University of Kerbala
College of Applied Medical Sciences
Department of Clinical Laboratories

Isolation and characterization of causative bacteria of catheter related blood stream infection and the role of interleukin-10 in chronic renal disease patients on hemodialysis

A Dissertation Submitted to The Council of the College of Applied Medical Sciences University of Kerbala in Partial of Fulfillment of the Requirements for The Degree of Master in Clinical Laboratories

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بِسۡمِ ٱللَّهِ ٱلرَّحۡمَٰنِ ٱلرَّحِيمِ

﴿وَأَنزَلَ ٱللَّهُ عَلَيۡكَ ٱلۡكِتَٰبَ وَٱلۡحِكۡمَةَ وَعَلَّمَكَ مَا لَمۡ تَكُن تَعۡلَمُۚ وَكَانَ فَضۡلُ ٱللَّهِ عَلَيۡكَ عَظِيمًا ﴾

صدق الله العلى العظيم

النساء (113)

Dedication

At First, I Am Grateful to Allah for The Good Health and Wellbeing That Were Necessary to Complete This Research....

To My Family (Father and Mother) And to My Sweet and Loving Husband Header, To My Kids (Maryam and Karrar).

Who Supported Me and They Were Proud of Me and Helped Constantly to Complete This Research....

Duha ,2023

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Supervisor's certification

I certify the thesis entitled (**Isolation and characterization of causative bacteria of Catheter related blood stream infection and The role of interleukin-10 in chronic renal disease patients on hemodialysis)** was prepared under my supervision by **Duha Hussein Jiyad** at the department of Clinical Laboratories\ College of Applied Medical Sciences\ University of Kerbala, in partial fulfillment of the requirements for the degree of Master in Clinical Laboratories.

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/ / 2023

Head of Department Recommendation

In view of the available recommendation, I forward this thesis for debate by the examining committee.

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/ /2023

Approval Certification

We certify that the thesis entitled (**Isolation and characterization of causative bacteria of Catheter related blood stream infection and The role of interleukin-10 in chronic renal disease patients on hemodialysis**) fulfills partial requirements of the degree of Master in Clinical Laboratories.

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4 \10\ 2023

Committee Certification

We, the examining committee, certify that we have read the thesis entitled " **Isolation and characterization of causative bacteria of Catheter related blood stream infection and The role of interleukin-10 in chronic renal disease patients on hemodialysis"** and have examined the student **(Duha Hussein Jiyad)** in its content and that in our opinion it is accepted as a thesis for degree of Master of **Clinical Laboratories.**

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/ / 2023

I have certified upon the discussion of the examining committee.

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Assist. Prof. Dr. Huda Abdalreda Abdullah

Dean of the College of Applied Medical Sciences / University of Kerbala

4 /10/ 2023

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Table of Abbreviations	
Abbreviations	Full Nomenclature
AG	Antigen
AKD	A cute kidney disease.
AMR	Antimicrobial resistant
AMX	Ammoxillin
AST	Antimicrobial susceptibility test
AVF	Arteriovenous fistulas.
AVG	Arteriovenous graft
BSI	Blood Stream infection
CID	Clindamycin
CKD	Chronic kidney disease
CN	Gentamycin
CRBSIS	Catheter-related blood stream infection
CRF	Chronic renal failure.
CSIF	Cytokine Synthesis inhibitor factor
CTM	Cefotaxime
CTX	Ceftriaxone
CVC	Central venous Catheter
EGFR	Estimated glomerular filtration rate
ESRD	End-stage renal disease
GFR	Glomerular filtration rate
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HD	Hemodialysis
HIV	Human immunodeficiency

IFN	Interferon
IL	Interleukin
IMI	Imepeneme
MDR	Multidrug-resistant
MEM	Meropeneme
MHC	Major histocompatibility Complex
MRSA	Methicillin-resistant- Staphylococci- aureus
NIH	Neointimal hyperplasia
NK	Natural killer
PAMPS	Pathogen-associated molecular patterns
PD	Peritoneal dialysis
PDR	Pan drag resistance
PEC	Pathogenic-Escherichia coli
PICC	Peripherally inserted Central Catheter
PMNLS	Poly morph nuclear Leukocytes.
PRRS	Pattern recognition receptors
RRT	Renal replacement treatment
TCF-B	Transforming growth factor b
TH	T-helper
TLR	Toll-like receptor
TZP	Piperacillin / Tazobactam
VA	Vascular access

Summary

Infection is a common complication and is the second leading cause of death in hemodialysis patients. The risk of bacteremia in hemodialysis patients is 26-fold higher than in the general population, and 1/2-3/4 of the causative organisms of bacteremia in hemodialysis patients are Gram-positive bacteria، hemodialysis patients have a higher risk of *Staphylococcus* infection and the most common site of infection causing bacteremia is internal prostheses.

The aims of the study are to Characterize and distribution of type of bacterial infection and antibiotic susceptibility test and the relationship of interleukin-10 with catheter related bloodstream infection.

The present study is designed to deal with blood Stream infection in hemodialysis Patient, after establishing the diagnosis via investigation and clinical diagnosis at the dialysis center in Imam AL-Hussein hospital in Kerbala province during the period from November 2022 to April 2023.

A total of (100) blood samples (70 patients and 30 controls), patients group sub divided 35 center venous catheter, 35 arteriovenous fistula), the age group varied from (10-80) year. Blood samples were collected with volume 10 ml, blood culture was done for bacterial isolation and identification, after that many analyses were performed, including kidney function test (urea, creatinine, sugar), immunological index (interleukin10), Microbiological test (Antibiotic susceptibility test).

The current study's results show that bacterial infection occurs in 48.6% of center venous catheter patients, 8.6%of arteriovenous fistula patients, *Staphylococcus epidermidis* was the most bacterial species isolated from hemodialysis patients.

The results of antibiotic resistance show that (85.7%) from resistant to Ammoxillin and (14.3%) of *Staphylococcus epidermidis* resistant to Cefotaxime, Ceftriaxone, Meropeneme, Clindamycin, (100%) *Staphylococcus aureus* resistant to Ammoxillin, 80% resistant to Ceftriaxone, (60 %) resistant to Gentamycin, (40%) resistant to Cefotaxime, (20%) resistant to , Meropeneme ,(80%)of *Staphylococcus hominis* resistant to Ammoxillin ,(60%), resistant to Gentamycin, Ceftriaxone (40%) resistant to Cefotaxime,(20%) resistant to Piperacillin/Tazobactam, (100%) *Escherichia Coli* resistant to Cefotaxime , Ammoxillin (66.7%) resistant to Ceftriaxone, Clindamycin, (33.3%) resistant to Gentamycin.

The results showed that there was a significant difference in serum level at ($P < 0.05$) 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* bacteria with an average of (62.981), followed by *Staphylococcus aureus* bacteria with an average of (24.977) and then *Staphylococcus Hominis* with an average of (11,054) and *Staphylococcus Epidermidis* with an average (10,650).

The result concluded that patient with center venous catheter type was the most bacterial infection than arteriovenous fistula in and the most predominant bacterial was *Staphylococcus epidermidis*, and the most effective antibiotic was Imepeneme for gram-positive bacteria, Piperacillin/Tazobactam for gram negative bacteria, IL-10 was high in patients with bacterial infection compared to patients without bacterial infection.

Chapter One

Introduction

1.1 Introduction

Chronic kidney disease is a degenerative condition that affects 8–16% of the world's population, or over 800 million individuals (Kovesdy, 2022) .

Patients with end-stage renal illness are in critical need of renal replacement therapy, Hemodialysis (HD) is a vital life-saving operation and is the most prevalent sort of kidney replace therapy in the world and has several problems ,one of these problem was bloodstream infections (BSIs) (Bazrafshan *et al*., 2023), Infection is a major cause of hospitalization in hemodialysis patients (Masakane *et al*., 2013), hemodialysis patients are at higher risk for infection, because uremia is known to make patients with ESRD more susceptible to infectious agents through defects in cellular immunity, neutrophil function, and complement activation (Pruthi *et al*., 2012)

Gram-positive bacteria are responsible for the great majority of blood stream infections in hemodialysis patients, the most common of Gram-positive bacteria are *S. epidermidis,* methicillin-resistant *S. aureus* (MRSA), and coagulase negative *staphylococcus* ,(*E. coli*) are the common Gram-negative organisms that isolated from blood samples patients (Aslam *et al*., 2018)

Automated systems, such as Vitek 2 (bioMérieux) are accurate identification of the causative agents of bloodstream infections and determination of antibiotic susceptibility profiles are vital in guiding effective targeted antimicrobial treatment choices, Standard protocols for microbial identification and antimicrobial susceptibility testing (AST) involve blood culture in liquid medium using commercial systems, Gram staining and overnight sub-culturing of signal-positive samples on solid medium to obtain isolated colonies (Fothergill *et al*., 2013).

The isolated colonies are then used for identification and susceptibility testing, increasing rates of antibiotic resistance contribute to use of empiric broad-spectrum antibiotics (A *et al*., 2012)

During extracellular and highly pro-inflammatory bacterial infection, the pathogen mostly neutralizes or eliminates the immune response effectors. In this context, the production of IL-10 modulates the immune response intensity and allows a successful bacterial clearance, without excessive host tissue damage. Although in some cases the absence of IL-10 makes the immune response more effective to clear the pathogen, the damage produced on host tissues is more severe and compromise host survival (Penaloza et al., 2016)

1.2 Aim of study

The purpose of the present Study was to characterize and distribution of type of bacterial infection and antibiotic susceptibility test and the relationship of Interleukin-10 with catheter related bloodstream infection.

1.3 Objectives

The goal of the present to study the connection of infecting organism with the

1. Identification Specific microorganism, Causes of Catheter related blood stream infection in patient on hemodialysis, using blood culture and vitike 2 technique.
2. Determine Serum level of IL-10 in patient and control groups by ELISA technique.
3. Determine antibiotic susceptibility test for each microorganism obtain by vitike 2 technique.
4. Correlated Catheter-related blood stream infection with clinical presentation of patient group.
5. correlated IL-10 with specific Catheter related Blood stream infection.

Chapter two

Literatures Review

Literatures review

2.1 Acute kidney disease

A sudden disruption of normal kidney function. This fast decline in organ function is related to rising creatinine levels in the blood and a fall in urine production below 500 mL/day. Because of the increased likelihood of developing chronic and end-stage renal disease, this illness has a significant influence on both the patient's short-term and long-term survival (Mertowska *et al*., 2022).

Rapid and reversible loss of renal function due to acute kidney injury is linked to a more rapid progression of chronic kidney disease CKD(Zhong *et al*., 2020).

There are three main types of causes for AKI, and they are called pre-renal, intra-renal, and post-renal. Impairment in renal perfusion, leading to a decrease in GFR without additional damage to the renal parenchyma, is the outcome of pre-renal causes of acute kidney injury. Possible problems include hypovolemia, decreased heart function, systemic vasodilation, and increased vascular resistance Damage to the kidney's tubules, glomeruli, interstitial tissue, or vascular structures within the kidney itself (intrinsic AKI) are the cause of kidney failure. Finally, post-renal AKI develops once urine flow is blocked due to an acute blockage in the extra renal or intracranial space (Yun & Hur, 2022).

2.2 Chronic Kidney disease

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 (Evans *et al*., 2022).

Toxins can build up in the serum when damaged kidneys are unable to excrete the waste products that are created during the metabolic process. The subsequent symptoms, which are referred to collectively as uremic symptoms or uremic syndrome," impact each and every one of the body's systems (Smeltzer *et al*. 2008), including renal impairment on a continuum from mild to severe and from there to end-stage renal disease (Su, 2009).

The world's aging population faces an increasing burden of illness. It is characterized by several kidney abnormalities, including a reduction in renal mass, renal fibrosis, and a decreased glomerular filtration rate (Schroth and colleagues, 2020).

Renal failure is the ultimate phase of both acute and chronic renal illness and may need dialysis or transplantation. Early stages of kidney dysfunction are 10–1000 times more widespread in the population than kidney failure, and they are linked to cardiovascular disease, electrolyte and acid–base disorders, excessive fluid intake, metabolic and endocrine problems, drug toxicity released by the kidneys, and metabolism and endocrine complications (Levey *et al*., 2013). Kidney damage is accelerated by variables such as obesity, poor management of diabetes type 2, smoking dyslipidemia, anemia, related vascular disease and UTI (Balderas-Vargas, 2020).

CRF can be determined through evaluation of serum concentrations of creatinine, a breakdown derived from muscle protein. The creatinine level indicates the glomerular filtration rate (GFR), and elevated creatinine levels in CRF indicate a decreased GFR (AdakedathV & Kandi, 2017).

Homeostatic deregulation of the synthesis, release, and degradation of soluble molecules are disrupted in people with chronic kidney disease. This

includes immune system disruption due to alterations in cytokines and inflammatory mediators, as well as increased cytokine levels in the blood due to decreased renal clearance. Interstitial fluid from patients on prolonged peritoneal dialysis has been shown to produce pro-inflammatory cytokines and has an elevated absorptive gradient (Tinti *et al*., 2021).

The categorization of CKD relies on the estimated rate of glomerular filtration (eGFR) and albuminuria in order to better manage CKD and offer better treatment for patients. (Evans *et al*., 2022).

Glomerular filtration rate (GFR) is often regarded as the most practical general indicator of renal health, playing an essential part in the criteria for the diagnosis and classification of kidney disease as well as in the dose selection for many therapy drugs (Miller & Jones, 2018).

There are six different eGFR levels. Damage to the kidneys becomes more severe with time, therefore an eGFR of a flow rate of 60 milliliters per 1.73 square meters for more than 3 months is grounds for worry.

- In the first two stages of the illness, patients have eGFR values that are normal to mildly reduced (60 to C 90 mL/min per 1.73 m2).
- Stage 3 patients had eGFR values between 45 and 59 mL/min per 1.73 m2, indicating a modest to moderate reduction in kidney function.
- Stage 4 and 5 eGFR values (15-29 and 15 mL/min per 1.73 m2) are associated with severe disease and renal failure, respectively.

(Murton *et al*. 2021).

The end outcome with certain kidney disorders is chronic renal failure, when kidney function progressively declines and treatment with renal replacement therapy (dialysis or transplantation) is required (Vaidya & Aedula, 2021).

2.3 Hemodialysis

Patients with stage V or terminal persistent renal disease, which is described as an average glomerular filtration rate of 15 mL/min/1.73 m2, will require some form of treatment to replace kidney function this form of therapy may involve a kidney transplant or one of the dialysis options available, such as hemodialysis (Andreoli *et al*., 2020).

Hemodialysis (HD) 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 (Guney, 2020).

2.3.1 Hemodialysis mechanism

Throughout hemodialysis, waste products and excess fluid are removed using an external filter termed a dialyzer, which contains a semipermeable membrane. The waste is separated by producing a counter-current flow a gradient in which blood flows in one direction and dialyzer fluid circulates in the opposite way (Nl *et al*., 2015).

