NEAR EAST UNIVERSITY

INSTITUTE OF GRADUATE STUDIES

DEPARTMENT OF MEDICAL MICROBIOLOGY AND CLINICAL MICROBIOLOGY

INVESTIGATION OF THE PREVELANCE AND RISK FACTOR OF BACTERIAL AND VIRAL INFECTIONS IN HEMODIALYSIS PATIENTS IN MILITARY HOSPITAL IN JORDAN

M.Sc. THESIS

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Nicosia

June,2022

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We certify that we have read the thesis submitted by Razan Khater titled **"Investigation of the Prevalence and Risk Factors of Bacterial and Viral Infections in Hemodialysis Patients in Jordan**" and that in our combined opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science.

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Declaration

I hereby declare that all information, documents, analysis and results in this thesis have been collected and presented according to the academic rules and ethical guidelines of Institute of Graduate Studies, Near East University. I also declare that as required by these rules and conduct, I have fully cited and referenced information and data that are not original to this study.

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I owe everything to my family, who have supported and encouraged me throughout my personal and academic life and have a strong desire to see this achievement come true, without the encouragement and support of my family members, I would not be where I am today. Thank you so much for everything.

I dedicate this work to my sincere and generous father and my lovely mother, in appreciation of their glorious sacrifices for our success on our trail. Also, i'd like to convey my gratefulness to my sisters, who have always been there for me. In honor of their valiant sacrifices, this thesis is dedicated to them. This thesis is theirs.

Thank you all,

Razan Khater

Abstract

Prevalence and Risk Factors of Microbiological Infections in Hemodialysis Patients in Private Hospital in Jordan

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Hemodialysis is the treatment used in balancing/improving acid-base and electrolyte abnormalities in patients with acute and chronic kidney disease who are refractory or unresponsive to medical treatment. Infections are among the most important risk factors for hemodialysis patients. The main reasons for the high mortality and morbidity rate in hemodialysis patients due to viral and bacterial infections.

factors of HBV, HCV, HIV and catheter associated infections among acute and chronic hemodialysis patients in a military hospital in Jordan. Data were obtained by retrospective examination of patients' age, gender, and diagnosis, Hemodialysis frequency, cultures, and antibiotic treatments received by patients', duration and frequency of dialysis, presence of a catheter and fistula, and liver function tests, HBsAg, anti-HBs, anti-HCV, anti-HBs, anti-HCV, anti-HIV values of the patients were recorded from the files.

According to these data that was obtained, we observed the most common bacteria were MRSA (24.5%), followed by Klebsiella spp. (19.5%) and E. coli (17.1%). When anti-HCV, HBsAg, HB-core, Anti-HIV, and HIV-RNA serology results are evaluated in hemodialysis patients, the following results were obtained: hepatitis B surface antigen was positive in (8.1%), HCV was positive in (17.7%), and HB-core was positive in (11.3%) hemodialysis patients.

Since vascular procedures are applied for a long time in patients receiving hemodialysis with other patients in the hemodialysis unit, it is possible to add

infectious agents even in units with good infection control. These findings are an indication of insufficient adherence to optimal infection control procedures.

This study was conducted retrospectively. Therefore, if standard infection control measures are followed while patient follow-up in hemodialysis units, the frequency of bacterial and viral infections can be reduced

***Key Words**:* Chronic kidney disease, Hemodialysis, Bloodstream infection**,** Hepatitis, Viral infection

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List of Abbreviation

A. baumanii:	*Acinetobacter baumanii*
C. freundii:	*Citrobacter freundii*
Candida spp.:	*Candida species*
CRBSI:	Catheter Related Blood Flow Infection
CAS:	Catheter-Associated Sepsis
CDC:	Centers for Disease Control and Prevention
CVCs:	Central Venous Catheters
CKD:	Chronic Kidney Disease
CNS:	Coagulase Negative *Staphylococci*
DOPPS	Dialysis Outcomes and Practice Patterns Study
E. cloacae:	*Enterobacter cloacae*
E. coli:	*Escherichia coli*
ESRD:	End Stage Renal Failure
GFR	Glomerular Filtration Rate
Gr (-):	Gram-Negative
Gr (+):	Gram-Positive
HBV:	Hepatitis B Virus
HCV:	Hepatitis C Virus
HD:	Hemodialysis
HB-core:	Hepatitis B Antigen
HBsAg:	Hepatitis B Surface Antigen
HDV:	Hepatitis D virus
HIV:	Human Immunodeficiency Virus
K. pneumoniae:	*Klebsiella pneumoniae*
***Klebsiella spp*.:**	*Klebsiella species*
M. morganii:	*Morganella morganii*
MRSA:	Methicillin Resistant *Staphylococcus aureus*
MDR:	Multi-Drug Resistant
NKF-DOQI:	National Kidney Foundation-Dialysis Outcomes Quality Initiative
P. aureginosa:	*Pseudomonas aureginosa*
Pseudomonas spp.:	*Pseudomonas species*

S. aureus:	*Staphylococcus aureus*
SF:	Serum Physiological
Spp:	*Species*
S. epidermidis:	*Staphylococcus epidermidis*
Streptococcus spp.:	*Streptococcus species*
VRE:	Vancomycin-Resistant *Enterococci*

CHAPTER I

Introduction

Hemodialysis (HD) is the treatment used in balancing/improving acid-base and electrolyte abnormalities in patients with patients having acute and chronic renal disease refractory or unresponsive to medical treatment. HD is not only used in these abnormalities, but also before kidney transplantation and in some acute poisonings (Elliott, 2000). Infections are among the most significant risk factors for people with HD. According to reports publish, there is a positive correlation between HD patients and the risk of infection (Collins et al., 2011; Hanafusa et al., 2015; Ishigami et al., 2017). However, the relationship between dialysis modality and infectious diseases in HD patients remains unclear due to the limited number of studies (Banshodani et al., 2021). The reports of the Japanese and United States Renal Data System of HD treatment draw attention to the increase in mortality rates and hospitalization rates for infectious diseases in people with end-stage renal disease (ESRD) who are undergoing HD in recent years (Banshodani et al., 2021).

Viral infections such as hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) associated with complications are common in HD patients (Bahri et al., 2016; Mhalla et al., 2018).

In addition to hepatitis B infection, occult hepatitis B can also be seen in HD patients. Although there is HBV replication is active, and there is a detectable DNA load in occult hepatitis B, there is no hepatitis B surface antigen (HBsAg) detection (Bläckberg and Kidd-Ljunggren 2000; Bréchot et al., 2001). Systematic vaccination against HBV and hygiene rules greatly contributed to reducing HBV infections in HD patients.

HCV, which is one of the blood-borne viruses, is one of the most important viral infections seen in HD units, both in dialysis patients and among healthcare workers. Machine sharing and close contact between patients are considered among the reasons for encountering this virus frequently in HD centres. Anti-HCV positive prevalence in HD units is 0.7-18.1 in Asia-Pacific countries; In Venezuela, 71% varies between 2.6 and 22.9% even in developed countries (Fissell et al., 2004; Johnson et al., 2009; Jadoul et al., 2019). As with HBV, HCV continues to be the main infection risk associated with HD if vaccination against HCV infections is not performed. The prevalence of HCV in chronic HD patients reaches up to 90% for some countries (Hinrichsen et al., 2002).

HEV is mainly transmitted by the faecal-oral route. However, this is not the only transmission route. Some other modes of transmission of HEV include blood transfusion, organ transplantation, and HD. HEV is mainly transmitted by the faecal-oral route. However, this is not the only transmission route. Some other modes of transmission of HEV include blood transfusion, organ transplantation, and HD (Taherkhani and Farshadpour, 2016). HEV, which is one of the common agents transmitted through the hospital in HD patients, is due to its parenteral transmission and sensitivity to the infection of HD patients who are immunocompromised (Scotto et al., 2015). Although HEV infection progresses with a mild clinical course, serious infections can be seen in HD patients (Hosseini-Moghaddam et al., 2010; Wedemeyer et al., 2012). Despite the severity of the situation, HEV is neglected in HD patients, especially in endemic countries, and HEV screening is not routinely performed in HD centres (Kamar et al., 2017; Ouji et al., 2021).

The main reason for the high mortality and morbidity rate in hemodialysis patients as a result of viral infections like HBV and HCV are acute and chronic liver inflammation and damage, ranging from cirrhosis to hepatocellular carcinoma (Lodhi et al., 2019). All actions are intended to detect the incidence of HBV and HCV infections in HD units and address the risk factors for their spread, allowing for more efficient healthcare in that country.

The most common pathogens encountered in HD patients are Staphylococcus aureus, Gram-positive cocci followed by coagulase-negative staphylococci (Wang et al., 2006). There is a rise in the incidence of infections multi-drug resistant (MDR) organisms due to the continuous involvement of HD patients in the health system and the increase in antibiotic treatments. Among resistant pathogens, MRSA and MDR Gram-negative bacilli are among the most common pathogens in HD patients (Calfee, 2013).

CHAPTER II

General Information

2.1. Kidney

A healthy adult individual has a pair of kidneys, each weighing an average of 150 g. The kidneys are one of the best-preserved organs in the human organism in the anatomical structure. Although both kidneys are located behind the abdominal wall, they are not actually in the abdominal cavity (Wallace, 1998; Glassock and Rule, 2016) (Figure 1).

