Original Research Article

"Clinical and Microbiological Evaluation of Bloodstream Infections in Patients Undergoing Maintenance Hemodialysis: A Study in Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh"

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Abstract

Introduction: Chronic kidney disease (CKD) is one of the most common non communicable diseases throughout the world. According to the data of Bangladesh Renal Registry almost twenty millions of Bangladeshi adults are suffering from various stages of CKD. Many of these CKD patients ultimately developed ESRD when life is not sustainable unless renal replacement therapy is initiated. *Objective:* The purpose of the present study was to estimate the rates of infections and clinical and microbiological evaluation of bloodstream infections in patients undergoing maintenance hemodialysis. *Methods*: This cross sectional study was conducted from January 2014 to December 2015 for a period of 2(two) years in the Department of Nephrology at Bangabandhu Sheikh Mujib Medical University, Dhaka. All adult patients underwent hemodialysis of both sexes fulfilling the inclusion and exclusion criteria were included in the study. Then each patient was evaluated during each hemodialysis session for the (1) presence of bloodstream infection (BSI) using CDC (Centre for disease control) case definitions by blood cultures (Two samples were sent for cultures one from peripheral veins and another from vascular access either from fistula or from central venous catheter) and (2) clinical features. *Result*: The mean age of the patients were 38.26 (15.26) years. In this present study male (71.7%) are predominant than female (28.3%). Maximum (51.7%) patients were under weight. In this study 50 (83.3%) patients had anemia. Mean (SD) WBC, Hb, S. uric acid, FPG, Plasma glucose 2h ABF, HbA1C, S. total protein and S. albumin were 14415 (4000) count/cmm, 9.61 (1.62) g/dl, 417.67 (100.87) μmol/l, 5.37 (1.18) mmol/l, 7.27 (2.18) mmol/l, 6.42 % (0.68), 62.71 (5.82) g/l and 28.97 (4.99) g/l respectively. Out of 46 AV fistula cases, culture was positive in vein 8 (13.3%) cases and in fistula 5 (10.8%) cases. Out of 11 permanent CV catheter cases, culture was positive in vein 6 (54.5%) cases and in catheter 7 (63.3%) cases. Out of 3 catheter tip cases, culture was positive in catheter tip 2 (66.7%) cases. Among 28 bacteremic episodes Pseudomonas aeruginosa were 53.57%, Acinetobacter spp. were 35.71% and Klebsiella spp. were 10.71%. Blood stream infection rate due to hemodialysis in fistula was 0.24/1000 patient-days, in catheter was 3.05/1000 patient-days and total was 1.19/1000 patient-days. Acinetobacter spp (6.7%) and Pseudomonas aeruginosa (16.7%) were found in peripheral vein. Acinetobacter spp in 3(6.5%) and Pseudomonas aeruginosa were present in 2(4.3%) cases in AV fistula. Klebsiella spp. were present in 3 (21.4%) cases, Acinetobacter spp were in 3 (21.4%) cases and Pseudomonas aeruginosa were in 3(21.4%) cases in Central venous catheter. *Conclusion:* The risk of BSI in patients undergoing hemodialysis is related to the vascular access (tunneled central venous catheter), low haemoglobin, underweight, low serum total protein and low serum albumin.
Keywords: Mevaluation, Bloodstream infections, Plasma glucose 2h ABF, BSI, CDC.

INTRODUCTION

Chronic kidney disease (CKD) is one of the most common non communicable diseases throughout the world. According to the data of Bangladesh Renal Registry almost twenty millions of Bangladeshi adults are suffering from various stages of CKD. Many of these CKD patients ultimately developed ESRD when life is not sustainable unless renal replacement therapy is initiated. Incidence rate (number of patients/million population/year) and prevalence (number of patient/million) of ESRD in different countries (2010) :

In USA : incidence rate 348 and prevalence rate 1752, In Japan incidence rate 288 and prevalence rate 2260 and in Bangladesh incidence rate 20 and prevalence rate 158 [1].Options for renal replacement therapy in Bangladesh are: 1) Pre-emptive transplantation, 2) Transplantation after starting hemodialysis, 3) In-center hemodialysis 4) Intermittent peritoneal dialysis and 5) Continuous ambulatory peritoneal dialysis (CAPD). Renal transplantation is the best form of renal replacement therapy though it has some disadvantages like insufficient suitable donor, need for compliance with immunosuppression drugs. Continuous ambulatory peritoneal dialysis (CAPD): it preserves residual renal function, have independence and relatively simple but it is associated with high rate peritonitis. Most of the countries of the world and even in Bangladesh hemodialysis is the mostly used renal replacement therapy. A small amount of glucose is also commonly used. Note that this is a different process to the related technique of hemofiltration [2]. Bleeding may also occur; again the risk varies depending on the type of access used. Infections can be minimized by strictly adhering to infection control best practices [3]. Ideally hemodialysis access would be established in advance of starting dialysis. Functional vascular access is needed for all extracorporeal dialytic therapies and remains the life line for patients with ESRD who need chronic intermittent hemodialysis therapy. Ideally a first access should be an aretiovenous fistula placed at the wrist though upper arm access site also used. The next is central venous catheter (CVC) either permanent tunneled CVC or temporary untunneled CVC. In Bangladesh, vascular access for maintenance hemodialysis patients is AV fistula and untunneled CVC. Some hemodialysis centers in Bangladesh are using tunneled CVC, but the rates are still not high. AV grafts rarely used in our country. Data from the Dialysis Outcomes and Practices Patterns Study (DOPPS) shows that in the United States 25 % of dialysis patients are dialyzed with catheters; in other countries the use of catheters is even more common (Belgium, 41%; UK, 28%). Over 70% of patients with initiating chronic hemodialysis in the United States have a tunneled CVC as their first blood access device [4].Though the native AV fistulas are still the best suited accesses for hemodialysis, this option is impractical in many situations, so that several justifiable reasons exist for the use of CVC; these include the catheter as a bridge angioaccess device, while the patient is awaiting living-related kidney donor transplantation or maturation of an autologus fistula or graft, as the permanent vascular access for the patients unsuitable vascular anatomy who have exhausted all other options [5]. There are some advantages of tunneled CVC over untunneled CVCs: a tunneled CVC is associated with a reduced morbidity, mortality, infection rate as well as better and constant performance compared with untunneled catheter [6] observed that typical infections rate are 3 episodes of infection/ 1000 tunneled catheter