The transport or diffusion of solute particles via a semipermeable membrane is the underlying idea of dialysis. Diffusion is the technical term for this process. Dialysate is composed of sodium bicarbonate (NaHCO3), deionized water, sodium chloride (NaCl), and acid concentration. Urea and creatinine are metabolic waste products. are removed from the body by diffusing down the concentration gradient from the circulation into the dialysate. The pace at which particles diffuse through the membrane is determined, in turn, by the size of the particles as they pass through the membrane and into the dialysate. The rate of diffusion over a membrane is

proportional to the solute particle size. With increasing solute particle size, this rate decreases. When oxygenated blood-carrying arteries from the heart are redirected to a vein, this is called an arteriovenous shunt. Due to this, the vein becomes sturdy (by developing muscle surrounding it like an artery), and may be punctured several times; its pressure is also monitored during the dialysis process. (muafiah, 2019). Figure (2.1) is a schematic depiction of a dialyzer.

Dialysis has several drawbacks since it cannot fully substitute for the kidney. Patients not only face long-term consequences, but also issues during dialysis, which can result in the session being cut short, reducing the effectiveness of dialysis and negatively impacting patient care (Othman *et al*. 2022).

Another type of replacement therapy is called peritoneal dialysis the peritoneal membrane is used as an exchange surface in peritoneal dialysis, a kind of renal replacement therapy. This process is initiated by infusing a sterile fluid into the peritoneal cavity through a catheter (Andreoli & Totoli, 2020).

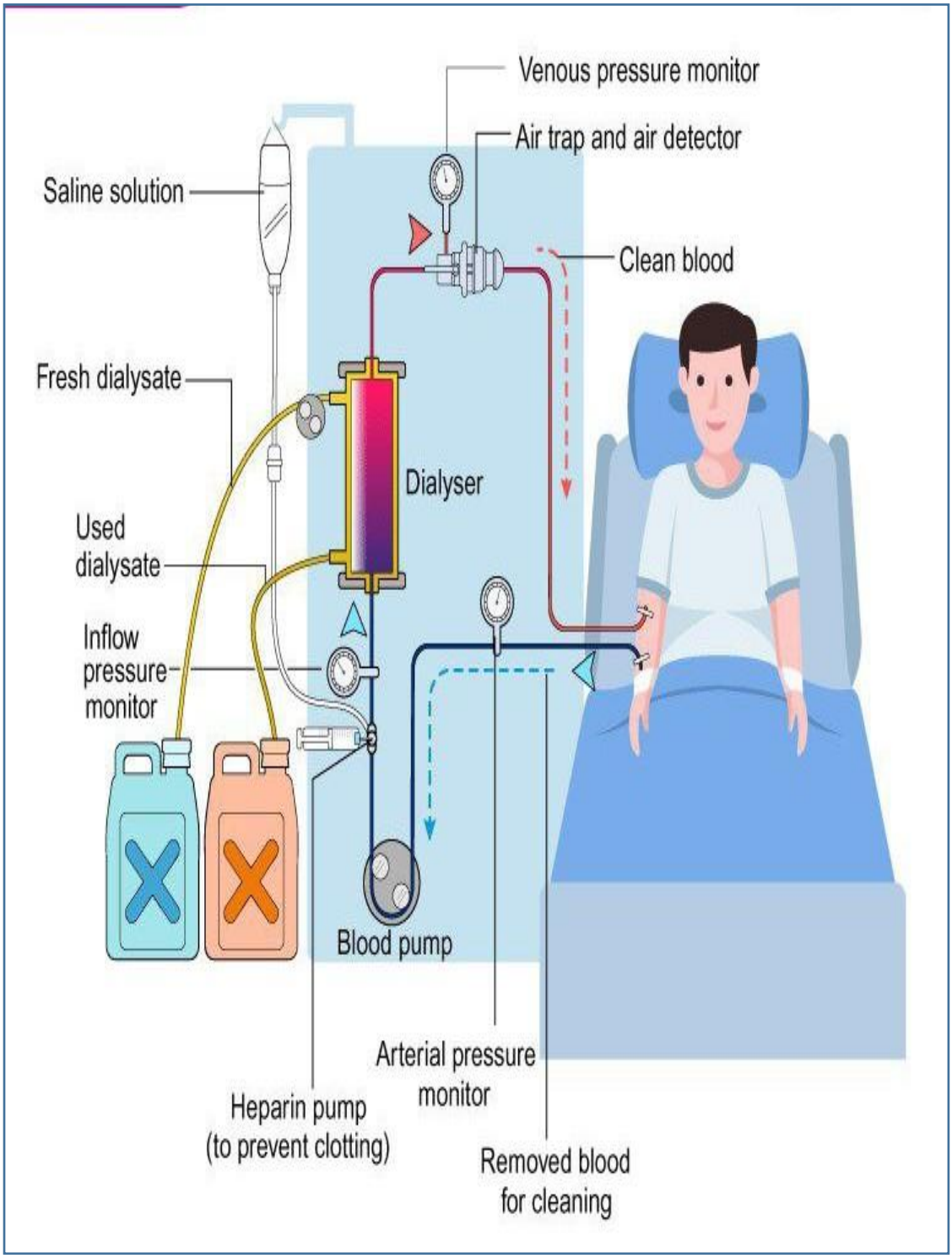


Figure (2.1) a schematic depiction of a dialyzer

https://byjus.com/biology/dialysis/

2.4 Vascular access(VA)

It is necessary to have a vascular access that is functional in order to obtain adequate levels of dialysis effectiveness, and it is regarded as the patients' lifeline when they are receiving HD maintenance. The perfect vascular access should have a number of precise properties, the most significant of which are as follows: 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), autologous arteriovenous fistulas (AVFs), and prosthetic arteriovenous grafts (AVGs) (Torreggiani *et al.,* 2021).

2.4.1 Arteriovenous fistula (AVF)

Arteriovenous fistula (AVF) is the kind of vascular access that is considered to be the first-line option and the ideal choice. However, there is a possibility that an AVF may not mature into a conduit that can be used, or that it will develop recurring stenoses, which will result in a high incidence of surgical re-intervention in order to preserve patency (Ondigui *et al*., 2022).

When compared to both arteriovenous grafts (AVGs) and central venous catheters (CVCs), AVFs had a reduced complication rate and higher patency. Hemodialysis is most effective when the vascular access channel is optimized to allow for a flow rate of at least 300 mL/min (Kaller *et al*., 2022).

It takes at least 12 weeks for the healing process to develop before an AVF can be used for dialysis therapy, and if the AVF fails or becomes entirely thrombosed within this time, the patient will have early AVF failure (Samra *et al*., 2022).

Injuries to the intima and malfunction of endothelial cells during the establishment of an AVF can all contribute to thrombosis, which in turn can cause persistent inflammation and the failure of outward remodeling. Additionally, neointimal hyperplasia (NIH), stenosis, and thrombosis. Stenosis in AV accesses is caused by neointimal hyperplasia, which is a myoendothelial growth of cells and matrix (Samra *et al*., 2022).

Successful AVF use in hemodialysis patients requires three major sequential processes of care: catheter and AVF placement by a surgeon, AVF maturation leading to its successful use for dialysis, and maintenance of primary AVF patency after its successful use (Qian *et al*., 2020).

2.4.2 Central venous catheter (CVC)

It is estimated that roughly five million central venous catheter (CVC) insertions take place annually in the United States. The surgical insertion of a central venous catheter (CVC) is a frequent medical operation, different kinds of catheters are introduced in different ways, including peripherally rather than centrally. These catheters can have either a big or a tiny diameter (Smith *et al*., 2022).

A central venous catheter (CVC) is a great option when an immediate or emergent HD is required, such as during the start of renal replacement therapy or when a permanent access gets ineffective and CVC is used as a temporary bridging access, or when the vascular anatomy is not suitable for the creation of an AVF or AVG. CVC is a wise decision ,particularly when immediate or emergent HD is needed (Rezapour *et al*., 2021).

The insertion of a central venous catheter is a common treatment that is also frequently required for patients who are in a severe condition. The delivery of whole parenteral nutrition, dialysis, plasmapheresis, medicine administration, and hemodynamic monitoring are just some of the numerous

indications that led to the development of various access procedures and devices. These were also created to permit additional sophisticated operations such as the insertion of trans venous pacemakers (Rezapour *et al.*, 2021).

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) (Al-Barshomy, 2021).

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 is linked to CVCs (Torreggiani *et al.*, 2021).

The patient's age, the length of time spent in the hospital, and the types of CVC that are chosen are some of the numerous factors that might have an impact on the success of the CVC. (Howthan *et al.*, 2020)

2.4.3 Arteriovenous Grafts (Avgs)

An arteriovenous (AV) graft is a plastic tube with loops that joins an artery to a vein. These connections are formed by sandwiching graft material between them. The decision to use an AV graft over another kind of hemodialysis access is dependent on a variety of considerations, including anatomy and life expectancy (Yuo and Theodore H., 2023).

Vein-to-artery grafts AVGs are the most prevalent kind of dialysis access, despite having greater infection rates and shorter lifespans than AVFs. Bacteremia caused by hemodialysis is more common in AVGs than AVFs by more than a factor of 10 (HentMschel, 2019).

Vein-to-artery grafts problems associated with the AVG genotype when compared to AVF, the functional survival of AVG is much lower. Thrombosis results from venous stenosis brought on by neointimal hyperplasia as the normal progression of AVG. The primary cause of thrombosis is an increase in the number of smooth muscle cells, myofibroblasts, and vessels inside the neointima. Multiple causes, including stenosis, hypotension, and severe compression for hemostasis, typically contribute to AVG thrombosis (Santoro *et al.*, 2014).

2.5 Infection

2.5.1 Hemodialysis Vascular Access Device (HVAD) Infections

Within the population that receives dialysis, the HVAD is the source of infection that occurs most frequently. Erythema, disintegration of the skin, purulent discharge, and even bleeding from a pseudo aneurysm can all be indicators that an infection is present (Berman *et al*., 2004). There is a possibility that fever and other symptoms of sepsis are present. Infections caused by VADs might vary in their clinical presentation, bacteriology, course of treatment, and likelihood of consequence depending on the type of access device and its location. Inflammation in the local area is typical across the board for infections involving shunts, AVFs, and AVGs. The most common signs of cellulitis, as determined by past research, were erythema and soreness of the soft tissues that were located above AVF or AVG, Less than half of the cases exhibited more concerning signs of a progressing infection, such as fever, drainage, or abscesses. These indicators were present in less than half of the cases. Nephrologists are well aware of the potential consequences that can arise from HVAD infections. (S. Berman, 2017).

2.5.2 Blood stream infection

Bloodstream infections (BSIs) are infections that are brought on by the existence of live bacteria in the bloodstream. They are frequently linked to severe diseases that have a high incidence of mortality and morbidity, and the worldwide increase in prevalence of these diseases has led to their emergence as one of the major causes of death (Peker *et al*., 2018).

Both hemodialysis and peritoneal dialysis patients are susceptible to bloodstream infections. dialysis patients, however they occur more often in hemodialysis patients (Patel *et al*., 2016).

Patients with end-stage renal illness have an infection as their second main cause of mortality. In most cases, the dialysis technique itself, and the method of vascular access in particular, are linked to an increased risk of infection in patients undergoing dialysis (Dalgaard *et al.*, 2015).

Patients who have reached the end stage of renal illness are required to have a vascular access in order to remove and replenish blood; nevertheless, these vascular accesses are a major source of infection and can lead to other complications. The types of vascular access that patients have can have an effect on the rates of bloodstream infections (BSI) that they have while receiving hemodialysis, the risk of bloodstream infections (BSIs) , from 0.5 to 27.1 per 100 patient-months among hemodialysis patients, according to data is collected in north America (alhazmi *et al.*, 2019).

The presence of comorbidities, inadequate nutrition, and uremia, the length of time the catheter is left in place, the site of insertion, and the manipulation of the catheter by the medical staff in charge of the hemodialysis treatment are all potential causes of these infections. The skin must be properly prepared, hand hygiene must be meticulously practiced, the most stringent sterile barrier precautions must be taken, and the most

appropriate insertion location must be selected. Inadequate use of aseptic methods during catheter insertion is another potential source of infection. This may also contribute to the lack of sterile procedures during catheter placement (Schwanke *et al*., 2018).

2.5.3 Catheter-related bloodstream infections

Patients with HD typically have central venous catheters, There are a significant number of bloodstream infections associated with vascular access, and seventy percent of those are specifically associated with catheters inserted into the central veins. The majority of vascular accesses in HD facilities are located in the arteriovenous fistulas and grafts are what make up the arteriovenous fistulas, but only 19% of the prevalent patients with HD typically have central venous catheters, 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(Hymes *et al*., 2017).

Bloodstream infections caused by bacteria are especially dangerous for dialysis patients because of their immune systems are already impaired and the dialysis catheter provides constant access to the bloodstream. Symptoms of a bacterial bloodstream infection in a hemodialysis patient may be comparable to those in other persons, but they may additionally include fever, redness or swelling at the dialysis access site, and low blood pressure when the patient is undergoing dialysis (Bhojaraja *et al*., 2022).

Preventing problems and the infection from spreading throughout the body requires a speedy diagnosis and the administration of medicines. The seriousness of the disease, the patient's general health, and the type of bacteria responsible all play a role in determining the best course of therapy. Dialysis catheter removal or replacement may also be necessary to stop the spread of infection (Soi *et al.* 2016).

2.6 Pathogens Association of Blood Stream Infection

2.6.1 Bacterial blood stream infection

Patients with ESRD are more likely to get infections, due to immune system changes, higher rates of colonization with organisms, more frequent hospitalizations, and more contacts with the healthcare system, when a central venous catheter (CVC) is used for hemodialysis, the vascular access might become a portal of entry for pathogen **(**Kellum *et al*., 2021**)**.

1- *Staphylococcus aureus* *(S. aureus)* is still one of the leading causes of potentially fatal infections of the skin, blood, and other soft tissues, as well as infectious diseases of the lower respiratory tract and other vital organs, such as endocarditis, mastitis, and osteomyelitis. Several components of the bacterial surface and extracellular proteins contribute to *S. aureus*' pathogenicity (Silva *et al*., 2023).

Staphylococci, which are members of the family Micrococcaceae, are round bacteria that can range in size from 0.5 to 1.8 m in diameter. These bacteria cluster microscopically are Gram-positive cocci that are catalase-positive but oxidase-negative (Amourl-D *et al*., 2023).

Staphylococcus aureus is a highly adaptable pathogen that may proliferate and invade neighboring tissues due to the expression of a wide variety of virulence factors (Al-Ugaili, 2013). The vast range of these

virulence factors is seen in figure (2.2), and includes structural and secreted components that contribute to the pathophysiology of infection.

S. aureus may persist as a colonizer and can cause invasive infections due to its wide repertoire of immune evasion strategies. To avoid being destroyed by the human immune system, *S. aureus* has evolved a large repertoire of virulence and immune evasion proteins (Howden *et al*., 2023).