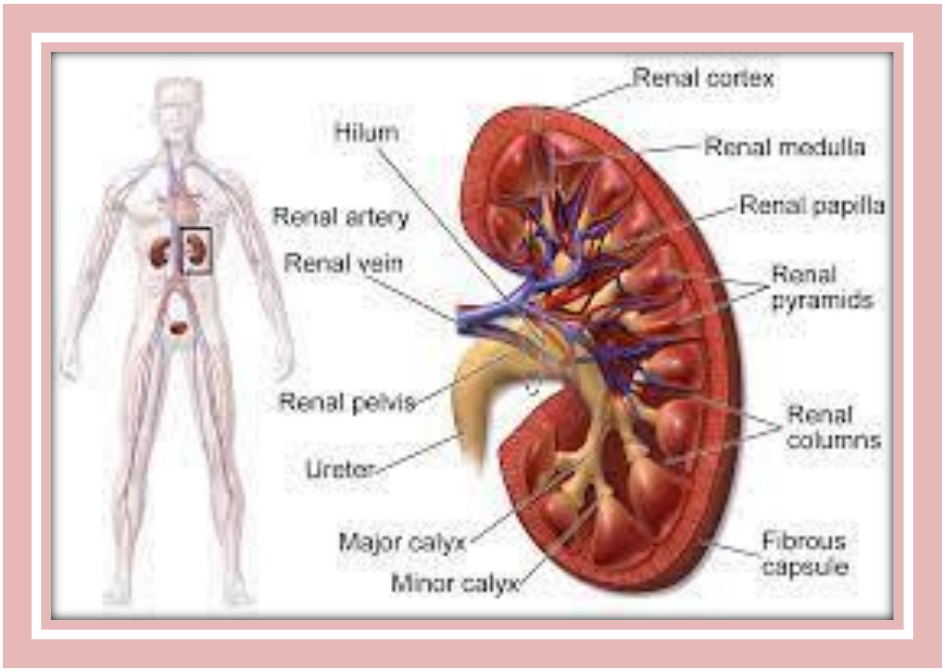

Figure 1:
Kidney Anatomy (https://en.wikipedia.org/wiki/Kidney)

They have a retroperitoneal location, meaning that they are located just behind the peritoneum, which covers the intra-abdominal cavity. The kidney has a dense vascular network to which 20-30% of cardiac output is directed. In a person with a body weight of 70 kg, the amount of blood passing through the kidney in 1 minute is approximately 1200 ml/min. It is very important to maintain the state of homeostasis in the body. The maintenance of the chemical structure of the internal environment is largely done by the lungs and kidneys. The kidneys regulate the body fluid and electrolyte balance. In order to keep the osmotic pressure of the blood constant, they remove different amounts of electrolytes and clean the body from harmful substances (Figure 2). They ensure the removal of toxic substances such as urea, uric acid, and

creatinine, which are the waste products produced as a result of metabolism, from the body. At the same time, they prevent the loss of substances by providing the reabsorption of substances necessary for the body (such as glucose and amino acids). They also help regulate the body's normal acid-base balance. Another function of the kidneys is their contribution to gluconeogenesis. They are also involved in the hormone synthesis and enzymes. Production of erythropoietin is a hormone that regulates the production of red blood cells.

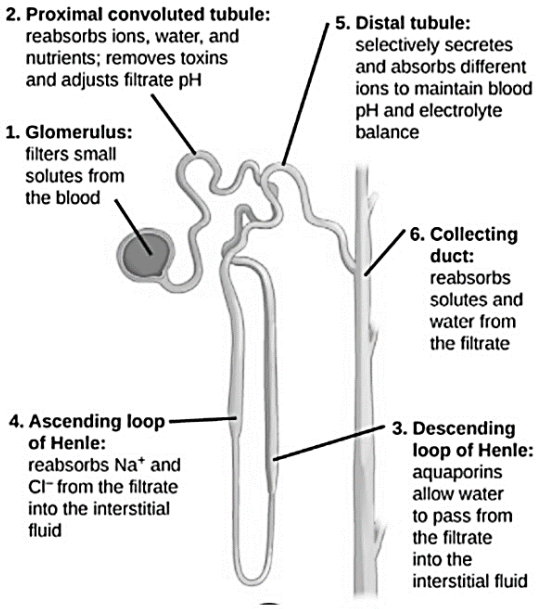

Figure 2:

The Different Functions of The Nephron in Filtering Waste and Maintaining Homeostatic Balance (https://courses.lumenlearning.com/wm-biology2/chapter/kidney-function-and-physiology/)

Other functions of the kidneys include the production of renin is an enzyme that regulates the production of angiotensin, that affects blood pressure and sodium balance, as well as 25-hydroxyvitamin D conversion, which affects calcium balance, to 1,25-dihydroxyvitamin D. There are approximately two million nephrons in each kidney. Each nephron consists of two parts, called the Tubules and glomeruli. Glomerular filtration, tubular reabsorption, and tubular secretion all contribute to the formation of urine in nephrons (Widmaier et al, 2018).

Kidney failure is divided into both acute and chronic. Acute renal failure is a condition for which deterioration of kidney function occurs within hours or days. It is

characterized by an acute onset of 24-h urine output below 400 ml in most patients and accumulation of nitrogen residues (as urea, nitrogen, and creatinine) within the blood (Ferenbach, 2016; Figure 3).

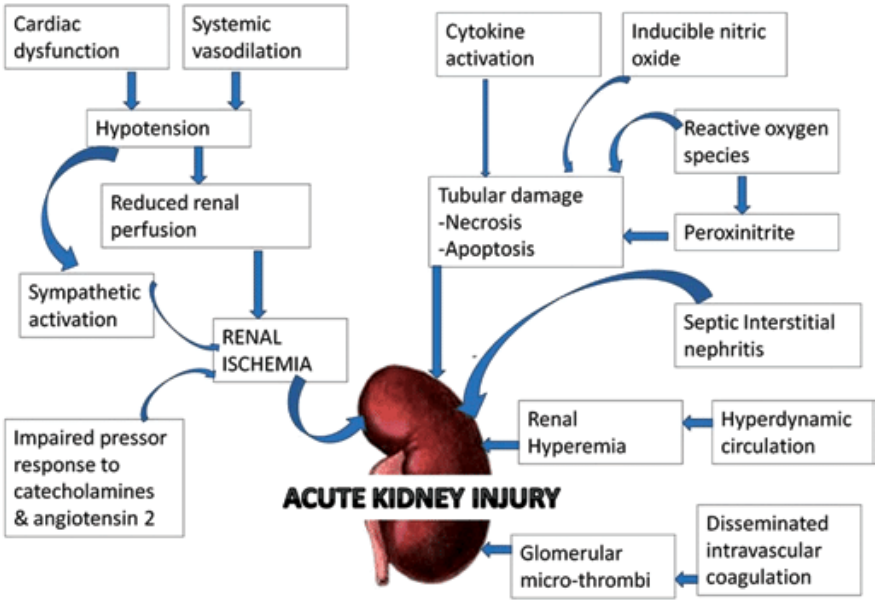

Figure 3:

Acute Kidney Injury

(https://www.researchgate.net/publication/320733753/figure/fig2/AS:555506961588224@1509454588747/Pathogenesis-of-acute-kidney-injury-in-sepsis_W640.jpg)

It is a clinical picture dominated through of a sudden decline in glomerular filtration rate and abnormalities in fluid electrolyte homeostasis. Regardless of the cause of chronic kidney failure, it arises as a result of long-term, progressive and irreversible destruction of over 80% of nephrons. It can be defined as a chronic progressive deterioration in the regulation of the fluid-solute balance of the kidney and metabolic and endocrine functions when the glomerular filtration rate decreases below 80 ml/min. As a result, nitrogenous substances such as urea, creatinine, and other metabolic residues excreted in the urine cannot be eliminated and accumulate in the blood. When the glomerular filtration value decline to 5-10 ml/min, end-stage renal failure (ESRD) is mentioned and patients require renal replacement therapy as dialysis and kidney transplantation (Schrier, 2017).

2.2. Chronic Kidney Disease (CKD)

Chronic kidney disease (CKD) is a multisystemic disease characterized by progressive and irreversible damage to the nephrons as a result of many systemic and primary kidney diseases. Glomerular filtration rate (GFR) gradually decreases over the years, and the rate of this decrease varies greatly depending on the different causes (Glassock and Winearls, 2009; Vaidya and Aeddula, 2021).

The classic symptoms of CKD appear with the development of uremia. Uremic symptoms usually occur after the GFR falls below 10-15 ml/min. Uremia causes deterioration in the functions of almost all organs (Azer et al., 2015) (Table 1).