days in tunneled catheter and infection rates are high with nontunneled catheter. Vascular access is an established risk factor for sepsis in patients on renal replacement therapy, and different types of haemodialysis vascular access are associated with differing rates of bacteraemia. Patients dialysing through a central venous catheter are most at risk, with an associated bacteraemia incidence of 2–6 cases per 1000 catheter days. Within this group, those dialysing through a non-tunnelled central venous catheter have comparatively higher rates of bacteraemia than those using tunnelled central venous catheters [7]. Optimal survival and the quality of life of patients with end stage renal disease on long term hemodialysis is largely dependent upon the adequacy of dialysis through an appropriately placed and properly functioning permanent vascular access with minimal mechanical complications and infection rates. Vascular access related bloodstream infections and related complications requiring hospitalization, account for nearly one third of the cost of ESRD management with reported mortality rates of 12-25.9% [8]. Yet, despite these risks and international and national guidelines that recommend fistulas as the preferred form of dialysis access, the proportional use of tunneled catheters for dialysis access has steadily increased in many countries [32].Vascular access related bloodstream infections are a leading cause of hospitalization in patients treated with chronic hemodialysis. In addition, a catheter is used for the initial dialysis session in approximately 80 percent of incident hemodialysis patients [33].The majority of bacteremia in hemodialysis patients are caused by infection of vascular access catheters. In addition, catheter-dependent hemodialysis patients have a two- to threefold higher risk of infection-related hospitalization and infection-related death as compared with patients undergoing dialysis via a fistula or graft [34' 35]. Female gender, presence of diabetes mellitus, presence of central venous catheter rather than A/V fistula, low serum total protein, low serum albumin, high white cell count and low hemoglobin levels are associated with bloodstream infection [30]. Catheter can sometimes became colonized from more remote sites during bacteremia [36]. Bloodstream infection (BSI) is the leading cause of hospitalization and the second most common cause of death among patients receiving hemodialysis [29]. There may also be symptoms of specific infection, such as cough due to pneumonia, dysuria due to urinary tract infection [24].The diagnosis of catheter related bloodstream infection (CRBSI) is often suspected clinically in a hemodialysis patient using a CVC who present with fever or chills, unexplained hypotension and no other localizing sign [32]. Mild symptoms include malaise and nausea, in the setting of a normal catheter exit site or tunnel, on physical examination. More severe symptoms include high fever with rigors, hypotension, vomiting and change in mental status, in the setting of a norma catheter exit site or tunnel, on physical

examination. Both Gram-positive and Gram-negative organisms are responsible for BSI in patients on maintenance hemodialysis. Observed that central venous catheter-related bloodstream infection (CRBSI) was a major cause of morbidity and mortality in patients with end-stage renal disease treated with chronic hemodialysis [44]. The policy of increasing the AVF (arteriovenous fistula) prevalence beyond 50% while minimizing the use of CVCs, dependent largely upon the timely referrals and prudently implemented pre-ESRD program - ought to have a positive impact on long-term HD outcomes [8, 9] carried out a study to evaluate the clinical outcome and costs of nosocomial and community-acquired methicillin-susceptible Staphylococcus aureus (MSSA) or methicillin-resistant S. aureus (MRSA) bloodstream infection (BSI) in patients undergoing hemodialysis. This study also highlighted differences according to the source of BSI, including costs arising from hospitalization and treatment.

OBJECTIVES
A. General objective
1. To estimate the rates of infections and clinical and microbiological evaluation of blood stream infections in patients undergoing maintenance hemodialysis.

B. Specific objectives
1. To determine risk factors for developing bloodstream infections in subjects undergoing hemodialysis.
2. To detect the causative organisms of bloodstream infections in subjects undergoing hemodialysis and determine their antibiotic sensitivity pattern.
3. To assess the rate of infection in different types of vascular accesses (Fistula and permanent catheter)
4. To observe relation between risk factors with bloodstream infection in patients receiving hemodialysis.

MATERIALS AND METHODS
This cross sectional study was conducted from January 2014 to December 2015 for a period of 2(two) years in the Department of Nephrology at Bangabandhu Sheikh Mujib Medical University, Dhaka. All adult patients underwent hemodialysis of both sexes fulfilling the inclusion and exclusion criteria were included in the study. Sample size: Due to time constrain finally 60 samples were taken.Then each patient was evaluated during each hemodialysis session for the (1) presence of bloodstream infection (BSI) using CDC (Centre for disease control) case definitions by blood cultures (Two samples were sent for cultures one from peripheral veins and another from vascular access either from fistula or from central venous catheter) and (2) clinical features.

