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Research Article

INCIDENCE AND RISK FACTORS OF CENTRAL VENOUS CATHETER AND BLOOD STREAM BACTERIAL INFECTIONS IN HEMODIALYSIS PATIENTS: A CROSS SECTIONAL STUDY

Abdullah Khamees Jaudah[1] and Alaa Khattar Musa[2]

[1]*Al-Basra Specialized Renal center, Basrah College of Medicine, Basrah, Iraq .*

[2]*Department of Medicine, Basrah College of Medicine, Basrah, Iraq*

Abstract

Background: Central venous catheter remained the prevalent form for hemodialysis initiation in Iraq but associated with increased risk of infection specifically catheter-related bloodstream infection which is the major cause of morbidity and mortality among hemodialysis patients. **The Aim of the study:** Estimation of the incidence and predictors of the central venous catheter and bloodstream bacterial infection in hemodialysis patients, and the identification of the most common bacterial etiologies, and their antimicrobial susceptibility. **Materials and Methods:** A cross - sectional observational study, involving eighty end-stage renal disease patients on hemodialysis in the Dialysis Center of Basrah General Hospital Southern of Iraq, from March to September 2016. History, clinical examination and investigations were taken from the patients including catheter tip and blood culture, hemoglobin, serum albumin leukocyte count and random blood sugar. **Results:** 80 patients on hemodialysis, 45 % were male, 55 % were female, mean age was 54 years, 34 % were diabetics, 51 % had catheter tip infection, 25 % had catheter - related bloodstream infection, 59 % of cases with bloodstream infection were catheter-related, about 78 % of the males had catheter tip infection. Central venous catheter duration carries a sensitivity (78 %) and specificity (62 %) for catheter tip infection. Half of diabetic patients had catheter tip infection. The patients symptoms and local signs were present each in about (60 %) patients with catheter tip infection. Catheter infection with methicillin - resistant *Staphylococcus aureus* was a significant predictor for catheter - related blood stream infection. *Staphylococcus epidermidis* and *Staphylococcus aureus* were the most identified organisms in catheter tip infection and catheter - related blood stream infection respectively. **Conclusion:** The best significant predictors for the catheter tip infection are being a male, being diabetic, had a central venous catheter duration more than 20.5 days, with sign and symptoms of catheter - related infections. The main predictor for catheter-related blood stream infection is the catheter infection with methicillin - resistant *Staphylococcus aureus*. Severe anemia has a statistically weak yet significant association with catheter-related bloodstream infection.

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1. Introduction

Chronic kidney disease (CKD) is defined as the decreased glomerular filtration rate (GFR) to <60 ml/min/1.73 m^2 in the last three or more months, regardless of the cause (KDIGO, 2013). The latest updates of the Kidney Disease Improving Global Outcomes (KDIGO) use the

* *Corresponding author*: Abdullah Khamees Jaudah

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estimated glomerular filtration rate (eGFR) as a basis for classification from (Stage 1≥90 ml/min/1.73 m^2) as normal. In stage 2, eGFR is from 60 - 90 ml/min, in stage 3 is between 30 - 60 ml/min, in stage 4, 15-30 ml/min, and Stage 5 is less than 15 ml/min (Levey *et al*., 2003). Recently, there was an increased prevalence of end - stage renal disease (ESRD) worldwide with significant morbidity and mortality. The renal replacement therapy (RRT) is the treatment option at this stage and includes dialysis and transplantation (Hudson and Johnson, 2004).

Hemodialysis (HD) for ESRD may be achieved using an arterio venous fistula (AVF), graft (AVG) or central venous catheters (CVCs) which are either temporary (non-tunneled) catheters or long lasting (tunneled) catheter (Stevens and Levin, 2013). The AVF is the preferred vascular access for HD because of the reduced infections rate and improved delivery of adequate dialysis, unlike CVC that has lower patency rate, high infection rate, hospitalization and mortality mainly due to catheter - related bloodstream infection (CRBSI) (Vassalotti *et al*., 2012). Non - tunneled CVCs for HD primarily placed in internal jugular, sub-clavian or femoral vein, they are indicated for short-term HD access, and their use should be limited to less than three weeks; otherwise if we need it for more than three weeks, a tunneled catheter is the option (National Kidney Foundation, 2006; Allon and Work, 2007).