Table 1

Clinical and Laboratory Findings in CKD

Clinical and laboratory findings in CKD	
Cardiovascular System	Pericarditis, Pericardial Effusion, Hypertension, Diastolic Dysfunction, Atherosclerosis, Hypotension, Arrhythmias, Cardiomyopathy
Skin Findings	Melanosis, Nail Atrophy, Hypothermia, Delay in Wound Healing, Itching
Gastrointestinal System	Nausea, Vomiting, Gastritis, Peptic Ulcer, Bleeding, Uremic Fetor, Anorexia, Weight Loss
Central Nervous System	Coma, Stupor, Polyneuropathy, Dementia, Convulsion, Muscle Weakness, Headache, Sleeping Disorders, Restless Legs Syndrome Irritability, Cramp, Flap Tremor, Concentration Disorder
Respiratory System	Pulmonary Edema, Pleural Effusion, Uremic Lung
Endocrine System	Amenorrhea, Impotence, Infertility, Impaired Glucose Tolerance Decreased Libido, Developmental Delay, Hyperparathyroidism, Renal Osteodystrophy, Hypogonadism
Liquid Electrolyte Balance	Hypovolemia, Hyponatremia, Hyperkalemia, Hypocalcemia, Hyperphosphatemia, Metabolic Acidosis, Hypermagnesemia, Hypervolemia
Immune System	Susceptibility to Infection, Increased Incidence of Cancer, Insufficient Antibody Formation
Bone Mineral System	Hyperdynamic Bone Disease, Osteoporosis, Osteocalcin, Adynamic Bone Disease
Haematological System	Anemia, Increase in Bleeding Tendency, Lymphocytopenia, Thrombocytopenia

Complications of CKD include hypertension, dyslipidaemia, anemia, hyperkalemia, malnutrition, metabolic acidosis, neurological complications, GIS complications and endocrine abnormalities.

The main treatment approach in CKD is to enable the existing nephrons to do their job with minimal damage, to prevent the development of complications, and to slow down the progression if CKD complications have started to develop. When the GFR is less than 5-10 ml/min/1.73 m^2, hemodialysis (HD), peritoneal dialysis or kidney transplantation comes into question for the patient. Some studies suggest that dialysis treatment may be delayed until the GFR approaches 7 ml/min/1.73 m^2 in some patients instead of uremic signs. If uremic symptoms, volume load unresponsive to diuresis, and refractory hyperkalemia are associated with a GFR of 10-15 ml/min/1.73 m^2, dialysis now inevitable (Long et al., 2017).

2.2.1. HD: Although it varies according to the patient, the treatment is usually applied 3 days a week, and the session duration varies between 3-5 hours according to the patient's body square and the dialysis entrance route. In hemodialysis, vascular access is provided either with a prosthetic graft or with an arteriovenous fistula.

2.2.2. Peritoneal dialysis: In peritoneal dialysis, the dialyzer considers the peritoneal membrane. An indwelling catheter is inserted into the peritoneal cavity and dialysate is delivered through this catheter. Fluids and solutes pass through the capillary bed among the visceral and parietal layers of the peritoneal membrane in the dialysate. After equilibrium is reached, the dialysate is drained and replaced with fresh dialysate. This process is referred to as 'change'.

2.3. Infections in Chronic Kidney Patients

Infections are very common in Chronic Kidney patients and the leading cause of death is infections. Septicemia is most commonly encountered as pneumonia, intravenous access infection, wound infection and urinary tract infection. A significant increase is observed in both bacterial infections (pneumonia, urinary tract infections, catheter bacteremia, catheter access tract infection, tunnel infection) and Infections caused by viruses [Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Human Immunodeficiency Virus (HIV)] in these patients (Dounousi et al., 2006; Levey and Coresh, 2012: Caccamo, et al 2014). Infections are responsible for 15% of all deaths in patients with kidney damage (Dounousi et al., 2006).

Patients with ESRD are more susceptible to infections due to comorbid diseases with immunodeficiency, frequent hospitalizations, uremic toxicity, increase in nitrogenous products, lymphopenia, neutropenia, chemotaxis defect, cellular immunity disorder, hypoalbuminemia, anemia and complement deficiency (Naqvi and Collins, 2006; Dagher et al., 2015). In these patients, there is a rise in the risk of infection in direct proportion to the decrease in renal functions. While the risk is 16% when GFR > 60 ml/min, the risk of nosocomial infection quadruples when the GFR falls between 15-44 ml/dl. One of the reasons for this situation is the decrease in T-cell activation as well as the decrease in leukocyte, chemotaxis and phagocytosis functions in the immune system. Unfortunately, dialysis itself also worsens immune dysfunction through complement activation (Dounousi et al., 2006; Chung et al., 2012; Caccamo, et al 2014; Dagher et al., 2015). Uremia and HD treatment cause increased oxidative stress. It is known that oxidative stress is correlated with the progression of CKD (Abbott et al., 2001). Nosocomial infections in chronic HD patients are frequently in the form of bloodstream infections (BSI) and urinary tract infections. Infection risk factors in HD patients; previous bacterial infection, use of catheter instead of fistula as vascular access, and high serum ferritin levels (>500ug/lt). Impairment in phagocytosis function is one of the predisposing factors in HD patients. Phagocytic functions are affected by uremia and the type of dialysis membrane. Iron overload also leads to an increase in the risk of infection. In HD patients, *Escherichia coli (E. coli*) sepsis attacks are much more common in patients with iron overload. While iron overload increases the virulence of some bacteria, it also suppresses phagocytosis. The use of AV fistulas instead of external shunts has led to a marked reduction in the frequency of vascular structure-related infections. The most important pathogens reported by the Centers for Disease Control and Prevention (CDC) are *coagulase-negative Staphylococci* (CNS), E. coli, Enterococci and *Candida species* (*Candida spp.)*, respectively. The role of Enterococci in nosocomial infections is alarming due to the rise in the rates of *Vancomycin-resistant Enterococci* (VRE) in patients undergoing dialysis in recent years and limited treatment options against them. Moreover, almost all nosocomial infections and bacteremia are associated with mortality in this group of patients (Pittet et al., 1994; CDC, 2011). Similarly, Candida spp. it is an important nosocomial infection agent with high morbidity and mortality. In a study, it was shown that mortality due to Candida infection is higher than Gram-negative [Gr (-)] microorganisms (Pittet et al., 1994). Due to minimal urine output in

patients entering HD, the emergence of hospital infections can also be in the form of urinary tract infections. Urinary tract infection with symptoms occurs more prominently within these patients. The clinical picture begins with the growth of bacteria in the residual urine in the bladder with a positive urine culture, followed by fever. Limiting urinary catheterization plays an active role in reducing infection in many patients (Pittet et al., 1994; Naqvi and Collins, 2006).

CKD is a very important problem due to its morbidity and mortality. Due to the lack of curative treatment for chronic renal failure and inadequacy of donor for kidney transplantation, patients undergoing palliative treatment should undergo HD at intervals. For this purpose, peritoneal HD and more often HD is preferred.

Renal transplantation, peritoneal dialysis, or hemodialysis are possibilities for patients with ESRD, and the prevalence of these patients continues their lives dependent on dialysis. The basis of HD is based on renal function diffusion and ultrafiltration. With HD, metabolic end products are removed and thus the electrolyte and fluid balance of the body is provided. The necessary venous access route for HD is provided either by surgically created arterio-venous shunts or by HD catheters.

Central venous catheters (CVCs) are the most commonly used medical devices for the treatment and follow-up of many patients, especially those hospitalized in the ICU. Catheters are generally used to provide access for HD until the use of more permanent surgical fistulas is possible (Sohail et al., 2021).

There are three main indications for the use of temporary or permanent HD catheters:

1- Patients who need HD until the surgical fistula is opened or until the opened fistula matures.

2- HD patients in whom surgical fistula opening is not possible

3- A HD catheter is administered to patients who are scheduled for renal transplantation soon or who are waiting for peritoneal HD to be initiated.

The most important advantages of central venous catheters are that they can be used as soon as they are inserted, do not cause fistulas, and provide painless access to the patient's blood. However, there are also disadvantages such as the risk of occlusion and infection in the catheter, and catheterization increases the possibility of permanent central venous stenosis and occlusion. In addition, complications due to indwelling catheters increase as the duration of use increases. As a result of this, the National Kidney Foundation-Dialysis Outcomes Quality Initiative (NKF-DOQI) working

group recommends keeping the rate of using catheters as the permanent HD route below 10 % in chronic HD patients.

2.4. Complications of Catheterization of Central Veins

2.4.1. Catheter dysfunction causes: There are two types dysfunctions (Griffiths et al., 2011).

- Early-stage catheter dysfunction: The most common causes are the positioning of the catheter tip, the bends in the subcutaneous tissue of the catheter, and external pressure due to too tight binding of the fixation suture. Due to the very tight suture, external pressure can be detected by checking the insertion site of the catheter into the skin.
- Late-stage catheter dysfunction: The most common causes are occlusion of the catheter due to thrombosis, fibrin sheath development, venous thrombosis, displacement of the catheter tip over time, and catheter breakage. Catheter occlusion is often due to thrombus forming within the catheter lumen and is the result of not flushing the catheter with heparinized Serum Physiological (SF) after use. It is usually manifested by the inability to aspiration and infusion through the catheter.

2.4.2. Catheter Infections: Infections due to intravenous catheters can occur in a clinical spectrum ranging from simple colonization to sepsis. Existing definitions of infection are sometimes used interchangeably in practice. The defined definitions for infections due to intravenous catheters are as follows:

- Catheter colonization: Significant growth (> 15 cfu in semiquantitative culture or > 103 cfu in quantitative culture) in cultures taken from the catheter tip, a subcutaneous catheter part, or the catheter junction, without any clinical findings.
- Exit site infection: It has two definitions, microbiological and clinical.
    - Microbiological definition: Microorganism growth from the catheter exit location, with or without accompanying bloodstream infection.
    - Clinical definition: It means erythema, swelling and/or tenderness within 2 centimeters around the catheter exit location, with or without accompanying bloodstream infection. Other symptoms and signs of infection may also be present, such as abscess in the exit site or fever.