ENROLLMENT CRITERIA
Inclusion criteria
- Subjects on maintenance hemodialysis more than 3 months
- A patient with vascular access who developed the following clinical or lab criteria:
- Temperature:>100°F
- Heart rate:>90/minute
- Respiratory rate:>20/minute
- Peripheral white blood cell count:>12000/cmm
- Age: More than 18 years
- Sex: patients of both sexes
- Patients willing to participate in the study

Exclusion criteria
- Subjects with prophylactic antibiotic therapy
- Subjects with known infection within one month
- Acute renal failure
- Temporary venous catheter

DATA ANALYSIS
Data were recorded systematically in predesigned data collection form. Quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. Statistical analyses were performed by using window based computer software device with Statistical Packages for Social Sciences (SPSS-21) (SPSS Inc, Chicago, IL, USA). Association between categorical variables were analyzed by chi-squared test and continuous variable by unpaired student t-test used. For all statistical tests, p value <0.05 as was considered as statistically significant.

RESULTS AND OBSERVATION
The present cross sectional study was conducted to estimate the rates of infections and clinical and microbiological evaluation of bloodstream infections in patients undergoing maintenance hemodialysis in the Department of Nephrology of Bangabandhu Sheikh Mujib Medical University, Dhaka. A total number of 60 patients were included in the present study. The results of the present study are as follows:

Table-I: Distribution of patients according to age group (N=60)

Age group	Frequency	Percentage
≤20	6	10.0
21 – 30	17	28.3
31 – 40	12	20.0
41 – 50	7	11.7
51 – 60	15	25.0
>60	3	5.0
Total	60	100.0

[Table I] shows the text merits the description which refer to the percent distribution of patients/subjects in different age group.
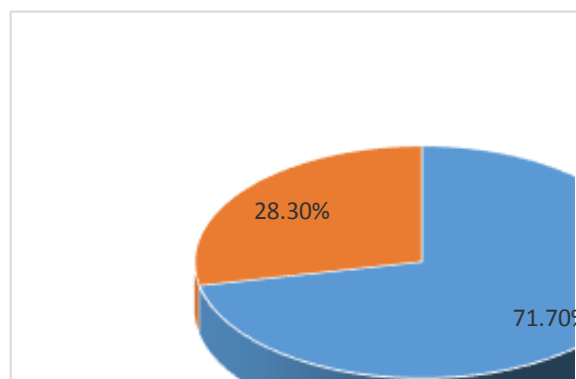

Fig-1: Pie chart of patients according to gender

Table-2: Distribution of patients according to body mass index (BMI) (N=60)

Nutritional status	Frequency	Percentage
Under weight	31	51.7
Normal	28	46.7
Over weight	1	1.7
Total	60	100.0

[Table 2] shows distribution of patients by body mass index. Most of the patients were either under weight (51.7%) or normal (46.7%). Body mass index (kg/m2) : <18.5=under weight, 18.5-24.9= normal, 25-29.9= over weight and > 30= obese

Table-3: Baseline clinical characteristics of the study sample (n=60)

Characteristic	Bacteremia		p value
	Negative (n=46)	Positive (n=14)	
Radial pulse rate /min	99.04 ± 8.54	98.07 ± 7.50	0.703[#]
Systolic blood pressure (mm of Hg)	154±22	143 ± 8	0.134[#]
Diastolic blood pressure(mm of Hg)	92 ± 9	86 ± 7	0.064[#]
Temperature (ºF)	101 ± 1	102 ± 1	0.055[#]
Respiratory rate (b/min)	22. 6 ± 1.6	22.7 ± 0.9	0.065[#]
Anemia			0.338[##]
Absent	9 (19.6)	1 (7.1)	
Mild	17 (37.0)	4 (28.6)	
Moderate	20 (43.5)	9 (64.3)	
Pneumonia	0 (0.0)	0 (0.0)	
Skin infection	0 (0.0)	0 (0.0)	
Urinary tract infection	0 (0.0)	0 (0.0)	
Infective endocarditis	0 (0.0)	0 (0.0)	
Septic arthritis	0 (0.0)	0 (0.0)	
Intra-abdominal abscess(by USG)	0 (0.0)	0 (0.0)	

[#] Unpaired t test was done to calculate statistical difference.
[##] Chi square test was done to calculate statistical difference.
Numeric data was expressed as Mean±SD and categorical data as number (percent)

[Table 3] shows that baseline clinical characteristics of both bacteremic and nonbacteremic patients are not significantly different statistically.

Table-4: Clinico-biochemical; hematological; comorbid condition and other associated factors in subjects with or without BSI in patients receiving HD (N=60)

Characteristic	Bacteremia		p value
	Negative (n=46)	Positive (n=14)	
Age, yr Mean(SD)	38 ± 16	37 ± 12	0.756[#]
Gender			0.513[##]
Male	32 (69.6)	11 (78.6)	
Female	14 (30.4)	3 (21.4)	
Diabetes mellitus			0.361[##]
Yes	12 (26.1)	2 (14.3)	
No	34 (73.9)	12 (85.7)	
Cerebrovascular disease			0.427[##]
Yes	2 (4.3)	0 (0.0)	
No	44 (95.7)	14 (100.0)	
Vascular Access			<0.001[##]
AV fistula	41 (89.1)	5 (35.7)	
Permanent catheter	5 (10.9)	9 (64.3)	
Surgical procedure within 1 month	3 (6.5)	5 (35.7)	0.005[##]
Current iron therapy	36 (78.3)	11 (78.6)	0.980
History of blood transfusion within 1 month	20 (43.5)	8 (57.1)	0.370[##]
Presence of intravenous canula	2 (4.3)	0 (0.0)	0.427[##]
S. total protein (g/L)	63.6 ± 6.1	59.5 ± 3.0	0.020[#]
S. Albumin (g/L)	30.2 ± 4.8	24.6 ± 2.4	<0.001[#]
White cell count/ cmm	14954 ± 4407	12642 ± 988	0.058[#]
Hemoglobin (g/dl)	9.6 ± 1.7	9.4 ± 1.2	0.720[#]

[# unpaired] t- test was done to calculate statistical difference
[##] Chi square test was done to calculate statistical association
Numeric data was expressed as Mean±SD and categorical data as number (percent).