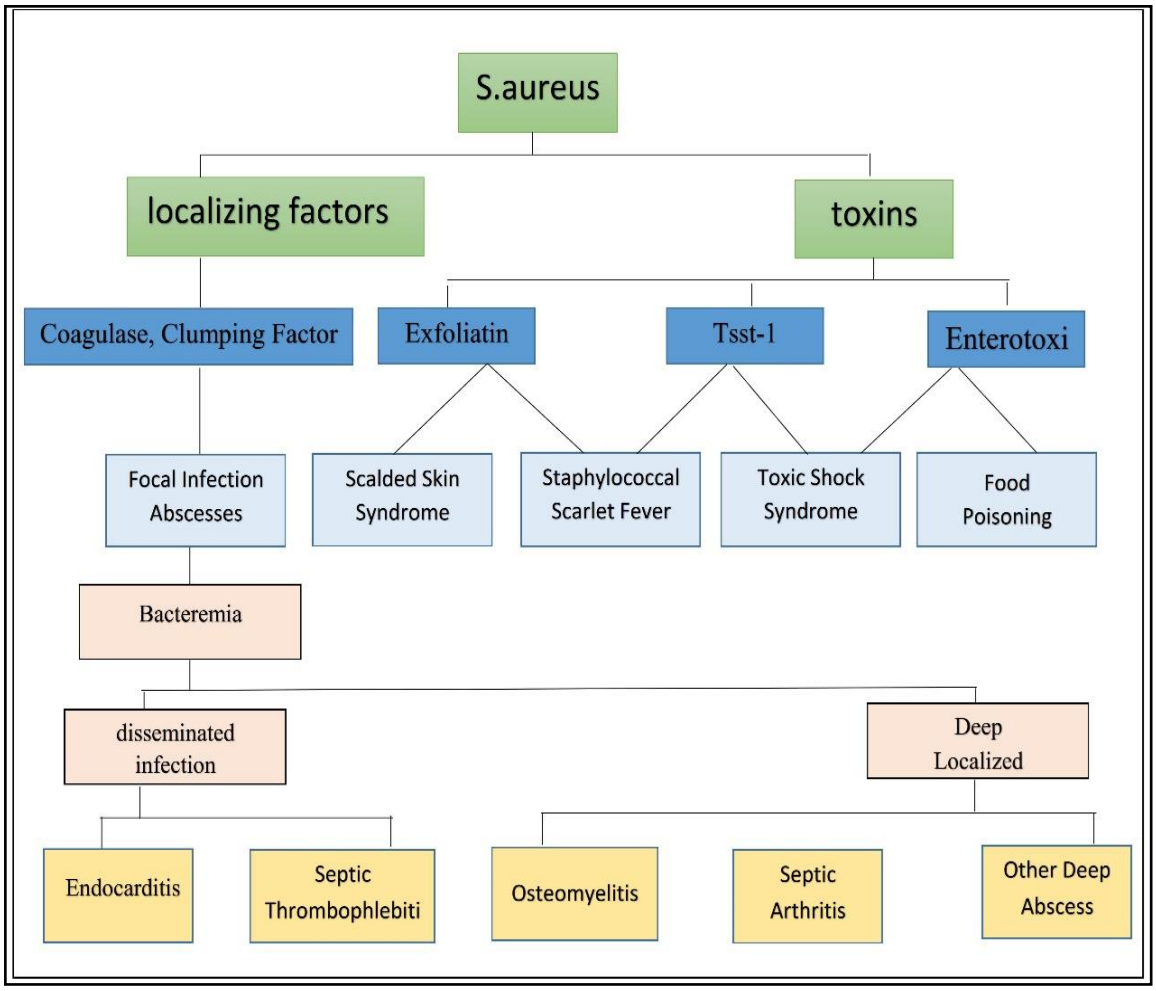


Figure (2.2) Correlation of staphylococcal virulence factors with disease https://clinicalgate.com/staphylococcus/

MDR *Staphylococci* are appearance of drug-resistant virulent forms of *Staphylococcus aureus*-particularly-methicillin-resistant *S. aureus* (MRSA), poses a significant challenge in the prevention, treatment, and management of Staphylococcal infections, Methicillin-resistant Staphylococci (MRS) cause infections that are difficult to cure. (Kaur & Chate, 2015)

Dialysis patients appear to have fast progression of bacterial infections, and their recovery time is significantly longer than that of non-uremic individuals. This information might be relevant to immunological changes that occur in patients who have terminal. These immunological changes involve a decline in humoral immunity as a result of deficits in amino acids, minerals B, C, D, and E, and zinc; an increase in the cellular suppressor activity anorexia caused by retention of nitrogenized products; and severe anemia brought on by a lack of erythropoietin. Amino acid, vitamin B, C, D, and E, and zinc deficiency are all causes of these immune alterations. Accidental iron loss that occurs during dialysis and lower erythrocyte survival in uremia are both factors that contribute to an increased danger of transmittable diseases, which is a prognostic factor for death. (Grothe *et al*., 2010).

2-*staphylococcus epidermidis* is a Gram-positive bacterium commonly found on the skin and mucosal surfaces and 30% of catheter-related bacteremia (CRB) is caused by *S. epidermidis* and are responsible for nosocomial infections due to the widespread use of medical implants and equipment, (Namvar *et al*., 2014).

S. epidermidis are formation of biofilm and biofilm can be described as the deposition of microorganisms and their extracellular products on the surface to form a highly organized bacterial population. Production of factors that mediate intercellular adhesion is a distinguishing feature of the biofilm accumulation and development phase. These factors include the extracellular polysaccharide, polysaccharide intercellular adhesion (PIA), and the biofilm-associated proteins Aap (accumulation associated protein) and These factors are produced by biofilm-forming microorganisms (Chabi & Momtaz, 2019).

During the second stage of the biofilm's proliferation, mushroom-shaped structures and channels appear. These structures serve to promote the transport of nutrients to the biofilm's deeper layers. The last stage in the formation of biofilm is characterised by the detachment of biofilm colonies and the subsequent spread of those clusters to faraway areas (Le *et al*., 2018)

3- *Staphylococcus hominis* is a type of the coagulase-negative staphylococci and is one of the three most often recognised isolates that may be collected from the blood of patients in hospitals. These bacteria are acknowledged as having the potential to behave as opportunistic pathogens and have been known to cause infections of the bone and joint, bloodstream, endocardium, and peritonium. The use of indwelling medical devices has been linked to the majority of infections caused by staphylococci. The precise methods that *S. hominis* uses to cause disease in humans have not yet been identified (Szczuka *et al*., 2018).

People whose immune systems are unusually compromised are more likely to get infections than other people. The great majority of the isolates can be treated with penicillin and erythromycin, if not all of them. Antibiotics are frequently prescribed as part of the treatment plan for patients who have bacteremia caused by *Staphylococcus hominis*. Additionally, the degree of severity of the infection and the sensitivity of the bacteria to the various medications will play a role in the decision of which antibiotic to use. It is essential to keep in mind that the detection of *Staphylococcus hominis* in the circulatory system does not automatically imply that this microorganism is the root cause of the infection. The overall health of the patient, the presence of other organisms, and the use of medical equipment (such as catheters or prosthetic valves) can all play a role in the progression of bacteremia (Osaki *et al*., 2020).

4- *Escherichia coli* (*E. coli*) Bacteria that are picked up in the community are some of the most prevalent bacteria that can cause a urinary tract

infection (UTI), and common in people who use hemodialysis. Many diseases of the bloodstream are caused by pathogenic E.coli(PEC) (Bahramian *et al*., 2021), a tiny percentage of *E. Coli* can spread outside the intestines and cause illness and these bacteria are thought to have a significant role in the etiology of Gram-negative bacillus-causing bacteremia agents (Koga *et al*., 2014).

2.6.2 Fungal blood stream infection

Fungi cohabit as commensals in humans, colonizing various bodily regions such as the epidermis, vaginal tract, and gastro-intestinal tract. Nonetheless, as an opportunistic pathogen, it can induce significant mucosal colonization and local and/or systemic illness anytime the immunological state of the host or its microbiota is altered (Costa-de-oliveira & Rodrigues, 2020).

Candidemia was described as the presence of Candida in a blood culture along with fever, chills, low blood pressure, and other symptoms of the disease. (Zhong *et al.'s* 2020)

Although *Candida albicans* was previously thought to be the most common causative agent of candidaemia in healthcare facilities, recent years have seen a shift in the distribution of candidaemia toward *Candida non-albicans,* and resistance to antifungal agents varies among Candida species and geographic regions (Ye *et al*., 2022).

Recent surgery, broad-spectrum antibiotic usage, and the presence of a catheter (CVC) are all common risk factors for candidemia in patients. (Zhong *et al*., 2020).

2.6.3 Virus blood stream infection

Hemodialysis patients are at an increased risk of contracting viruses such hepatitis B virus (HBV), hepatitis C virus (HCV), and the human immunodeficiency virus (HIV). Managing patients with ESRD is complicated by the fact that both patients and healthcare providers are at risk of contracting these viruses (Ephraim, 2022).

2.7 Immunity and Chronic Kidney Disease

During an HD session, the blood and materials contact, triggers the cells of the (innate immune system), specifically the neutrophils, monocytes, and macrophages. The recruitment of these cells and the consequent production of proinflammatory cytokines are what causes HD patients to have a higher incidence of cardiovascular disease, which in turn is caused by the maintenance of a pro-inflammatory condition. (Constancio *et al*., 2019).

This higher risk of infection is related to an immunological dysfunction that affects both the body's innate and adaptive immune system of CKD patients, resulting to a situation in which both immune activation and immunosuppression are present in CKD patients (Johansen, 2019).

Multiple factors, such as uremic, anemia, iron overload, vitamin deficiency, trace element buildup, and malnutrition, as well as the impairment of granulocyte and macrophage, have been linked to immunologic disorders in chronic renal failure (CRF) patients These factors contribute to immunologic disorders in CRF patients (Musia & Zwoliska, 2003).

The immune system is the body's natural defense mechanism, fending off both foreign and native pathogens. Non-specific immune activities (such cytokine production) are initiated upon detection of pathogen-associated

molecular patterns (pAMPs; for example, bacterial lipopolysaccharide). (Lee *et al.*, 2020).

Polymorph nuclear leukocytes (PMNLs) are primary neutrophils and essential components of the non-specific cellular immune response. The most numerous cell type in mammals, white blood cells are the first line of defense against extracellular microorganisms. Protective neutrophils arrive to the site of an infection quickly (within minutes) and engage in phagocytosis (the eating and destruction of bacteria of neutrophils in culture) to eliminate the possibility of infection (Espi *et al.*, 2020).

In patients with persistent kidney disease and end-stage renal disease (ESRD), there was an impaired immune system, and there was also a steady drop in the circulating numbers of natural killer cells (NK) and B cells. This loss was connected with the impairment of renal function (Austria & Wu, 2018).

For individuals who have renal function that is less than optimal, for instance, the quantity of lymphocytes will be lower. In addition, people with CKD have a reduced ability of their T cells to respond to antigen stimulation. In individuals with ESRD, the total number of neutrophils does not vary, in contrast to the lower lymphocyte count that is seen in these individuals, Persons with ESRD, on the other hand, seem to have a poorer ability for phagocytosis and a higher rate of apoptosis when compared to healthy participants (Ishigami & Matsushita, 2019).

Dysfunction of the adaptive immune respons is correlated with an increased likelihood of passing away. T-cell lymphopenia has been shown to be caused by reduced thymic output, increased apoptosis, and impaired proliferation in patients who are receiving hemodialysis. This stands in contrast to the increase in highly differentiated memory T cells (Campo *et al.*, 2022).

In addition to immunological cells, the complement system is involved in the pathophysiology of chronic kidney disease (CKD). The complement system is made up of more than 30 serum proteins that work together as a cascade and produce a membrane assault complex in order to destroy harmful microorganisms. There are three distinct ways that complement may be activated: the classical route, the alternate pathway, and the lectin pathway research. The activation of complement during CKD may affect renal cell function and lead to chronic damage (Shahbazi *et al*.'s 2019).

Patients suffering end-stage renal disease (ESRD) often display signs of inflammation, such as elevated C-reactive protein and pro-inflammatory cytokine levels and the soluble receptors that bind to them. Complement activation linked with uremia may potentially lead to immune system dysfunction. Low levels of IL-10 production correlate with elevated C-reactive protein in dialysis patients (Syed-Ahmed & Narayanan, 2019).

In addition, they may trigger the production of various chemokines, cytokines, growth factors, and matrix proteins that contribute to inflammation and scarring. Urine acidification may be triggered by modified C3 through the alternate route activation. Unregulated complement activation may also be brought on by the production of anaphylatoxins and a reduction in CD59 expression on tubular cell surfaces (Shahbazi, *et al.*, 2019).

2.8 Interleukin 10

The body's own immune system defends against both internal and external invaders. When pathogen-associated molecular patterns (pamps; for instance, bacterial lipopolysaccharide) are detected, they trigger non-specific immune actions (such as cytokine production) (Ren *et al*., 2019).

Interleukin -10 (IL-10) is an immunosuppressant and anti-inflammatory cytokine that is crucial for the body's defense systems. It was discovered in 1991. IL-10 is 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) (Sameer & Nissar, 2021) .

Interleukin 10 was thought to be a byproduct of CD4+T cells that assisted Th2 cells and was given the name cytokine synthesis inhibitor factor, or CSIF. In humans, the IL10 gene is found in the 1q32 region of the chromosome. This area is made up of six -helices (A-F) and connecting loops four of them are bundled together in the form of a traditional left-handed four-helix structure, which is typical of all the helix cytokines (Adane and Getawa 2021).

The physiologically active form of IL-10 that have 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 (Minsi *et al*., 2020).

Hemodialysis causes protein breakdown and promotes cell death. Independent risk factors for HD patients' morbidity and death include elevated interleukin levels and the presence of metabolic acidosis. Regular hemodialysis reduces mortality, however the disease is linked to inflammation (Gharib *et al*., 2022).

IL-10 suggested that has a role in the preservation of the pathogenicity and durability of some viral infections, such as HCV. This is achieved by the direct targeting of immune effector cell types or through the prevention of maturation of macrophages and dendritic cells indirectly through the limiting of the host's ability for antigen presentation and chemokine production (Yousry *et al.*, 2021).

The activities of IL-10 are not restricted to the downregulation of proinflammatory cytokines such as IL-1, IL-6, and TNF-a.Actually, IL-10 inhibits the generation of agents that stimulate migration, such as interleukin-8 or CC chemokines may cause more leukocytes to congregate at a site of inflammation(Stenvinkel *et al.*, 2005)**.**

Interleukin-10, is important for suppressing cell-mediated immunity and reducing the development of MHC class II molecules on monocytes and macrophages, so causing these cells to decrease their release of pro-inflammatory cytokines (Abdalla, 2018).

Because of its potential to begin communication in numerous immune cell types, (IL-10) has the ability to elicit both anti-inflammatory and immune stimulatory actions in vivo and is commonly dysregulated in human illness. While IL-10 stimulates pro-inflammatory IFN- production by stimulating CD8+ T-cells, its anti-inflammatory actions are mostly attributable to reduction of monocyte, and macrophage activity (Saxton *et al.*, 2021) , In addition, these important role in the defense system of the host against infection (Hirani *et al.*, 2022).

