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Complication of Hemodialysis Catheter Bloodstream Infections: Impact of Infecting Organism

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ABSTRACT:
Hemodialysis is a life-saving procedure in patients with chronic renal failure (CRF). However, in this procedure, infections, which often cause patient deaths, may develop due to catheter application. There were no data regarding catheter-related bloodstream infections (CRBSIs) in hemodialysis in Libya. In this study, we aim to study: To identify complications in patients with chronic renal failure associated with central venous catheter related infections in patients, undergoing hemodialysis, and to identify micro-organisms species, as well as their susceptibility profiles to the most commonly used antimicrobial agent.
We assessed common study testswas performed at the Microbiology Laboratory, from September to October 2022. 65 patients undergoing hemodialysis, at Janzour kidney service center, Tripoli, Libya.Were included in this research. Blood samples were collected from central venous catheter (CVC), and fistula-associated arteriovenous (AVF). The samples were cultured according to the standard microbiological procedures. Isolates were identified by conventional identification methods. Data was submitted to all patients to collect information such as age, gender, and health condition.

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We retrospectively examined65 patients hemodialysis, 33(51%) were female, and 32 (49%) were male. The mean age of the patients was 37.82 years ± 17.428 SD (range: 5-78). Hemodialysis access route was AVF in 55 patients (84.6%), and CVC in 10 patients (15.4%). Patients with use catheter days had higher cases of central venous catheter (CVC) 5(62.5%) compared to patients with was arteriovenous fistula (AVF) 3 (37.5%).Of the 65 blood cultures, 8(12.3%) tested positive. Among all microorganisms isolated, Candida albicans 2(25%) in the central venous catheter, and 1(12.5%) in the arteriovenous fistula. The second isolate the gram-positivebacteria were Staphylococcus aureus 3(37.5 %) in the central venous catheter, and gram-negative isolates organisms were Escherichia coli 2 (25%),) in the arteriovenous fistula. Identified bacteria isolates were tested for susceptibility to twelve antibiotics, high resistance in gram-negative isolates collection. E. coli was 100% resistant to CIP, AMP. Staphylococcus, aureus isolates showed extreme resistance against CFM, CL, IMI, C-5, MRP, F-300 and TOP 100%, 75%, respectively.

In conclusion, the fistula is the best available option for hemodialysis patients, with a much lower infection compared to patients with wasCentral venous catheter. A longitudinal study with comparison of multiple units representing different healthcare sectors would improve our knowledge on risk factors and practices associated withblood stream infection impact of infecting (BSIs) among hemodialysis patients in Libya.

Keywords: CVC, AVF, Bloodstream infections, Antimicrobial.

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مضاعفات عدوى مجرى الدم في قسطرة غسيل الكلى: تأثير الكائن الحي

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الملخص:
غسيل الكلى هو إجراء منقذ للحياة في المرضى الذين يعانون من الفشل الكلوي المزمن (CRF). ومع ذلك، في هذا الإجراء، قد تتطور الالتهابات، التي غالبًا ما تسبب وفاة المرضى، بسبب تطبيق القسطرة. لا توجد بيانات بشأن التهابات مجرى الدم المرتبطة بالقسطرة (CRBSIs) في غسيل الكلى في ليبيا. نهدف في هذه الدراسة إلى: التعرف على المضاعفات لدى مرضى الفشل الكلوي المزمن المرتبط بالعدوى المرتبطة بالقسطرة الوريدية المركزية لدى المرضى الذين يخضعون لغسيل الكلى، وتحديد أنواع الكائنات الحية الدقيقة، بالإضافة إلى مدى قابليتها بالعوامل المضادة للميكروبات الأكثر استخدامًا. قمنا بتقييم اختبارات الدراسة التي اجريت في مختبر الأحياء الدقيقة، في الفترة من سبتمبر إلى أكتوبر 2022. وقد تم تضمين 65 مريضًا يخضعون لغسيل الكلى، في مركز خدمات الكلى جنزور، طرابلس، ليبيا. تم تضمينها في هذا البحث، تم جمع عينات الدم من القسطرة الوريدية المركزية (CVC)، والناسور الشرياني الوريدي (AVF). وتمت زراعة العينات وفقاً للإجراءات الميكروبيولوجية القياسية. تم التعرف على العزلات بطرق التعريف التقليدية. تم تقديم البيانات لكل المرضى لجمع المعلومات مثل العمر والجنس والحالة الصحية. فحصنا بأثر رجعي 65 مريضا غسيل الكلى، 33 (51٪) كانوا من الإناث، و32 (49٪) كانوا من الذكور. كان متوسط عمر المرضى 37.82 سنة ± 17.428 SD (النطاق: 5–78). كان طريق الوصول إلى غسيل الكلى هو AVF في 55 مريضًا (84.6٪)، وCVC في 10 مرضى (15.4٪). كان المرضى الذين يستخدمون القسطرة