- Tunnel infection: Tenderness, erythema, and/or swelling spreading along the subcutaneous segment from the catheter in an area > 2 centimeter around the catheter exit site, with or without accompanying bloodstream infection.
- Pocket infection: Infected fluid in the pocket containing the devices placed completely under the skin; It is often the presence of tenderness, erythema and/or swelling in the overlying skin area, spontaneous rupture of the skin, discharge or necrosis.
- Bloodstream infection (BSI): It has two definitions: infusion fluid-related and catheter-related.
    - Infusion fluid-associated bloodstream infection (infusion fluid-associated bacteremia): Simultaneous growth of the same microorganism in blood samples and cultures of infusion fluid without any other source of infection.
    - Catheter-related bloodstream infection (CRBSI): Most of the catheter-related bloodstream infections (CRBSI) are associated with CVC use and are frequently seen in patients followed in the ICU.

According to standardized surveillance CDC criteria; laboratory-confirmed bloodstream infection must meet at least one of the following criteria;

- Fever, chills, chills and/or hypotension with one of the signs of infection, and in 2 or more blood cultures taken on different days or from different places (or by a non-culture-based microbiological method) the same skin flora member [diphtheroid (*C. diphtheriae*, *Corynebacterium spp.*) *Bacillus spp.* (except *Bacillus anthracis*), coagulase-negative staphylococci (*CNS*) [including *Staphylococcus epidermidis (S. epidermidis*)], viridians group streptococci, *Aerococcus* spp. and *Micrococcus spp*.] growth of the microorganism.
- Bacterial or fungal pathogen identified in one or more blood cultures cannot be explained by a focus other than the catheter.

The presence of at least one of the above criteria in patients who have had a central catheter for longer than 2 consecutive days; It is defined as KIKDE (Bloodstream infection event (central line-associated bloodstream infection and non-central line-associated bloodstream infection)." Device-associated Module BSI [Internet] Atlanta, GA: Centers for Disease Control and Prevention. (5 October 2020) https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc_clabscurrent.pdf.

- Possible catheter-related sepsis: Findings of sepsis in a patient with negative blood cultures, regression of these findings immediately after catheter removal, and growth of a significant number of microorganisms in the catheter segment or growth in the exudate in the exit site, or induration and erythema of the skin over the tunnel.
- Septic thrombophlebitis: It is an infection of the thrombus surrounding the cannula. It can be in peripheral or central catheters. The vein in which the catheter was inserted becomes an intravascular abscess. Blood cultures continue to be positive after the cannula is removed. More than half of the cases have signs of inflammation at the entry site. It may not cause clinical symptoms for a long time even after the catheter is removed.
- Infusion phlebitis: There is pain, erythema, tenderness or thrombosis in the vein where the cannula was applied. Risk factors such as cannula material (polyurethane and Teflon), experience of the operator, application area (hand and wrist), duration (> 48 h), fluid given (antibiotics), age, female gender, and underlying diseases were defined.
- Bloodstream infection associated with contaminated infusion fluid: Characterized by septic shock. Most infusion-related hospital-acquired outbreaks develop during the production of the infusion fluid or during preparation and administration in the hospital. The causative agents are often Gr (-) bacilli.

With all these definitions and etiology, catheter-related bacteremia and infections are the most common late complications. The risk of bacterial colonization increases in direct proportion to the length of stay and use of the catheter. If the patient is in the septic state, the catheter should be removed urgently and another vein should be inserted with a temporary catheter or replaced with a new one over the wire. In bacteremic patients without clinical signs of sepsis, treatment with intravenous antibiotics should be attempted first. If blood cultures continue to grow despite this treatment, the catheter should be replaced with a new one over a guidewire. Since venous pathways are vital in HD patients, it is tried to protect these pathways as much as possible. When a HD catheter that has been in use for a long time is removed, it may not be possible to use the same vein for catheterization once again due to possible stenosis and venous thrombosis. It has been shown that approximately 50% of the

permanent venous routes can be saved with antibiotic treatment and replacement of the catheter over the wire in catheter-related bacteremia.

2.5. Catheter-Associated Infections and HD

A central venous catheter is widely used for temporary vascular access in HD patients. The use of central venous catheters is often closely associated with local infections and bloodstream infections (Blot et al., 2005; Sahli et al., 2017). Sepsis caused by infectious complications especially seen in HD patients with ESRD is among the most common causes of death in this patient group. The occurrence of central venous catheter-related bloodstream infection ranges from 0.6 to 6.5 episodes per 1000 catheter/days (Saeed- Abdulrahman et al., 2002; Power et al., 2009). While the causative agent is mostly *Staphylococcus aureus* (*S. aureus*), central venous catheter time, old age, diabetes mellitus, and low hemoglobin and serum albumin levels are among the other factors (Lemaire et al., 2009; Sahli et al., 2017).

Catheter-Associated Infections are classified as follows (Pearson, 1996):

- Catheter colonization: In the absence of accompanying clinical symptoms, bacteria production of 15 CFU (colony forming units) and above at the catheter tip (semiquantitative culture).
- Catheter insertion site infection: Induration, redness, tenderness or purulent discharge of at least 2 cm of skin after the catheter insertion location.
- Catheter-associated sepsis (CAS): Production of the same microorganism from a semiquantitative culture of the catheter tip (and/or blood culture from the catheter) and blood culture from a peripheral vein in a patient with sepsis signs and no other infection source can be identified.
- Possible CAS: A patient with signs of sepsis, in which the microorganism cannot be grown, has a decrease in fever after removal of the catheter.

Many complications such as endocarditis, sepsis, pneumoniea etc are encountered in dialysis patients. Among the complications, the second highest morbidity and mortality rate is infection-related complications (Collins et al., 2015). The mortality rate due to sepsis when compared to the general population is at least 100 times higher in dialysis patients. (Sarnak and Jaber, 2000). Among the causes of susceptibility to infection seen in dialysis patients, factors such as violation of the skin and mucosal barriers of the patients, deterioration in the immune system, and generally

high average age are considered (Vanholder and Van Biesen, 2002; Naqvi and Collins, 2006; Wang et al., 2006). Although the most common pathogens encountered in HD patients are *S. aureus*, Gr (+) cocci and *CNS*, the incidence of infections with multi-drug resistant (MDR) organisms is also high due to the frequent use of antibiotics and their frequent presence in hospital settings (Wang et al., 2006; Klevens et al., 2008). Among these pathogens, it is known that methicillin-resistant *S. aureus* (MRSA), vancomycin-resistant enterococci (VRE) and MDR Gr (-) bacilli are the most common (Calfee, 2013). In HD patients, vascular-related infections are the most commonly identified source of infection. *S. aureus*, *CNS* and Enterococci are the most common microorganisms causing Catheter Related Blood Flow Infection (CRBSI). The pathogenesis of CRBSI includes the organism's adhesion to the catheter after entry into blood stream and the formation of colonization. Bloodstream infection is strongly associated with vascular access type, catheter position, and previous bacteremic episodes (Gupta and Yassin, 2013).

2.6. Hepatitis B Virus

HBV has infected almost 2 billion individuals worldwide, according to estimates (WHO, 2015). About 5% of the worldwide population is chronically infected with HBV, every year about half a million individuals die from HBV-related causes. The majority of chronic HBV differs from region to region; HBV epidemiology is changing with the adoption of universal vaccination programs in countries.

2.6.1. Transmission route of HBV infections: HBV, which can survive on inanimate surfaces for up to seven days, can exist at variable rates in blood, but also in other body fluids such as semen, saliva, tears, and cervical secretions (Alter, 2003; Thio et al., 2015; Figure 4).

Transmission occurs in four ways:

i) Percutaneous transmission: It occurs as a result of parenteral contact with infected blood or body fluids (Alter, 2003).

ii) Sexual transmission: Risky sexual activity is one of the most common ways of transmission for HBV, and the highest risk group is homosexuals.

iii) Perinatal-vertical transmission: It occurs as a result of transmission from the infected mother to the baby (Shiraki, 2000).

iv) Horizontal transmission: It is a form of transmission that occurs by non-sexual close contact with infected people, and it occurs mostly between family members. Although the mechanism of horizontal transmission is not known exactly, contact of infected blood or saliva with unhealthy skin or mucous membranes is thought to be the most likely mode of transmission (Alter, 2003).

