Prevalence of Catheter Related Blood Stream Infection among Patients on Maintenance Hemodialysis, Causative Organism and Catheter Outcome

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ABSTRACT

Background: Hemodialysis (HD) patients are at risk of several causes of morbidity and mortality especially cardiovascular related complications and Infection. In patients on maintenance HD infection and sepsis are major hospitalization cause and the second most common cause of mortality. **Objective:** The aim of the current study is to investigate the incidence of catheter related blood stream infection among HD patients.

Patients and methods: A total of 161 patients on maintenance HD at Ain Shams University Hospital Dialysis Unit for at least 3 months prior to start of study, and followed up for 12 consecutive months.

Results: A total of 161 patients were included in our study; mean age was 55.2 (SD 17.1) years old, and mean follow up was 10.9 (SD 2.7) months. Patients were observed for 12 months on maintenance HD, 102 (63.4%) of the patients' vascular access was arteriovenous fistula and 59 (36.6%) patients with dialysis catheter (tunneled or non-tunneled catheter). Patients older than 65 years old were independently associated with increased risk of CRBSI relative risk 1.13 (95%CI: 1.57-2.24) [P-value <0.001]. Prolonged of catheter indwelling was independently associated with higher CRBSI relative risk in patients with >12 months catheter indwelling time relative risk 1.75 (95%CI: 1.0-2.0) [P-value <0.001]. Diabetes is independently associated with higher relative risk of CRBSI 1.94 (95%CI: 1.15-3.26) [P-value <0.001]. Most common causative organism was gram-positive bacteria (65) %, followed by gram-negative bacteria (35%). gram negative CRBSI is independently associated with higher risk of catheter loss compared to gram positive organisms' relative risk 5.18 (95%CI: 1.76-15.18) [P-value <0.001].

Conclusion: CRBSI is common among patients on maintenance hemodialysis maximizing prevention strategies and tailoring treatment approaches is vital for the reduction of rate of CRBSI and appropriate catheter management.

Keywords: Hemodialysis, Catheter related blood stream infection, Bacteremia.

INTRODUCTION

End stage renal disease (ESRD) is a major public health problem and a significant financial burden [1]. Hemodialysis (HD) patients are at risk of several causes of morbidity &mortality especially cardiovascular related complications and Infection. In HD patients' infection and sepsis are major hospitalization cause and the second most common cause of mortality [2,3].

The exact definition of catheter-related blood stream infection (CRBSI) lacks consistency. In 2018, the Kidney Health Initiative's Catheter End Points Workgroup was performed by a multidisciplinary group of experts to establish a standardized definition of catheter-related bloodstream infection (CRBSI) in HD patients. The definition criteria for CRBSI diagnoses in HD patients: 1) Clinically (temperature more than 37.5 C or rigors or new predialysis hypotension or altered mental status), 2) Bacteremia confirmation (the same organism growing in the blood cultures from the HD catheter and a peripheral vein or dialysis bloodline), and 3) exclusion of any alternate infection [4].

The accurate diagnosis of CRSBI in HD patients face challenges as peripheral blood cultures are not obtained either because an existing vein is preserved for arteriovenous fistula (AVF) creation or veins cannot be accessed. Symptomatic HD patients with fever usually will go the hospital and not to the HD facility with antibiotics prescribed without taking blood cultures. Catheter tips are not routinely sent for culture due to catheter salvage [5,6].

Bacteremia had a high incidence among HD patients using tunneled catheters as compared to those an arteriovenous fistula (AVF) or even with a graft (AVG). Tunneled catheter is associated with an 8-fold greater bacteremia risk compared to AVF. CRBSI, exit-site infection and tunnel infection or colonization are common central venous catheter complication in HD patients [7,8]. There are 1.1 to 5.5 occurrences of catheter-related bloodstream infection per 1000 catheter days, and these episodes are more likely to result in hospitalization, morbidity, and fatality [9].

Gram-positive bacteria, particularly Staphylococcus aureus and coagulase-negative staphylococci, account for 40% to 80% of CRBSIs whereas gram-negative organisms account for 20% to 40%, polymicrobial infections account for 10% to 20%, and fungal infections account for 5%. Endocarditis, septic pulmonary emboli, osteomyelitis, spinal epidural abscess, septic arthritis, and brain abscess are possible CRBSI complications [10].

Management of CRBSI depends on the catheter type and the infection severity. As soon as a diagnosis is made, empirical systemic antibiotics should be given until the results of the culture and sensitivity test are available [11]. Decision for catheter removal depends on infection severity and the organism involved. Whenever catheter salvage is attempted, a systemic antibiotic and an antibiotic lock should be provided [12].

The objective of the current study is to study the incidence of catheter related blood stream infection

among our cohort of patients on maintenance HD, causative organism factors influencing occurrence of catheter related blood stream infection and factors associated with catheter loss as outcome.