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في أيام أعلى من حالات القسطرة الوريدية المركزية (62.5) 5 (CVC٪) مقارنة بالمرضى الذين يعانون من الناسور الشرياني الوريدي (37.5) 3 (AVF٪). من بين 65 مزرعة دم، كانت نتيجة 8 (12.3٪) إيجابية. من بين جميع الكائنات الحية الدقيقة المعزولة، المبيضات البيضاء 2 (25٪) في القسطرة الوريدية المركزية، و1 (12.5٪) في الناسور الشرياني الوريدي. أما العزلة الثانية فكانت البكتيريا موجبة الجرام هي المكورات العنقودية 3 (37.5%)في القسطرة الوريدية المركزية، و العزلات سلبية الجرام هي الإشريكية القولونية 2(25%) في الناسور الشرياني الوريدي. تم اختبار حساسية العزلات البكتيرية المحددة لاثني عشر مضادًا حيويًا.

العزل الثاني في مجموعة البكتريا سالبة الجرام، كانت الإشريكية القولونية مقاومة عالية بنسبة 100% للسيبروفلوكساسين (CIP) و الامبيسلين (AMP). المكورات العنقودية أظهرت عزلات المكورات العنقودية مقاومة شديدة ضد السيفيكسيم (CFM)، السيفالكسين (CL)، الإميبينيم (IMI)، الكلورامفينيكول(C–5)، الميروبينم (MRP)، النتروفورانتوين (F–300) و التوبراميسين (TOP) 100% ، 75% على التوالي.

في الختام، يعتبر الناسور أفضل خيار متاح لمرضى غسيل الكلى، مع نسبة إصابة أقل بكثير مقارنة مع المرضى الذين يستخدمون القسطرة الوريدية المركزية. إن إجراء دراسة طولية مع مقارنة وحدات متعددة تمثل قطاعات رعاية صحية مختلفة من شأنه أن يحسن معرفتنا بعوامل الخطر والممارسات المرتبطة بإلتهابات مجرى الدم(BSI) بين مرضى غسيل الكلى في ليبيا.

الكلمات الدالة: القسطرة الوريدية المركزية (CVC)، الناسور الشرياني الوريدي(AVF)، التهابات مجرى الدم، مضادات الميكروبات.

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INTRODUCTION :

Hemodialysis patients are at a high risk for infection because the process of hemodialysis requires frequent use of catheters or insertion of needles to access the bloodstream [1]. Hemodialysis patients have weakened immune systems, which increase their risk for infection, and they require frequent hospitalizations and surgery where they might acquire an infection [2]. 20% of prevalent hemodialysis patients depend upon central venous catheters as their primary vascular access [3]. Catheter-related bloodstream infection (CRBSI) is one of the most feared consequences of hemodialysis catheter use due to its associated increased risk of morbidity and mortality [4]. Some patients are successfully treated with intravenous antibiotics administered at their outpatient dialysis units, while others develop potentially life threating complications necessitating a high level of inpatient care .[5]