Temporary vascular access can be established using CVC in urgent HD for Bonfante *et al*. (2011): (i) Acute kidney injury (AKI), (ii) Patients with ESRD who require HD before maturation of their AVF or AVG, (iii) Patients experienced failures of their AVF and (iv) As a bridge to transplantation or peritoneal dialysis. Patients on HD suffer from impaired immunity, attributable to ESRD and the comorbid conditions such as diabetes mellitus (DM), malignancies, malnutrition especially in the elderly population, and disruption of skin barrier by HD. All these factors make them susceptible to infections, which are regarded now as the leading cause of morbidity and hospitalization and the second most frequent cause of mortality among RRT patients (Yoon *et al*., 2005; USRDS, 2013).

ESRD patients on HD are at risk for infections caused by nosocomial multidrug - resistant (MDR) bacteria showing decreased susceptibility to many antimicrobials, so the empirical administration of such antimicrobials may be inappropriate, increasing the morbidity, mortality, and health burden (Kollef, 2000). The use of culture especially when done using Minimum inhibitory concentration (MIC) helps determine which class of antibiotic is most effective, which lead to appropriate choice of an antibiotic leading to increase chances of treatment success and slow antibiotic resistance (Centre for Disease Control and Prevention, 2013). Dialysis - associated CRBSI can arise from one of two sources (Allon, 20147): (i) Migration from the skin along the outside of the catheter into the bloodstream and (ii) Direct inoculation from a biofilm containing pathogenic microorganisms that may form on the inner surface of the catheter.

The Aim of this Study

Estimation of the incidence and predictors of the central venous catheter and blood stream bacterial infection in hemodialysis patients, and the identification of the most common bacteria, and their antimicrobial susceptibility.

2. Materials and Methods

Study Design

A cross - sectional observational study, involving (80) ESRD patients on HD in the Dialysis Center of Basrah General Hospital Southern of Iraq, from March to September 2016.

Patients Selection

Initially, ninety - three patients gave consent for enrollment in the study. We excluded thirteen patients for different causes:

- Two patients had other than the jugular site for insertion.
- Seven patients were using antibiotic at the time of catheter removal for the last seven days.
- Four patients on immunosuppressive medication or steroids.

The remaining eighty patients were more than 18 years old, with their temporary CVC as a dialysis access, and without permanent vascular access i.e. AVF or AVG not present or mature at the time of the study. The causes for the catheter removal were:

- Catheter blockage.
- Suspected catheter infection by the presence of local signs of exit site infection or presence of fever and rigors.
- Change the temporary catheter to tunneled catheter, AVF or switch HD to peritoneal dialysis.
- Personal intention to quit the HD sessions.

The temporary HD catheter is the radiopaque polyurethane double lumen catheter (Gambro® Medical Technology Company, Germany). A detailed history and examination were recorded from all studied patients and classified accordingly to:

a) The patients age groups were: young age group < 45 years, middle-aged group between 45 - 65 years and elderly > 65 years old (National Council on Aging, 2002).
b) Symptoms of DM (American Diabetes Association, 2013) with a random value of the plasma glucose of 11.1 mmol/L, or a fasting plasma glucose of 7.0 mmol/L) or HbA1c > 6.5 % or Self - reported diabetes medication, or self - reported DM.

Data Registration

- The patients' files in the dialysis unit were the chief source of data for the current CVC status.
- According to the duration of catheter placement till removal, there were three groups of patients: (≤ 14 days, 15 - 21 days and >21 days).
- We examine the catheter exit site for local signs of infection (Safdar and Maki, 2002).
- Measurement of the temperature by a mercurial thermometer on axillary site. We considered the patient as feverish if the corrected axillary temperature was more than (37.8 °C), then we question the patient about any rigors.

