13.9)	0.002*
Recent admissions		33 (37.1)	37 (30.1)	0.285
Number of previous admissions		0.6 ± 1.4	0.7 ± 1.7	0.762
Recent antibiotic use		28 (30.8)	15 (12.2)	0.001*

Data as mean ± SD For quantitative variables or numbers (percentages) are presented for bilateral variables. BMI: Body mass index, DM: Diabetes mellitus, HTN: Hypertension, UTI: Urinary tract infection, GN: Glomerulonephritis, ADPKD: Autosomal dominant polycystic kidney disease, AKI: Acute kidney injury, CVC: Central venous catheter, GI: Gastrointestinal, RTI: Respiratory infection.

Table 4. Frequency distribution of microorganisms in patients based on cultures (N = 91)

Gram-positive	Catheter - drawn blood cultures	Venipuncture blood cultures	Catheter - tip culture
	Number (%)	Number (%)	Number (%)
Staphylococcus aureus	21 (41.2)	9 (33.3)	8 (40.0)
Staph epidermidis	10 (19.6)	7 (25.9)	2 (10.0)
Enterococcus spp.	8 (15.7)	3 (10.7)	2 (10.0)
Gram - negative			
Escherichia coli	5 (9.8)	3 (11.1)	3 (15.0)
Pseudomonas aeruginosa	3 (5.9)	3 (11.1)	0
Acinetobacter baumanni	3 (5.9)	1 (3.7)	2 (10.0)
Other gram negatives	1 (2.0)	2 (7.4)	3 (15.0)
Total	51	27	20

Discussion

To the authors' knowledge, this is the second study to obtain data on CVC-RI in HD in Iran (12). Our results documented a high frequency for CVC-RI. Of these hospitalizations, 57 (26.6%) were diagnosed as definite CVC infection and 34 hospital admissions (15.9%) as possible CVC infection. Our study findings revealed a high prevalence of CVC-RI among patients on hemodialysis. This is consistent with previous literature reporting similar infection rates in this patient population (13, 14). The percentage is higher in our study than that found by Nabi (15) et al and Thompson et al (16). Overall, vascular access infection accounts for nearly 28% of all infections affecting ESRD hospitalizations (17). Other studies demonstrated CVC-RI are among the most serious complications of chronic HD and these individuals are especially vulnerable to these infections because of immunosuppression and frequent puncture of their vascular access site (18). Also, sepsis is a potentially preventable cause of mortality in HD population, and a significant percentage is vascular access related (19). In the US, from 2003 to 2013 the hospitalization rate for vascular access infections declined in patients on HD. However, there was a simultaneous rise in the rate of hospitalization for bacteremia / sepsis in these patients (20). One explanation may be a change in the frequency of coding from the diagnosis "vascular-access infection" to an increase in the use of the code "bacteremia."

The results of the study showed that the incidence of infection was not significantly different between different age groups, and BMI. There was no significant relationship between catheter - related infection, gender, occupational status, marital status, education, underlying disease, etiology of kidney failure, and incidence. In the analysis of variables such as catheter type, catheter placement, emergency catheter placement, previous catheter history, and previous catheter number, previous catheter infection history, catheter replacement, and antibiotic use in the last month were associated with an increased incidence of catheter - related infection. The previous studies dealt with diverse numerous risk factors related to catheter infections. According to the literature, the most frequent risk factors for CVC-RI in HD patients include, but are not limited to female gender, diabetes, urgent catheter placement, and previous hospitalization (6). Recent antibiotic use is reported as a risk factor for multidrug-resistant organisms colonization in patients undergoing HD (21).

In our study, we found that CVC-RIs were highest in the Jugular site, and the location of the CVC was a significant risk factor. Specifically, we observed that Subclavian CVCs had lower rates of CVC-RI compared to Jugular and femoral CVCs. The risk factors for BSI in permanent catheters include the duration of the catheter (22), past catheter-related bacteremia (23), and left-sided internal jugular vein catheters (24). Similar to our study, Merrer et al. demonstrated that among patients with catheters, the subclavian site (rather than a jugular or a femoral site) is associated with lower infection (25). In opposite to our study, Lemaire et al demonstrated that jugular venous access reduces the risk of infection as compared with femoral catheters (26).