Patients undergoing hemodialysis are liable to infection cited for several predisposing issues, ,Impaired immunity due to renal failure, comorbidities, malnourishment that increase the virulence and the adherence properties of hospital bacteria as well as the breakdown of the protective anatomical barriers due to repeated intravascular intervention required for hemodialysis, represent the main reasons for the high prevalence of bloodstream infection in those patients [6,7]. Recurrent exposure to hospital instruments, as well as microbial colonization of the hemodialysis catheter during hemodialysis sessions [8]. It is proposed that microbial bloodstream invasion and subsequent CRBSI can occur by one of 2 routes. An extra luminal pathway, in which the microorganisms are transferred

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from the skin insertion site to the catheter tip and then invade the blood stream .[9]

Alternatively, the intraluminal pathway involves adventitious contamination of the catheter hub and subsequent microbial colonization of the lumen secondary to improper aseptic precautions during catheter manipulation by the health-care personnel. Regardless of the 2 pathway of infection, whenever the pathogen is introduced into the bloodstream, it may adhere to the catheter surface or become embedded within a fibrin layer [10]. Being an inanimate medical device, microbial attachment to the catheter surface stimulates biofilm formation which is an orchestrated community of microorganisms living within an exopolysaccharide matrix [11]. CRBSIs are frequently caused by Gram-positive bacteria, particularly coagulase-negative staphylococci (CONS) and Staphylococcus aureus [12]. Currently, Gram-negative bacteria are condemned to be etiologic agents for CRBSIs [13]. Accumulating evidence points to a growing burden of infection among patients on dialysis. The risk of infection varies with the characteristics of the patients who are selected for dialysis. Increased access to dialysis has led to less-stringent selection of patients, as characterized by an increasing proportion of elderly patients, those with diabetes, and frail individuals with complex coexisting conditions [14]. In addition, the trend towards advancing age among patients receiving dialysis is expected to confer an increased susceptibility to infection; older age has repeatedly proven to be an independent risk factor for infection in dialysis populations [15]. Previous studies suggested that the vascular access for hemodialysis is the major risk factor for bacteremia in patients with end stage renal disease.[16]

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MATERIALS AND METHODS:

Study design :

This study has conducted at the microbiology laboratory, and collected specimens from patients' hemodialysis at Janzour kidney service center, Tripoli, Libya, from September to October 2022. The ethical research committee gave ethical approval for the study. Data was submitted to all patients to collect information such as age, gender, and health condition.

Study population :

A total of 65 patients, were included in the study 32 male and 33 female. Aged were between 5-78 years. The patients who participated in the study were from different regions of Libya. In this study two samples were taken: Blood samples were collected from central venous catheter (CVC) , and arteriovenous fistula (AVF).

Sample Collection and Transport :

Ten ml of blood collected from the patients undergoing hemodialysis course, were collected aseptically using a sterile needle and syringe from the distal edge of directly from the central venous catheter or fistula after disinfection, with chlorhexidine-alcohol 0.5%. Inoculated into aerobic culture bottles, and transported to the microbiology laboratory, for analysis within 30 minutes.

Isolation and Identification of Microorganisms :

Blood culture bottles, which were incubated at 37°C for 18-24 hours (up to 1 week if necessary). After incubation, the bacterial growth on the cultures isolated onto Bloodagar, Mannitol salt agar, MacConkey agar, and sabouraud dextrose. All strains isolated

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identification, according to the standard microbiological methods. Characteristics morphological description of colonies is hemolytic pattern, microscopic examination, and biochemical reactions.

Bacterial Antibiotic Susceptibility Testing :

Antimicrobial susceptibility testing was performed based on the Kirby Bauer disc diffusion method using Clinical and Laboratory Standard Institute guidelines [14]. Pure colonies of respective bacteria isolate and inoculated to Mueller Hinton agar plates. The inoculated plates were left at room temperature to dry for 3–5 min and a set of antibiotic discs were 7placed on the plates. The following antibiotic discs with their respective concentrations were used: Methicillin [MET,5µg]; Cefixime [CFM,5µg]; Vancomycin [VA,5µg]; Ciprofloxacin [CIP,5µg]; Cephalexin [CL,30µg]; Ampicillin [AMP,10µg]); Fucidic acid [FC.,10µg]; Tobramycin [TOP,1µg]; Nitrofurantion [F,300 µg]; Chloramphenicol [C,5µg]; Meropenem [MRP,10µg]; Imipenem [IMI,10µg [.