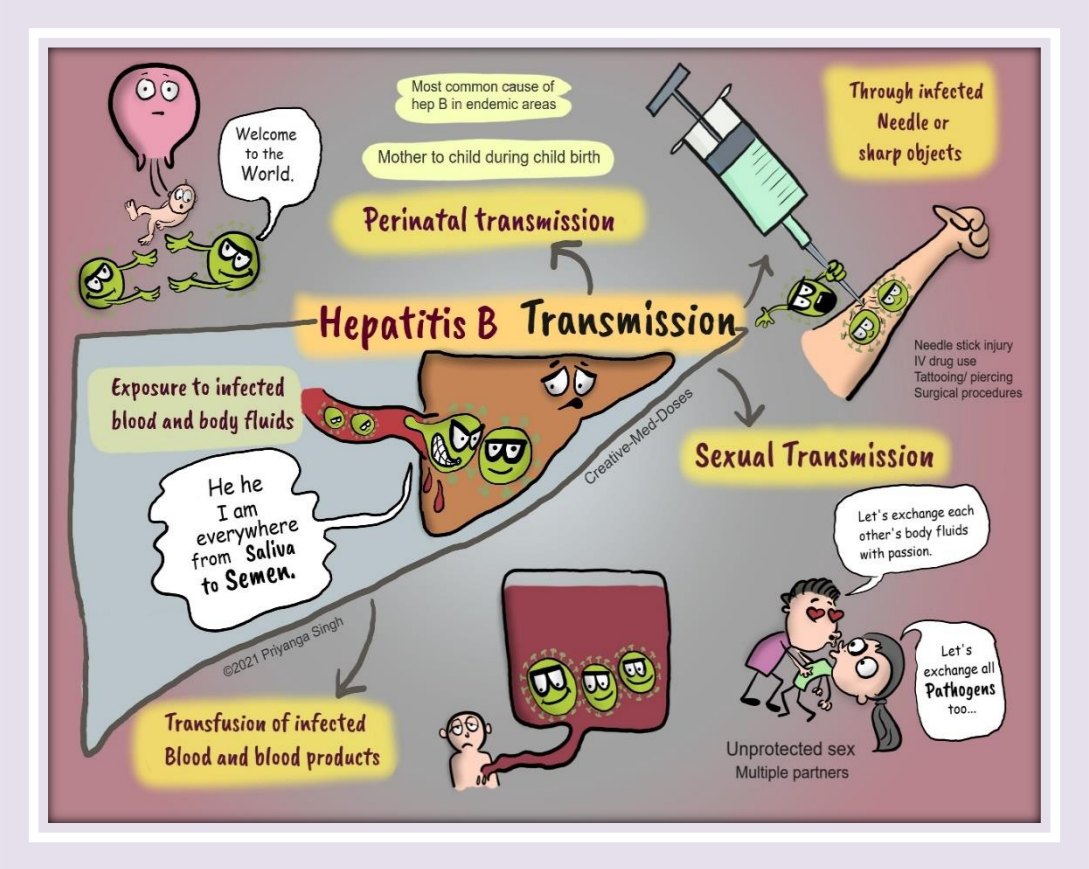

Figure 4:

*Transmission Route of HBV Infections (*https://creativemeddoses.com/topics-list/hepatitis-b-transmission-and-clinical-presentation/)

Poor hygiene, low socioeconomic status and mental retardation are risk factors for horizontal transmission. The type of transmission also varies with the prevalence of infection. While perinatal transmission is more common in regions with high prevalence, horizontal and percutaneous transmission is more common in regions with moderate prevalence, and transmission associated with unprotected sexual intercourse and intravenous drug use is more common in regions with low prevalence (Thio et al., 2015).

2.6.2. Occult HBV infection and HD: The most important transmission route of HBV infection, which has a serious mortality and morbidity rate around the world, is the transfusion of blood and blood products. Therefore, HBV is a viral agent that can spread very easily in the dialysis environment.

Although the detection of serological indicators is important in determining the infection, it is often insufficient. Although occult HBV infections are more common in hepatitis and hepatocellular carcinoma cases, factors such as HD and transplantation are reported to be effective in occult HBV infections (Torbenson and Thomas, 2002; Ergünay, 2005; Figure 5).

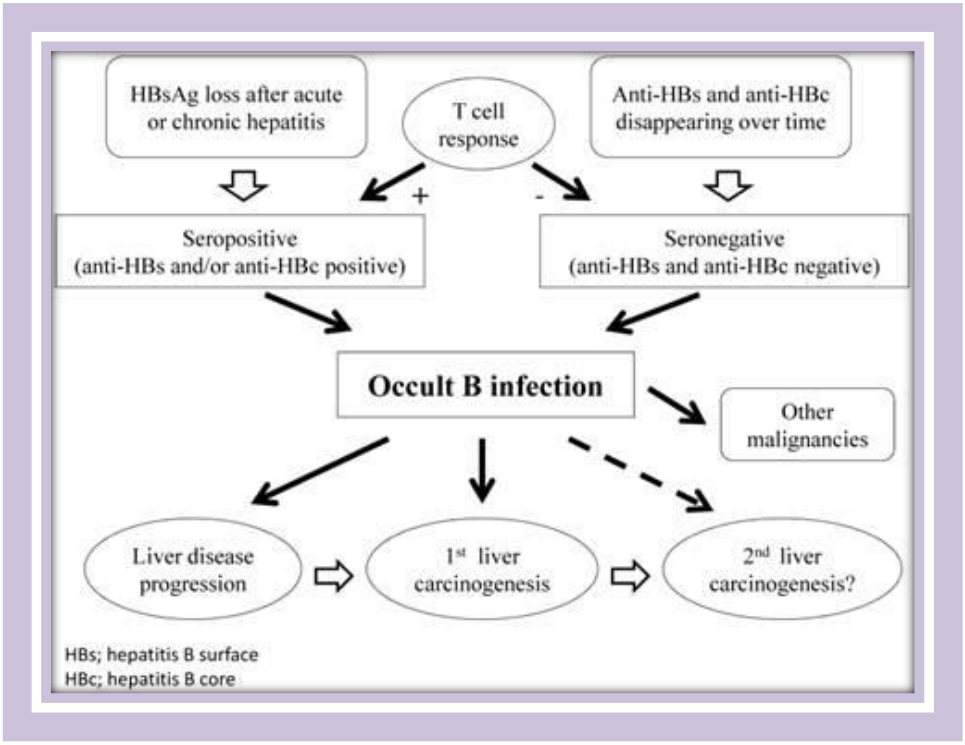

Figure 5:

Occult HBV Infection

(https://www.jcancer.org/ms/getimage.php?name=jcav04p0473g01.jpg&type=thumb)

In chronic HD patients, the immune response is impaired as a result of conditions such as renal anemia, chronic inflammation and nutritional deficiency (Saijo et al., 2015). Impaired immune response, need for frequent transfusions, shared use of dialysis machines and low response to hepatitis B vaccine are risk factors for occult HBV transmission. In HD patients, protective antibody response developed in only 50-60% of patients after hepatitis B vaccination, and it was found that acute hepatitis B was more likely to become chronic in HD patients. According to studies,

the prevalence of occult HBV in HD patients varies between 0-58% (Fontenele et al., 2013).

2.7. Chronic Renal Failure and Hepatitis C Virus Infection

Anti-HCV positivity in HD units differs between 4-70%. The high rate of nosocomial HCV transmission in dialysis units cause more increased rate of HCV infection in these patients' comparison with the general population (Karkar, 2007).

HCV infection is a major cause of mortality and morbidity in patients who have ESRD. Between 1992 and 1999, the prevalence of HCV decreased from 21% to 12.5% in the USA. This lowering in the prevalence and incidence of HCV infection in dialysis patients has been achieved by increasing infection control measures. "The Dialysis Outcomes and Practice Patterns Study" (DOPPS) is a prospectively designed study that included France, Spain, Germany, Italy and Japan. 308 dialysis centres participated in the study and the prevalence of HCV was 12.5% (UpToDate Infection with the Hepatitis C virus in patients).

Compared to HD patients, peritoneal dialysis patients were detected to have a lower prevalence of HCV infection. In Singapore in a single-center study, the prevalence of anti-HCV was shown to be present in 6.5% between peritoneal dialysis patients and 28% between HD patients. Also, a high incidence was found in HD centers with a high HCV seroprevalence. Patients undergoing HD in the same centre are more likely to be infected with the same genotype. If the prevalence of HCV infection in the dialysis unit is below 19%, the incidence of anti-HCV in that centre is 2.5%, while if the prevalence of HCV infection is above 60%, the incidence rises to 35% (UpToDate Hepatitis C virus infection in patients). Although patient-to-patient transmission of HCV through contaminated instruments it is the most likely transmission route in HD units, changing heparin bottles and not changing gloves between HCV and non-HCV patients explains the cause of HCV outbreaks. Physical proximity of infected or uninfected patients and sharing of HD machines appear to increase the risk of transmission (dos Santos et al., 1996; Coppala et al., 2015).

HCV transmission in HD patients can be through blood and blood product transfusions, surgical interventions and nosocomial transmission from the HD unit (from the hand of the personnel or dialysis machine). It has been proven by various studies that blood transfusion is the most important transmission route for HCV. After the use of erythropoietin, this transmission route has been significantly controlled. The

length of stay of patients on HD is another important risk factor. Detection of anti-HCV positivity in patients who have never been transfused is proof that HD is an independent risk factor, in other words, HCV infection is a nosocomial infection. The type of dialysis administered in patients with ESRD is another risk factor for HCV infection. The prevalence of HCV in peritoneal dialysis patients is significantly less than in HD patients. While the annual seroconversion rate in 129 anti-HCV negative patients is 0.15/patient-year in HD patients, this rate is 0.03/patient-year in peritoneal dialysis patients (Jadoul et al., 1998). The incidence of HCV infection in patients on home HD and continuous ambulatory peritoneal dialysis is less than that in the HD unit. Homogeneity between HCV types in the same HD unit, higher anti-HCV prevalence in patients undergoing HD in machines close to anti-HCV positive patients, and lower incidences in units where isolated rooms and machines are used can be listed as evidence of nosocomial transmission.