[Table 4] shows that in the analysis of variables, Type of vascular access (Permanent catheter), surgical procedure within one month, low serum total protein and low serum albumin were significantly more frequently associated with bacteremia.

Table-5: Distribution of patients according to co-morbidities (N=60)

Co-morbidity	Frequency	Percentage
DM	14	23.3
Cerebrovascular disease	2	3.3

[Table 5] shows co-morbidities of the patients. DM was in 14 (23.3%) patients and cerebrovascular disease was in 2 (3.3%) patients. [DM=Diabetes mellitus]

Table-6: Distribution of patients according to anemia in two access types (N=60)

Anemia	Access type		Total n (%)	p value
	AV Fistula n (%)	Central venous catheter n (%)		
Absent	9 (19.5)	1 (7.1)	10 (16.7)	0.525
Mild	16 (34.8)	5 (35.7)	21 (35.0)	
Moderate	21 (45.7)	8 (57.2)	29 (48.3)	
Total	46 (100.0)	14 (100.0)	60 (100.0)	

Chi-square test was done to calculate statistical significance [Table 6] shows distribution of patients according to anemia in two different access types. Anemia was moderate in 57.2% cases in central venous catheter and 45.7% cases in AV fistula. Mild anemia was presence in 35.7% cases in central venous catheter and 34.8% cases in AV fistula. Most of the patients of both groups are anemic, but there is no significant difference between two groups regarding anemia.

Table-7: Hematological and biochemical variables in two groups of access type for hemodialysis (N=60)

	Access type		Total	p value
	AV Fistula	**Central venous catheter**		
WBC (count/cmm)	14652±4209	13635±3229	14415 ± 4000	0.410
Hemoglobin (g/dl)	9.67 ± 1.75	9.41 ± 1.13	9.61 ± 1.62	0.599
S. Uric acid (μmol/l)	410.45± 108.65	440.35±69.56	417.67 ± 100.87	0.338
Plasma glucose				
Fasting (mmol/l)	5.31±1.29	5.55± 0.73	5.37 ± 1.18	0.508
2 hours ABF	7.29±2.27	7.20±1.94	7.27 ± 2.18	0.885
HbA1c (%)	6.41 ± 0.65	6.46 ± 0.78	6.42 ± 0.68	0.800
S. total protein (g/l)	63.79±5.87	59.14 ± 4.09	62.71 ± 5.82	0.008
S. albumin (g/l)	30.01 ± 5.01	25.52 ± 3.07	28.97 ± 4.99	0.003

Unpaired t test was done to calculate statistical difference. [Table 7] shows laboratory findings in two different access types. Serum total protein and serum albumin were significantly higher in cases of AV fistula comparing central venous catheter type. WBC, Hemoglobin, Serum Uric acid, plasma glucose and HbA1c were almost similar in both cases.

Table-8: Bloodstream infection rate of the patients (N=60)

	Peripheral Vein	AV fistula	Catheter	Total
No of infection episodes	14	5	9	28
Total patient-days	23340	20390	2950	23340
Infection rate (per 1000 patient-days)	0.59	0.24	3.05	1.19

[Table 8] shows blood stream infection rate due to hemodialysis. Infection rate in fistula was 0.24/1000 patient-days, in catheter was 3.05/100 patient-days and total was 1.19/1000 patient-days.

Table-9: Distribution of culture positivity according to site of sampling (N=60)

	Total	Positive					
		Peripheral Vein	**Fistula**	**Catheter**	**Catheter tip**	**Urine**	**Pleural fluid**
Both peripheral vein + AV fistula	46	8 (13.3)	5 (10.8)				
Both peripheral vein + permanent CV catheter	11	6 (54.5)		7 (63.3)			
Both peripheral vein + permanent CV catheter + Catheter tip culture	3	0 (0.0)		0 (0.0)	2 (66.7)		
Urine culture	7					0 (0.0)	
Pleural fluid culture	1						0 (0.0)

[Table 9] shows output of culture according to culture sites. Out of 46 AV fistula cases, culture was positive in peripheral vein 8 (13.3%) cases and in fistula 5 (10.8%) cases. Out of 11 permanent CV catheter cases, culture was positive in vein 6 (54.5%) cases and in catheter 7 (63.3%) cases. Out of 3 catheter tip cases, culture was positive in catheter tip 2 (66.7%) cases. Urine and pleural fluid culture revealed no growth of bacteria.

Table-10: Names of organisms isolated from total bacterial episodes (N=60)

Pathogen	Frequency	Percentage
Pseudomonas aeruginosa	15	53.57
Acinetobacter spp	10	35.71
Klebsiella spp.	3	10.71

[Table 10] shows among 28 bacterial episodes Pseudomonas aeruginosa were 53.57 %, Acinetobacter spp. were 35.71 % and Klebsiella spp. were 10.71 %

Table-11: Outcome of bacterial culture in samples from AV fistula and central venous catheter (N=60)

Culture	Access type		p value
	AV Fistula (n=46)	Central venous catheter (n=14)	
No growth	41 (89.1)	5 (35.7)	<0.001
Positive	5 (10.9)	9 (64.3)	

Chi-square test was done to calculate statistical association.

[Table 11] shows comparison of growth between AV fistula and central venous catheter site. Positive growth was significantly higher in central venous catheter 9 (64.3%) than that of AV fistula 5 (10.9%) cases.