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 (Almuhayawi *et al.*, 2021).

2.9 Diagnosis

2.9.1 Diagnosis of acute and chronic kidney disease

Early identification is essential for accurate diagnosis of both acute and chronic kidney illnesses; yet, early stage kidney disease is often , and can only be identified by laboratory testing. (Levey *et al.*, 2013). The diagnosis can be done either clinically by measuring the amount of urine that is produced or biochemically after tests such as blood urea nitrogen and creatinine have been ordered. Both values are functional, and neither one reflects the histological damage that has been done to the kidney (Olvera-Posada, 2016). as well as electrolytes, in addition to the acid-base balance. In the oliguria phase of AKI, certain patients may experience metabolic acidosis, hyperkaliemia, hypomagnesaemia hyperphosphatemia, hyperuricemia, and hyperuricemia (N *et al*., 2013).

2.9.2 Diagnosis of blood stream infection

Blood culture is still considered the diagnostic method of choice for blood stream infections (BSIs). On the other hand, it has been estimated that the sensitivity of blood culture is just about fifty percent. Blood culture is the diagnostic method that is used the majority of the time in order to identify bacteremia, and fungemia (Howthan and coworkers, 2020).

For aerobic and anaerobic growth conditions, respectively, standard bottles containing rich media have been produced. A blood culture is defined as a culture that was acquired by one venipuncture or line draw. They may hold as much as 10 milliliters (mL) of blood. However, because the

difficulties of getting large quantities of blood, special pediatric blood bottles have been devised for the culture of amounts less than 3 milliliters. These bottles may hold up to 10 milliliters of blood, to neutralize antibiotics administered before to sampling (Opota *et al*., 2015).

There are several benefits associated with blood cultures. To begin, they have been utilized in the medical field for more than a century and are effectively included into the clinical workflow as well as clinical standards. Second, the use of semi-automated culture methods has vastly reduced the amount of manual labor required in the microbiological laboratory, which has reduced the amount of time spent doing hands-on work. Third, there is the possibility of isolating and identifying a wide variety of bacterial and fungal pathogens In addition, isolating the pathogen is a precondition for phenotypic susceptibility testing, which enables doctors to begin antimicrobial medication that is specifically tailored to the patient's condition (Abedelnasser *et al*., 2020).

BCs are simple to carry out and show high sensitivity for the infections that may be cultivated. There are, however, significant limitations:

- The turnaround time is quite a little longer than usual. The failure to identify pathogens that cause bloodstream infections in patients who have been treated with antimicrobials in the past
- An inability to identify other than bacteria or yeast any slow-growing or obligatory intracellular microorganisms and pathogens
- A significant delay in the detection of microorganisms involved in BSIs, or even their complete absence (Peker *et al*., 2018).

2.10 Treatment

When a catheter-related bloodstream infection (CRBSI) is suspected, treatment should begin initially with a CVC block (high dose of of antibiotic administered into catheter for 12-24 hours and then pumped into the circulation) and a systemic antimicrobial agent, typically given via a peripheral catheter or PICC, depending on the local microbiological guidance. This should be done while blood culture results are awaited. The first selection of antibiotics will be made according to the the severity of the patient's condition clinical, the risk factors for infection, and the potential bacteria linked with the specific vascular device, among other criteria.Practically speaking, it is essential to have coverage for both Gram positive bacteria (which involves coagulase-negative *staphylococci*) and Gram-negative microbes. depending on local susceptibility patterns and allergy status (Lal & Chadwick, 2019).

Antibiotic treatment that is started as soon as possible and suitable, is a critically essential component of the treatment of patients with BSI. For a therapy to be effective, it is necessary that all of the organisms that were isolated from the blood be sensitive in vitro to the antimicrobials that were selected, that the appropriate route and dosage are used, and that the antimicrobials are administered as soon as possible after the blood cultures were collected (Timsit *et al*., 2020).

2.11 Antibiotic resistant

Antibiotics are medications that either kill or slow the growth of microorganisms. Antiviral, antifungal, and antiparasitic medications are all examples of different types of antimicrobial medication. Antibiotics are compounds that may either be made or obtained from microorganisms (bugs or germs such as bacteria and fungus). Antibiotics are used to treat bacterial

and fungal infections. Alexander Fleming's discovery of the first antibiotic in 1928 marked the beginning of a new era in the annals of medical history. Antibiotics are one of the therapies that are recommended the most frequently in contemporary medicine. Some antibiotics have bactericidal properties, which means that they eliminate bacteria. The majority of antibiotics fall into the bacteriostatic category, which mean they prevent the development of germs (Abdulhussein, 2022).

In many underdeveloped nations, antimicrobial medications are easily accessible without the need for a prescription from a medical professional or another skilled health practitioner. This has led to an excessive amount of their use. In both instances, a common misconception exists. Antibiotics are referred to be "wonder medications" because of their ability to efficiently treat a wide variety of illnesses in a very short length of time. The length of a patient's stay in the hospital is one of the elements that can have a role in the development and spread of infections that are extremely resistant to antibiotics that occur in hospitals. Other factors to take into account include the presence of immunocompromised individuals (such as patients diagnosed with acquired immunodeficiency syndrome (AIDS) or recipients of transplants), invasive procedures, and the intensity of clinical care. Antibiotics are not only administered in inappropriate amounts (inadequate doses, lack of adherence to treatment standards), but they are also used inappropriately too often (Prestinaci *et al*., 2015).

Antibiotics are utilized in both the medical treatment of humans and agricultural practices all over the world. Antibiotics are often unnecessary or dubious treatments, depending on the circumstances. Use of antibiotics has been connected to resistance to antibiotics, with the most frequent antibiotic-resistant bacteria seen in hospitals being methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, and gram-negative rods such as

Enterobacteriaceae and Pseudomonas aeruginosa. Antibiotic resistance has been linked to the development of superbugs, which are strains of bacteria that are able to withstand treatment with antibiotics. Recent research uncovered a strain of *S. aureus* that is intermediate in vancomycin yet resistant to the antibiotic, presenting a new therapeutic challenge. (Laxminarayan *et al*., 2013).

Antimicrobial resistance (AMR) is the capacity of microbes to withstand the action of drugs that are aimed to eliminate them. Antibiotic resistance is globally recognized as a threat to the health of humans because it renders treatment of microbial infections more difficult, increases the risk of disease spread and degree of severity, and these Antibiotic- resistant pathogens cost billions of dollars in healthcare (Marini *et al.*, 2022) .

There are three categories of bacteria that show signs of resistance to multiple classes of antimicrobial drugs.

1) Microorganisms with multidrug resistance (MDR) have developed immunity to at least one antibiotic from three or more different classes.

2) Extremely resistant microorganisms (XRMs) are bacteria that have developed resistance to all but two or fewer types of antibiotics.

3) Pan drag resistance refers to microorganisms that are resistant to all agents in all antimicrobial classifications (Alkofide *et al*., 2020).

Drug inactivation (which is typically characterized by an irreversible cleavage catalyzed by an enzyme), alteration of the antibiotic linking site, and minimized storage of the drug as a result of either reduced membrane permeability or increased drug efflux are the mechanisms that contribute to antimicrobial resistance. It is possible for bacteria to pass on the gene that is responsible for a particular resistance mechanism to bacteria that also carry genes for other resistance mechanisms. This can lead to species that are

resistant to several drugs, which is the fundamental cause of the current problem with our public health. During this process, resistance genes can be acquired by a bacterium in one of three different ways: either directly from the environment (transformation), from another bacterium in the form of plasmids (conjugation), or through phages (transduction) (Baier *et al.*, 2020).

Bacterial infections cause more illness than any other cause. Now that laboratories can cultivate microorganisms in a suitable medium, or "culture," doctors need to know how susceptible or resistant various pathogens are to various antimicrobials so they can quickly and effectively treat their patients (Bayot & Bragg, 2019).

Medical technologists (clinical laboratory scientists) perform antimicrobial susceptibility testing (AST) to determine what antimicrobial therapy is most effective for individual patients and to prevent the inappropriate emergence of resistant pathogens in those who are ill. Isolates with well known strategies for resistance, AST can help identify bacteria are of great importance to infection prevention and control, including *S.aureus* that is resistant to methicillin carbapenemase-producing Enterobacteriaceae, broader range lactamase producers, and vancomycin-resistant enterococci. AST also helps identify wider range lactamase producers, carbapenemase-producing Enterobacteriaceae. Epidemiological research focusing on the genesis and dissemination of resistance rely heavily on AST to measure resistance incidence and prevalence (van Belkum *et al.*, 2019).

Chapter Three

Material & Method

3.1. Study design

This case-control research was carried out in the dialysis unit in Imam Hussein Teaching Hospital. All of patients were registered with hemodialysis from November (2022) to April (2023).

3.2. Subjects Group:

One hundred (100) participants were enrolled in this study including three groups involved in this case-control study according to clinical diagnosis by a clinician: the first one includes patients with symptoms involved center venous catheter (CVC) [35 (22 male, 13 female), the second group includes asymptomatic arteriovenous fistula (AVF) [35 (18 male, 17 female) and the third group includes [30 (18 male, 12 female)] apparently healthy control group. All of the groups' ages range from 10 to 80 years in figure (3.1). Detailed case information sheets involving age, sex, full history and other variables were carried out for each patient by a questionnaire as in (Appendix 1). Figure (3.1) shows scheme of study.

control

3.3. Control

Thirty person who appeared to be healthy Condition and whose age ranged from (10-80 years) and sex matching with patient group .

3.4 Inclusion Criteria

All cases in hemodialysis center diagnosis which have fever, chill, swelling at the catheter site, asymptomatic people also included in this study.

3.5. Exclusion Criteria

Individuals who have diabetic mellitus, autoimmune condition, viral hepatitis, and patients who are already taking antibiotics are not eligible to participate in this study.

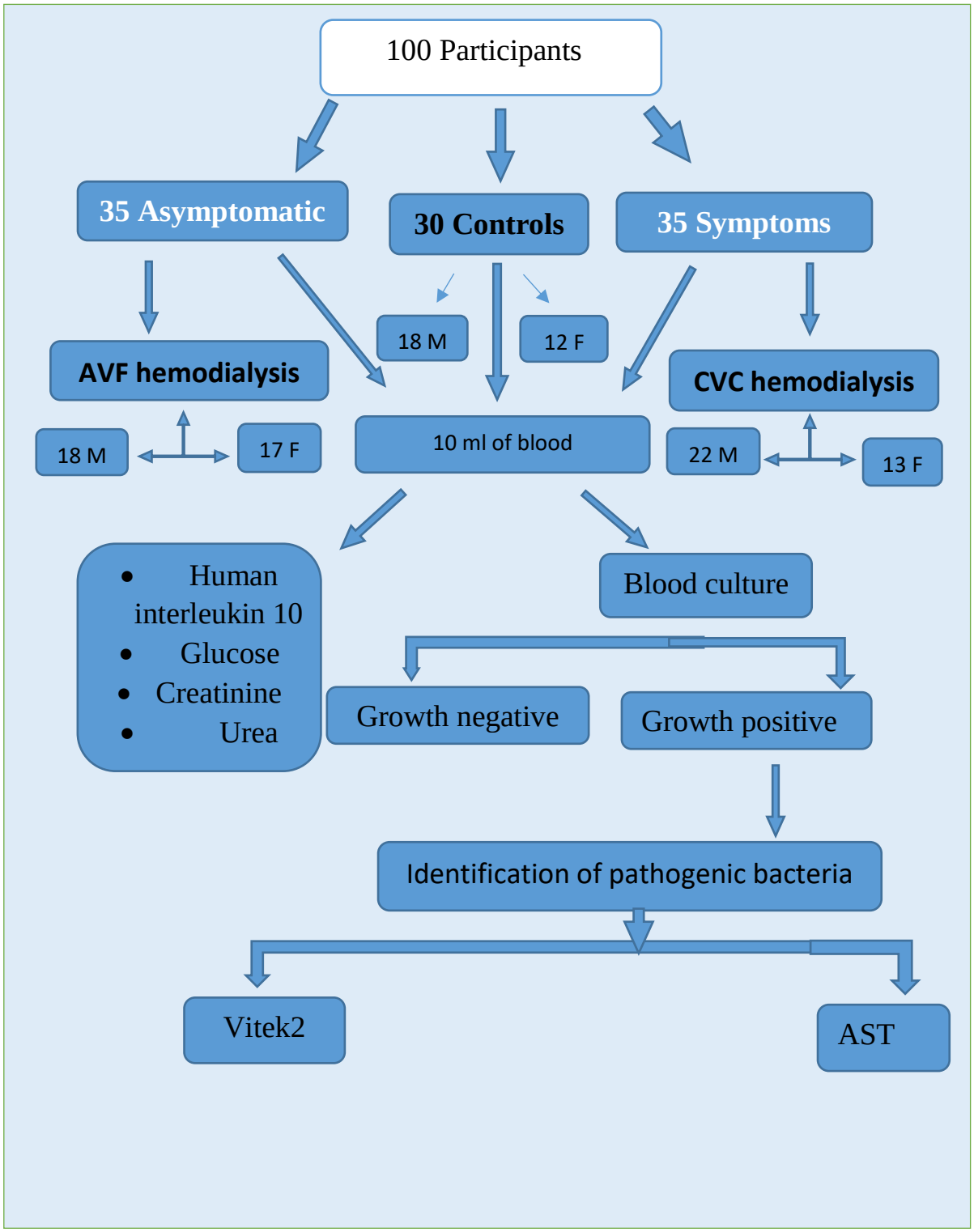


Figure (3.1): scheme of study

3.6. Ethical Approval

Biological materials and potentially harmful microbes were handled according to protocols established by Kerbala University's the Department of Clinical Laboratories in the College of Applied Medical Sciences. Samples for this study were collected from patients undergoing dialysis at the Kerbala Health Directorate after getting the requisite approval from the hospital administration and the patients.

3.7. Materials

3.7.1. Equipment and Tools Utilized in the Study

The following tools and instruments were employed in this investigation in Table (3.1).

Table (3.1): Devices and Instruments.