Statistical analysis :

The raw data were entered into excel spreadsheets and later imported to SPSS software version 26 (IBM Corp., Armonk, N.Y, USA). Descriptive statistics were used to calculate the mean standard deviation, and median. For the total number, Chi-square test was used to compare blood stream infection impact of Infectingcases according to demographic and clinical variables.

RESULTS :

Of the 65 patients hemodialysis, 33(51%) were female, and 32 (49%) were male. The mean age of the participants was 37.82 years ± 17.428 SD (range: 5-78). The participants were

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eitherhypertension, and diabetes mellitus, 35 cases (53.8%), 25(38.5%) respectively. Hemodialysis access route was AVF in 55 patients (84.6%), and CVC in 10 patients (15.4%), as show in table (1). The main signs and symptoms observed in patients with BSI were fever, 7 (87.5%), and nausea, 2 (25%), as shown in table (2). The results show that there was a statistically significant difference patients infection incidence according to types catheters ($\chi 2$ (1) = 3.841, P = 0.002). Patients with use catheter days had higher cases of Central venous catheter (CVC) 5 (62.5%) compared to patients with was arteriovenous fistula (AVF) 3 (37.5%), as shown in table (1). Of the 65 blood cultures, 8 (12.3%) tested positive. Among all microorganisms isolated, Candida albicans 2(25%) in the central venous catheter, and 1(12.5%) in the arteriovenous fistula. The second isolate the gram-positive bacteria were Staphylococcus aureus 3 (37.5 %) in the central venous catheter, and gram-negative isolates organisms were Escherichia coli 2 (25%),) in the arteriovenous fistula, as show in table (3).Identified bacteria isolates were tested for susceptibility to twelve antibiotics. High resistance in gram-negative isolates collection, E. coli was 100% resistant to all tested antimicrobials. S. aureus isolates showed extreme resistance againstS. aureus were the most frequent (100%) resistant to, Cefixime, Tobramycin,Nitrofurantion,Chloramphenicol, Meropenem, and Imipenem, 100%, E. coli was the most frequently isolated (25%), and they were 100% resistant to Ciprofloxacin, and Ampicillin, as shown in Table [4].

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Table 1. Clinical Characteristics of the study population

Clinical Characteristics	All patient (n=65)	Patient with bloodstream infection (n=8)	Patients without bloodstream infection (n=57)
Gender: Male Female	32(49%) 33(51%)	5(16%) 3(9%)	27(47%) 30 (53%)
Vascular access: Arteriovenous fistula Central venous catheter	55(84.6%) 10(15.4%)	3(37.5%) (62.5%) 5	52(91%) 5(9%)
Causes of renal failure: Hypertension Diabetes mellitus	35(53.8%) 25(38.5%)	3(37.5%) 4(50%)	32(56.1%) 21(36.8%)
Serological tests: Hepatitis C virus positive Hepatitis B virus positive	5(7.7%) -	- -	- -
Duration of hemodialysis: Frequency of hemodialysis (days)	All 3 days a week	All 3 days a week	All 3 days a week

Note: Values are presented as number of patients (n) and percentage (%), $P < 0.001$

Table 2. Frequency and percentage of clinical signs of the study population

Complications	All patients, (n=65)	Patients with bloodstream infection (n=8)	Patients without bloodstream infection (n=57)
Fever	9(13.8%)	7(87.5%)	2(3.5%)
Chills	-	-	-
Nausea	7(10.8%)	1(12.5%)	5(8.8%) 4(7.0%)
Vomiting	-	-	-
Cramps	4(6.2%)	-	

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TABLE 3.Pathogen types isolated from blood culture from vascular access.

