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Original article

Bacterial pattern of hemodialysis central catheter associated infections in end stage renal disease patients in North Eastern Egypt

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ABSTRACT

Background: Hemodialysis-catheter associated infections are a crucial problem for hemodialysis patients in the inpatient and outpatient venues. So, our aim was to identify bacterial pattern of hemodialysis central catheter associated infection (HD-CAI) and study the risk factors in developing HD-CAI in end stage renal disease (ESRD) patients admitted and followed in the Clinical Nephrology unit, Suez Canal University Hospital, Ismailia, Egypt. **Methods:** The study was a cross sectional descriptive study that was conducted on 62 patients who admitted and followed in the Clinical Nephrology unit, Suez Canal University Hospital, Ismailia, Egypt. From each patient with evidence of Catheter Related Infections (CRI), three specimens (swabs, catheter tips and blood cultures) were aseptically collected and processed in the Microbiology Department. Isolated colonies from catheter tip culture and blood culture were identified by colony morphology, Gram staining and biochemical tests. The antibiotic susceptibility testing was performed using disc diffusion method outlined by Clinical and Laboratory Standard Institute depending on the isolated organism**. Results:** The prevalence of HD-CAI was 14.5%. It was found that 88.9% of the study participants who developed HD-CAI did not use skin antiseptics. Also the Gram positive bacteria represented 88.9% of the isolated organisms, comprised mainly of *S.epidermidis)* representing 55.6%, followed by *S .aureus* in 33.3%. While, Gram negative bacteria were recovered from 11.1% of the isolated organisms. All isolates of *S. epidermidis* and *S. aureus* were sensitive to amoxicillin (100%) & linezolid (100%), while *S. epidermidis* showed resistance to cefoxitin (80%). **Conclusion:** The frequency of HD-CAI was 14.5%. Gram positive bacteria represented 88.9% of the isolated organisms, comprised mainly of *S.epidermidis* (55.6%), and followed by *S .aureus* (33.3%).

Introduction

Catheter-associated blood stream infections (CABSI) are known as the presence of bacteremia arising from an intravascular catheter. It is one of the most frequent, serious and costly complications related to central venous catheterization. It represents the most common cause of nosocomial bacteraemia. There are many microbial causes of CABSI. However, certain organisms as staphylococci and candida can secrete a biofilm layer giving them protection and resistance against antimicrobial agents [1].

Hemodialysis-catheter associated bloodstream infections (HD-CABSI) are a serious problem for hemodialysis patients in the inpatient and outpatient compartments. Morbidity burden includes admission, line exchange, damage to the site of

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insertion, discomfort, temporary access, antibiotics side effects, infection complications including potential mortality, damage to access sites, inadequate dialysis with complications of uremia, acid/base imbalance, electrolyte abnormalities, volume overload, etc. Expense burden includes prolonged hospital stay, financial and human resources needed to replace lines, drug acquisition costs, etc [2].

Risk factors for CABSI include factors related to patient-, catheter-, and doctor. Patient-related factors include severity of illness, leucopenia, impaired integrity of the skin, and presence of distant infection. Catheter type influences risk of bloodstream infection and risk of bacteremia increases for each catheter type with increasing lumen number. Antiseptic or antimicrobial coating of catheters is reported to reduce risk of CABSI. For non-tunneled catheters, risk of bloodstream infection differs according to the site of insertion such that risk is greatest for groin insertion, intermediate for neck venous catheter insertion, and lowest for chest or upper extremity venous catheter insertion. Risk of CABSI increases after breaks in aseptic technique during placement and maintenance and with increases in the frequency of catheter access [3,4].

Catheter- related infection (CRI) prevention depends on evidence-based measures. The most effective measures are hand hygiene before catheter insertion and maintenance, full-barrier precautions during insertion, 2% alcoholic chlorhexidine usage in skin preparation, groin catheterization avoidance whenever possible and prompt removal of useless lines. The use of care protocols and the training of the workers in the field must be considered. Implementation of these bundled measures shown in high-quality studies to reduce CABSI incidence by 50% [5].

Patients and Methods

This cross-sectional descriptive study was performed over 62 adult patients with end stage renal disease (ESRD) admitted for central catheter insertion in HD unit. The consent was obtained from all patients included in the study. The study aimed to identify bacterial pattern of hemodialysis central catheter associated infection (HD-CAI) and study the risk factors in developing HD-CAI in HD-CAI in ESRD patients admitted and followed in the Clinical Nephrology unit, Suez Canal University Hospital, Ismailia, Egypt. All patients admitted for central catheter insertion were followed up over 1 month.