Investigations

1. Under aseptic conditions, we remove the catheter, and cut about 4 cm segment from the catheter tip by a sterile scissor, then place it in a sterile container to be transported to the lab for a catheter tip culture (CTC) as early as possible to prevent dryness (Center for Disease Control and Prevention, 2015).
2. We used two cubital venous sites sampling for blood culture (BC) and sensitivity.
3. Confirmed catheter - related bloodstream infection (CRBSI) is the isolation of the same organism from the culture of the distal segment of the catheter, and from peripheral blood of a patient in the absence of any other noticeable source of infection (Horan *et al*., 2008).
4. In the lab, both catheter tips after special processing and blood sample were placed separately in a culture device (VITEK®2 system bio Mérieux).
5. Blood cultures as well as antibiotic sensitivity performed in the same device by minimum inhibitory concentration (MIC) using the Guidelines of Advanced Expert System (AES), Global Clinical and Laboratory Standards Institute (CLSI) (Advanced Expert System, 2016; National Committee for Clinical Laboratory Standards, 2016).
6. The MIC is the lowest concentration (mg/ml) of an antibiotic that inhibits the growth of a given strain of bacteria (Center for Disease Control and Prevention, 2013).
7. We draw another 4 - 5 ml blood samples for estimation of the Hemoglobin (Hb), Leukocytes Counts, and Serum Albumin. The results divide the cohort to: (i) Three groups according to their Hb level (WHO, 2011): those with severe < 8 g/dL, moderate 8 – 10.9 g/Dl, and mild anemia to Hb ≥ 11 g/dL, (ii) Two groups according to the leukocytes count (Steven *et al*., 2015): those with normal leukocyte count 4 – 11 × 10^9/L, and leukocytosis > 11 × 10^9/L of note, there

was no patients with leukocyte count < 4 × 10^9/L, (iii) Three categories according to the albumin level (Daniel Pratt, 2015): those with normal serum albumin ≥ 3.5 g/dL, mild hypoalbuminemia 3 - 3.49 g/dL and moderate to severe hypoalbuminemia < 3 g/dL.

Statistical Analyses

Data are tested using IBM SPSS statistical software version 22.0 for Windows (SPSS Incorporation, Chicago, Illinois, USA) with many continuous and categorical variables:

- The (Mean value ± SD) for the description of the continuous variables.
- The (Frequencies and Percentages) for the description of the categorical variables.
- Chi-Square Test X^2 is used to test and compare the categorical variables.
- The General Linear Model Univariate Analyses were executed to check the variables for any significant association.
- The use of Binary Logistic Regression Analysis for the independent variables to show the Odd Ratio (OR) i.e. Exp (B), and 95 % confidence intervals (C.I.).
- The use of the Receiver Operating Characteristic Curves (ROC) to compare the predictive value of the different predictors, the area under the curve (AUC), and the cutoff values of the binary variables, with both the sensitivity and the specificity.
- The study adopts the two-tailed probability values with ($p \leq 0.05$) to be statistically significant.

3. Results and Discussion

A cross - sectional study involved eighty patients with ESRD on HD *via* temporary double lumen CVC with 41 patients had Catheter - Tip Infection (CTI), half of them were additionally had CRBSI afterward Patients with blood stream infection (BSI) were 34, from them the majority 20 (59 %) are CRBSI comprising quarter of the cases in the study and the rest of blood stream infection 14 (41%) were not associated with catheter infection.

The cohort included 36 (45 %) males, with a male to female ratio of 8:10. About 78 % of the males had CTI compared to only 30 % of the opposite sex that was proved to be a statistically significant predictor for CTC positivity in HD patients in univariate and binary logistic regression. On the other hand, there were 33 % of males had CRBSI, compared to only 18 % of the opposite sex. Sex cannot be considered as a predictor for CRBSI because it lacked the significance.

About half of our cohort is middle aged, and the other half is distributed equally among the young and old age group, with a mean age (54±13 years). Age groups had no association to the CTI. Although, the middle age group was found to associate significantly with the CRBSI, it cannot be heightened to be a predictor for the CRBSI as it lacks the significance in the regression analysis. Even though, we have nine cases out of total CRBSI cases are in the elderly. On catheter removal, the mean CVC duration was (25.26 ± 15.55 days), half of the patients had CVC duration >21 days, 19 (24 %) with ≤ 14 days, 21 (26 %) with (15 - 21 days). The duration was a powerful and significant predictor for the CTC positivity but not the CRBSI, carrying a good sensitivity (78 %) and fair specificity (62 %) with a cut - point of (20.5 days), using the univariate, regression, and the ROC curves.

Diabetes mellitus is another powerful and significant predictor for the CTC but not the CRBSI. About 34 % of our patients were diabetics; half of them are CTC positive compared to about a quarter of them that had CRBSI. The mean value of serum albumin was 3.2 ± 0.5 g/dL. There were fourteen patients had moderate to severe hypoalbuminemia. About 70 % of them are CTC positive, compared to about 31 % of patients with normal albumin. There were only five patients with moderate to severe hypoalbuminemia and positive CRBSI compared to a similar number with normal albumin. The level of serum albumin whether low, normal or borderline has a relationship to neither the CTC nor the CRBSI.