Table-12: Organisms isolated from peripheral vein (N=60)

Gram-negative bacteria	Frequency	Percentage
Acinetobacter spp	4	6.7
Pseudomonas aeruginosa	10	16.7

[Table 12] shows organisms isolated from peripheral vein. Acinetobacter spp was present in 6.7% cases and Pseudomonas aeruginosa was present in 16.7% cases.

Table-13: Peripheral vein sensitivity pattern of Acinetobacter spp. (N=60)

Antibiotics	Sensitive	Resistant
Piperacillin + Tazobactum	4 (100.0)	
Cefuroxime		2 (100.0)
Ceftazidime		3 (100.0)
Ceftriaxone		1 (100.0)
Imipenem	1 (33.3)	2 (66.7)
Amikacin	4 (100.0)	
Netilmicin	3 (75.0)	1 (25.0)
Amoxicillin		3 (100.0)
Ciprofloxacin	4 (100.0)	
Co-trimoxazole	3 (75.0)	1 (25.0)
Colistin	4 (100.0)	
Cefotaxime		2 (100.0)
Ticarcillin		2 (100.0)
Aztreonam		4 (100.0)

[Table 13] shows sensitivity pattern of Acinetobacter spp. Piperacillin + Tazobactum(4/4), Amikacin(4/4), Ciprofloxacin(4/4) and Colistin(4/4) antibiotics were sensitive in 100% cases. Imipenem

(1/3) was sensitive in 33.3% cases. Netilmicin(3/4) and co-trimoxazole(3/4) was sensitive in 75% cases. Cefuroxime (2/2), Ceftazidime (3/3), Ceftriaxone (1/1), Amoxicillin (3/3), cefotaxime(2/2), Ticarcillin(2/2) and Aztreonam(4/4) were resistant 100% cases.

Table-14: Peripheral vein sensitivity pattern of Pseudomonas aeruginosa (N=60)

Antibiotics	Sensitive	Resistant
Piperacillin + Tazobactum	10 (100)	
Cefuroxime		5 (100)
Ceftazidime		9 (100)
Ceftriaxone		3 (100)
Cefepime		5 (100)
Imipenem	2 (50)	2 (50)
Amikacin	9 (90)	1 (10)
Netilmicin	6 (60)	4 (40)
Gentamicin	5 (50)	5 (50)
Amoxicillin		3 (100)
Ciprofloxacin	10 (100)	
Co-trimoxazole	2 (66.7)	1 (33.3)
Colistin	10 (100)	
Cefotaxime	2 (100)	
Ticarcillin	6 (60)	4 (40)
Aztreonam	8 (100)	

[Table 14] shows sensitivity pattern of Pseudomonas aeruginosa. Piperacillin + Tazobactum (10/10), Ciprofloxacin (10/10), Colistin(10/10), Cefotaxime (2/2) and Aztreonam(8/8) antibiotics were sensitive in 100% cases. Imipenem (2/4) was sensitive in 50% cases, Amikacin (9/10) was sensitive in 90% cases, Netilmicin (6/10) was sensitive in 60% cases, Gentamicin (5/10) was sensitive in 50% cases, co-trimoxazole(2/3) was sensitive in 66.7% cases, Ticarcillin(6/10) was sensitive in 60% cases. Cefuroxime (5/5), Ceftazidime (9/9), Ceftriaxone (3/3), Cefepime(5/5) and Amoxicillin(3/3) were resistant in 100% cases.

Table-15: Organisms isolated from vascular access sites (N=60)

Gram-negative bacteria	Access type		p value
	AV Fistula n (%)	Central venous catheter n (%)	
Klebsiella spp.	0 (0.0)	3 (21.4)	0.001
Acinetobacter spp	3 (6.5)	3 (21.4)	0.104
Pseudomonas aeruginosa	2 (4.3)	3 (21.4)	0.043

Chi-square test was done to measure the level of significance [Table 15] shows organisms isolated from vascular access site. Acinetobacter spp were present in 3(6.5%) cases and Pseudomonas aeruginosa

were present in 2(4.3%) cases in AV fistula. Klebsiella spp., Acinetobacter spp and Pseudomonas aeruginosa all were present in 3 (21.43) cases in Central venous catheter.

Table-16: Central venous catheter sensitivity pattern of Klebsiella spp. (N=60)

Antibiotics (sensitive)	Access type			
	AV Fist	ula	Central venous catheter Sensitive	Resistant
Cefuroxime				2 (100.0)
Ceftazidime				2 (100.0)
Ceftriaxone				2 (100.0)
Imipenem			2 (100.0)	
Amikacin			1 (50.0)	1 (50.0)
Gentamicin			2 (100.0)	
Amoxicillin				2 (100.0)
Ciprofloxacin			2 (100.0)	
Co-trimoxazole				2 (100.0)
Colistin			2 (100.0)	
Nalidixic			1 (50.0)	1 (50.0)
Cefradine			1 (50.0)	1 (50.0)

[Table 16] shows sensitivity pattern of Klebsiella spp.: Imipenem (2/2), Gentamicin (2/2), Ciprofloxacin(2/2) and Colistin(2/2) antibiotics were sensitive in 100% cases. Amikacin (1/1), Cefradine(1/1) and Nalidixic acid(1/1) were sensitive in 50.0% cases. Cefuroxime (2/2), Ceftazidime (2/2), Ceftriaxone (2/2), Amoxicillin (2/2) and Co-trimoxazole(2/2) antibiotics were resistant in 100% cases.