In our study, infection of catheters was more common in patients without previous intravascular lines than in other patients. Important issues that cannot be overemphasized are the education of ESRD patients who previously had no intravascular line. Proper hygiene after insertion of the catheter is essential for the prevention of CVC-RI. Another explanation of this finding is partial natural immunity, because primary infection provides partial immunity to early reinfection. Vaccines can certainly confer partial immunity against S. aureus bacteremia in patients on HD, after which protection wanes as antibody levels decrease (27, 28). An old study by Johanovsky showed that mild staphylococcal infection in rabbits produced both "partial immunity" as evidenced by increased bactericidal activity of leukocytes and increased clearing of injected staphylococci from blood and organs, as well as a state of cutaneous and systemic hypersensitivity which was associated with lowered resistance to staphylococcal reinfection (29).

The pathogenesis of infections associated with catheters among patients on HD is similar to that among other patient groups. Resident skin flora can be introduced at the time of catheter insertion at the insertion / exit site. These organisms can colonize the catheter tip or contaminate the hub and enter the lumen of the catheter. S. aureus, adheres to catheters promoted by host proteins coating the catheter (30, 31). In addition, extrinsically contaminated infusates can

lead to catheter-associated infections. Once intraluminal, organisms can be embedded in a biofilm or disseminated over the catheter surface (22). Also, catheters can cause mural thrombus in the vein; a characteristic noted to predispose to catheter colonization and infection (32).

Staphylococcus aureus (*S. aureus*) was the most common causative organism in our study, which is comparable to most reports (13-15, 26). The recent National Healthcare Safety Network report on ARBSI associated with in-center HD highlights the continued dominance of *S. aureus* (33). *S. aureus* is known to cause high morbidity, mortality, and hospitalization along with secondary metastatic infections such as endocarditis, osteomyelitis, septic arthritis, epidural abscess, and cross - infection of implantable cardiac devices and other intravascular devices (32). In patients on HD, the risk of death within 15 days of infection, or hospitalization for treatment of infection, is > 8 times higher in *S. aureus*-BSI than in BSI with other organisms (34). Although the most frequent etiological culprits of infections are gram-positive microorganisms, bacteremia can be caused by gram-negative microorganisms as well (6, 33).

Our study has several limitations. First, the number of catheter tip cultures was small because removing the HD catheter solely for diagnostic purposes is impractical, places patients at unnecessary risks associated with catheter intervention, and leaves the patient without access to dialysis. Secondly, peripheral venipuncture was often not possible, impractical, or purposefully avoided to preserve veins for future arteriovenous access creation. Finally, we did not do a survival analysis of catheters with duration use.

Conclusion

Based on the findings of this study, the incidence of CVC-related infection was high in our patients on hemodialysis. Smokings, CVC location, number of previous catheters, presence of previous infection history, and antibiotic use in one recent month were risk factors related to infection in the patients on HD. Education of ESRD patients who previously had no intravascular line on proper hygiene of inserted catheter seems to be essential for the prevention of CVC-RI. *S. aureus* must be taken into account for empirical therapy.

Acknowledgments

We would like to express our gratitude to Ali Sohrabi, Chief of the Microbiology Laboratory at BouAli Sina Hospital, for his assistance in collecting blood samples and conducting the cultures during our study.

Conflict of Interest

The authors declare no conflicts of interest.

Funding/Support

This research received no external funding.

Ethics

The authors have observed ethical considerations in informed consent, double publication and / or submission and redundancy, plagiarism, misconduct, data fabrication, and / or falsification. The study protocol was approved by the medical ethics committee of Qazvin University of Medical Sciences (Approval ID: IR.QUMS.REC.1396.6).

Authors' contributions

HN and AK conceived and designed the study. AA and BB performed the statistical analyses. AA, BB, and LA drafted the manuscript. HN, AK, AA, and BB made substantial contributions to the interpretation of the results and the development of the manuscript. All authors were involved in revising it for important intellectual content and approving the final version.

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