Microorganisms isolated n=8	Central venous catheter	Arteriovenous fistula
S. aureus	3	-
E.coli	-	2
Candidiaalbicans	2	1

TABLE4. Prevalence and resistance of bacterial agents isolated vascular access.

Antibiotic	S.aureus	E. coli
Methcillin[5µg] MET	1(33.33%)	0
Cefixime[5µg] CFM	3(100%)	0
Vancomycin[5µg] VA	2(66.7%)	0
Ciprofloxacin[5µg] CIP	2(66.7%)	2(100%)
Cephaalexin [30µg] CL	3(100%)	0
Ampicillin [10µg] AMP	2(66.7%)	2(100%)
Fucidic acid [10µg] FC	2(66.7%)	0
Imipenem [10 µg] IMI	3(100%)	0
Chloramphenicol [5 µg] C-5	3(100%)	0
Meropenem [10 µg] MRP	3 (100%)	0
Nitrofurantoin [300 µg] F-300	3(100%)	0
Tobramycin [10 µg] TOP	3(100%)	0

Note: 0 = Resistant microorganisms

DISCUSSION:

The prevention and control of bacterial and fungal infections in patients receiving hemodialysis via CVCs is a constant concern for health professionals. Although CVCs are an important component in the management of patients, these catheters also significantly

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contribute to BSIs [15]. In study in Saudi Arabia, involving 57 patients undergoing hemodialysis via temporary CVC, 19.3% developed catheter related infection [16]. Such variations in BSI rates are possible because of differences in the characteristics of patients and vascular access management protocols that are applied at different hemodialysis units. Type of vascular access is a known risk factor for BSI among hemodialysis patients. Several studies have found that rates of BSI in patients undergoing hemodialysis appear to vary depending on the type of vascular access .[17]

Use of AVF in the current study was higher (84.6%), compared to CVC (15.4 %), as in the study by Karkar et al who found a significant increase in the use of AVF and a reduction in CVC implantation associated with a decrease in infection rates [18]. Findings showed that the use of CVC was the independent risk factor for the occurrence of BSI among hemodialysis patients compared to AVF. This finding is consistent with those of Fram et al who reported an 11.2-fold increase the chance of developing BSIs with the use of CVC, compared to AVF P<.001.[19]

In another study, the absence of fistula was a risk factor for developing BSI P=.047 [20]. Use of AVF is thought to be the most appropriate vascular access, with a lower risk of complications including infection [21]. Our findings emphasize the importance of reducing the use of catheters in hemodialysis patients as much as possible and using a fistula instead. However, the use of a fistula has some limitations and is not always possible especially in elderly and diabetic patients [22]. Regarding isolated microorganisms previous studies [15]. We have reported a high prevalence of gram-positive organisms in patients undergoing hemodialysis treatment, mainly

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S.aureus [17, 19, 21]. However, we observed that gram-negative organisms were the predominant organisms (54.6%). E. coli was the most frequently isolated (25%), and they were 100% resistant to Ciprofloxacin, and Ampicillin. Gram-positive organisms represented 37.5% S. aureus were the most frequent (100%) resistant to, Cefixime, Tobramycin, Nitrofurantion ,Chloramphenicol , Meropenem, and Imipenem. Infections in hemodialysis patients are often caused by resistant microorganisms, due to the frequent need for antimicrobial therapy and frequent hospitalizations [20]. Antimicrobial susceptibility in this study showed that more than a third of isolated bacteria were multiply resistant. According to the United States Centers for Disease Control, the rational use of antibiotics is an important measure for controlling the spread of multiply resistant microorganisms [23]. Fram et al found that prior antimicrobial use was associated with a higher occurrence of BSI P=.013.[19]

CONCLUSION :

Type of vascular access represents the main risk factor associated with BSI in patients undergoing hemodialysis. Vascular access has a strong influence on the clinical outcomes of hemodialysis treatment. The fistula is the best available option for hemodialysis patients, with a much lower infection rate compared to the catheter. A longitudinal study with comparison of multiple units representing different healthcare sectors would improve our knowledge on risk factors and practices associated with BSIs among hemodialysis patients in Libya.

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