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RESEARCH ARTICLE

Relationship between Interluekine-10 and Bacterial Infection in Hemodialysis Patients

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ABSTRACT

Hemodialysis (HD) is a vital life-saving operation accounting for around 69% of all kidney replacement therapy and 89% of all dialysis, but dialysis has various issues, one of which is bloodstream infections (BSIs), which are the second leading cause of mortality in end-stage renal disease patients. Interleukin-10 (IL-10) is an anti-inflammatory cytokine that helps to regulate the immunological response to infection. To study the correlated catheter-related blood stream infection with the clinical presentation of the patient group and the correlated IL-10 with a specific catheter-related blood stream infection. This is a case-control research conducted in the dialysis unit. The central venous catheter was used to collect 7 ml of blood from the patient and control groups, 5 ml of which was transferred to a blood culture container for culturing, and the remaining 2 ml was immediately deposited in a gel tube. Interleukin 10 was measured using conventional sandwich ELISA research kits. The results show that bacterial infection occurs in 48.6% of center venous catheter patients and 8.6% of arteriovenous fistula patients. IL-10 was high in patients with bacterial infection compared to patients without bacterial infection. Patients with center venous catheter types had more bacterial infections than arteriovenous fistulas. IL-10 levels were higher in patients with bacterial infections compared to patients without bacterial infections.

INTRODUCTION

End-stage renal disease (ESRD), which affects about 13% of the world's population, is brought on by chronic kidney disease (CKD), which is now considered a concern for the world's health due to its growing rates of morbidity and mortality, association with poorer quality of life, and high associated costs. [1], when kidney function progressively declines and treatment with renal replacement therapy (dialysis or transplantation) is required [2], it is necessary to have a vascular access that is functional in order to obtain adequate levels of dialysis effectiveness. The perfect vascular access should have a number of precise properties, the most significant of which are as follows: With the simplicity of installation, there are several desirable qualities in a kidney transplant, including the capacity to provide enough blood flow for effective dialysis, high primary patency rates, low rates of problems and side effects, a long lifespan, and minimal economic costs. The three most common vascular accesses for extracorporeal hemodialysis are central venous catheters (CVCs), arteriovenous fistulas (AVFs), and prosthetic arteriovenous grafts (AVGs) [3].

Hemodialysis (HD) is a vital life-saving operation, accounting for around 69% of all kidney replacement therapy and 89% of all dialysis, and is the most popular treatment for renal replacement therapy. The purpose of hemodialysis is to restore the fluid inside the cell environment. This is a feature of normal renal function. It does this by transporting dissolved chemicals such as urea from the blood into the dialysate and also by conveying dissolved substances such as bicarbonate through the dialysate into the blood [4].

Dialysis has many complications, one of which is bloodstream infections (BSIs), which are the second leading cause of mortality among end-stage renal failure patients. The risk of infection is generally associated with the dialysis operation itself, specifically the kind of vascular access [5]. Central venous connections increase the risk of infection in patients undergoing continuous hemodialysis by two to three times compared to arteriovenous fistulas or grafts. Most often encountered are infections at the point of departure, infections in the tunnel, and CRBSIs (catheter-related bloodstream infections) [6]. Central line-associated bloodstream infection (CLABSI) occurs when an invasive device, such as a central vascular catheter (CVC), is inserted into a vein; however, only a small percentage of nosocomial infections are linked to CVCs [3]. Whenever a pathogen enters the bloodstream, it can stick to the catheter site or implant itself in a fibrin layer. As the catheter is an inactive medical product, microbial adhesion to its surface triggers the formation of biofilm, which is an organized community of microorganisms residing within an exopolysaccharide matrix. Bacterial biofilms that form within the catheter lumen are a source of catheter-associated bacteremia [7]. Bloodstream infections caused by bacteria are especially dangerous for dialysis patients due to immune system changes, higher rates of colonization with organisms, more frequent hospitalizations, and more contacts with the healthcare system [8]. When pathogen-associated molecular patterns (pamps); for instance, bacterial lipopolysaccharide) are detected, they trigger non-specific immune actions (such as cytokine production) [9].Interleukin 10 (IL-10) is an immunosuppressant and anti-inflammatory cytokine that is crucial for the body's defence systems and a member of the class-2 cytokine group, which also consists of IL-19, IL-20, IL-22, and IL-24, as well as interferons type I (IFN-alpha, beta, epsilon, kappa, omega), type II (IFN-gamma), and type III (IFN-lambda) [10]. The physiologically active form of IL-10 has a short half-life and is easily broken in vivo. The secretion of IL-10 always lags behind the release of pro-inflammatory factors by a few hours, and it may exert its effects locally, via autocrine or paracrine mechanisms, or systemically, via a more hormonal mechanism [11]. Interleukin-10, which is important for suppressing cell-mediated immunity and for reducing the development of MHC class II molecules on monocytes and macrophages, so causing these cells to decrease their release of pro-inflammatory cytokines [12]; addition (IL-10) has an important role in the defence system of the host against infection; cytokine, controls the production of both Th1 and Th2, respectively [13].The capacity of type 1 regulatory (Tr1) cells to generate large quantities of IL-10 and transforming growth factor-b (TGF-b) is what distinguishes these cells from other types of regulatory cells. In the patients, the feedback mechanism of IL10 that is responsible for lowering monokine production seems to be functional. Because of this, the release of IL-10 might be considered a compensatory mechanism that limits the induction of monokine production caused by chronic renal failure and the therapy of hemodialysis [14].