Equipment & Instruments	Manufacturing Company	Origin
Autoclave	Hirayama HVE-50	Japan
Biological safety cabinet	EuroClone Safemate	Italy
Burner	Amal	Turkey
Centrifuge	Kokusan	Japan
Cool box	VB	China
Cotton	BDH	England
Deep freezer	Hettich	Korea
Electric oven	Olympus	Japan
ELISA Devices(washer & reader)	Human	Germany
ELISA printer	Epson	Japan

Eppendorf tube 0.5 ml	ALS	China
Flasks (different size)	Jlassco	India
Gel Tubes 10 ml	ALS	China
Gloves	ALS	China
Graduated glass cylinder	Supc orior	Germany
Incubator	Memmert	Germany
Light microscope	Olympus	Japan
Loop	Himedia	India
Micropipette set	SLAMED	Germany
Pipette tip	ALS	China
Refrigerator	Panasonic	Korea
Sensitive balance	Sartorius	Germany
Slides	Himedia	India
Syringe 10 ml	Arrow	Egypt
VITECK® 2 compact system	Bio merieux	France
Water bath	Polyscience	USA
Water distillatory	GFL	Germany

3.7.2. Chemicals and Biological materials

Table (3.2): The chemicals and biological materials

Chemicals and biological materials	Company	Country of origin
Absolute alcohol	Bioneer	Korea
Glycerol	Biolife	Italy
Gram's stain kit	Biolife	Italy
Normal saline (0.9 %)	choueifat	Lebanon
Oil immersion	BDH	England

3.7.3. Culture media

Table (3.3): Culture media used in the current study

Culture media	Company	Country of origin
Blood agar base (BAB)	Himedia	India
Blood culture bottle	Microxpress	Spain
MacConky agar	Oxoid	England
Muller Hinton agar	Himedia	India

3.7.4 Antibiotic dick as mentioned in table (3.4)

Table (3.4) Antibiotic Dick

Antibiotic dick	Assembly	Disk potency
Ammoxillin	AMX	10 µg
Cefotaxime	CTM	30 µg
Ceftriaxone	CTX	30 µg
Clindamycin	CID	2 µg
Gentamycin	CN	10 µg
Imepeneme	IMI	5 µg
Meropenem	MEM	10 µg
Piperacillin/tazobactam	TZP	20/10 µg

3.7.5. Commercial kits

Table (3.5): The commercial kits which are used in the study.

Kits	Company
Human interleukin 10 (IL-10) Elisa kit	Sunlong / china
Urea kit	Linear / spain
Creatinine kit	Linear /spain
Glucose kit	Biolabo / France
ID (VITEK2) Cards Cassette	Biomerieux

Table (3.6): components and quantity (IL-10) Elisa kits.

Components	Quantity
User manual	1
Closure plate membrane	2
Sealed bags	1
Microelisa stripplate	1
Standard： 135 pg/ml	0.5ml×1 bottle
Standard diluent	1.5ml×1 bottle
HRP-Conjugate reagent	6ml×1 bottle
Sample diluent	6ml×1 bottle
Chromogen Solution A	6ml×1 bottle
Chromogen Solution B	6ml×1 bottle
Stop Solution	6ml×1 bottle

Table (3.7): Reagents of Urea kit

Reagents	QUANTITE
CAL Urea standard	1 x 3 mL
R2 Buffered chromogen	1 x 48 mL
R3 Alkaline hypochlorite	1 x 50 mL
R1 Enzyme reagent Urease	1 x 2 mL

Table (3.8): Reagents of Creatinine kit

Reagents	QUANTITE
R1 Picric acid	1 x 50 mL
R2 Alkaline buffer	1 x 50 mL
CAL Creatinine standard	1 x 3 mL

Table (3.9): Reagents of Glucose kit

Reagents	QUANTITE
R1 Monoreagent.	2 x 50 mL
CAL Glucose standard	1 x 3 mL

3.8 Diagnosis of bacteria

3.8.1. Blood Sample collection

Ten ml of blood were collected from each patient groups and control group, for patient via the central venous catheter and 5ml was transferred to a blood culture bottle for cultivating, other 5ml of blood was immediately placed in a gel tube, and permitted to coagulate at room temperature (20-25 °C) for 15 minutes. The collected specimens were centrifuged at 3000 rpm for about 15 minutes to separate the serum, which was then divided into 2 parts, one part was stored at -20 C until the immunological assay and the second part was immediately used for investigation of chemical makers (urea, creatinine, sugar) using the DRUi.

3.8.2. Blood culture

is an important diagnostic tool for determining the presence of microorganisms. Blood sample will be collected using a sterile needle and syringe and transferred to a culture bottle. The BacT/ ALERT® 3D system (bioMeriéux, Marcy l'Etoile, France) was utilized for the initial examination of the blood cultures(Arif *et al*., 2021). The bacteria were collected and inoculated onto blood agar plates (BAP; Asan Pharmaceutical Co., Ltd., Seoul, Korea) and MacConkey agar plates (Becton Dickinson, Sparks, MD,

3.8.3 Conventional workflow of positive blood cultures

Following a positive signal from the BacT/ALERT® 3D Device, Gram staining was conducted, after that, the bacteria are cultured on a solid agar medium. The colonies on the agar plates were used for identification and antibiotic susceptibility testing (AST) using the commercial automated Vitek2 system (bioMeriéux) after an overnight incubation period. The ID and AST values produced using this method served as a benchmark against which the institution's methods could be compared (Ha *et al.*, 2018).

1. After primary organism isolation, minimal treatment is required using a simple homogenous inoculum.
2. Insert the inoculum into the VITEK® 2 Cassette at the Smart Carrier Station TM.
3. The VITEK® 2 Card and the sample are linked via a barcode.
4. Once the Cassette has been loaded, the gadget will handle the incubation and results readout (Arif *et al.*, 2021).

VITEK® 2 Compact is a biochemically based automated microbiological identification tool with 48 biochemical attributes that is extensively used in clinical laboratories (Książczyk *et al*., 2016). VITEK® 2 Compact can identify microorganisms for up to 4 hours. Each well evaluates the metabolic performance of a strain, including its capacity to acidify, alkalize, Enzymatically hydrolyze substrates, as well as bacterial proliferation in the presence of inhibitors.Fluorescence-based sensors are used to track bacterial growth and metabolic changes in the microwells(Arif *et al.,* 2021). Bacterial incubation conditions, such as media composition and pH, influenced the outcomes of biotyping and biochemical-based techniques (Książczyk *et al*., 2016). A sterile microloop was used to collect a few colonies from a pure culture that had grown for 18 to 24 hours on blood or macconkey agar. Using a VITEK® 2 DensiChek (bioMérieux, Warszawa, Poland), a bacterial culture was calibrated to the McFarland Turbidity Standard of 0.5–0.63 in 3 mL of a 0.45 % sodium chloride solution (Arif *et al.,*2021). The GP card was placed on the cassette and placed in the instrument if the gram stain was negative; otherwise, the GN card was placed on the tape and placed in the instrument if the gram stain was positive. To avoid turbidity changes, the duration between suspension preparation and card filling was shorter than 30 minutes. At 35.5 1 °C, the cards were incubated. After each card was withdrawn from the incubator, colorimetric

measurements were obtained automatically every 15 minutes. After 10 to 18 hours of incubation, the findings were read (Morka *et al.,* 2018).

3.8.4 Determination of antibiotic susceptibility

Additionally using vitike 2 to determines antibiotic susceptibility testing ,it was also used Disk diffusion method to determines Antibiotic susceptibility test of different isolates were carried out according to the criteria of the Clinical and Laboratory Standards Institute using disk diffusion method by Kirby-Bauer method(Hudzicki,2009), bacterial cells were suspending then adjusted to a 0.5 McFarland standard tube and spread on surface of Mueller Hinton Agar by using disks commercially obtainable antibiotics (Bioanalyse, Turkey) and the plates were incubated at 37ºC for 18-24 hours. After incubation, the antibiotic inhibition zone diameters (IZD) were measured in millimeters (mm) (CLSI,2016).

3.9. Sterilization Methods

A. The culture medium utilized in the current investigation was autoclave sterilized at 121Co for 15 minutes.

B. The glasswares are sterilized using dry heat in an electric oven set to 180 degrees Celsius for a period of two hours.

3.10 Media Preparation

3.10.1 Blood agar medium

To prepare this medium, we followed the instructions on the package and dissolved 40 gm of blood agar base in 1000 ml of D.W. After 20 minutes of autoclaving at 121 degrees Celsius, the medium was cooled to 45 degrees Celsius and 5 percent of fresh human blood was added. It was used to test the hemolytic potential of bacterial isolates and as an enrichment medium for the isolates (MacFadden, 2000).

3.10.2 MacConky agar medium:

The agar for this medium may be mixed with 1000 ml of D.W. for 40 grams, and then the mixture can be sterilized in an autoclave at 121 degrees Celsius for twenty minutes. After cooling, it was poured to the plates, this type of media used selective gram-negative media (MacFadden, 2000).

3.10.3 Muller- Hinton agar medium

It is used in assessing the effectiveness of various antibiotics after being prepared in accordance with the manufacturing firm. (McFadden, 2000).

3.11 Preparation of Solutions and Reagent

Solutions for Gram staining: These solutions have been prepared in accordance with the necessary microbiological procedures. The solutions included crystal violet, iodine, pure alcohol, and safranin. There were four different solutions in all (Leboffe and Pierce, 2012).

3.12. Biomarker Profile Assay by ELISA Technique:

The serum level of interleukin 10, was determined by classic sandwich-ELISA using ELISA research kits.

3.12.1 Determination of the level of Human Interleukin 10 (Cat. No SL0967Hu), china.

3.12.1.1. Principle of Sandwich ELISA technique: /

Sandwich-ELISA is the technique used in this ELISA kit. The IL-10-antibody that has already been coated onto the Micro Elisa strip plate included within this package. In a Micro Elisa strip plate, the standard or sample is mixed with the appropriate antibody and placed in the wells.Each well of a Micro Elisa strip plate is then treated with an antibody against IL-10 that has been conjugated with Horseradish Peroxidase (HRP). Unbound substances are flushed out. Each well is dosed with the TMB substrate solution. Only when IL-10 and HRP conjugated IL-10 antibody are added to a well will appear blue and subsequently certain antibodies become yellow. The optical density (OD) at 450 mn, as determined by spectrophotometry.

The amount of IL-10 present can be calculated from the resulting OD value. The IL-10 concentration in the samples may be calculated by comparing the optical density (OD) of the samples to the OD of the standard curve.

3.12. 1. 2 Procedure of Sandwich ELISA technique:

1. Dilution of Standards Dilute the standard by small tubes first, then pipette the volume of 50ul from each tube to microplate well, each tube use two wells, total ten wells.

90pg/ml	Standard No.1	300µl Original Standard + 150µl Standard diluents
60pg/ml	Standard No.2	300µl Standard No.1 + 150µl Standard diluents
30pg/ml	Standard No.3	150µl Standard No.2 + 150µl Standard diluent
15pg/ml	Standard No.4	150µl Standard No.3 + 150µl Standard diluent
7.5pg/ml	Standard No.5	150µl Standard No.4 + 150µl Standard diluent

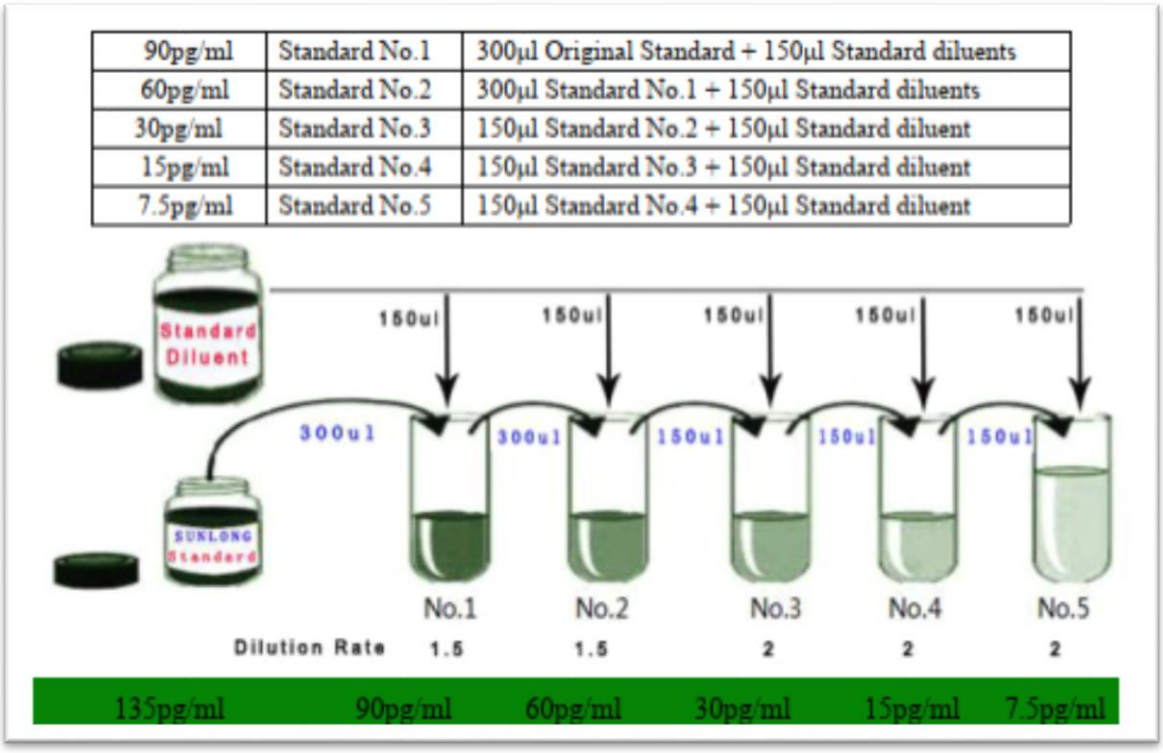


Figure (3.2): Concentration of standards of IL-10

2. In the Micro Elisa strip plate, leave a well empty as blank control. In sample wells, 40µl Sample dilution buffer and 10µl sample are added (dilution factor is 5). Samples should be loaded onto the bottom without touching the well wall. Mix well with gentle shaking.

3. Incubation: incubate 30 min at 37℃ after sealed with Closure plate membrane.

4. Dilution: dilute the concentrated washing buffer with distilled water (30 times for 96T and 20 times for 48T).

5. Washing: carefully peel off Closure plate membrane, aspirate and refill with the wash solution. Discard the wash solution after resting for 30 seconds. Repeat the washing procedure for 5 times.

6. Add 50 µl HRP-Conjugate reagent to each well except the blank control well.

7. Incubation as described in Step 3.

8. Washing as described in Step 5.

9. Coloring: Add 50 µl Chromogen Solution A and 50 µl Chromogen Solution B to each well, mix with gently shaking and incubate at 37 ℃ for 15 minutes. Please avoid light during coloring.

10. Termination: add 50 µl stop solution to each well to terminate the reaction. The color in the well should change from blue to yellow.

11. Read absorbance O.D. at 450nm using a Microtiter Plate Reader. The OD value of the blank control well is set as zero. Assay should be carried out within 15 minutes after adding stop solution.

3.12.1.3. Calculation of Result

The human IL-10 levels that have been calculated using the Standard are presented on a logarithmic scale (x-axis), and the read ODs that correspond to those concentrations are shown on a logarithmic scale (y-axis), respectively. The amount of Human IL-10 present in a sample is shown along the X-axis, while the sample's optical density is displayed along the Y-axis. Multiplying the dilution factor by itself is one way to get the beginning concentration of the substance. (Appendix 3).

3.13. biochemical tests

3.13.1 Urea Test

3.13.1.1. Principle of Urea Test

The generation of ammonia and carbon dioxide is the end consequence of urea being hydrolyzed by the enzyme urease1,2. The created ammonia reacts with alkaline hypochlorite and sodium salicylate in the presence of sodium nitroprusside, which acts as a coupling agent. This results in the production of a green cromophore. The intensity of the color that is produced is proportional to the amount of urea that is present in the sample.

