World Journal of Medicine and Medical Science
Vol. 4, No. 1, May 2016, pp. 1-10, ISSN: 2330 - 1341 (Online)
Available online at http://www.wjmms.com

Research article

Prevalence of Central venous catheter - Related Bacteremia Among Chronic Hemodialysis Patients in Main Hospitalsof Gaza Strip, Palestine

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ABSTRACT :

Central venous catheter-related bloodstream infection (CRBSI) is associated with high rates of morbidity and mortality on patients with end-stage renal disease treated with chronic hemodialysis. The Rates of complication and readmission are high among hemodialysis patients with bacteremia, resulting in increased demands on resources and serious complications **.** blood samples were collected from one catheter lumen, where a single blood culture was collected for each patient of 50 HD patientswith indwelling subclavin CVC (42% male and 58% female). Each sample was cultured on blood agar, MacConkey agar and chocolate agar. The isolated bacteria was identified by biochemical test.Pus swabs from catheter exit siteswereperformed on certain cases. Antibiotic susceptibility test was accomplished using Kirby-Bauer method and the antibiotics that were selected for isolated bacteria and their result interpretation were determined based on clinical and laboratory standards institute 2007 (CLSI) for antimicrobial susceptibility testing.The results showed that 60% of the sample population had bacteremia of which77% were gram positive cocci (GPC) and 23% were gram negative bacilli (GNB). The main causes of renal failure were found to bediabetic nephropathy and hypertensive nephropathy (28% for each). Moreover, This implies that staphylococcus hemolyticus (27%) followed by staphylococcus epidermidis (23%) were the main etiologies for CVC associated bacteremia.All of identified GPC were sensitive to vancomycin except 25% of isolated Staphococcushemolyticus were resistant to it. All of GNB were sensitive to gentamycin except 50% of Klebsiella pneumonia and 100% of Escherichia coli were resistant to it.Gram positive cocci were the main etiologies for CVC associated Bacteremia among cases .The findings suggest that care of catheter exit site and catheter itself willcontribute to reducing the prevalence of bacteremia.Antibiotic susceptibility test , like antibiogram , is an important test in the determination of the appropriate antibiotic to be given for a particular patient in order to confirm the patient's empiricaltherapy.

Key words : bacteremia , hemodialysis , central venous catheter , Gaza Strip

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INTRODUCTION

Central venous catheter (CVC) is a commonly used device in haemodialysis (HD). Patients who are not suitable for creation of arterial-venous (AV) fistula or graft require catheters to receive HD. Catheter-related blood stream infection (CRBSI) is a major complication in patients with CVC [1].Chronic dialysis patients are at risk for infections caused by nosocomial multidrug resistant (MDR) pathogens exhibiting decreased susceptibility to many antimicrobials. Hence, empirical administration of such antimicrobials may be inappropriate. Antimicrobial administration would therefore result in increased morbidity, mortality and cost to the health care system [2].

The main reasons for the high prevalence of bloodstream infection in chronic dialysis patientsare a) Impaired immunity due to renal failure, comorbidities, malnourishment that increase the virulence and the adherence properties of hospital bacteria and b) the breakdown of the protective anatomical barriers due to repeated intravascular intervention required for HD[3] .Rates of complication and readmission are high among HD patients with bacteremia ,results in increased demands on resources. Serious complications include infective endocarditis, septic arthritis, septic pulmonary emboli, osteomyelitis, spinal epidural abscess and severe sepsis. More severe cases lead to death which have been reported in 20% of cases[4].

This study aimed to achieve three objectives a) determining the prevalence of central venous catheter-related bacteremia among chronic hemodialysis patients (CHP) in the two main hospitals of Gaza Strip (Al-Shifa and Nasser), b) assessing the risk factor that causes renal failure among CHP, c) identifying the antimicrobial resistance pattern of identified bacteremia.

Methods

▪ samples population and collection

This study followed the Descriptive Analytical approach and was carried out within eight months between April 2014 and November 2014. The sample size was 50 (HD) patients with indwelling subclavin CVC. Samples collected from thetwo main hospitals in Gaza Strip , Nasser hospital 24patients (48%) and Al-Shifa hospital 26 patients (52%).4 ml of blood sample collected from one catheter lumen of each patient and injected in single blood culture bottles for bacterial isolation and identification , Pus samples collected using a sterile cotton wool swab by extend the swab deeply into the depth of infected region around the catheter exit site , then immersed the swab into tube contain 4ml ofthioglycolate broth mediafor bacterial isolation and identification .