Definitions

According to (CDC 2016) recommendations, central line-associated blood stream infections (CLABSI) is defined as a laboratory-confirmed bloodstream infection (LCBI) where central line was in place for more than two calendar days on the date of event. The day of device placement considered being day one supported by the fact that the line secured in place on the date of event or the day before. laboratory-confirmed bloodstream infection was identified if a pathogen was isolated from one or more blood specimens and the organism identified is not related to infections at another site (LCBI-1). Or if the patient had at least one of these signs or symptoms; fever (>38.0^{o}C), chills, or hypotension, and the organism identified in blood was not related to infections at sites and the same common commensal is identified from two or more blood specimens drawn on separate occasions (LCBI-2) [6,7]. laboratory-confirmed bloodstream infection which is not related to the central line was excluded from the study.

Collection and processing of specimens [8]:

From each patient with evidence of CRI, three specimens (swabs, catheter tips and blood cultures) were aseptically collected to make sure that the blood stream infection is related to the catheter. Samples were processed in the Microbiology Department, Faculty of Medicine, Suez Canal University for the isolation and identification of the causative microorganisms.

Swab specimens were aseptically collected from exudate presented at the exit site or deeper in tunnel infections. Semi-quantitative culture technique was performed by rolling 5 cm segment from removed catheter four times across a blood agar plate with firm downward pressure. Cultures yielded 15 or more colonies were considered significant, potentially indicating a CRI.

Blood samples were collected, whenever possible, before starting antimicrobial treatment. Five ml of blood were withdrawn under aseptic conditions. Blood was added to culture bottle and incubated at 37°C and examined daily (up to 10 days) for evidences of growth. Subculture of blood culture broth was performed on blood agar and MacConkey's agar aerobically at 37°C [9]. Confirmation of HD-CAI was done according to the clinical diagnosis (signs and symptoms) and culture results from catheter tips and blood culture.

Microorganism identification

Isolated colonies from catheter tip culture and blood culture were identified by colony morphology, Gram staining and biochemical tests. For Gram positive bacteria, catalase, coagulase and mannitol fermentation tests were done. While Gram negative bacteria identified by indole production, Voges-Proskauer, citrate, motility, lysine decarboxylase, oxidase, sugar fermentation, urease, gas production, H2S production tests [10].

Antibiotic susceptibility testing

The antibiotic susceptibility testing was performed using disc diffusion method outlined by Clinical and Laboratory Standard Institute depending on the isolated organism [11].

Data management

The data obtained from the records were coded and these codes were entered into computer through Microsoft Excel software. The final study results were stated using the SPSS (statistical package for social sciences) version 18 and data was presented in tables and graphs. Data was compared by using Chi-square test for qualitative variables while independent t-test was used for quantitative variables. Statistical significance was considered at *P-value <0.05* and highly significance at *P-value <0.01*.

Results

This study included 62 adult patients known to have ESRD depending on regular hemodialysis of both sexes. The mean age ±SD of patients was 50.2±13.3 years with 53.2% of them were males (33 patients) as shown in **table (1)**.

Table 1. Basic data of the studied subjects.

		Frequency n=62	**Percent**
Gender	Male	33	53.2
	Female	29	46.8
	Total	62	100.0
Age (years)			
Mean ±SD		50.2±13.3	
Range		20-80	

The frequency of HD-CAI was 14.5% (9 patients) as shown in **figure (1)**.

The majority of patients developed exit infection followed by tunnel infection representing 44.4% and 11.1% respectively as shown in **figure (2)**.

Staphylococcus epidermidis was the most common isolated organisms accounts for 55.6% of cases (n=5\9) followed by *S. aureus* and *pseudomonas aeruginosa* representing 33.3% (n=3\9) and 11.1% (n=1\9) respectively as shown in **figure (3)**.

Figure 1. Frequency of infection among the study participants.

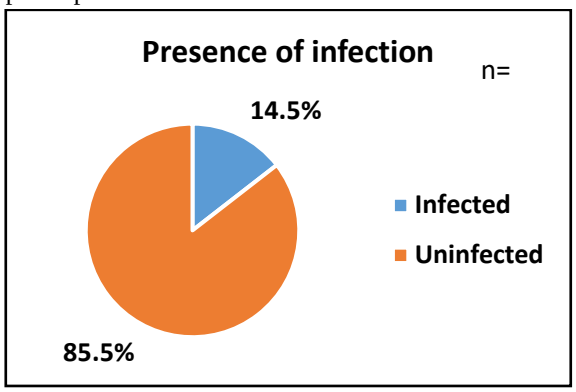


Figure 2. Type of infections detected among the study participants.