Half of the patients had Hb level (8-10.9 g/dl), 34 (42 %) had Hb level <8 g/dl and the minority 6 (8 %) had Hb level ≥11g/dL with a mean Hb level of (8.3 ±1.8 g/dl). More than half

of our severely anemic patients (18 out of 34 patients) are CTC positive, compared to only 2 out of 6 patients in the mildly anemic or normal Hb level patients. It appeared that the severe anemia below 8 g/dl has a statistically weak yet significant relation to the CRBSI but not the CTC with the cut-off value of 7.7 g/dl with a sensitivity of only 50 % and a specificity of 64 %. This was evident by the use of ROC curve that fail to reach the value of the predictability of the CRBSI. The mean leukocytes count was (9.1 $\times 10^9$/L ± 4.5 $\times 10^9$/L). All the patients who had their leukocytes count >11 cells $\times 10^9$/L had CTI, and half of them had CRBSI, but this relation did not reach the level of significance in CTC nor CRBSI group.

The patients' symptoms i.e. fever and rigor was a powerful predictor that had a significant relation to the CTC positivity after adjustment for other confounders in univariate and regression analysis, but no such relation to the CRBSI. There were 34 patients with this symptomatology, 25 (74 %) of them had CTI initially. And then, about half of the patients with fever and rigor have CRBSI. The patients local signs of the catheter exit site were a powerful predictor that had a significant relation to the CTC positivity after adjustment for other confounders in univariate and regression analysis, but no such relation to the CRBSI. Local signs of exit site infection were evident in 32 patients of whom 75 % were CTC positive initially. And then about half of them were proved to be CRBSI positive.

Catheter infection with Methicillin - resistant *Staphylococcus aureus* (MRSA) strain when compared to other bacterial pathogens that were encountered in our cohort was a powerful and a significant predictor for CRBSI. There were only 10 patients whom catheters were infected with MRSA, eight of them had CRBSI. All *Staphylococcus aureus* bacteria isolated in our cohort were methicillin resistant. In addition to MRSA, we encountered another seven bacterial pathogens that carried no association of statistical significance. There were seven pathogens in the CTC; *Staphylococcus epidermidis* (44 %), *Staphylococcus aureus* (24 %), *Pseudomonas aeruginosa* and *Staphylococcus hemolyticus* (10 % each), *Escherichia coli* and *Klebsiella pneumoniae* (5 % each), and the *Enterobacter* sp. in 2 % of cases. On the other hand, there were only four bacterial pathogens that caused CRBSI; MRSA (40 %), *Staphylococcus epidermidis* (30 %), *Pseudomonas aeruginosa* (2 0%), and *Staphylococcus hemolyticus* (10 %).

Table - 1: Incidence of Positive CTC with the Specific Patients Demographic Characteristics and Variables

Variables		CTC N (%)		Total (%)
		Positive (N = 41)	Negative (N = 39)	
Age (years)	<45	12 (54.5 %)	10 (45.5 %)	22 (28 %)
	45-64	15 (41.7 %)	21(58.3 %)	36 (45 %)
	≥65	14 (63.6 %)	8 (36.4 %)	22 (28 %)
Gender	Male	28 (77.8 %)	8 (22.2 %)	36 (45 %)
	Female	13 (29.5 %)	31 (70.5 %)	44 (55 %)
CVC Duration (days)	≤ 14	5 (26.3 %)	14 (73.7 %)	19 (24 %)
	15-21	8 (38.1 %)	13 (61.9 %)	21 (26 %)
	> 21	28 (70 %)	12 (30 %)	40 (50 %)
Diabetes Mellitus	Yes	13 (48.1 %)	14 (51.9 %)	27 (34 %)
	No	28 (52.8 %)	25 (47.2 %)	53 (66 %)
Albumin (g/dL)	< 3	10 (71.4 %)	4(28.6 %)	14 (18 %)
	3-3.49	22 (59.5 %)	15 (40.5 %)	37 (46 %)
	≥ 3.5	9 (31 %)	20 (69 %)	29 (36 %)
Hb (g/dL)	< 8	18 (52.9 %)	16 (47.1 %)	34 (42 %)
	8-10.9	21 (52.5 %)	19 (47.5 %)	40 (50 %)
	≥ 11	2 (33.3 %)	4 (66.7 %)	6 (8 %)
Leukocyte Count (cell×10^9/L)	4-11	28 (41.8 %)	39 (58.2 %)	67 (84 %)
	> 11	13 (100 %)	0 (0 %)	13 (16 %)
Fever and Rigors	Yes	25 (61 %)	9 (23 %)	34 (42 %)
	No	16 (39 %)	30 (77 %)	46 (58 %)
Local Signs of Exit Site Infection	Yes	24 (58.5 %)	8 (20.5 %)	32 (40 %)
	No	17 (41.5 %)	31 (79.5 %)	48 (60 %)