MATERIALS AND METHODS

Study Design

The dialysis unit at Imam Hussein Teaching Hospital served as the site of this case-control study. Every patient had a hemodialysis registration between December 2022 and April 2023.In this study, one hundred (100) participants were enrolled, with three groups participating in a case-control analysis based on a clinician's clinical diagnosis: the first group consists of patients with fever and chills, which were confirmed to be caused by bacterial infection and who have a central venous catheter (CVC) [35 (22 males, 13 females]; the second group consists of 35 asymptomatic

hemodialysis patients, which were confirmed to have an arteriovenous fistula (AVF) (18 males, 17 females); and the third group consists of thirty healthy control groups (14 males, 16 females). The age range of each group is from (10 – 80) years old.

Inclusion and exclusion criteria

This research covered all cases in hemodialysis centers with or without fever, chill, or oedema at the catheter site, as well as healthy individuals, but this research is not suitable for participants who are suffering from an autoimmune illness , viral hepatitis, diabetics, and those taking antibiotics.

Blood sample collection

Each patient group and control group had 7 milliliters of blood drawn via a central venous catheter, of which 5 milliliters were transferred to a blood culture container in order to be cultured. The other 2 ml of blood was immediately placed in a gel tube and was permitted to coagulate at room temperature [20 to 25 °C] for 15 minutes. The gathered specimens were centrifuged at 3000 rpm for approximately 15 minutes to separate the serum. The serum was kept at -20°C until the immunological test. The blood level of interleukin 10 was measured using conventional sandwich ELISA research kits.

When the blood culture test is positive, the samples are plated onto a variety of culture media, including "blood agar, MacConkey, and brain heart infusion broth enrichment media", and then cultured at 37 degrees for a whole day. The recovered bacteria were identified using morphological and microscopic features. Bacterial type was confirmed using automated VITEK2.

Automated techniques are the fastest and most accurate approach to identify microorganisms. To produce a biochemical profile for organism diagnosis, the VITEK2 system employs plastic reagent cards with Microliter quantities. of several biochemical test mediums in 30 wells. Automatic inoculation from cultured samples is conducted, and the colour change of the card caused by the microbe's metabolic activity is measured at regular intervals using a photometer. Several types of cards, involving those for Gram-negative GN identification and Gram-positive GP identification, are now accessible since the data is assessed recorded and printed in a computer database[15].

Statistical analysis

Data analysis was done statistically using "IBM SPSS" statistical packages version 23. The analysis results were summarized using descriptive statistics. Additionally, statistical differences between two independent groups have been determined using the Mann-Whitney test and the independent T-test. Besides, the analysis of variance (ANOVA) was carried out to conduct multiple comparisons between groups.

RESULTS

A total of 100 blood samples (70 patients and 30 controls) patients subdivided into 35 center venous catheters and 35 arteriovenous fistulas. The age group varied from 10 to 80) years. Blood samples were collected with volume 10 ml, blood culture was done for bacterial isolation and identification. The current study's results show that bacterial infection occurs in 48.6% of center venous catheter patients and 8.6% of arteriovenous fistula patients. The results showed that there was a significant difference in serum level ($P < 0.05$) between interleukin-10 and infected and non-infected patients with bacteremia, where the concentration of IL-10 was high in patients with bacteremia compared to patients without bacteremia, and there was a significant difference between interleukin-10 and types of bacteria, as it was high in *Escherichia coli*, followed by *Staphylococcus aureus*.