Table-17: Sensitivity pattern of Acinetobacter spp. (N=60)

Antibiotics (sensitive)	Access type		Central venous catheter Sensitive	Resistant
	AV Fistula Sensitive	Resistant		
Piperacillin + Tazobactum	3 (100.0)		3 (100.0)	
Cefuroxime		3 (100.0)		3 (100.0)
Cefixime		3 (100.0)		1 (100.0)
Ceftazidime		3 (100.0)		3 (100.0)
Ceftriaxone		3 (100.0)		2 (100.0)
Imipenem	1 (33.3)	2 (66.7)	2 (66.7)	1 (33.3)
Amikacin	3 (100.0)		3 (100.0)	
Netilmicin	3 (100.0)		2 (100.0)	
Gentamicin			1 (100.0)	
Amoxicillin	1 (33.3)	2 (66.7)		3 (100.0)
Ciprofloxacin	3 (100.0)		3 (100.0)	
Co-trimoxazole	2 (66.7)	1 (33.3)	1 (100.0)	
Colistin	3 (100.0)		2 (100.0)	
Aztreonam	1 (33.3)	2 (66.7)		2 (100.0)
Nalidixic	1 (33.3)	2 (66.7)		
Cefotaxime		3 (100.0)		

[Table 17] shows sensitivity pattern of Acinetobacter spp. in AV fistula and central venus catheter. In AV fistula: Colistin(3/3), Amikacin(3/3), Netilmicin(3/3), Ciprofloxacin(3/3) and Piperacillin + Tazobactum(3/3) were sensitive in 100% cases. Cefuroxime (3/3), Cefixime(3/3), Ceftazidime(3/3), Ceftriaxone(3/3) and Cefotaxime(3/3) were resistant in 100% cases. Imipenem (2/3), Amoxicillin(2/3), Aztreonam(2/3) and Nalidixic(2/3) were resistant in 66.7% cases. In central venous catheter: Colistin(2/2), Amikacin(3/3), Netilmicin(2/2), Ciprofloxacin(3/3), Gentamicin(1/1), Co-trimoxazole(1/1) and Piperacillin + Tazobactum(3/3) were sensitive in 100% cases. Imipenem (2/3) was sensitive in 66.7% cases. Cefuroxime (3/3), Cefixime(1/1), Ceftazidime(3/3), Ceftriaxone(2/2), Amoxicillin(3/3) and Aztreonam(2/2) were resistant in 100% cases.

Table 18: Sensitivity pattern of Pseudomonas aeruginosa (N=60)

Antibiotics (sensitive)	Access type			
	AV Fistula		Central venous catheter	
	Sensitive	Resistant	Sensitive	Resistant
Piperacillin + Tazobactum	2 (100.0)		2 (100.0)	
Cefixime				2 (100.0)
Ceftazidime		2 (100.0)		2 (100.0)
Ceftriaxone				2 (100.0)
Cefepime		2 (100.0)		
Imipenem		2 (100.0)	1 (50.0)	1 (50.0)
Amikacin	2 (100.0)		2 (100.0)	
Netilmicin	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)
Gentamicin	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)
Amoxicillin				2 (100.0)
Ciprofloxacin	2 (100.0)		2 (100.0)	
Colistin	2 (100.0)		2 (100.0)	
Ticarcillin	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)
Aztreonam		2 (100.0)	1 (50.0)	1 (50.0)

[Table 18] shows sensitivity pattern of organisms (Pseudomonas aeruginosa) isolated from vascular access site: In AV fistula: Piperacillin + Tazobactum(2/2), Amikacin(2/2), Ciprofloxacin(2/2) and Colistin(2/2) were sensitive in 100% cases. Ticarcillin(1/1), Gentamicin(1/1) and Netilmicin(1/1) were sensitive in 50% cases. Ceftazidime (2/2), Cefepime(2/2), Aztreonam(2/2) and Imipenem(2/2) were resistant in 100% cases. In Central venous catheter: Piperacillin + Tazobactum(2/2), Amikacin(2/2), Ciprofloxacin(2/2) and Colistin(2/2) were sensitive in 100% cases. Ceftazidime (2/2), Cefixime(2/2), Ceftriaxone(2/2) and Amoxicillin(3/3) were resistant in 100% cases. Imipenem (1/2,)Ticarcillin(1/2), Gentamicin(1/2), Netilmicin(1/2) and Aztreonam(1/2) were resistant in 66.7% cases.

Table-19: Organisms isolated from catheter tip (N=60)

Gram-negative bacteria	Frequency	Percentage
Klebsiella spp.	1	33.3
Pseudomonas aeruginosa	1	33.3

[Table 19] shows organisms isolated from catheter tip. Klebsiella spp. was present in 33.3% case and Pseudomonas aeruginosa was present in 33.3% case.

Table-20: Catheter tip sensitivity pattern of Klebsiella spp. (N=60)

Antibiotics	Sensitive	Resistant
Cefuroxime		1 (100.0)
Ceftazidime		1 (100.0)
Ceftriaxone		1 (100.0)
Imipenem		1 (100.0)
Amikacin		1 (100.0)
Netilmicin		1 (100.0)
Gentamicin	1 (100.0)	
Amoxicillin		1 (100.0)
Ciprofloxacin	1 (100.0)	
Colistin	1 (100.0)	
Nalidixic	1 (100.0)	

[Table 20] shows sensitivity pattern of Klebsiella spp. Gentamicin, Ciprofloxacin, Colistin and Nalidixic antibiotics were sensitive in Klebsiella spp bacteria but Cefuroxime, Ceftazidime, Ceftriaxone, Imipenem, Amikacin, Netilmicin and Amoxicillin antibiotics were resistant in Klebsiella spp bacteria.