Table - 2: Incidence of CRBSI with the Specific Patients' Demographic Characteristics and Lab Variables

Variables		CRBSI N (%)		Total
		Positive (N = 20)	Negative (N = 60)	
Age (years)	<45	6 (27.3 %)	16 (72.7 %)	22
	45-64	5 (13.9 %)	31 (86.1 %)	36
	≥65	9 (40.9 %)	13 (59.1 %)	22
Gender	Male	12 (33.3 %)	24 (66.7 %)	36
	Female	8 (18.2 %)	36 (81.8 %)	44
CVC duration (days)	≤ 14	5 (26.3 %)	14 (73.7 %)	19
	15-21	6 (28.6 %)	15 (71.4 %)	21
	> 21	9 (22.5 %)	31 (77.5 %)	40
Diabetes Mellitus	Yes	7 (25.9 %)	20 (74.1 %)	27
	No	13 (24.5 %)	40 (75.5 %)	53
Albumin (g/dL)	< 3	5 (35.7 %)	9 (64.3 %)	14
	3-3.49	10 (27 %)	27 (73 %)	37
	≥ 3.5	5 (17.2 %)	24 (82.8 %)	29
Hb (g/dL)	< 8	10 (29.4 %)	24 (70.6 %)	34
	8-10.9	10 (25 %)	30 (75 %)	40
	≥ 11	0	6 (100 %)	6
Leukocyte Count (cell×10^9/L)	4-11	13 (19.4 %)	54 (80.6 %)	67
	> 11	7 (53.8 %)	6 (46.2 %)	13
Patients with CTI showing MRSA	Yes	8 (80 %)	2 (20 %)	10
	No	12 (17.1 %)	58 (82.9 %)	70
Fever and Rigors	Yes	16 (80 %)	18 (30 %)	34
	No	4 (20%)	42 (70 %)	46
Local Signs of Exit Site Infection	Yes	12 (60%)	20 (33.3 %)	32
	No	8 (40%)	40 (66.7 %)	48

Table - 3: Univariate Analysis for CTC and CBRSI

	Fixed Factors	B	Exp (B) (Odd Ratio)	*p*	95 % CI	
					Lower Bound	Upper Bound
CTC	Male Gender	-0.516	0.597	<0.005	-0.720	-0.312
	DM	0.336	1.400	<0.005	0.161	0.510
	CVC Duration	0.429	1.536	<0.005	0.216	0.642
	Fever and Rigor	-0.474	0.623	0.002	-0.769	-0.178
	Local Signs of Exit Site Infection	-0.211	0.810	0.030	-0.401	-0.021
CRBSI	Age (45-65 years)	0.276	1.318	0.008	0.076	0.475
	Severe Anemia(Hb< 8 g/dl)	-0.357	0.700	0.034	-0.688	-0.027
	MRSA	-0.664	0.515	<0.005	-0.945	-0.383

Table - 4: Binary Logistic Regression for CTC and CBRSI

	Predictors	B	Exp (B) (Odd Ratio)	*p*	95 % Confidence Interval	
					Lower Bound	Upper Bound
CTC	Male Gender	4.511	90.977	<0.005	10.216	810.156
	DM	-3.000	0.050	0.004	0.007	0.375
	CVC Duration	-1.645	0.193	0.003	0.065	0.571
	Fever and Rigor	1.659	5.255	0.001	2.025	13.638
	Local Signs of Exit Site Infection	1.923	6.842	0.029	1.211	38.654
CRBSI	Severe Anemia(Hb< 8 g/dl)	1.536	4.645	0.016	1.335	16.161
	MRSA	4.084	59.411	<0.005	6.674	528.851

Table - 5: ROC Curve Statistics for CTC and CBRSI

	Predictors	AUC	Asymptomatic Significance	95% CI		Sensitivity %	1 - Specificity
				Lower	Upper		
CTC	CVC Duration	0.732	<0.005	0.622	0.843	77.9	0.3819
CRBSI	Severe Anemia	0.503	0.973	.339	.666	50.0	0.3637

The data in Table - 6 illustrated the antibiotic sensitivity for bacterial pathogens that were isolated in CRBSI in MIC by mg/ml. The MRSA, *Staphylococcus epidermidis* and *Staphylococcus hemolyticus* shared the sensitivity to four drugs with a valid MIC (gentamycin, Daptomycin, Linezolid, and Vancomycin). Other bacterial pathogens are sensitive to many types of drugs of different etiologies.