PATIENTS AND METHODS
A single center, retrospective, observational follow up study was conducted on 161 patients on maintenance HD at Ain Shams University Hospital dialysis unit for at least 3 months prior to start of study and followed up for 12 consecutive months. Data collected included age, gender, vascular access, diabetic status, and catheter dwell time, incidence of CRBSI, underlying organism and catheter outcome. Blood culture was taken from peripheral and central catheter upon suspicious. Catheter loss was defined as removing a catheter within two weeks of being diagnosed with CRBSI.

Inclusion crieteria:
- All patients age 18 years and above.
- Patients on maintenance Hemodialysis for at least 3 months.
- Patient followed up for 12 months.

Exclusion crieteria:
- Patient with missing data or failure of follow up.
- Patient with active or obvious source of infection other than CRBSI.
The definition criteria for CRBSI diagnoses in HD patients: 1) Clinically (temperature more than 37.5 C or rigors or new predialysis hypotension or altered mental status), 2) Bacteremia confirmation (the identical bacterium is present in blood cultures from a dialysis bloodstream and a peripheral vein), and 3) Excluding any additional infections [4].

Ethical consent:
An approval of the study was obtained from Ain Shams University Academic and Ethical Committee. After explaining our research objectives, written informed consent was obtained from all study participants. This study was conducted in compliance with the code of ethics of the world medical association (Declaration of Helsinki) for human subjects.

Statistical analysis
The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 26 for windows. Qualitative data were defined as numbers and percentages. Chi-Square test and Fisher's exact test were used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by Kolmogorov-Smirnov test.

Normal distribution of variables was described as means and SD, and independent sample t-test and ANOVA test were used for comparison between groups. Binary logistic Regression analysis to study the relative risk of occurrence of CRBSI and Catheter outcome among different study Variables to determine relative risk independent of confounders age, diabetes, catheter dwell time, underlying causative organism for both incidence of CRBSI and catheter loss as outcome. P value ≤0.05 was considered to be statistically significant.

RESULTS
A total of 161 patients were included in our study; mean age was 55.2 (SD 17.1) years old, and mean follow up was 10.9 (SD 2.7) months. We observed for 12 months 161 patients on maintenance HD, 102 (63.4%) of the patients vascular access was arteriovenous fistula and 59 (36.6%) patients with dialysis catheter (tunneled or non-tunneled catheter).
As shown in **Table 1**, we found statistically significant increase in incidence of CRBSI with advancement of age. **Table 1** shows among study groups showing significant higher risk for CRBSI associated with diabetes, prolonged catheter indwelling time and elder age group.

Table (1): Factors associated with increased risk of CRBSI.

Comparison groups		N (all patients)	Episode of CRBSI				CRBSI /100 patient dialysis month				P-value
			No		CRBSI		Mean	SE	Range	SD	
			N	%	N	%					
DM	Non-diabetic	72	63	87.5%	9	12.5%	0.51	0.16	4.73	1.36	0.003
	Diabetic	89	60	67.4%	29	32.6%	1.30	0.20	5.29	1.92	
Gender	Female	71	53	74.6%	18	25.4%	0.99	0.21	5.29	1.74	0.45
	Male	90	70	77.8%	20	22.2%	0.91	0.18	4.73	1.73	
Age	≤ 21 years old	6	6	100%	0	0.0%	0.00	0.00	0.00	0.00	0.008
	22-44 years old	33	28	84.8%	5	15.2%	0.61	0.26	4.73	1.49	
	45-64 years old	70	56	80%	14	20%	0.81	0.20	4.61	1.64	
	65-74 years old	37	27	73%	10	27%	1.03	0.29	5.29	1.75	
	≥ 75 years old	15	6	40%	9	60%	2.49	0.56	4.73	2.16	
Catheter duration	Less than 12 months	17	11	64.7%	6	35.3%	1.30	0.44	3.80	1.82	<0.001
	More than 12 months	42	10	23.8%	32	76.2%	3.11	0.28	5.29	1.83	

As illustrated in **Table 2**, a significant higher risk of CRBSI in diabetic patients (Mean 1.3, SD 1.92) than non-diabetic (Mean 0.51, SD 1.36) [P-value <0.003]. Our finding showed a significant higher risk of CRBSI in subjects had catheter indwelling >12 months (Mean 3.11, SD 1.83) compared with catheter indwelling <12 months (Mean 1.3, SD 1.82) [P-value <0.001]. **Table 2** shows significant higher risk for CRBSI associated with diabetes, prolonged catheter indwelling time and age ≥65 years old.

Table (2): Risk estimate for catheter related blood stream infection among study groups.