Table-21: Catheter tip sensitivity pattern of Pseudomonas aeruginosa (N=60)

Antibiotics	Sensitive	Resistant
Piperacillin + Tazobactum	1 (100.0)	
Cefepime	1 (100.0)	
Imipenem	1 (100.0)	
Amikacin	1 (100.0)	
Netilmicin	1 (100.0)	
Gentamicin	1 (100.0)	
Ciprofloxacin	1 (100.0)	
Colistin	1 (100.0)	
Ticarcillin	1 (100.0)	

[Table 21] shows sensitivity pattern of Pseudomonas aeruginosa. Tazobactum, Cefepime, Imipenem, Amikacin, Netilmicin, Gentamicin, Ciprofloxacin, Colistin and Ticarcillin antibiotics were sensitive in Pseudomonas aeruginosa.

DISCUSSION

Bloodstream infection (BSI) is the leading cause of hospitalization and the second most common cause of death (after cardiovascular death) among patients receiving regular hemodialysis [29]. In the present cross sectional study the rates of infections was estimated and clinical and microbiological evaluation of bloodstream infections in patients undergoing hemodialysis was done. In this study mean (SD) age of the study population was 38.26 (15.26) within the range of 16-70 years. Maximum (28.3%) patients were in age group 21-30 years followed by (25.0%) were in age group 51-60 years. Mean age was comparatively higher in others studies [30, 31]. Patient at any age may require hemodialysis. Males (71.7%) were predominant

than females (28.3%). Male female ratio was 2.52:1. Any gender may require hemodialysis [30, 31]. Females are associated with more bacteremia than the males [23, 30]. Most of the patients were either under weight (51.7%) or normal (46.7%). Evaluation of baseline clinical characteristics such as pulse, blood pressure, respiratory rate, temperature and anemia, body mass index of both bacteremic and nonbacteremic patients revealed no significant difference. During further evaluation no patient was found to have urinary tract infection, pneumonia, infective endocarditis, skin infection, septic arthritis [32]. Stated that hemodialysis patient may be suspected for bloodstream infection who present with fever or chills, unexplained hypotension, and no other localizing sign [24]. Found pneumonia 0.84/100 patient-month, urinary tract infection 0.29/100 patient-month, wound infection 1.29/100 patient-month for all access. In this study risk factors for bloodstream infections were searched and found that tunneled central venous catheter, surgical procedure within one month, low serum total protein and low serum albumin were significantly associated with bacteremia [33]. Showed the risk of bacteremia was highest in hemodialysis patients using central venous catheter as vascular access and the incidence rate of CRBSI was 2.5 to 5.5 cases/1000 catheter days. Risk factors described in other studies include: older age [42] higher total intravenous iron dose [38, 39] increased recombinant human erythropoietin dose [6], lower hemoglobin level [39, 40] low serum albumin level [42, 24]; Diabetes mellitus [32] and recent surgery [24]. Regarding co-morbidities of the patients, DM was in 14 (23.3%) patients and cerebrovascular disease was in 2 (3.3%) patients [31]. Found DM (32.0%) in their study [30]. Found DM (39.0%) and Coronary disease (18.8%). Most of the patients were found to have mild to moderate anemia. Anemia was moderate in 57.2% cases in central venous catheter and 45.7% cases in AV fistula. Mild anemia was presence in 35.7% cases in central venous catheter and 34.8% cases in AV fistula [40]. Showed anemia were significantly associated with bacteremia. Bloodstream infections rate due to hemodialysis were recorded. In this study, total 28 bacteria were identified at a infection rate of 1.19/1000 patient-days. Of the 28 bacteria 5 involved permanent fistula (0.24/1000 patient-days); and 9 involved permanent-tunneled central venous catheter (3.05/1000 patient-days). There were 14 bloodstream infections (0.59/1000 patient days). In the study of [30] the BSI rate was 0.52 per 1000 patient-days. Of the 148 episodes, 34 occurred in patients with permanent fistula (0.18/1000 patient-days); 19 in patients with grafts (0.39/1000 patient-days); 28 in patients with permanent tunneled central catheters (1.03/1000 patient-days); and 67 in those with temporary catheter (3.18/1000 patient-days) [43]. Identified a total of 109 infections, for a rate of 11.32/1000 dialysis sessions (ds). Of the 109, 23 involved permanent fistulae or grafts (4.23/1000 ds); 18 involved permanent-tunneled central catheter infections