3.13.1.2 Procedure of Urea Test

1. Bring both the samples and the reagents to the same temperature, which is room temperature.
2. pipette into cuvette

TUBES	Blank	Sample	CAL.Standard
Working reagent	1.0 mL	1.0 mL	1.0 mL
Sample	–	10 µL	–
CAL.Standard	–	–	10 µL

3. Combine all of the components and incubate them for either five minutes at a temperature of 37 degrees Celsius or ten minutes at a temperature ranging from 16-25 degrees Celsius.
4. Pipette

R3	1.0 mL	1.0 mL	1.0 mL

5. At a wavelength of 600 nanometers, compare the absorbance (A) of the samples to that of the standard, and also compare it to the absorbance (A) of the reagent blank..

3.13.2. Creatinine test

3.13.2.1 Principle of Creatinine test

An adaptation of the classic picrate reaction forms the basis of this method. When exposed to an alkaline environment, creatinine forms a crimson complex with picrate ions. The concentration of creatinine in a sample is inversely proportional to the rate of complex formation, which is expressed as an increase in absorbance over a specified time period.

3.13.2.2 Procedure of Creatinine test

1. Bring the reaction temperature (about 37 degrees Celsius), the samples, and the standard to the working reagent.
2. Second, use distilled water to calibrate the photometer to a reading of zero.
3. Pipette contents into a cuvette

Working reagent	1.0 mL
Sample or Standard	100 µL

4. Blend softly (4). Put the cuvette into the instrument's temperature control and start the timer.
5. After adding either the sample or the standard, record the intensity of absorption at 510 nm after 30 seconds (A1) and 90 seconds (A2) respectively.

3.13.3 Glucose Test

3.13.3.1 Principle of Glucose Test

In an enzymatic indicator test that is based on the Trinder reaction, the synthesis of a pink quinoneimine dye is employed as a quantitative indication. This dye is formed during the process. After enzymatic oxidation and in the presence of glucose oxidase, glucose is found to be the product of this process. The pigment indicator is produced when the hydrogen peroxide

that has been created is activated by the enzyme peroxidase and then combines with phenol and 4-aminoantipyrine.

3.13.3.2 Procedure of Glucose Test

Pipette into test tubes as follows:		
	Reagent Blank	**Standard / Sample**
Standard / Sample	---	10 µl
Reagent	1 ml	1 ml

A serum based calibrator or aqueous glucose reference can be utilised to calibrate the assay. Shake and incubation for 10 min at 15-25oC in water bath or minutes at 37 degrees Celsius. Evaluate the standard, samples, and reagent blank for absorbance ‹the end-point is stable for 60 minutes.

Calculation:

$$\text{Glucose conc.} = \frac{\text{Sample abs.}}{\text{Standard abs.}} \times \text{Standard conc.}$$

3.14. Statistical analysis

Data analysis has been done statistically utilizing IBM SPSS statistical packages version 23. The analysis outcomes have been summarized using descriptive statistics. In addition, Mean and Standard Deviation have been computed and in order to determine if the experimental results were statistically significant, the $p < 0.05$ probability threshold was utilized. Furthermore, the Shapiro-Wilk test has been employed to check the normality of the data, while the Levene test has been utilized to examine the homogeneity of variance. Chi-square have been performed in order to investigate the association of the categorical and numerical variables, respectively. Additionally, statistical differences for two independent groups have been determined using the Mann-Whitney Test and Independent T-Test. Besides, the analysis of variance (ANOVA) was carried out to conduct multiple comparisons between groups. Moreover, Scheffe's post-hoc test was utilized at ($p < 0.05$) for multiple comparisons within groups. Asterisks indicate data having a P value below 0.05.

Chapter Four

Results and Discussion

4. Results

4.1 Distribution of Subject Groups according to Age and sex

One hundred (100) participants were enrolled in this study including three groups involved, the first one includes patients with symptoms involved bacterial infection like fever chill that founded have center venous catheter (CVC) [35 (22 males, 13 female)], the second group includes 35 asymptomatic hemodialysis patient which founded have Arteriovenous fistula (AVF) (18 male, 17 female) and the third group includes 30 healthy control group (18 male, 12 female).

4.2 Biochemical Parameters of age patient Groups

The results show that there were no significant differences in level ($P<0.05$) between age groups and biochemical Parameters, as show in table (4.1).

Table (4.1) Distribution of Biochemical Parameters according to age for patient group

Age Group	Number	Mean ± Std. Deviation		
		Creatinine mg/dl	Urea mg/dl	Glucose mg/dl
<20	5	9.04 ± 0.86	176.48 ± 104.06	119.06 ± 23.66
20-29	6	9.37 ± 1.30	138 ± 39.76	153 ± 39.75
30-39	7	9.51 ± 2.40	148.49 ± 29.90	175.86 ± 56.04
40-49	17	8.29 ± 2.03	107.60 ± 29	137.15 ± 33.03
50-59	18	8.26 ± 2.11	123.74 ± 41.4	147.56 ± 39.90
≥ 60	17	7.92 ± 2.66	138.01 ± 47.12	139.24 ± 25.02
P. value		0.51	0.17	0.30

Anova has been used in comparison, sig: significant, nsig; not significant P. value (≤ 0.05)

The current study found that there was no significant difference in the levels of creatinine, urea, or glucose between age groups in hemodialysis patient that agreement with study presented by (Foley *et al*., 2004), (Al Saran *et al*., 2011),while previous studies found that elderly hemodialysis patients had lower levels of creatinine and, which may reflect differences in muscle mass and protein metabolism(Al-Hwiesh *et al*., 2015).

(Garibotto & Russo., 2012) suggested that relationship between aging, muscle mass, and creatinine explains that age-related reductions in muscle mass can lead to lower creatinine production, which can in turn lead to lower creatinine levels in the blood, However another study, suggested that older age is associated with lower GFR and higher serum creatinine levels, but also cautioned that creatinine levels can be influenced by a variety of factors, including muscle mass and dietary protein intake. (Zoccali & Mallamaci, 2016). (Cheng *et al*., 2018) suggested that older age was associated with lower creatinine levels among patients receiving continuous renal replacement therapy (CRRT) may be due to reduced muscle mass and other age-related changes in body composition included in current study.

4.3 Association of positive and negative blood culture according to type of vascular access.

This study approved that there was significant difference at ($p < 0.05$) in rate of positive blood culture in patient with CVC compared with patient an AVF as show in table (4.2)

Table (4.2) 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)

There are many study shows that the incidence of positive blood cultures was significantly higher in patients with CVCs compared to those with AVFs, 15% of patients with CVCs had positive blood cultures, compared to only 2% of patients with AVFs (Al-Jaishi *et al*., 2012) ,and previous study founded positive blood cultures was significantly higher in patients with CVCs compared to those with either AVFs or AVGs. Specifically, 22% of patients with CVCs had positive blood cultures, compared to 3.5% of patients with AVFs and 6% of patients with AVGs (Farouk *et al*., 2017) ,and another study presented by (Selby *et al*., 2018) found that 8.3% of patients with CVCs had positive blood cultures, compared to only 1.1% of patients with AVFs, (Alzahrani et a., 2020) founded that central venous catheters (CVCs) are more prone to bloodstream infections than arteriovenous fistulas (AVFs) in hemodialysis patients ,that agree with the current study ,and the similar study confirmed that vascular access of the CVC (Double lumen) which has

responsible for about (30– 60%) of catheter-related infection in hemodialysis patients and hospitalization rates are higher among patients with CVCs (Double lumen) than among AVF (native arteriovenous fistula)(Abduzzahra *et al*., 2022)

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 (Thongprayoon *et al*., 2021).

Catheters provide a direct route for bacteria to enter the bloodstream along the catheter surface (Thomson *et al*., 2007), catheters are requiring frequent manipulation and access that can introduce bacteria (Ramanathan *et al*., 2012).

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 (National Kidney Foundation, 2020).

4.4 Distribution of isolated bacterial infection according to age and sex

The present study's finding of bacterial growth showed that all age groups have bacterial growth, but age level of (>60) years were the most associated with infection as recorded in table (4.4), However, the growth was analyzed compared to sex of the two groups of patient, the result approved that there was no significant difference between male and female according to bacterial infection .

Table (4.3): Distribution of isolated bacterial infection according to age and sex

Patients		BC Positive		P. value
		CVC No= 17	AVF No=3	
Age (year)	<20	2	0	0.400
	20-29	2	1	
	30-39	2	0	
	40-49	4	1	
	50-59	2	0	
	≥60	5	1	
SEX	Male	11	3	0.169
	Female	6	0	
	Total	17	3	

Chi square has been used in comparison, sig: significant, nsig; not significant

P. value (≤ 0.05)

The current study found that older age was associated with a higher risk of bloodstream infections among hemodialysis patients this study corresponds with (Ibrahim *et al*, 2014) and (Alzahrani *et al,* 2020). which may be due to age-related changes in immune function, such as decreased T-cell function and impaired phagocytosis, which can make older adults more vulnerable to infections. Another study presented by (Rhee& Kovesdy., 2021) shows that there were other factors can increase from risk of bacterial infections among hemodialysis patients over 60 years of age which include comorbidities such as diabetes, hypertension, and cardiovascular disease, as well as exposure to infectious agents in healthcare settings. While previous studies found that age

was not a significant predictor of bloodstream infections among hemodialysis patients and suggested that this may be due to differences in patient characteristics and healthcare (Al-Otaibi et a., 2018). Another study shows that the risk of bloodstream infections among hemodialysis patients in the United States was highest in patients aged 18 to 44 years, rather than in older adults, that this may be due to differences in the prevalence of risk factors for infections, such as the use of catheters, between younger and older patients(Al Ammary et a., 2019) .

According to sex, the current study shows that prevalence of positive blood culture between male and female found that males were relatively dominant than females but statistically non- significant in the studied groups. These findings consistent with that reported in previous study (Alirezaei *et al*., 2019), (Nasiri *et al*., 2022) ,On the other hand, the incidence of infection has been higher in females, than males in previous studies presented by (OnVillal *et al*, 2018) .Also, another study presented by (Jaber *et al*, 2008), found men tend to have higher rates of comorbidities such as diabetes, hypertension, and cardiovascular disease, which are all risk factors for bacterial infections.

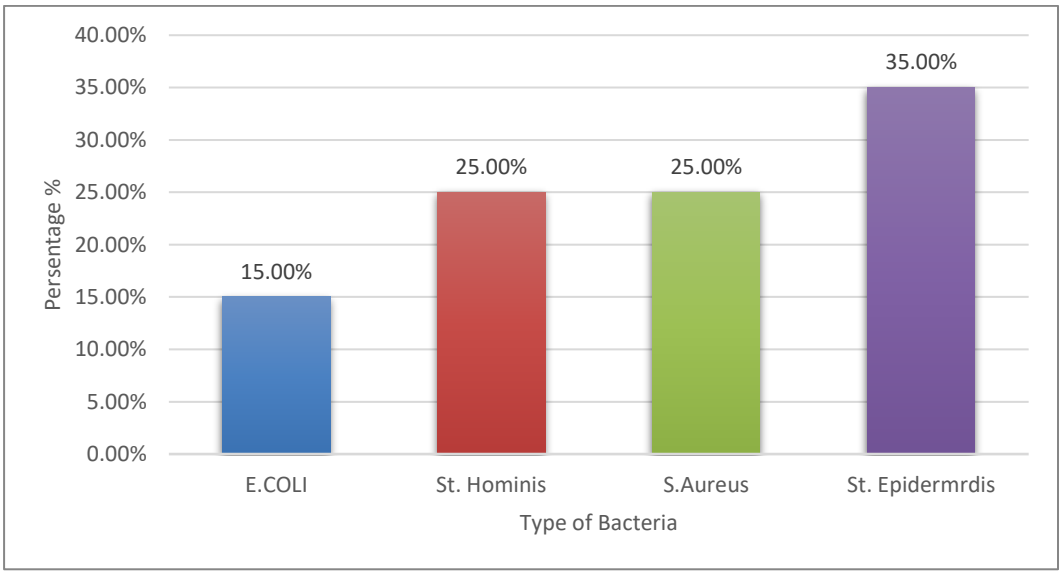
These comorbidities can lead to immune dysfunction and impaired wound healing, making patients more vulnerable to infections and the similar study suggested that men might be more likely than women to engage in behaviors that increase the risk of infection, such as smoking or poor hygiene practices (Kumar *et al*, 2004).

Another factor that may contribute to the gender difference in infection risk is hormonal differences between men and women, Estrogen a hormone found predominantly in women has been shown to have a protective effect against infection, Estrogen has been shown to stimulate the immune system, enhance wound healing, and inhibit bacterial growth (Klein *et al*., 2018).

Female X chromosome mosaicism provides an expanded repertoire of immune functions in females as compared with males, since a large number of genes related to immune functions are located on the X chromosome (Vázquez-Martínez *et al*., 2018).

4.5 Common bacterial infection in hemodialysis patients

Results in figure(4.1) show significant differences at (P<0.05) between bacterial types isolated from hemodialysis patient, gram positive was the most bacterial species than gram negative in hemodialysis patients, *S. epidermidis* was the most bacterial species isolated from hemodialysis (7) with percentage of (35%), while the other two bacterial species were equal in proportion and they were (5) with percentage (25%) for each of *S. aureus* and *S. Hominis*. However, *E- Coli* (3) with percentage (15%).



Cross tabulation test

Figure (4.1) Common bacterial species that isolated from hemodialysis patients

some study showed nearly same results that were reached in this research such as (Hadian *et al*., 2020), the most common organisms are gram-positive organisms (52-84%) ,and the similar study by (Prasansah, 2015) showed that Gram-positive bacteria were isolated with the highest frequency (88.5%). In

addition, previous study presented by(Rteil *et al*., 2020) show that *E. coli* (24.4%) followed by coagulase negative *staphylococci* (22.2%). *S. aureus accounted* for only 5.6% of cases, this is not consistent with the results of current study. While certain studies presented by(McCann *et al*., 2008) and(Chabi & Momtaz, 2019) corresponding with the current study show that coagulase negative *S. epidermidis* are the most common bacterial isolated from hemodialysis patients and which emerged as a prominent nosocomial pathogen and the leading cause of infections in implanted prostheses and other indwelling devices in recent years. This is due to *S .epidermidis* forming avid biofilms on device surfaces. Bacteria are stick to the surface , and then form cell-cell aggregates and a multilayered architecture , autolysin protein, promotes bacterial adhesion to the surface of medical devices(Dai *et al*., 2012)

4.6 comparison between Biochemical parameter and type of bacteria

This study found that there was no significant difference in level ($p \leq 0.05$) when Comparison among Creatinine glucose and urea with type of bacteria as shown in table (4.4).