Risk estimate				P-value
Variable	RR	95% Confidence Interval		
		Lower	Upper	
Diabetic versus non diabetic	1.94	1.15	3.26	<0.001
female versus male	1.22	0.62	2.38	0.375
Catheter indwelling more than 12 months versus less than 12 month	1.75	1.08	2.81	<0.001
Age ≥ 65 years versus < 65 years old	1.13	1.57	2.24	<0.001

As illustrated in **Figure 1**, we found the most common causative organism was gram-positive bacteria (65%), followed by gram-negative bacteria (35%). We did not encounter fungal infection among our cohort during the 12 months follow up period. Coagulase negative Staphylococcus species were predominant in the gram-positive bacteria with 39%, Staphylococcus aureus (16%), Streptococcus (5%) and Enterococci (5%). The most common gram-negative bacterias were Pseudomonas aeruginosa (16%), followed by Escherichia coli (8%), Klebsiella pneumonia (5%) and Citrobacter (5%).
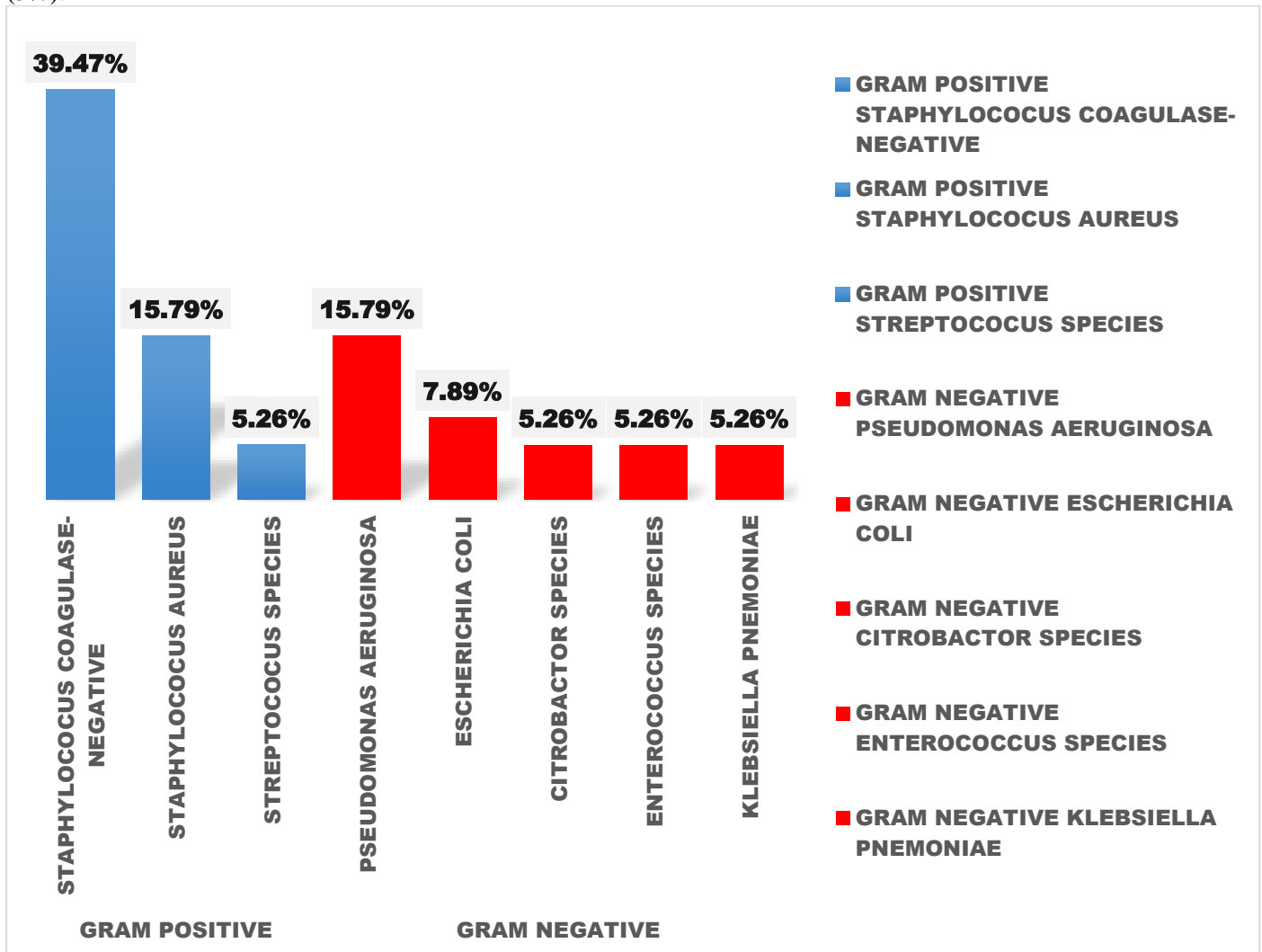

Figure (2): CRBSI causative organism showing predominant gram positive organisms 65% than gram negative 35%.