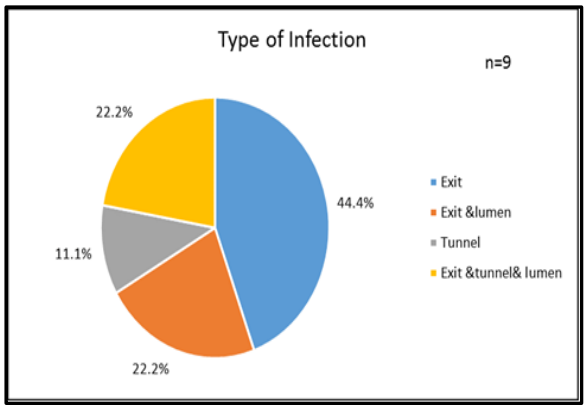
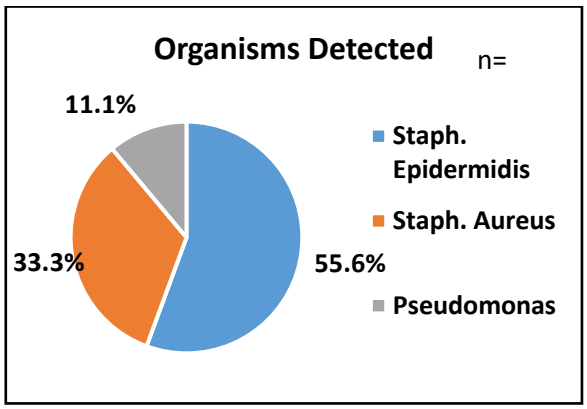


Figure 3. Organisms detected by cultures from infection sites.



All isolates of *S. epidermidis* were sensitive to amoxicillin (100%) & linezolid (100), while showed resistance to cefoxitin (80%). All isolates of *S. aureus* were sensitive to amoxicillin (100%) & linezolid (100). Gram negative organisms were sensitive to quinolones and trimethoprim/sulfamethoxazole, while showed

resistance to amoxicillin, linezolid and cefoxitin **(Table 2)**.

The mean age of patients who developed HD-CAI (no= 9 patients) was 45.4 years, 22.2% of them were males, while 77.8% were females. Most of them (44.4%) had mixed chronic illnesses (4 cases) followed by hypertension (3 cases), ischemic heart diseases (1 case) and chronic obstructive pulmonary diseases (1 case) (33.3%, 11.1% and 11.1% respectively) (*p= 0.37*).

In this study, we found a significant relation between the use of skin antiseptics and the development of HD-CAI. Meanwhile, 88.9 % of the studied participants who developed HD-CAI did not use proper skin antiseptics while 67.9% of the study participants who did not develop HD-CAI used skin antiseptics (*p= 0.002*) as shown in **table (3)**.

The results showed that in patients with HD-CAI, 44.4% had mixed chronic illness, 33.3% had isolated HTN and11.1% had isolated IHD & isolated COPD as shown in **table (4).**

Table 2. Results of antimicrobial susceptibility testing for the isolated organism.

	S. epidermidis **(n=5)**				***S. aureus*** **(n=3)**			
	Sensitive		Resistant		Sensitive		Resistant	
	N	%	N	%	N	%	N	%
Amoxicillin	5	100	0	0	3	100	0	0
Cefotaxime	4	80	1	20	0	0	3	100
Linezolid	5	100	0	0	3	100	0	0
Ciprofloxacin	4	80	1	20	0	0	3	100
Trimethoprim/Sulfamethoxazole	4	80	1	20	1	25	2	75
Clindamycin	3	60	2	40	0	0	3	100
Cefoxitin	1	20	4	80	1	25	2	75
Erythromycin	3	60	2	40	0	0	3	100

Table 3. Relation between the use of skin antiseptics and occurrence of infection.

			Infection		
			Infected	**Uninfected**	**Total**
Usage of local skin antiseptics	Use of skin antiseptics	number	1	36	37
		% within column	11.1%	67.9%	59.7%
	No use of skin antiseptics	number	8	17	25
		% within column	88.9%	32.1%	40.3%
Total		number	9	53	62
		% within column	100.0%	100.0%	100.0%

Table 4. Relation between occurrence of infection and chronic illnesses.

			Infection		
			Present	**Absent**	**Total**
Chronic illness	DM	number	0	13	13
		% within column	0.0%	24.5%	20.9%
	HTN	number	3	9	12
		% within column	33.3%	17.0%	19.3%
	COPD	number	1	2	3
		% within column	11.1%	3.8%	4.8%
	IHD	number	1	4	5
		% within column	11.1%	7.5%	8 %
	Mixed	number	4	25	29
		% within column	44.4%	47.2%	46.7%
Total		number	9	53	62
		% within column	100.0%	100.0%	100.0%

Discussion

This study was performed as a prospective descriptive study aiming at improving the outcome of patients who develop HD-CAI and improving anti-microbial prescription in HD-CAI in ESRD patients admitted and followed in the Clinical Nephrology unit, Internal medicine, Suez Canal University Hospital.