(10.1/1000 ds); and 68 involved temporary-catheter infections (28.23/1000 ds). There were 38 bloodstream infections (3.95/1000 ds). Positive growth was significantly higher in central venous catheter 9 (64.3%) than that of AV fistula 5 (10.9%) cases. In their study [40, 41] described hemodialysis catheter were major risk factors for bacteremia particularly when compared to synthetic graft or native arteriovenous fistula. Out of 46 AV fistula cases, culture was positive in peripheral veins 8 (13.3%) cases and in fistula 5 (10.8%) cases. Out of 11 permanent CV catheter cases, culture was positive in peripheral veins 6 (54.5%) cases and in catheter 7 (63.3%) cases. Out of 3 catheter tip cases, culture was positive in catheter tip 2 (66.7%) cases. Out of 7 Urine for C/S & 1 pleural fluid culture revealed no growth. Regarding source of bacteremia: 3 cases were primary bacteremia and rests of the cases were either due to permanent catheter or due to AV fistula [30]. Found primary bacteremia 51%, CRBSI 28% and 21% secondary to other sources. Regarding causative organisms causing bacteremia: All identified bacteremia were gram-negative and the high prevalence of gram-negative bacteria may be due to immunocompromised states of the patients, contaminated infusate and misuse of antibiotics. Pseudomonas aeruginosa were 53.57 %, Acinetobacter spp. were 35.71 % and Klebsiella spp. were 10.71 %. In their study, Al muneef *et al*. (2006) noted a total 50 CRBSI episodes; among them 48% were polymicrobial, 32% were due to gram-negative bacilli and 10% due to gram-positive organisms. The most common organisms isolated were Klebsiella 16%, coaglase- negative staphylococci 14% and Pseudomonas aeruginosa 11% [30]. Noted gram-negative bacteria as a cause of bloodstream infections in 33% cases. Among them Escherichia coli were 39%, Klebsiella spp. were 17%, Acinetobacter spp. were 14% and Enterobacter spp. were 14%. Regarding organisms isolated from peripheral veins, Acinetobacter spp. was present in 6.7% cases and Pseudomonas aeruginosa was present in 16.7% cases. Sensitivity pattern of Acinetobacter spp and Pseudomonas spp. in peripheral vein were recored. Most sensitive antibiotics were Piperacillin + Tazobactum, Amikacin, Ciprofloxacin and Colistin. Moderately sensitive antibiotics were Imipenem, Co-trimoxazole and Netilmicin. Most resistant antibiotics were Cefuroxime, Ceftazidime, Ceftriaxone, Amoxicillin, cefotaxime, Gentamicin and Ticarcillin. Regarding organisms isolated from vascular access site, Acinetobacter spp in 3(6.5%) and Pseudomonas aeruginosa were present in 2(4.3%) cases in AV fistula. In Central venous catheter. Klebsiella spp in 3(21.4%). Acinetobacter spp in 3(21.4%) and Pseudomonas aeruginosa in 3(21.4%) cases were present. Sensitivity pattern of Klebsiella spp. in central venous catheter: Imipenem, Gentamicin, Ciprofloxacin and Colistin antibiotics were sensitive in 100% cases. Cefuroxime, Ceftazidime, Ceftriaxone, Amoxicillin and Co-trimoxazole antibiotics were resistant in 100% cases.

Sensitivity pattern of Acinetobacter spp. in AV fistula and central venus catheter. Most sensitive antibiotics were: Colistin, Amikacin, Netilmicin, Ciprofloxacin and Piperacillin + Tazobactum. Moderately sensitive antibiotics were Imipenem, Aztreonam and most resistant antibiotics were Cefuroxime, Cefixime, Ceftazidime, Ceftriaxone and Cefotaxime. Sensitivity pattern of organisms (Pseudomonas aeruginosa) isolated from vascular access sites: Most sensitive antibiotics were Piperacillin + Tazobactum, Amikacin, Ciprofloxacin and Colistin. Most resistant antibiotics were Ceftazidime, Cefepime, Aztreonam and Imipenem. Regarding organisms isolated from catheter tip, Klebsiella spp. was present in 33.3% case and Pseudomonas aeruginosa was present in 33.3% case. Sensitivity pattern of Klebsiella spp.in catheter tip: Gentamicin, Ciprofloxacin, Colistin and Nalidixic antibiotics were sensitive in Klebsiella spp bacteria but Cefuroxime, Ceftazidime, Ceftriaxone, Imipenem, Amikacin, Netilmicin and Amoxicillin antibiotics were resistant in Klebsiella spp bacteria. Sensitivity pattern of Pseudomonas aeruginosa in catheter tip: Tazobactum, Cefepime, Imipenem, Amikacin, Netilmicin, Gentamicin, Ciprofloxacin, Colistin and Ticarcillin antibiotics were sensitive in Pseudomonas aeruginosa. Arterial catheters used for hemodynamic monitoring (0.8%, 1.7 per 1000 catheter-days) and peripherally inserted central catheters used in hospitalized patients (2.4%, 2.1 per 1000 catheter-days) posed risks approaching those seen with short-term conventional CVCs used in the Intensive care unit. Surgically implanted long-term central venous devices--cuffed and tunneled catheters (22.5%, 1.6 per 1000 IVD-days) and central venous ports (3.6%, 0.1 per 1000 IVD-days)--appear to have high rates of infection when risk is expressed as BSIs per 100 IVDs but actually pose much lower risk when rates are expressed per 1000 IVD-days. The use of cuffed and tunneled dual lumen CVCs rather than noncuffed, nontunneled catheters for temporary hemodialysis and novel preventive technologies, such as CVCs with anti-infective surfaces, was associated with considerably lower rates of catheter-related BSI. Regardless of the repeated reservations raised by countless researchers with reference to the use of catheters as vascular access for hemodialysis (HD), central venous catheters (CVCs) remain irreplaceable tools of the modern dialysis delivery system as a reliable option for the clinical situations requiring instant access to circulation, for various reasons. Patients on long-term hemodialysis are therefore at a significantly high risk for catheter related bloodstream infections (CRBSI) and ensuing serious complications.

CONCLUSIONS

In hemodialysis patients, the risk of bacteremia can be stratified according to vascular access type. Infections rates were highest in hemodialysis patients with central venous catheter access, compared with rate in those with AV fistula. Low serum total protein, low serum albumin, low hemoglobin and poor nutrition are risk factors for bloodstream infections (BSI). To reduce the rates of bloodstream infections careful clinical evaluation, limitation of the catheter use as vascular access, improvement of nutritional status, correction of anemia and hypoalbuminaemia are essential. BSI is responsible for mortality, morbidity, cost and hazards of the patients. The 1st step to minimize BSI is to dialysis through AV fistula, next step is to recognition of risk factors and their management and the 3rd step is to early recognition and treatment BSI.

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