▪ Bacterial identification

Bacterial identification was performed using biochemical tests and culture characteristic according to the procedures explained by Bailey and Scotts in 'Diagnostic Microbiology'[5]. An oxidase test was used to differentiate *Pseudomonas aeruginosa* from *Enterobacteriaceae*. Gram stain and biochemical tests were used to identify the isolated gram negative bacteria. To identify gram positive bacteria, catalase, hemolysis on blood agar, coagulase and other tests were used[6] .In order to confirm the diagnostic results of identified bacteria,the advanced bacterial identification software online (ABIS online) was used [7].

▪ Performance of antimicrobial susceptibility test

Antibiotic susceptibility test was accomplished using disk diffusion method (Kirby- Bauer method) according to World Health Organization (WHO) 2003 [8]. The selected antibiotics for isolated bacteria and the interpretation of their results (i.e. whether

sensitive, intermediate or resistant) were determined according to the Clinical and Laboratory Standards Institute 2007 (CLSI) for antimicrobial susceptibility testing[9].selected antibiotics were Penicillin G (P) , Ampicillin (AM) , Vancomycin (VA) , Tetracycline (TE) , Ciprofloxacin (CIP) , Chloramphenicol (C) , Rifampin (RIF) , Doxycycline (DXT) , Erythromycin (E) , Cefuroxime (CXM) , Gentamycin (CN) , Piperacillin (PRL) , Ceftazidim (CAZ) , Cefotaxime (CTX) andAmikacin (AK) .

- **Determination of risk factors of ESRD**

Risk factors of end stage renal disease was obtained from the medical profile of patients .

Results

The study subjects (n=50 patients) consisted of 42% (21 cases) males and 58% (29 cases) females. The mean age of sample population was 43.38 years old. The distribution of isolated bacteremia regarding to gender of patient showed the percentage of bacteremic cases of female (16 cases) was 32% and it was higher than male (14 cases) 28%. The distribution of blood culture results of patients by hospitalsrevealed that the total positive blood culture was 60% among subjects, 32% of them were from Al-Shifa hospital and 28% were from Nasser hospital. No significant correlation (p = 0.817) between positive culture and hospitals was found.

- **Risk factors of ESRD among CHP**

The etiologies of renal failure for the study sample were diabetic nephropathy (28%), Hypertensive nephropathy (28%),glomerulonephritis (16%), unknown (20%) ,Renal trophy and Lupus nephritis (4% for each) .

- **Bacteria isolated from Pus swab from catheter exit site .**

Five species of bacteria were isolated from pus on catheter exit site , the major isolated bactereia are gram positive cocci and their *Staphylococcus aureus* , *Staphylococcus hemolyticus* , *Staphylococcus epidermidis and Enterococcus spp*followed by one species of gram negative bacilli and its *Pseudomonas spp* , the isolated bacteria are identified on certain cases of CVC not from all cases involved in this study .

- **Percentage of bacterial isolated among sample population .**

Table 1 : Percentage of bacterial isolated among sample population .

Group		Bacteria species	Number	Percentage (%)
GPC (77%)	CONS (50%)	*Staphylococcus hemolyticus*	8	27
		Staphylococcus epidermidis	7	23
	COPS (7%)	*Staphylococcus aureus*	2	7
		Enterococcus spp	6	20
GNB (23%)		*Serratiaspp*	2	7
		Klebsiella pneumonia	2	7

		Escherichia coli	1	3
		Pseudomonas aerogenosa	1	3
		Enterobacterspp	1	3
Total			**30**	**100**

The results of study showed that 9 species of bacteria were identified in 60% of sample population as shown in table 1 above , the GPC was the main causative agent of bacteremia 77% while GNB was responsible for 23% , *Staphylococcus hemolyticus* was the most predominant of GPC 27% but *Staphylococcus aureus* was the lowest frequency 7% as shown in Figure 1 below , *Serratiaspp* and *Klebsiella pneumonia* were the higher percentage (7% for each) in GNB .