The total number of patients in this study was 62 patients. In our study the mean age of the patients with HD-CAI was 45.4 year & 22.2% of them were males while 77.8% were females.

The frequency of HD-CAI was 14.5%. In the study done by **Leou and his colleagues**, the frequency of hemodialysis-catheter associated infection was 17.4% [12]. Our results more in agreement with another cohort study done in a large patient population in a United States-based health care claims database after central venous catheter placement. Catheter-related complications occurred mostly during the first 90 days after catheter insertion. Incidence rate was highest for CABSIs and it was 5.1 [13].

A retrospective cohort study on haemodialysis patients (emergency-only hemodialysis) were done in Texas reported a high CRBSI with a rate of 0.84 infections per 1000 catheter-days with increased morbidity and mortality [14].

The study results are less in agreement with a study done in a hemodialysis unit in southeastern Brazil. It presented data from prospective surveillance carried out from March 2010 through May 2012. It revealed that the overall incidence of BSI was 1.12 per 1000 access-days. The rate was higher for patients performing dialysis through CVC [15].

There were a total of 109,929 catheter days of follow-up in the study period. 20% of patients had temporary percutaneous catheters, while 80% had permanent tunneled catheters. There were 40 episodes of CRBSI of which 20 occurred in those with temporary catheters and 20 in those with permanent catheters. The overall CRBSI rate was 0.36/1000 catheter days [16].

Also our study showed that in patients with HD-CAI, 44.4% had combined chronic illness, 33.3% had isolated hypertension & 11.1% had isolated ischemic heart diseases & 11.1% had isolated chronic obstructive pulmonary diseases. Review of literatures revealed that People with the previous co-morbid conditions are at a higher risk of developing HD-CAI. On the other hand, in 2017, **Thompson and his colleagues** reported that only liver disease was independently associated with CRBSI (RR 2.11; 95% CI 1.15, 3.86) [17].

In this study, the Gram positive bacteria represented 88.9% of the isolated organisms, comprised mainly of *S.epidermidis* representing 55.6%, followed by *S .aureus* in 33.3% . Similarly, Gram negative bacteria were recovered from 11.1%

of the isolated organisms. These results are in agreement with the results obtained from another prospective study done in four medical centers and Spanish dialysis facilities revealed that CRBSI was caused by gram-positive coccus in 91.7% of the cases [18] .

In another recent study reported that the predominance of Gram positive organisms while most of the *S.aureus* isolates were methicillin sensitive while the vast majority of the CONS were methicillin resistant. The Gram negative isolates showed significantly less antimicrobial resistance as compared to Gram negative isolates [15]. At the same time, an Irish study reported 84% infections to be due to staphylococcus (61% CONS, 23% *S.aureus*), a study from Saudi Arabia reported 60% of infections due to Gram negative organisms [19,20]

These results are in agreement with those obtained by **Safdar & his colleagues** who reported that the four groups of microbes commonly cause CRBSI were CoNS spp., *S.aureus*, Candida spp, gram-negative bacteria [21]. *Staphylococcus epidermidis* was considered specifically a major concern for people with catheters or other surgical implants because it is known to cause biofilm that grows over these devices [22]. In our study, exit infection represented 44.4%, while tunnel infection represented 11.1% of the patients with HD-CAI.

In the present study, all isolates of staphylococci were sensitive to amoxicillin & linezolid. On the other hand 80% of *S. epidermidis* showed resistance to cefoxitin, and these results are in agreement with these obtained by **Hellmark colleagues** who reported that 58% of *S. epidermidis* was resistance to cefoxitin [23]. In another study, **Contreras & his colleagues** founded that 95 % of *S.epidermidis* isolates which cause blood stream infection was mecithillin-resistant *Staph.epidermidis* [24] .

Also in our study, *S. epidermidis* isolates showed resistance to doxycyclin (60%), erythromycin (40%), and gentamycin 80%. In study done by **Robert &his colleagues**, 43.7% of CoNS strains were resistant to erythromycin. 70.5% and 71.9% of the isolated strains were susceptible to clindamycin and trimethoprim/sulfamethoxazole respectively, these results were found to agree with our results [25].

Conclusion

The study showed that the frequency of HD-CAI was 14.5%. Gram positive bacteria represented 88.9% of the isolated organisms, comprised mainly of *S.epidermidis* (55.6%), and followed by *S .aureus* (33.3%). Also in this study, *S.epidermidis* isolates showed resistance to doxycycline (60%), erythromycin (40%), and gentamycin (80%).

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