Before the introduction of anti-HCV tests, blood product transfusions were the major cause of HCV spread. In a study conducted in Saudi Arabia, it was reported that 74% of anti-HCV positive patients who undergone both HD and intermittent peritoneal dialysis had a blood transfusion history (Al-Wakeel, et al., 1996; Shaheen et al., 1995). However, the presence of anti-HCV in some of the HD patients who have never been transfused indicates that nosocomial infections are also seen (Jadoul et al., 1998). Failure to take universal precautions, resulting in exposure to blood or blood-contaminated equipment rather than blood transfusions, could be a major cause of HCV transmission in patients with renal failure. The presence of infection, which is reported as high as 10% each year in dialysis units, revealed that HCV-contaminated areas, environmental surfaces and instruments are responsible for nosocomial transmission in these units (Nguyen, et al., 2016). It has been reported that the incidence of infection will be lower in centers where anti-HCV positive patients use separate machines (dos Santos et al., 1996). HBV and HCV transmission to the dialysate does not seem possible due to the large diameter of the viruses (35-40 nm). The dialysis membrane may act as a physical barrier to HCV, and disruption of membrane integrity may lead to HCV penetration into the dialysate (WHO, 2003). Therefore, the contamination caused by the HD environment rather than the contamination caused by the machines itself comes to the fore. HCV particles have been calculated diameter of 40-60 nm and are larger than the most permeable dialysis membrane's pores. It is not known whether there is a relationship between membrane

type and HCV infection. It is also unknown whether reuse of dialyzers will contribute to the nosocomial transmission of HCV. The lowest anti-HCV seroprevalence was found in centers where dialysis machines were not reused separately or in isolation in all HCV-infected patients (dos Santos et al., 1996). There are also studies showing that isolation and separate dialysis machines may not be necessary. For example, in one study, although separate devices were used in anti-HCV-positive patients, it was observed that nosocomial HCV transmission was higher in centers where anti-HCV positive and negative patients received dialysis together compared to centers where only anti-HCV-negative patients were on dialysis (Taskapan et al., 2001). When all studies were evaluated, it was shown that HD machines do not have an essential role in the transmission of nosocomial HCV (Shamshirsaz et al., 2004). It is recommended by the CDC that dialysis machines should not be separated in patients with HCV infection. Compliance with general infection control precautions and good sterilization are recommended. It has been stated that conventional cleaning and sterilization is sufficient for the inactivation of the virus. The other way of transmission is from personnel to patient, and it is rarely seen (UpToDate Epidemiology and transmission of HCV).

2.8. Hepatitis D virus (HDV)

HDV is an RNA-defective virus that can infect only HBsAg-positive individuals. HDV prevalence has different prevalence according to geographical regions. HDV, which is considered endemic in the Brazilian Amazon, is generally seen with higher rates in low-income countries. It is evaluated that 5% of HBV carriers worldwide are coinfected with HDV. HBV infection is still a major cause of liver disease in HD patients and kidney transplant recipients. Considering that HBV and HDV are transmitted in the same way, it is thought that HD and kidney transplant patients are also at risk for HDV infection (Pierre et al., 2018). There are very few studies of HDV infection in HD and kidney transplant patients worldwide. While the reported HDV prevalence of HD patients with hepatitis B in Iran is 44.5%, no marker of HDV infection was noticed in a study performed in France (Pierre et al., 2018).

2.9. HD and HIV

Although HD has been associated with increased risk of healthcare-associated HCV and HBV infections (Archibald et al., 2011; Patel, et al., 2011), it is considered

to be a low-risk setting HIV transmission (Patel, et al., 2011). Five outbreaks of HD-associated HIV occurred from 1990 to 1994 in 3 developing countries (Hassan et al., 38 1994; Velandia et al., 1995; El Sayed et al., 2000). In these outbreaks, epidemiologic findings sustaining HD-associated HIV transmission were related with directly observed or reliably reported evidence of egregious breaks in infection prevention and control practices (Mashragi et al., 2014).

CHAPTER III

Methodology

The aim of this study was to determine the seroprevalence and associated risk factors of HBV, HCV, HIV and catheter associated infections among HD (acute and chronic) patients in the HD unit of a military hospital in Jordan.

3.1. Patient Groups and Ethics

After obtaining ethics committee approval from the Near East University Faculty of Medicine Ethics Committee on NEU 2022/104-1576 the files of patients who underwent routine HD in the HD unit of a military hospital in Jordan were reviewed. It is a retrospective study involving 62 patients who received treatment in the HD Unit between January 1, 2015 and August 31, 2021.

3.2. Data Collection

Data were obtained by retrospective examination of patients' age, gender, and diagnosis, HD frequency (weekly), cultures (blood, urine and swab), and antibiotic treatments received by patients. Inclusion criteria included patients receiving regular HD (for at least 6 months).

Duration of dialysis, frequency of dialysis, presence of a catheter, presence of fistula, and for liver function tests, in the hospital, they use Cobas c411 by Roche company and manual by Bio-rad kit for detecting HBsAg, anti-HBs, and anti-HCV, anti-HIV, Hbcore, HBV-DNA, HBeAg, Anti-HBe, HCV-RNA, HIV-RNA values of the patients were recorded from the files.

3.3. Statistical Analysis

Statistical analyses were carried out through the Statistical Package for the Social Sciences (version 20.0, SPSS Inc., Chicago, IL, USA) program. As descriptive statistics; Number (n) and percentage (%) were used in the evaluation of categorical variables. Statistical power analysis of the sample number was done by Student’s t-test (Çapık, 2014). Presence of microorganisms (Gr (+) and Gr (-) bacterial growth) according to culture results; Correlations between sex, age and year were analyzed using the Pearson chi-square test. $p < 0.05$ was considered significant.

CHAPTER IV

Results

4.1. Demographic Features

Among 62 patients included in the study, 42 (%) were male and 20 (%) were female (Figure 6). Male patients were between 12 and 77 years old with a mean age of 65.0 ± 14.0, and female patients were between 14 and 67 years, and their mean age was 53.0 ± 16.0.

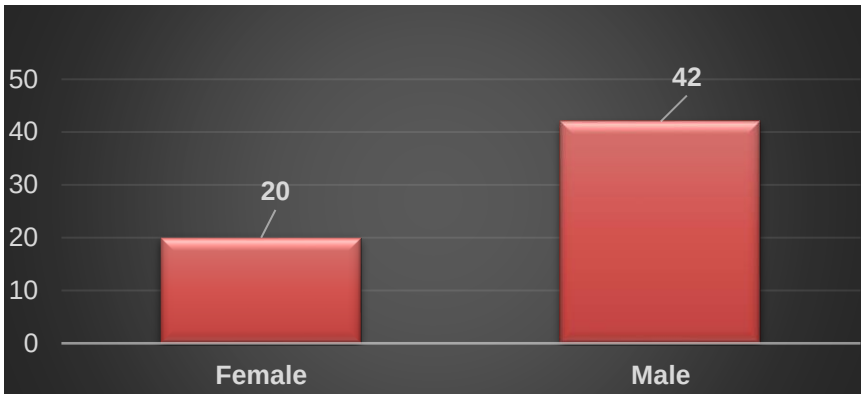

Figure 6:

Distribution of Patients Admitted to The HD Unit of a military Hospital Between January 1, 2017 and December 31, 2019, By Gender.

When the age distribution of the patients is analysed; The number of patients in the range of 1-20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 and over 61, respectively 3 (4.8%), 6 (9.7%), 5 (8.1%), 9 (14.5%), 21 (33.9%) and 18 (29.0%) (Figure 7).

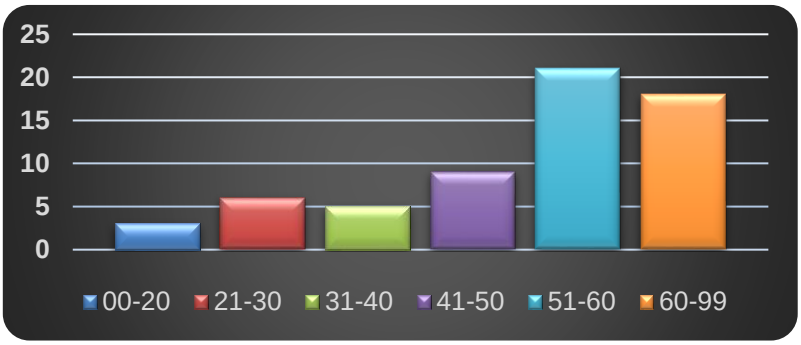

Figure 7:

Distribution of Patients Admitted to The HD Unit of a military Hospital Between January 1, 2017 and December 31, 2019, By Age.

When the years of admission to the hospital of HD patients were examined, it was determined that there was 1(1.6%) applied in 2015, 6(9.6%) in 2016, 4(6.5%) in 2017, 13(21%) in 2018, 7(11.3) in 2019, 9(15%) in 2020 and, 22(35.5) in 2021 (Figure 8).