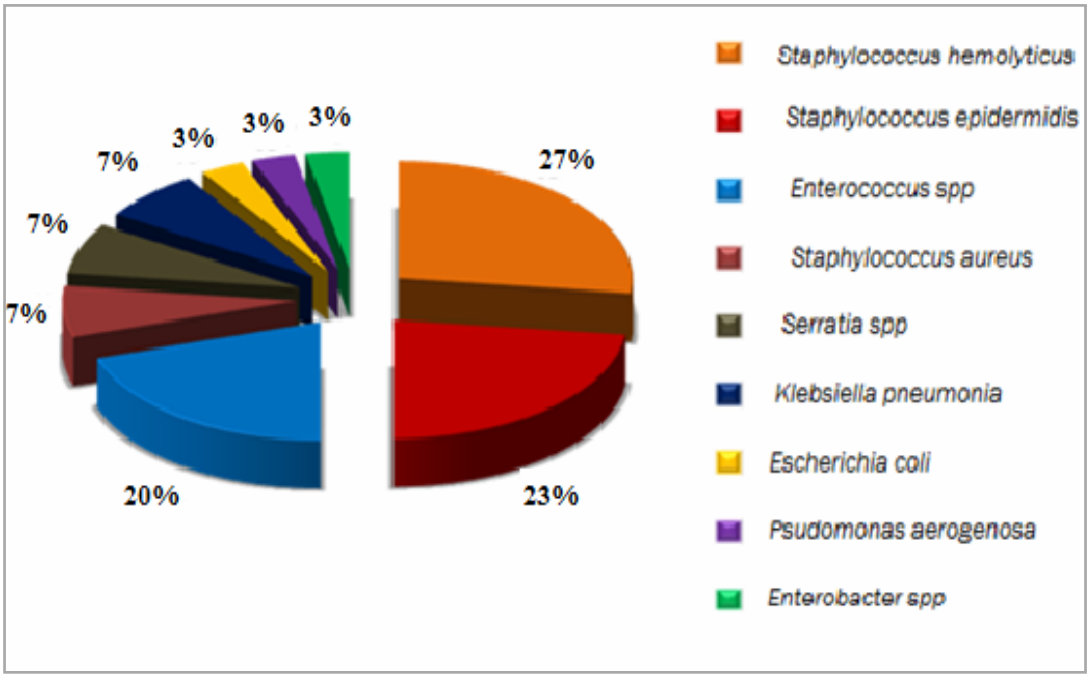

Figure 1: Distribution of bacteria among sample population

- **Antimicrobial susceptibility test results**

Escherichiacoli showed resistance to Ampicillin, Amoxicillin, Cefotaxime, Gentamicin, Ciprofloxacin and Chloramphenicol. It was only sensitive to Tetracycline and Amikacin. However, isolated Klebsiellapneumonia were found to have resistance to Ampicillin, Amoxicillin, Cefotaxime, Amikacin, Teteracycline as shown in table 2. Only 50% of them were resistant to Gentamicin. Pseudomonasaeruginosa showed resistance to Cefotaxime and Tetracycline only , All of isolated Staphylococcusaureus and Staphylococcushemolyticus were resistant to penicillin and ampicillin while 86% of Staphylococcusepidermidis were resistant to them. While all of isolated Staphylococcusaureus were resistant to cefuroxime, 50%ofStaphylococcushemolyticus and 71% of Staphylococcusepidermidis were resistant to it. 25% of Staphylococcushemolyticus were resistant to vancomycin. , all of isolated Enterococcusspecies were sensitive tovancomycin and chloramphenicol .

World Journal of Medicine and Medical Science
Vol. 4, No. 1, July 2015, pp. 1 -9, ISSN: 2330 - 1341 (Online)
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Table 2 : Percentage (%) of Antimicrobial Susceptibility Tests Results