Table - 6: Antibiotic Sensitivity for Bacteria Isolated in CRBSI in MIC

Types of Bacteria		Most Sensitive Antibiotics with MIC≤ 1 mg/ml	MIC mg/ml	N (%)
Staphylococcus aureus	MRSA	Gentamicin	≤ 0.5	8 (10 %)
		Daptomycin	0.5	
		Linezolid	≤ 1	
		Vancomycin	1	
		Teicoplanin	1	
	MSSA	---	---	---
Staphylococcus epidermidis		Tigecycline	≤ 0.12	6 (7 %)
		Gentamicin	≤ 0.5	
		Daptomycin	0.5	
		Vancomycin	1	
		Linezolid	1	
Pseudomonas aeruginosa		Colistin	≤ 0.5	4 (5 %)
		Ceftazidime	≤ 1	
		Piperacillin	≤ 1	
		Piperacillin/Tazobactam	1	
Staphylococcus haemolyticus		Gentamicin	≤ 0.5	2 (3 %)
		Daptomycin	0.5	
		Linezolid	0.5	
		Doxycycline	≤ 1	
		Vancomycin	1	
Total				**20 (25 %)**

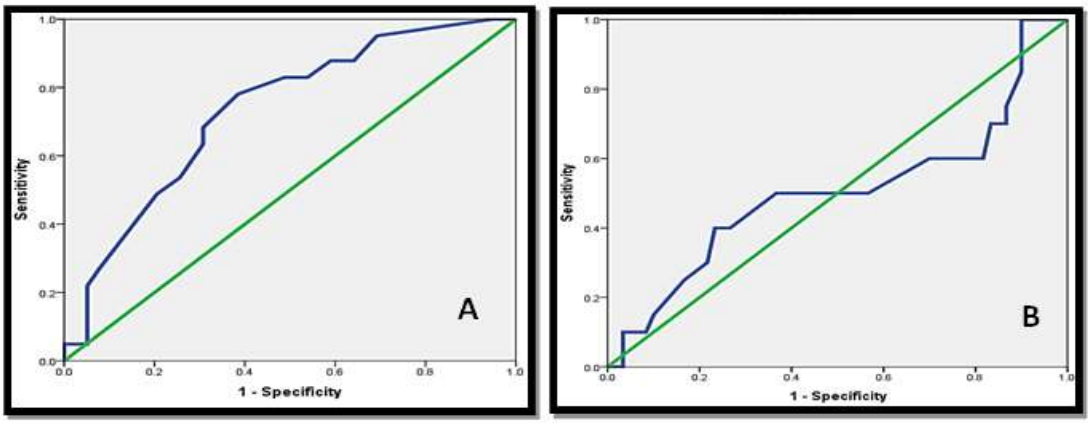

Figure - 1: A) ROC Curve for CVC Duration in CVC Culture (Cut-Point= 20.5 Days)
B) ROC Curve for Hemoglobin in CRBSI (Cut-Point= 7.7 g/dl)