Table (4.4) comparison between Biochemical parameter and type of bacteri

Parameter	Type of Bacteria	Mean ± Std. Deviation	P. value
Creatinine	*E.COLI*	6.933 ± 2.468	0.996
	St. Hominis	7.960 ± 2.239	
	S.aureus	8.080 ± 2.206	
	St. Epidermidis	8.400 ± 2.181	
Urea	*E.COLI*	192.267 ± 54.918	0.661
	St. Hominis	162.320 ± 106.668	
	S.aureus	127.060 ± 33.295	
	St. Epidermidis	117.929 ± 17.094	
Glucose	*E.COLI*	125.000 ± 19.079	0.664
	St. Hominis	145.400 ± 35.275	
	S.aureus	129.700 ± 34.223	
	St. Epidermidis	141.114 ± 42.868	

ANOVA Test between Groups for patients

This study was agreement with (Wang *et al*., 2016) found that elevated levels of urea were associated with increased levels of harmful bacteria of hemodialysis patients. Also (Lin *et al*., 2013) suggested that elevated levels of urea were associated with an increased risk of bloodstream infections in hemodialysis patients.

The similar study show Blood Urea Nitrogen levels were positively correlated with the levels of infection(Li *et al*., 2021) .

The increase of urea level and the proliferation of urease bacteria in patients with CKD led to an accumulation of ammonium in the gastrointestinal tract, raising the intestinal pH and weakening the junctions of intestinal cells, ultimately altering the permeability of the intestinal mucosa. In the course of CKD, the alteration of intestinal barrier, intestinal permeability, and gut bacterial community contributed to disruption of gut epithelial barrier ,complexes so that endotoxins and other harmful substances could flow into systemic circulation, inducing the occurrence of systemic inflammation(Liu *et al*., 2023).

Uremia, greatly increased concentrations of urea, creatinine and other nitrogenous metabolites reach the gut and become subject to microbial metabolism. Uremic patients show greatly increased counts of both aerobic and anaerobic organisms in the duodenum and the jejunum. Intestinal bacteria are involved in the generation of uraemic toxins such as indoxyl sulphate and p-cresol, and the latter has recently been linked with mortality in dialysis patients (bammens *et al*., 2021) .

4.7 Antibiotic susceptible test of bacterial isolated

This study included that AST to the bacterial species isolated from hemodialysis patient the result in figure (4.2) show 85.7% from *S. epidermidis* resistant to Ammoxillin and 14.3% of *S epidermidis* resistant to Cefotaxime, Ceftriaxone, Meropeneme, Clindamycin, 100% ***S. aureus*** resistant to Ammoxillin ,80% resistant to Ceftriaxone, 60 %resistant to Gentamycin، 40%resistant to cefotaxime, 20% resistant to , Meropeneme, 80% of *S. hominis* resistant to Ammoxillin ,60%, resistant to Gentamycin, Ceftriaxone 40% resistant to Cefotaxime, 20% resistant to piperacillin/Tazobactam, 100% *E. coli* resistant to Cefotaxime , Ammoxillin 66.7% resistant to Ceftriaxone, Clindamycin, 33.3% resistant to Gentamycin.

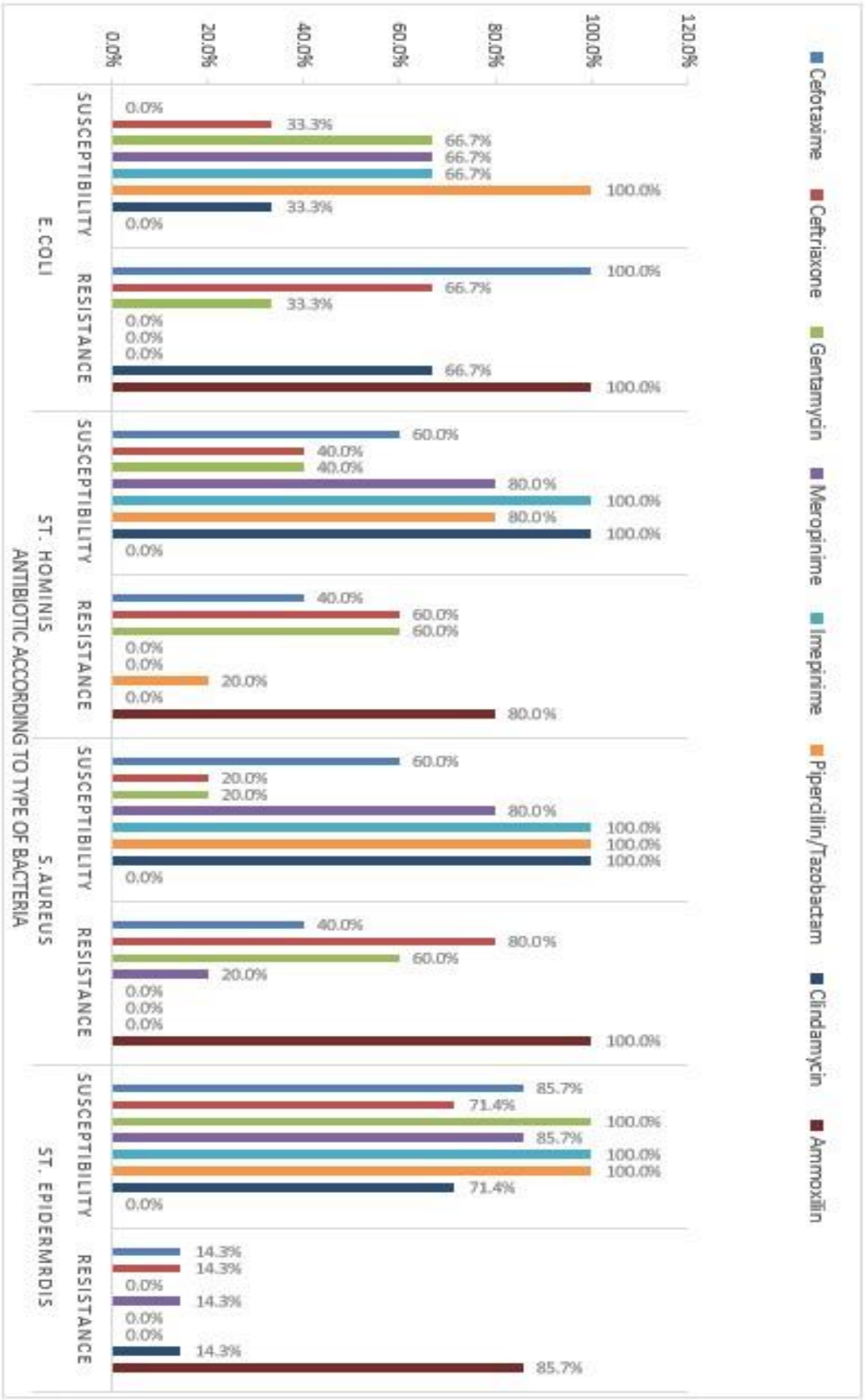


Figure (4.2) antibiotic susceptibility

(Ghafourian, *et al*. 2020) found that *E. coli* strains are isolated from clinical samples in a hospital in Iran, 82.4% were resistant to amoxicillin, 52.3% were resistant to ceftriaxone, and 35.7% were resistant to gentamicin. 40.2% were resistant to clindamycin. 83.3% were resistant to cefotaxime, also another study presented by (Badawy *et al*., 2021) found that 81.6% of the *E. coli* isolates were resistant to amoxicillin and 45.6% were resistant to ceftriaxone, also found that 47.8% of the isolates were resistant to clindamycin. Another study presented by (Akingbade *et al*., 2019) in Nigeria found that 66.7% of the isolates *E coli* from human clinical specimens were resistant to cefotaxime

(Sivick *et al*., 2012) found that 88.2% of *S. Epidermidis* isolates were resistant to amoxicillin (Otto, 2014) highlighted the high levels of resistance to beta-lactam antibiotics, including amoxicillin, due to the production of beta-lactamases. and alterations in penicillin-binding proteins (Deveci *et al*., 2021) found that 84.6% of of *S. epidermidis* isolates were resistant to amoxicillin, 76.9% of the isolates were resistant to cefotaxime. Another study by(Fiebelkorn *et al*., 2003) found that 34% of *S. epidermidis* isolates were resistant to ceftriaxone , 7.7% of of isolates were resistant to meropenem, (Miragaia *et al*., 2016) found that 7.5% of *S. epidermidis* isolates from patients with bloodstream infections were resistant to meropenem,

(Sammarraie & Al-Azawi, *et al*., 2017) found 100% of *S. aureus* resistant to amoxicillin, ceftriaxone ,(25%) gentamicin that agree with current study,(Al-Mohana *et al*., 2012) Showed that MRSA strains were 27.7% resistant to gentamicin ,(ElFeky *et al*., 2019). who found that63%of MRSA strains were resistant to gentamicin and the previous study by(Al-Anbari, *et al*., 2018) found that *S. aureus* bacterial strains were highly resistant to amoxicillin with percentage between 90% to 100%,(Deveci *et al*., 2021)

found that 41.8% of of *S. aureus* isolates from patients with bloodstream infections were resistant to cefotaxime. This study is consistent with the current study but the previous study showed 72.8% of *S. aureus* isolates were resistant to cefotaxime, (Abdel-Hady & Matter , 2015), (Deveci *et al*., 2021)found that 57.6% of the isolates were resistant to ceftriaxone, (Wang *et al*., 2015) found the antimicrobial susceptibility of *S. aureus* isolates from patients with bloodstream infections 0.9% of the isolates were resistant to Meropeneme. Another study showed that none of the isolates *S. aureus* were resistant to Meropeneme (Abdel-Hady & Matter , 2015).

(Lakhundi *et al*., 2018) found 52.8% of *S. hominis* isolates from patients with bloodstream infections were resistant to amoxicillin, 58.3% of of *S. hominis* were resistant to cefotaxime, 36.1% of the isolates were resistant to ceftriaxone,33.3% of *S. hominis* were resistant to gentamicin, 27.8% of the isolates were resistant to piperacillin/Tazobactam. While the previous study presented by(Choudhury *et al*., 2020) 66.7% of *S. hominis* from patients with bloodstream infections were resistant to amoxicillin, 33.3% of *S. hominis* isolates were resistant to gentamicin, 66.7% of *S. hominis* isolates were resistant to ceftriaxone, 41.7% were resistant to piperacillin/tazobactam.

Resistance in bacteria is caused by the overuse and misuse of antibiotics. When antibiotics are used too frequently or not used properly, bacteria can develop resistance to them over time, This occurs because bacteria have the ability to adapt and evolve in response to their environment, including exposure to antibiotics, bacteria can develop antibiotic resistance through several mechanisms, including Mutation .The bacteria can acquire mutations in their DNA that make them resistant to antibiotics, This occurs naturally over time and can be accelerated by the overuse or misuse of antibiotics (Centers for Disease Control and Prevention 2020) and gene transfer Bacteria can also acquire resistance genes from other bacteria through a process called gene transfer. This can occur through the exchange of

plasmids, which are small, circular pieces of DNA that can carry antibiotic resistance genes (Ventola., 2015).

All isolates showeed that ampicillin and amoxicillin possess the lower efficacy (Al-Jebouri & Mdish *et al*., 2019) , resistance to amoxicillin through several mechanisms. One of the most common mechanisms is the production of beta-lactamase enzymes, which can break down the beta-lactam ring in amoxicillin. Another mechanism is the alteration of penicillin-binding proteins (PBPs) in the bacterial cell wall, which can prevent amoxicillin from binding to its target site and inhibiting bacterial cell wall synthesis. In addition, some strains of *S. aureus* can acquire resistance genes through gene transfer, which can confer resistance to multiple antibiotics including amoxicillin (Chambers& Deleo.,2009).

Cefotaxime and other beta-lactam antibiotics bind to specific proteins called PBPs that are involved in building the bacterial cell wall. Some Staphylococcus strains have developed altered PBPs that have reduced affinity for antibiotic, making the antibiotic less effective(Bush& Bradford.,2016).

Some bacteria have developed efflux pumps, which are membrane proteins that actively pump antibiotics out of the bacterial cell before they can have an effect. This can reduce the concentration of antibiotic in the bacterial cell and make it less effective (Nikaido., 2018).

4.8 Immunological Parameter Serum Interleukin 10 (IL-10)

4.8.1 Comparison Between Subjects study groups according to Serum (IL-10) levels

This study founded that there was significant difference ($p<0.05$) between CVC, AVF and control groups as shown in the table (4.5) .

Table (4.5) comparison between subjects 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

Interleukin-10 (IL-10) is an anti-inflammatory cytokine, that plays an important role in regulating the immune response, (jaudah & Musa, 2017) found that IL-10 levels were significantly higher in hemodialysis patients who had central venous catheters compared to those with arteriovenous fistulas. Similarly, (Panichi *et al*., 2012) found that IL-10 levels were higher in hemodialysis patients with catheters compared to those with arteriovenous fistulas or grafts that is consistent with the results of current study presented, while the study shows that IL-10 levels were significantly higher in hemodialysis patients with vascular access dysfunction compared to those without dysfunction (Dheenan *et al*., 2019), similarly, found that IL-10 levels were higher in hemodialysis patients with arteriovenous fistula dysfunction compared to those without dysfunction(Kim *et al*., 2017).

4.8.2 Distribution (IL-10) According to the result of blood culture

Table (4.6) the results of statistical analysis that revealed the comparison between the level of IL-10 in patient with positive and negative blood culture, it found that there was significant difference in level of (IL-10) at ($P<0.05$) between positive and negative blood culture.

Table (4.6) 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

This study was similar to study presented by(Yang *et al*., 2021)found that IL-10 levels were significantly higher in patients with bacterial infections compared to those without infections .Also, another study shows that IL-10 levels were significantly higher in infected patients compared to non-infected in hemodialysis patients (Sidiq *et al*., 2020).The similar study conducted by(Fang *et al*., 2019) found that IL-10 levels were significantly higher in patients with sepsis compared to those without sepsis, and that IL-10 levels were associated with an increased risk of mortality.

Another study has suggested that 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 (Kato *et al*., 2013), and previous study suggested immune system activates a complex network of signaling pathways and cytokines, including IL-10, in an

attempt to fight off the infection and limit inflammation(Stenvinkel *et al*., 2005).

4.8.3 Difference between type of bacteria according serum to IL-10 levels

This study found that there was significant difference between type of bacteria and the level of IL-10, the level of IL-10 was found highly among bacteria *E. coli* and *S. aureus* at ($p < 0.006$) as show in table (4.7) .

Table (4.7) 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

There were many study investigated IL-10 level as (Bardoel *et al*., 2012), founded that IL-10 was produced in response to *S. aureus* and *E. coli* the study suggests that the IL-10 response may be specific to certain bacterial species, while (Himmelfarb *et al*., 2004) founded that the immune system of hemodialysis patients may be compromised, leading to a lower IL-10 to response to certain bacterial species , another study presented by (Wu, *et al*., 2012) investigated that patients infected with *S. aureus* had a higher IL-10

response, and that the IL-10 response to bacterial infections may be influenced by the specific bacterial species and the host's immune status.

Lipopolysaccharide (LPS) is the major component of Gram-negative bacteria cell walls and can cause an acute inflammatory response by triggering the release of a vast number of inflammatory cytokines in various cell types (Ngkelo *et al.,* 2012), interleukin-10 helps prevent excessive inflammation caused by *E. coli* infection, by suppressing the immune response, interleukin-10 helps reduce tissue damage caused by inflammation. (Rittirsch *et al*., 2008), , E. coli may dampen the immune response and improve survival (Steidler et al., 2013).