Table 1: Association of positive and negative blood culture according to type of vascular access

Type of Vascular Access	Result of BC		Total	*p*. value
	Negative	Positive		
CVC	18	17	35	0.001
	51.4%	48.6%	100%	
AVF	32	3	35	
	91.4%	8.6%	100%	
Control	30	0	30	
	100%	0%	100%	
Total	80	20	100	
	100%	100%	100%	

Chi square has been used in comparison, sig: significant, nsig; not significant *p*. value (≤ 0.05)

Table2: Comparison between subject's study group according to(IL-10)

parameter	Subject group		P. value
IL-10	CVC	AVF	0.001
		Control	0.000
	AVF	CVC	0.001
		Control	0.773
	Control	CVC	0.000
		AVF	0.773

Schiff's post-hoc test was utilized at ($p < 0.05$) for multiple comparisons within groups

Table 3: Distribution (IL-10) according to the result of blood culture

parameter	result of BC	Mean		*SD*	*p*. value
IL- 10	Negative	6.887	±	17.666	0.005
	Positive	22.182	±	19.670	

Mann-Whitney Test

Table 4: Difference between Type of Bacteria according to IL-10

Parameter	Type of bacteria		*p*. value
IL- 10	E.coli	S. hominis	0.000
		S.aureus	0.006
		S. epidermidis	0.000
	S. hominis	E.coli	0.000
		S.aureus	0.600
		S. epidermidis	1.000
	S.aureus	E.coli	0.006
		St. Hominis	0.600
		S. epidermidis	0.494
	S. epidermidis	E.coli	0.000
		S. hominis	1.000
		S.aureus	0.494

Scheffe's post-hoc test was utilized at ($p < 0.05$) for multiple comparisons within groups

Table (1) shows that there was a significant difference (p <0.05) in the rate of positive blood culture in patients with CVC compared with patients with AVF.

Table (2) shows that there was a significant difference at (p<0.05) between the CVC, AVF, and control groups.

Table (3) the results of the statistical analysis that revealed the comparison between the levels of IL-10 in patients with positive and negative blood cultures. It found that there was a significant difference in the level of IL-10 (p<0.05) between the positive and negative blood cultures.

Table (4) found that there was a significant difference between the type of bacteria and the level of IL-10. The level of IL-10 was found to be highly high among the bacteria *E. coli* and *S. aureus* (p < 0.006).

DISCUSSION

Interleukin-10 (IL-10) is an anti-inflammatory cytokine that plays an important role in regulating the immune response [16]. During an extracellular, highly pro-inflammatory bacterial infection, the pathogen primarily neutralizes or kills immune response effector cells. In this setting, the synthesis of IL-10 controls the severity of the immune response, allowing for effective bacterial clearance without causing severe tissue damage. Although in certain circumstances the lack of IL-10 makes the immune response more efficient to remove the infection, the damage caused the host tissues is more severe and threatens host survival. [17]. [18] found that IL-10 levels were significantly higher in patients with bacterial infections compared to those without infections. The presence of bacterial endotoxins in the bloodstream, which can occur during bacterial infections, may also stimulate the production of IL-10. Bacterial endotoxins are known to activate Toll-like receptors on immune cells, leading to the production of pro-inflammatory cytokines and chemokines, as well as anti-inflammatory cytokines such as IL-10 [19]. A previous study suggested the immune system activates a complex network of signalling pathways and cytokines, including IL-10, in an attempt to fight off the infection and limit inflammation [20].

There are many studies showing that the prevalent fistula was associated with lower risk for BSI compared with prevalent CVC [21], and previous studies found that positive blood cultures were significantly higher in patients with CVCs compared to those with either AVFs or AVGs, and another study presented by [22] found that 1.86% of patients with CVCs had positive blood cultures, compared to only 0.8% of patients with AVFs. [23] founded that central venous catheters (CVCs) are more prone to bloodstream infections than arteriovenous fistulas (AVFs) in hemodialysis patients, which agrees with the current study, and a similar study confirmed that vascular access of the "CVC" double lumen, which is responsible for about 30 to 60% of "catheter-related infection in hemodialysis patients", and hospitalization rates are higher among patients with "CVCs" than among AVF (native arteriovenous fistulas) [24].

The previous studies demonstrated that CVCs are more prone to the formation of biofilms, which are layers of bacteria that can adhere to the surface of the catheter. Biofilms can protect bacteria from the immune system and antibiotics [25], catheters provide a direct route for bacteria to enter the bloodstream along the catheter surface [26], and catheters require frequent manipulation and access that can introduce bacteria [27].

AVF is the preferred vascular access for hemodialysis patients because it provides better blood flow and is associated with a lower risk of complications such as infection and thrombosis compared to other types of vascular access, including intravenous catheters. AVF is created by connecting an artery and a vein in the patient's arm, allowing for repeated access for hemodialysis without the need for repeated needle punctures [28].

CONCLUSION

Patients with centre venous catheter types had more bacterial infections than arteriovenous fistulas, and the most predominant bacterial was Staphylococcus epidermidis. IL-10 levels were higher in

patients with bacterial infections compared to patients without bacterial infections. Staph aureus and E. coli were the most common bacteria species that increased the level of IL-10.

Ethical approval

The Department of Clinical Laboratories at Karbala University's College of Applied Medical Sciences devised standards for handling biological materials and potentially hazardous bacteria. After getting approval from the patients and hospital management, samples were collected from dialysis patients at the Karbala Health Directorate for the purpose of this study.

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