Antibiotics	Enterobacterace												*Pseudomonas aeruginosa*			*staphylococcus species*									*Enterococcus species*		
	Escherichia coli [1]			*Klebsiella pneumonia* [2]			*Enterobacter species* [1]			*Serratia Species* [2]			*Pseudomonas aeruginosa* [1]			*Staphococcusaureus* [2]			*Staphococcushemolyticus* [8]			*Staphococcusepidermidis* [7]			*Enterococcus species* [6]		
	R	**I**	**S**	**R**	**I**	**S**	**R**	**I**	**S**	**R**	**I**	**S**	**R**	**I**	**S**	**R**	**I**	**S**	**R**	**I**	**S**	**R**	**I**	**S**	**R**	**I**	**S**
AM	100	-	-	100	-	-	100	-	-	-	100	-				100	-	-	100	-	-	86	-	14	17	-	83
AX	100	-	-	100	-	-	100	-	-	-	-	100															
CTX	100	-	-	100	-	-	-	-	100	-	-	100	100	-	-												
CN	100	-	-	50	50	-	-	-	100	-	-	100	-	-	100	50	-	50	12.5	-	87.5	14	-	86			
AK	-	-	100	100	-	-	-	-	100	-	-	100	-	-	100												
TE	-	-	100	100	-	-	-	100	-	-	-	100	100	-	-	-	-	100	37.5	12.5	50	71	-	29	50	-	50
CIP	100	-	-	-	-	100	-	-	100	-	-	100	-	-	100										67	-	33
C	100	-	-	-	50	50	-	-	100	-	50	50				-	-	100	-	-	100	14	-	86	-	-	100
PRL													-	-	100												
CAZ													-	-	100												
P																100	-	-	100	-	-	86	-	14	17	-	83
CXM																100	-	-	50	-	50	71	-	29			
VA																-	-	100	25	-	75	-	-	100	-	-	100
E																100	-	-	37.5	50	12.5	57	-	43	50	-	50
RIF																50	-	50	25	-	75	14	-	86	33	17	50
DXT																									33	17	50

Discussion

- **Isolated Bacteria from Pus swab from catheter exit site .**

All of identified bacteria from pus around the catheter exit site were similar to the bacteria isolated from patient's blood. This proves that the catheter exit site infection was the main source of GPC bacteremia. None of the referred previous studies explained the catheter exit site infection or attempted to identify the bacteria responsible for the infection. The results indicated that catheter exit site infection was one of several routes of the pathogenesis of bacteremia among CVCs. The results also is agreement with O'Grady who found that CVC can become contaminated with microorganisms via two major routes. The first of these routes was Extraluminally route which means that the patient's skin organisms at the insertion site can migrate along the surface of the catheter into the cutaneous catheter tract surrounding the catheter. Such migration results in colonization of the organisms at the catheter tip. For short-term catheters (non-tunneled CVCs in place less than 10 days), this is the most common source of infection [10].

Previous study suggested the use of either sterile gauze or sterile, transparent, semi permeable dressing to cover the catheter site [11],anduse a 2% chlorhexidine wash for daily skin cleansing to reduce CRBSI [12].Also, proper hand hygiene can reduce CRBSI and it can be achieved through the use of either an alcohol-based product [13] orwith soap and water with adequate rinsing [14]. A sample of correct method of hand hygiene was described by WHO and is presented in [15].

- **Prevalence of CVC related bacteremia among chronic hemodialysis patients**

In the present study, identified a total of 30 bacterial isolates which were collected from 30 infected catheters out of a total of 50 CVCscollected from kidney dialysis department . The percentage of CVC related bacteremia was (60%) among sample population. This bacteremia prevalence in the present study was higher than the bacteremia prevalence of a study conducted by Khalid Al Saran who showed that the prevalence of bacteremia was (56%) [16]. However, there are three previous studies referred to in this research whose reported prevalence ofbacteremia was higher than the prevalence of bacteremia in the present study. First of them, a study conducted by Zipporah Krishna Sami in USA reported that the prevalence of bacteremia was (79%) among sample population [17].The second study was done by Abdul Halim Abdul Gaforin Malaysia who found the prevalence ofbacteremia to be (64%) of the cases[18]. The third study was accomplished byNasserHussain et al. and they found the prevalence ofbacteremia was (89.5%) separated intotemporary catheter (39.5%) and permanent (50%)catheter[19] .

In the present study the results of distribution of bacterial isolates revealed that out of 30 bacteria recovered from patients, 23 (77%) were GPC while 7 (23%) were GNB. The predominance of GPC isolates in blood cultures of patients in the present study was in accordance with the findings of Al Saran in Saudi Arabia single center experience who showed that (67.3%) of CVC related bacteremia were caused by GPC while the GNB were responsible of (32.7%) of CVC related bacteremia [20]. Moreover, a study conducted by Zipporah Krishna Sami who reported (50%) of bacteremia cases were caused byGPC while (30%) of bacteremia cases caused byGNB [21].However, Gafor's study showed that (44.4%) of BSI were caused by GNB while (38.9%) of BSI were caused by GPC[22] and this distribution is not agreement with the findings of the present study.