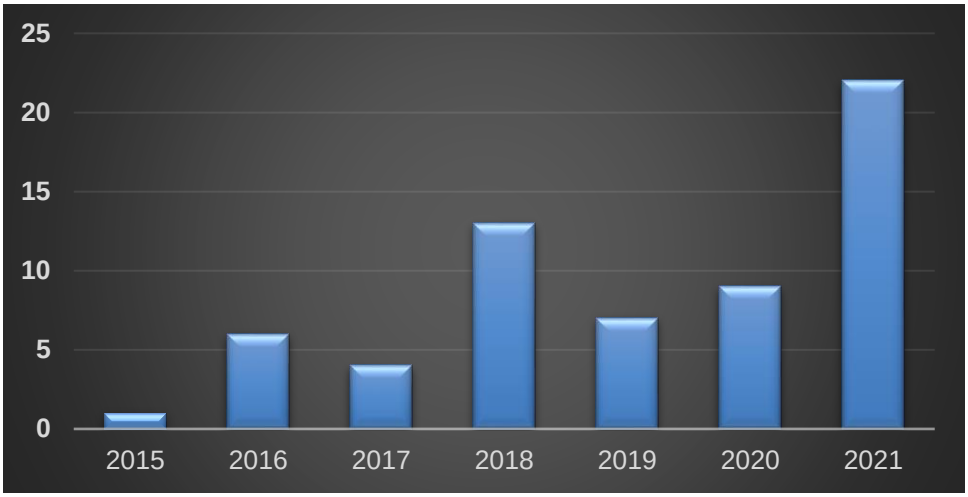

Figure 8:

Distribution of Patients Admitted to The HD Unit of a military Hospital Between January 1, 2017 and December 31, 2019, By Years.

When the weight changes of the patients receiving HD treatment at the start of the treatment and after the treatment were examined, weight loss was observed in 82.3% of the patients. In others HD, no weight change was determined (17.7%). 27(44%) of the HD patients included in the study were ESDR and 11(17.7%) were CKD patients. Among sixty-two HD patients, 5(8.1%) patients had diabetes mellitus. 1(1.6%) of the HD patients included in the study was a chronic hepatitis patient, while another HD patient was both HCV and HBV carriers. Hepatitis B vaccination was given to all HD patients in the study.

The demographic characteristics of the patients included in the study are shown in Table 2. Among the HD patients, 46 (74.2%) had an AV catheter, 5 (8.1%) a jugular, 8 (12.9%) a SC perma- catheter, 2 (3.2%) a femoral and 1(1.6%) a subclivian catheter.

Table 2

The Demographic Characteristics of The Patients Included in The Study

		n	%
Age	20 ≥	3	4.8
	21-30	6	9.7
	31-40	5	8.1
	41-50	9	14.5
	51-60	21	33.9
	61 ≤	18	29
Genders	Male	42	67.7
	Female	20	32.3
Diseases	ESRD	27	43.5
	CKD	11	17.7
	Diabetes mellitus	5	8.1
	HBV	5	8.1
	HCV	11	17.7
Year of admission to hospital	2015	1	1.6
	2016	6	9.7
	2017	4	6.5
	2018	13	21.0
	2019	7	11.3
	2020	9	14.5
	2021	22	35.5

Abbreviation: ESRD (end stage renal disease), CKD (chronic kidney disease).

4.2. HD Frequency

The frequency of HD applied to the patients per week varies between 2-3. The number of patients undergoing HD twice a week is 27 (43.5%).

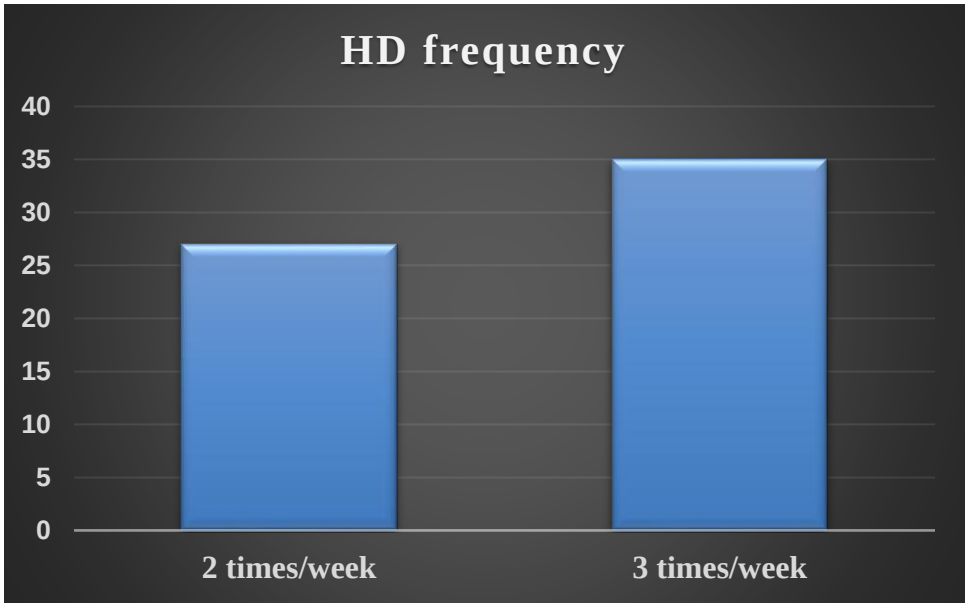

Figure 9:

HD Frequency of Patients (Weekly)

4.3. Culture Results

Cultures were taken from 21 (33.9%) of 62 HD patients due to infection. While there was no growth in blood, urine and catheter culture samples in 15 (36.5%) of 41 samples cultured (followed up) in the microbiology laboratory, growth was observed in 26 (63.5%) samples (Figure 10).

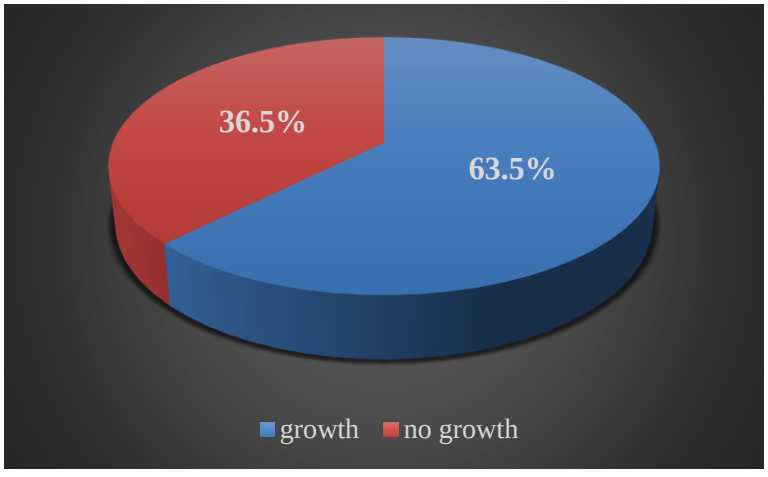

Figure 10:

Growth Rates of Bacteria Grown in Cultures (Blood, Urine and Swab)

According to our results, the most common bacteria was MRSA (n=10, 24.5%), followed by *Klebsiella spp*. (n=8, 19.5%) and *E. coli* (n=7, 17.1%) (Figure 11 and Table 3).