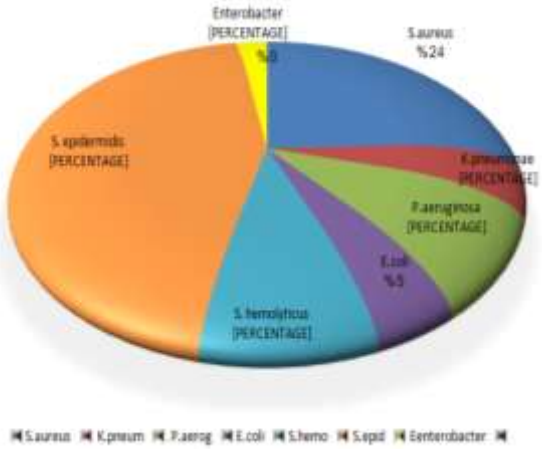

Figure - 2: Percentage of Bacteria Found in Catheter Tip Cultures

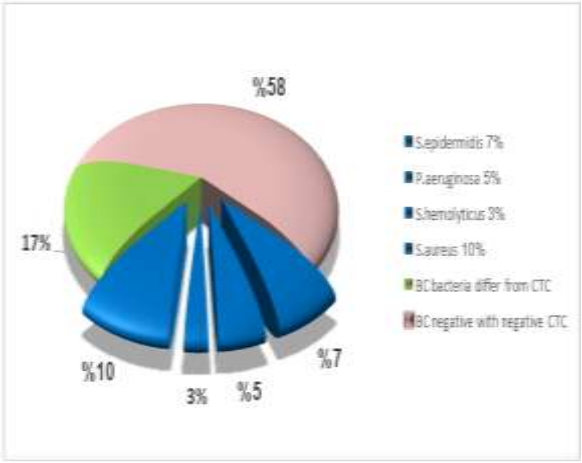

Figure - 3: Percentage of CRBSI to all cases in the study

Infection of CVC forms more than half of cases in our cohort. The patients with uremia demonstrate considerable deficit in cell - mediated immunity, phagocytosis and antibody production in addition to disruption of the protective skin barrier by HD catheter (Vandecasteele *et al*., 2009). The above result is similar to three studies by De Freitas *et al*. (2008), Qureshi *et al*. (2010) and Ghonemy *et al*. (2015). Furthermore, CRBSI constitute about (60 %) of cases with bloodstream infection in HD patients which is approximately similar to results obtained by Sanavi *et al*. (2007). The catheter is a foreign body that causes a local immune deficiency induced by exhausted neutrophils that display a decreased bactericidal activity causing bacteremia (Vandecasteele *et al*., 2009).

The factors affecting CTI and CRBSI were linked to each other in the net result, being catheter - related and sharing the same organism (Horan *et al*., 2008), i.e. the factors that affect CTI indirectly will affect CRBSI. CTI, not CRBSI, was closely linked to male gender; as most infections were male -predominant (Guerra Silveira and Abad-Franch, 2013). The results here are similar to Gupta and Ghonemy *et al*. (2016). Gender was not associated with CRBSI which may be due to the small sample size. CTI and CRBSI had no association with a particular age group; this is similar to studies done by Stefan and Ghonemy *et al*. (2013). As the CVC remain for more than 21 days, the risk of CTI is more. However, there is no significant direct effect of CVC duration on CRBSI, this is same to the result obtained by many studies (Nabi *et al*., 2009; Sahli *et al*., 2016).

Diabetes acts as an important factor for CTI, with an increased likelihood of catheter colonization as in two studies (Sahli *et al*., 2016). This result looks accepted by knowing that Diabetes Mellitus will increase the tissue susceptibility to infection (Alvin *et al*., 2015). DM had no significant association with CRBSI comparable to Stefan *et al*. (2013), and on the contrary to other studies of Allon *et al*. (2003) and Usman *et al*. (2013) due to predictor regression dilution bias. Although, the serum protein status is a vital contributor to the overall protective immunity measures (Douglas *et al*., 2015). We found a relation between the serum albumin and CTI by bivariate analysis that was not proved to be of any significance due to the effects of other confounders in linear univariate analysis. Ghonemy *et al*. (2015) had found a significant relation between hypoalbuminemia and the risk of CTI that was not evident in our study as they take a larger cohort with different comorbidities. Additionally, serum albumin level has no significant association with CRBSI which is similar to result obtained by Sanavi *et al*. (2007) but against some studies (Fysaraki *et al*., 2013; Gauna *et al*., 2013). Severe anemia was a predictor for the CRBSI supporting the results of Katneni and Hedayati (2007). Anemia lead to impaired host defense mechanism against

infection with the iron overload may lead to enhance bacterial growth and impair the phagocytic function (Joanne *et al*., 2015).

Leukocyte count has no significant association with CTI or CRBSI. We could not differentiate the causality from association of leukocyte in relation to either infections due to our study design, as leukopenia specially neutropenia will increase the risk and severity of bacterial infection, on the reverse leukocytosis happened usually as a response to infection, the above result is similar to Nabi *et al*. (2009) study and unlike that of Fysaraki *et al*. (2013) and Kurango *et al*. (2014) because of the different study design and inclusion criteria.