- **Antibiotic Susceptibility Test Results of isolated bacteremia**

All of isolated *Staphylococcus aureus* were resistant to cefuroxime but 50% of *Staphylococcus hemolyticus* and 71% of *Staphylococcus epidermidis* were resistant to it. All of isolated *Staphylococcus species* were sensitive to vancomycin except two (25%) cases of *Staphylococcus hemolyticus* were resistant to it, not agreement to the results of the study accomplished by J. Gilad in southern Israel who found all gram-positive isolates were vancomycin-susceptible [23].

50% of *Staphylococcus aureus,* 12.5% of *Staphylococcus hemolyticus* and 14% of *Staphylococcus epidermidis* showed resistance to Gentamycin. Some studies suggested that this resistance was due to the adherence propertiesofagiven microorganism in relation to host factors whicharealso important in the pathogenesis of CRBSI. For example, *Staphylococcus aureus* can adhere to host proteins (e.g., fibrinogen and fibronectin) commonly present on catheters by expressing clumping factors (ClfA and ClfB) that are bound to the protein adhesions [24].

For Erythromycin, there were 100% of *Staphylococcus aureus*, 37.5% of *Staphylococcus hemolyticus* and 57% of Staphylococcus epidermidis resistant to it. Finally, 50% of *Staphylococcus aureus*, 75% of *Staphylococcus hemolyticus* and 86% of *Staphylococcus epidermidis* were sensitive to Rifampin. Certain strains of *Staphylococcus epidermidis*appear to be uniquely suited for causing catheter-related infections because of their ability to produce a biofilm or “slime” thatconsists of complex sugars (polysaccharides) which are believed to help the organism adhere to the catheter’s surface [25]. Another interpretation conducted by Humphreys from London reported that the main mechanism of resistance of *Staphylococcus. epidermidis* to β-lactams is mediated by β- lactamase production [26] .

ZipporahKrishna Sami reported that recent data suggest that biofilms in the catheter lumen are responsible for the bacteremia, and that instillation of an antibiotic lock (highly concentrated antibiotic solution) into the catheter lumen after dialysis sessions can eradicate the biofilm[27].Another study also reported thatinstillation of concentrated antibioticsolutions into the lumen of silicone vascular catheters(antibiotic lock) in vitro eliminates the biofilm[28].

Only 17% of isolated *Enterococcus species* were resistant to penicillin and ampicillin but all of themwere sensitive to vancomycin and chloramphenicol. This result differs from that ofAnandhiLakshmanan whoshowed one case out of three *Enterococcus species* cases wasresistant to vancomycin[29].

Enterobacterace showed resistance of *Escherichia coli* to Ampicillin, Amoxycillin, Cefotaxime, Gentamicin,Ciprofloxacin and Chloramphenicol and it was only sensitive to Teteracycline and Amikacin. Also, isolated *Klebsiella pneumonia* were showed resistant to Ampicillin, Amoxycillin, Cefotaxime, Amikacin, Teteracycline and only 50% of them were resistant to Gentamicin while all of isolated *Klebsiella pneumonia* were sensitive to Ciprofloxacin and 50% of them were sensitive to Chloramphenicol and this resistance of *Klebsiella pneumonia and Escherichia coli* against antibiotic may causes many of serious complication on patient and this agreement with ZipporahKrishna Sami who found that serious systemic complications occurred in 11 cases or 18% of the total sample[30].

A careful and correct selection of antibiotics is important to increase the chance of successful treatment and to reduce the rate of bacterial resistance and this is achieved using antibiogram. Antibiogramis a list of laboratory testing for the sensitivity of an isolated bacterial strain to different antibiotics Antibiograms are often used by doctors to assess local susceptibility rates, to select empiric antibiotic therapy, and to monitor resistance trends within an institution [31]

Conclusion

We conclude that in our study, the identified bacteria was similar to bacteria isolated from pus around the catheter exit site which proved that the catheter exit site infection plays an important role in the pathogenesis of bacteremia. Care of catheter exit site by physician, nurse and patient may help reduce the prevalence of bacteremia cases to lower limits. Gram positive cocci were the main etiologies for CVC associated infection among sample population at the hospitals involved in the study. Finally, Diabetic nephropathy and Hypertensive nephropathy were the main etiology of end stage renal disease among sample population.Antibiotic susceptibility test, like antibiogram, is an important test in the determination of the appropriate antibiotic to be given for a particular patient in order to confirm the patient's empiricaltherapy. Hence, the lab results are helpful to prevent the misuse of antibiotics when the appropriate antibiotic is selected that reduces the prevalence of antibiotic resistance phenomena.

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