S. aureus secrete pyrogenic exotoxins called super antigens because they evoke a vastly exaggerated immune response that renders them lethal to humans (Arad *et al.,* 2002), super antigens bind directly, as intact proteins, to the MHC-II molecule and the TCR on the cell surface, without need for antigen processing, bypassing thereby the restriction that limits T-cell activation by conventional antigens to some 0.01% of all T cells, as opposed to some 20% by the super antigens (Miethk *et al*., 2017).

Chapter five

Conclusion and Recommendation

Conclusion

- *Staphylococcus epidermidis* was the most bacterial species isolated from hemodialysis patients.
- Older age was associated with a higher risk of bloodstream infections among hemodialysis patients.
- blood stream infection was found that Most predominant in CVC than AVF (48.6%to 8.6%).
- All gram positive bacterial species that isolated from hemodialysis patient resistant to amoxicillin and sensitive to Imepeneme.
- IL-10 higher in patients with bacterial infections compared to those without infections in hemodialysis patients.
- Staph aureus and E-Coli were the most bacteria species that increase level of IL-10.

Recommendations

1. Study of other type of microbial agent like viral and fungal infection among hemodialysis Patient.
2. Study The catheter related of blood stream infection in all Iraqi region for give clear operation for the most predominant type of infection in Iraqi patient.
3. Studying the effect of high interleukin 10 in the long term.

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Appendix

Appendix 1: Questionnaire of patients

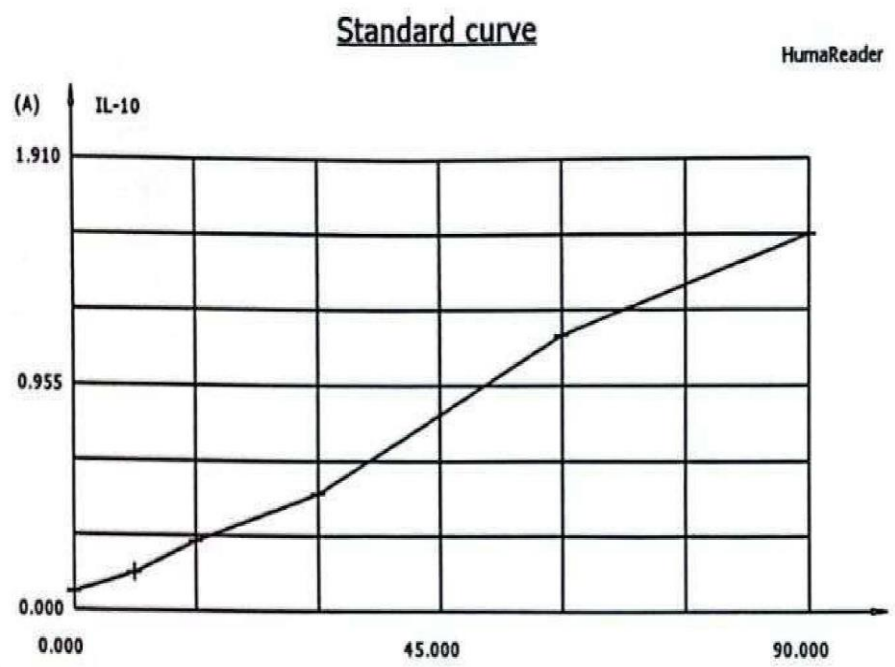
Name :		
Age :		
Sex :		
Antibiotics	yes	No
D.M	yes	No
Hepatitis	yes	No
immune disease	yes	No
Fever	yes	No
vascular access type	CVC	AVF

Appendix 2: Antibiotics susceptibility profile of Gram positive and gram negative bacteria (R-resistance, S-sensitive).

التسلسل	name	TUPE OF VASCULAR ACCESS	SEX	AGE	RESULT OF BC	type of bacteria	Cefotaxime	Ceftriaxone	Gentamycin	Meropinime	Imepinime	Piperacillin / tazobactam	Clindamycin	Ammoxilin	creatinine(0.7-1.4)mg/dl	urea(20-45)mg/dl	glucose(65-220)mg/dl	IK 3.6-5.2
1	patient	AVF	Male	60	N										13.8	212	138	3.76
2	patient	AVF	Female	51	N										7.3	98.6	193	2.569
3	patient	AVF	Male	52	N										6.9	104	113	0.015
4	patient	AVF	Female	53	N										7.7	80	205	3.749
5	patient	AVF	Female	65	N										5.6	118	161	3.246
6	patient	AVF	Male	46	N										11.6	158.9	128.5	4.931
7	patient	AVF	Female	60	N										7.4	110	117	3.941
8	patient	AVF	Male	50	N										7.9	168	240	0.512
9	patient	AVF	Female	40	N										7.7	80	205	0.104
10	patient	AVF	Female	46	N										8.4	142	189	4.725
11	patient	AVF	Male	56	N										9.8	163	132	4.282
12	patient	AVF	Male	62	N								r		6.5	117.1	109.6	7.241
13	patient	AVF	Male	70	N										7.4	131	167	2.837
14	patient	AVF	Female	43	N										8.8	94	114	4.087
15	patient	AVF	Male	28	P	s.epidermidis	s	r	s	r	s	s	s	r	9.2	134	200	9.618
16	patient	AVF	Male	60	N										12.8	231	127	7.715
17	patient	AVF	Male	43	P	st.hominis	r	r	s	s	s	r	s	r	5.2	52.4	127	11.5
18	patient	AVF	Female	38	N										8	113	163	7.415
19	patient	AVF	Male	52	N										9.4	88	189	2.92
20	patient	AVF	Male	57	N										10	177.5	180	6.12
21	patient	AVF	Female	20	N										10.5	99	143	2.197
22	patient	AVF	Male	47	N										9.8	112	134	7.48
24	patient	AVF	Female	43	N										11.7	136	110	6.081
25	patient	AVF	Female	32	N										5.6	185.4	265	2.797
26	patient	AVF	Female	31	N										7.7	141	122	7.539
27	patient	AVF	Male	44	N										10.5	52.3	135	0.219
28	patient	AVF	Male	58	N										5.4	124	98.5	3.688
29	patient	AVF	Female	40	N										9.8	99.8	188	2.139
30	patient	AVF	Female	66	N										9.6	147	152.9	1.085
31	patient	AVF	Male	33	N										11.5	188	201	0.738
32	patient	AVF	Male	62	P	st.epidermidis	s	s	s	s	s	s	r	r	8.1	93	101	9.887
32	patient	AVF	Female	51	N										12	118	135	4.752
33	patient	AVF	Female	36	N										11	145	167	1.189
34	patient	AVF	Male	55	N										11.9	113	111.4	0.569
35	patient	AVF	Female	24	N										10	91.8	141	3.909

الرقم	name	TYPE OF VASCULAR ACCESS	SEX	AGE	RESULT OF BC	type of bacteria	Ceftaxime	Ceftriaxone	Gentamycin	Meropirime	Imepinime	Piperillin / tazobactam	Clindamycin	Ammoxillin	creatrime(0.7-1.4)mg/dl	urea(20-45)mg/dl	glucose(65-120)mg/dl	IK-1(4.0-2.8)
1	patient	AVF	Male	60	N										13.8	212	138	3.78
2	patient	AVF	Female	51	N										7.3	98.6	193	2.569
3	patient	AVF	Male	52	N										6.9	104	113	0.015
4	patient	AVF	Female	58	N										7.7	80	205	3.749
5	patient	AVF	Female	65	N										5.6	118	161	3.246
6	patient	AVF	Male	46	N										11.6	158.9	128.5	4.931
7	patient	AVF	Female	60	N										7.4	110	117	3.941
8	patient	AVF	Male	50	N										7.9	168	240	0.512
9	patient	AVF	Female	40	N										7.7	80	205	0.104
10	patient	AVF	Female	46	N										8.4	142	189	4.725
11	patient	AVF	Male	56	N										9.3	163	132	4.262
12	patient	AVF	Male	62	N									r	6.5	117.1	109.6	7.241
13	patient	AVF	Male	70	N										7.4	131	167	2.837
14	patient	AVF	Female	43	N										8.8	94	114	4.087
15	patient	AVF	Male	28	P	s.epidermidis	s	r	s	r	s	s	s	r	9.2	134	200	9.618
16	patient	AVF	Male	60	N										12.8	231	127	7.715
17	patient	AVF	Male	43	P	st.hominis	r	r	s	s	s	r	s	r	9.2	52.4	127	11.5
18	patient	AVF	Female	38	N										8	113	183	7.415
19	patient	AVF	Male	52	N										9.4	88	189	2.92
20	patient	AVF	Male	57	N										10	177.5	180	6.12
21	patient	AVF	Female	20	N										10.5	99	143	2.197
22	patient	AVF	Male	47	N										9.8	112	134	7.48
24	patient	AVF	Female	43	N										11.7	136	110	5.081
25	patient	AVF	Female	32	N										5.6	185.4	265	2.797
26	patient	AVF	Female	31	N										7.7	141	122	7.539
27	patient	AVF	Male	44	N										10.5	52.3	135	0.219
28	patient	AVF	Male	58	N										5.4	124	98.5	3.668
29	patient	AVF	Female	40	N										9.8	99.8	188	2.139
30	patient	AVF	Female	66	N										9.6	147	152.9	1.085
31	patient	AVF	Male	33	N										11.5	188	201	0.738
32	patient	AVF	Male	62	P	st.epidermidis	s	s	s	s	s	s	r	r	8.1	93	101	9.887
32	patient	AVF	Female	51	N										12	118	135	4.752
33	patient	AVF	Female	38	N										11	145	167	1.189
34	patient	AVF	Male	55	N										11.9	113	111.4	0.569
35	patient	AVF	Female	24	N										10	91.8	141	3.909

Appendix 2: Calculation of Result



Program: IL-10 IL-10 Caculation: Curve Wavelength(nm): 450

Standard sample	#1	#2	#3	#4	#5	#6
Concentration(pg/ml)	0.000	7.500	15.000	30.000	60.000	90.000
Abs(A)	0.073	0.158	0.290	0.497	1.164	1.592

Operator: Checker:

الخلاصة

تعد العدوى من المضاعفات الشائعة وهي السبب الرئيسي الثاني للوفاة بين مرضى غسيل الكلى. إن خطر تجرثم الدم لدى مرضى غسيل الكلى أعلى بـ 26 مرة من عامة السكان ومن (2/1 الى 4/3) من الكائنات المسببة لتجرثم الدم لدى مرضى غسيل الكلى هي البكتيريا الموجبة لصبغة كرام ، ان مرضى غسيل الكلى لديهم خطر أعلى للإصابة بعدوى المكورات العنقودية حيث ان الموقع الأكثر شيوعًا للعدوى المسببة لتجرثم الدم هو الأطراف الاصطناعية الداخلية.

تهدف الدراسة إلى توصيف وتوزيع نوع العدوى البكتيرية واختبار الحساسية للمضادات الحيوية وعلاقة الإنترلوكين-10 مع عدوى مجرى الدم المرتبطة بالقسطرة.

عنيت هذه الدراسة بدراسة التهاب مجرى الدم في مرضى غسيل الكلى حيث تضمنت هذه الدراسة جمع(100 عينه دم) لكل من المرضى والاشخاص الأصحاء حيث جمعت 70 عينة دم (35 من المرضى الذين ظهرت عليهم الاعراض و35 من المرضى الذين لم تظهر عليهم الاعراض) ، و 30 عينه من الأشخاص الأصحاء خلال الفترة من تشرين الثاني 2022 الى نيسان 2023 من مركز الديلزه في مستشفى الامام الحسين التعليمي في مدينة كربلاء المقدسة، وتم الحصول على عينه الدم من الـ catheter بحجم 10مل من المرضى ومن الوريد بالسنبة للأشخاص الأصحاء، أجريت زراعة الدم لعزل البكتيريا والتعرف عليها وبعد ذلك تم اجراء العديد من التحليلات منها اختبار وظائف الكلى (اليوريا ، الكرياتينين، السكر) ، (اختبار حساسية البكتريا للمضادات الحيوية) ،المؤشر المناعي (إنترلوكين 10مع الدم) ،

أظهرت نتائج الدراسة الحالية أن العدوى البكتيرية تحدث في48.6% من مرضى القسطرة الوريدية المركزية، و8.6% من مرضى الناسور الشرياني الوريدي، وكانت *Staphylococcus epidermidis* أكثر الأنواع البكتيرية المعزولة من مرضى غسيل الكلى.

وأظهرت نتائج مقاومة المضادات الحيوية أن (85.7%) من *Staphylococcus epidermidis* مقاومة للأموكسيللين و (14.3%) مقاومة للمضادات الحيوية سيفوتاكسيم ، سيفترياكسون ، ميروبينيم ، كليندامايسين ، و (100%) من *Staphylococcus Aureus* مقاومة للأموكسيللين و(80%) مقاومة للسيفترياكسون و (60%) مقاومة للجنتامايسين و (40%) مقاومة للسيفوتاكسيم و (20%) مقاومة ميروبينيم و (80%) من بكتيريا *Staphylococcus hominis* مقاومة للأموكسيللين و (60%) ، مقاومة للجنتامايسين و سيفترياكسون و(40%) مقاومة للسيفوتاكسيم و (20%) مقاومة للبيبراسيلين / تازوباكتام ، و

(100%) من E. coli مقاومة لسيفوتاكسيم و للأموكسيللين و (66.7%) مقاومة لسيفترياكسون و كليندامايسين و (33.3%) مقاومة للجنتامايسين.

اظهرت النتائج وجود فرق معنوي عند المستوى ($P< 0.05$) بين الانترلوكين 10 والمرضى المصابين وغير المصابين ببكتيريا الدم حيث كان تركيز الانترلوكين 10 مرتفع في المرضى المصابين بالتهاب بكتيريا الدم مقارنه بالمرضى الغير مصابين بالتهاب بكتيريا الدم، واظهرت الدراسة وجود فرق معنوي بالنسبة للانترلوكين 10 بين انواع البكتيريا حيث كان مرتفع في بكتيريا *E. coli* وبمتوسط (62.981) ويليها بكتريا *Staphylococcus aureus* بمتوسط (24.977) ومن ثم *Staphylococcus Hominis* بمتوسط (11.054) و *Staphylococcus Epidermidis* بمتوسط (10.650)

جامعة كربلاء

كلية العلوم الطبية التطبيقية

قسم التحليلات المرضية

عزل وتوصيف البكتيريا المسببة لعدوى مجرى الدم المتعلقة بالقسطرة ودور الانترلوكين-10 في مرضى الفشل الكلوي المزمن مع غسيل الكلى

رسالة مقدمة

الى مجلس كلية العلوم الطبية التطبيقية جامعة كربلاء

وهي جزء من متطلبات نيل شهادة الماجستير في التحليلات المرضية

كتبت بواسطة

ضحى حسين جياد عزوز

بكالوريوس علوم الحياة / جامعة كربلاء /2012

بأشراف

أ.م. د أسراء سعيد عباس

هـ 1445 **م 2023**