Fever and rigors have a statistically significant correlation with CTI, not CRBSI, this is supported by a study done by Al-Solaiman *et al*. (2011), which may be because of half of the patients had concomitant CRBSI. Some CTI patients had coexistent BSI from variable sources (cases with bloodstream infection which are not catheter - related were 14, some of them are with CTI), or there is a non-infectious cause of the fever. The local signs of exit-site infection were closely related to CTI similar to Kaur *et al*. (2015) as most of the isolated organisms from catheter tip were skin commensals. The local signs have no significant relation to CRBSI comparable to Safdar *et al*. (2002) which shows that erythema, pain, swelling, purulence and other stigmata were rarely present and had a poor sensitivity for predicting BSI.

Most of the patients whom catheters colonized with MRSA will develop CRBSI like the results of Ekkelenkamp *et al*. (2008) and Nguyen *et al*. (2013) and explained by the fact that MRSA bacteria highly pathogenic organism with a high risk of morbidity and mortality. *Staphylococcus epidermidis* followed by *Staphylococcus aureus* were the most common bacteria identified in CTI like many other international studies (Sahli *et al*., 2016). Only four bacterial pathogen causing CRBSI and the most common was *Staphylococcus aureus* followed by *Staphylococcus epidermidis* which is similar to the results obtained by Oncu *et al*. (2003) and Kaur *et al*. (2015) suggesting a hub colonization by the skin flora of the patient or medical personnel. The isolation of *Staphylococcus aureus* points towards the catheter care lapse (Kaur *et al*., 2015). The *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Staphylococcus hemolyticus* shared approximately the same antibiotic sensitivity and being MDR, comparable to the studies of Katneni and Hedayati (2007), Leone *et al*. (2010) and Sahli et al. (2016). Unlike the *Pseudomonas aeruginosa* that had a different antibiotic sensitivity like that of Gupta *et al*. (2016). The assessment of the importance of each predictorby bivariate analysis such as Chi-square alone without predictability estimation is sub-optimal. We adopt the binary logistic regression in our cohort to evaluate the independent predictors of CTI and CRBSI.

5. Limitations of the Study

- Inadequately adjusted confounders may lead to bias, towards over- or under estimation of the effects of the predictors. Despite risk factors adjustment, it is likely that there may be a residual confounding from unknown comorbidities and drugs not included in the assessment.
- Limited external validity and generalizing ability of the observation i.e. the study was conducted in a relatively homogenous small number high - risk population (100 % ESRD on HD by temporary CVC), and as with all observational data analyses, we cannot distinguish causality from the association. It is unknown whether the chosen predictors would similarly predict the catheter - related infections outcome in low - risk patients.
- All current computerized blood cell counters account leukocyte as a part of the complete blood picture. Although, different algorithms used to eliminate artifacts and extremes fluctuate to some extent between manufacturers.

6. Conclusions

- The most powerful significant predictors for the CTC positivity are being a male, being diabetic, had a CVC duration more than 20.5 days, with sign and symptoms

of catheter - related infections, with a GOOD sensitivity and specificity.

- The most powerful significant predictor for the CRBSI is the Methicillin - resistant *Staphylococcal aureus* (MRSA) infection in the blood stream.
- Although, the severe anemia below the level of 7.7 g/dl has a significant association with CRBSI, it lacks the predictability given its very low, unacceptable sensitivity.
- The age of the patients loses its significance as a CRBSI predictor after the final adjustment of the variables. The age has not predictive value at all in CTC positivity.
- The other factors like biochemical measures (Leukocyte count and Serum albumin) have no predictiveness for either the CTC or CRBSI.
- The MRSA, *Staphylococcus epidermidis* and *Staphylococcus hemolyticus* shared the sensitivity to four drugs with MIC (Gentamycin, Daptomycin, Linezolid and Vancomycin).

7. Recommendations

- Hemodialysis *via* a CVC had a higher rate of infection and we should encourage the use of AVF. CKD patients are in need for HD in the future better to have AVF or AVG before initiation of HD.
- Limit the duration of temporary hemodialysis catheter for less than twenty days in case of the jugular site, especially in male diabetic patients who have signs and symptoms of catheter - related infections.
- Follow sterile techniques for the catheter insertion and access with regular surveillance of catheter exit site for local signs of infection and checking the temperature before each dialysis session.
- We should avoid using antibiotic routinely in HD to decrease the false negative results in the culture and sensitivity.
- We urge for a better awareness by the patients for the symptoms of catheter-related infections, and by the treating personals for the signs of the catheter exit site infections.

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