Table 3 shows significantly higher catheter loss with Gram negative Bacterial infection than Gram positive.

Table (3): Catheter outcome after CRBSI by underlying organism.

Variable		Catheter salvaged		Catheter removed		P-value
		N	%	N	%	
Gram stain	Gram negative	5	39.5%	8	61.5%	<0.001
	Gram positive	20	80%	5	20%	
Organism	Citrobactor species	1	50%	1	50%	0.005
	Enterococcus species	1	50%	1	50%	
	Escherichia coli	1	33.3%	2	66.7%	
	Klebsiella pnemoniae	1	50%	1	50%	
	Pseudomonas aeruginosa	2	33.3%	4	66.7%	
	Staphylococus aureus	6	100%	0	0.0%	
	Staphylococus coagulase-negative	11	73.3%	4	26.7%	
	Streptococus species	2	100%	0	0.0%	

Table 4 shows significantly higher catheter loss with Gram negative Bacterial infection than Gram positive.

Table (4): Risk estimate for catheter outcome after CRBSI episode.

Risk Estimate				
	Relative Risk	95% Confidence Interval		P-value
Organism: gram negative versus gram positive		Lower	Upper	
	5.182	1.768	15.185	<0.001

DISCUSSION

The aim of our retrospective cohort study was to investigate the prevalence of CRBSI among our patients on maintenance HD at Ain Shams University Hospital Dialysis Unit, causative organism factors influencing occurrence of catheter related blood stream infection and factors associated with catheter loss as outcome.

We observed for 12 months 161 patients on maintenance HD, 102 (63.4%) of the patients vascular access was arteriovenous fistula and 59 (36.6%) patients with dialysis catheter (tunneled or non-tunneled catheter). We found a significant increase risk of CRBSI in elder age group (>65 years old) in comparison to younger group (<65 years old) A meta-analysis of multiple studies showed 80% higher risk of primary AVF failure in elder age group (>65 years old). Age was associated with higher risk of CRBSI in some studies **Powe et al.** [13] while other studies **Sedlacek et al.** [14] did not report. Advanced age is a risk factor for primary AVF failure caused by atherosclerotic arteries and weak veins. Elder patients usually presented with multiple comorbidities and weak veins requiring dialysis catheter and are more dependent on others regarding catheter care [15].

Our finding showed a significant higher risk of CRBSI in subjects had catheter indwelling >12 months compared with catheter indwelling <12 months. The prolongation of catheterization was associated with RR 1.75 (95%CI: 1.0-2.0) [P-value <0.001]. This comes in accordance with published data reporting higher CRBSI with prolonged catheter dwelling time [16].

There was a significant higher risk of CRBSI in diabetic subjects than non-diabetic and this match with several studies **Jean et al.** [17], **Huifen et al.** [18] and **Jie et al.** [19] and this may be explained by that long term of hyperglycemia is associated with increased blood viscosity, abnormal cytokines, faster protein break down, reduced antibodies synthesis besides that hyperglycemia is a very good environment for bacteria reproduction and enhances bacteria virulence [20].

In our study, the most common causative organism was gram-positive bacteria, followed by gram-negative bacteria and fungi. Coagulase negative Staphylococcus aureus were predominant in the gram-positive bacteria with 39%, Staphylococcus aureus 16%, Streptococcus 5% and Enterococci 5%. The most common gram-negative bacteria were Pseudomonas aeruginosa 16% followed by Escherichia coli, Klebsiella and Citrobacter, which was consistent with the finding of **Dreesen et al.** [21] and **Tao et al.** [22]. However the distribution of the causal organism was slightly different from that reported by **Wisplinghoff et al.** [23], they imply that these potential regional disparities should be taken into account when choosing preventive and therapy.

We found catheter loss as outcome following CRBSI is higher among patients with gram negative organisms number of catheter lost (% of episodes caused by group) 8 (61.5%) than gram positive organisms 5 (20%), with P-value <0.001. In multivariate analysis gram negative CRBSI is independently associated with higher risk of catheter

loss compared to gram positive organisms RR 5.18 (95%CI: 1.76-15.18) P-value< 0.001, this come in agreement with recently published studies on the determinants of catheter outcome among patients on maintenance HD [24].

Limitations to our study were the lower number of patient cohort involved , short duration of follow up, we recommend large cohort of patients and longer follow up period of different patients cohort will help improving prevention, treatment and catheter salvage strategies.

CONCLUSION

CRBSI is common among patients on maintenance HD maximizing prevention strategies and tailoring treatment approaches is vital for the reduction of rate of CRBSI and appropriate catheter management. Older age, diabetes and prolonged catheter indwelling time are independent risk factors for CRBSI, gram positive infection predominates most of the cohorts and gram negative organisms associated with higher rate of loss of catheter.

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