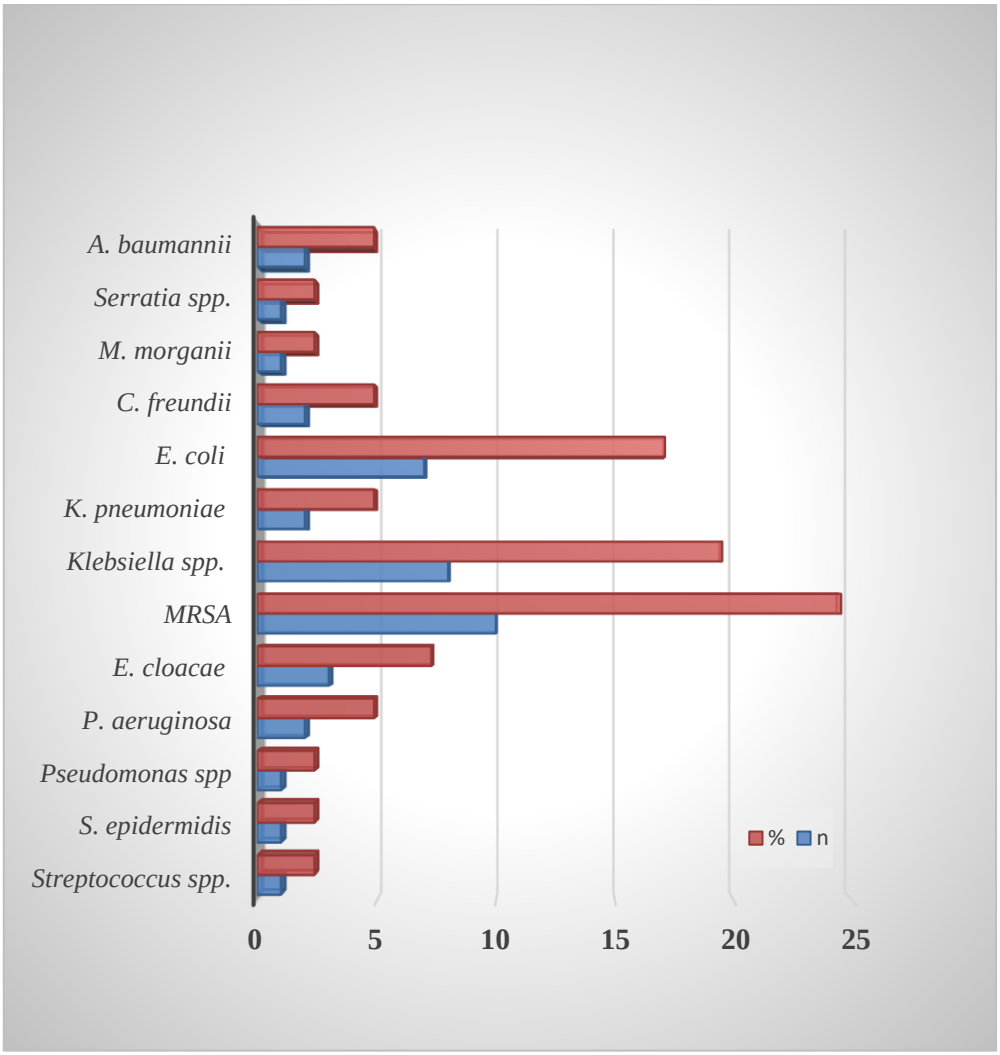

Figure 11:

Types of Microorganisms Contained in Culture Samples.

Table 3

Distribution of Microorganism in Blood, Urine and Swab Culture Samples.

	Species	**n**	**%**
Blood	*MRSA*	4	36.4
	E. cloacae	3	27.2
	S. epidermidis	1	9.1
	Pseudomonas spp	1	9.1
	P. aeruginosa	1	9.1
	Streptococcus spp.	1	9.1
	Total	**11**	**100**
Urine	*Klebsiella spp.*	8	47.1
	E. coli	4	23.5
	K. pneumoniae	2	11.7
	C. freundii	1	5.9
	P. aeruginosa	1	5.9
	M. morganii	1	5.9
	Total	**17**	**100**
Swab(wound)	*MRSA*	6	46.1
	E. coli	3	23.1
	A. baumannii	2	15.4
	Serratia spp.	1	7.7
	C. freundii	1	7.7
	Total	**13**	**100**

4.3.1. Gr (-) and Gr (+) bacteria distributions

The distribution of Gr (-) and Gr (+) bacterial species according to blood, urine and swab culture results obtained from HD patients is given in Table 4 and Table 5, respectively.

Table 4

Presence Gr (-) and Gr (+) Bacteria Types in Different Cultures in Samples Taken from HD Patients

Gr (-) %	**Gr (+) %**
Klebsiella species (Klebsiella spp.) **(27.6%)**	*Methicillin-resistant Staphylococcus aureus (MRSA)* **(83.4%)**
Escherichia coli (E. coli) **(24.1%)**	*Staphylococcus epidermidis (S. epidermidis)* **(8.3%)**
Enterobacter cloacae (E. cloacae) **(10.3%)**	*Streptococcus spp.* **(8.3%)**
Citrobacter freundii (C. freundii) **(6.9%)**	
Klebsiella pneumoniae (K. pneumoniae) **(6.9%)**	
Pseudomonas aeruginosa (P. aeruginosa) **(6.9%)**	
Acinetobacter baumannii (A. baumannii) **(6.9%)**	
Serratia spp. **(3.4%)**	
Morganella morganii (M. morganii) **(3.4%)**	
Pseudomonas spp. **(3.4%)**	

Gr (-) bacteria were: *A. baumannii, C. freundii, E. cloacae, E. coli, Klebsiella spp., K. pneumoniae, M. morganii, Pseudomonas spp., P. aeruginosa, Serratia spp.*

Table 5

Presence Gr (-) Bacteria According to Culture Results

Gr (-)	**n**	**%**
Klebsiella spp.	8	27.6
E. coli	7	24.1
E. cloacae	3	10.3
K. pneumoniae	2	6.9
C. freundii	2	6.9
A. Baumanii	2	6.9
P. aeruginosa	2	6.9
M. morganii	1	3.4
P. aeruginosa	2	6.9
Pseudomonas spp.	1	3.4
Serratia spp	1	3.4
Total	**29**	**100.0**

A total of 29 Gr (-) bacteria were detected in blood, urine and swab culture samples, of which 27.6% (n=8) were found to be *Klebsiella spp.* (Figure 12).

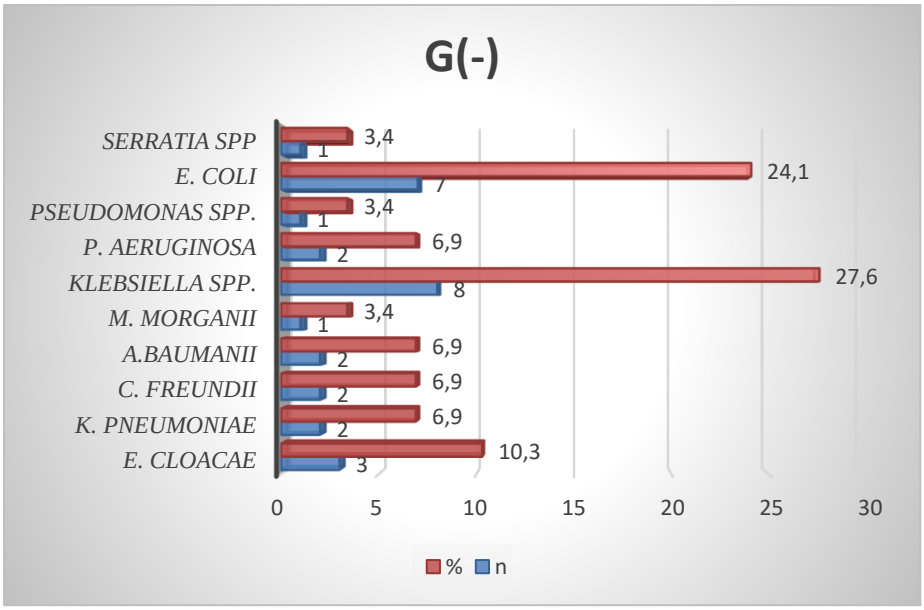

Figure 12:

Distribution Of Gr (-) Bacteria Obtained from Blood, Urine and Swab Culture Samples.

Gr (+) bacteria were: *S. epidermidis, MRSA and Streptococcus spp.* (Table 6).

Table 6

Presence Gr (+) Bacteria According to Culture Results.

Gr (+)	**n**	**%**
MRSA	10	83.4
Streptococcus spp	1	8.3
S. epidermidis	1	8.3
Total	**12**	**100.0**

A total of twelve Gr (+) bacteria were detected in blood, urine and swab culture samples, of which 83.4% (n=10) were found to be *MRSA.*

4.4. Antibiotic Resistance Patterns

When the antibiotic resistance patterns of *Klebsiella spp*. were examined, it was determined that the antibiotic to which it was the most sensitive was amikacin (n=5, 63% Figure 13), and the antibiotic to which it was the most resistant was ampicillin (n=5, 63% Figure 14). Antibiotic resistance patterns of *Klebsiella spp.* are shown in (Table 7).

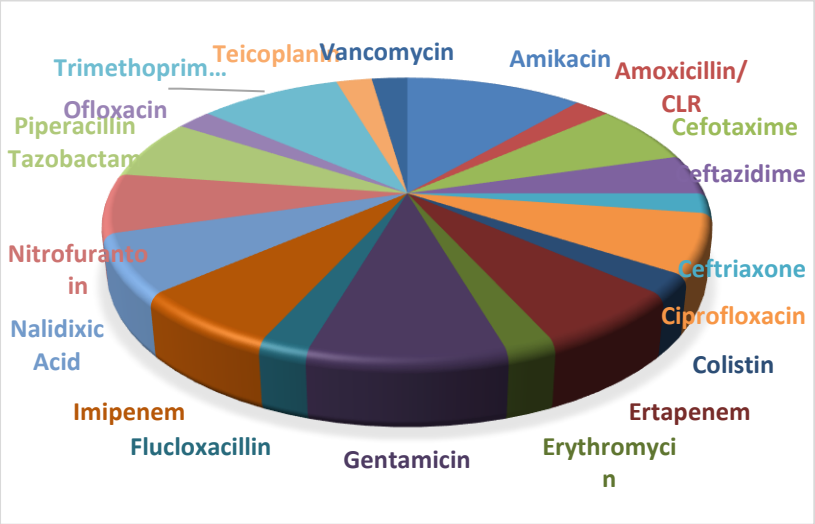

Figure 13:

Antibiotics to which Klebsiella spp.is sensitive

Table 7

The Antibiotic Resistance Patterns of Klebsiella spp.

Antibiotics	**I**	**R**	**S**	**n**
Amikacin	-	1	5	6
Amphotericin	-	1	-	1
Amoxicillin	-	5	1	6
Ampicillin	-	5	-	5
Cefotaxime	-	4	2	6
Ceftazidime	-	3	2	5
Ceftriaxone	-	1	-	1
Ciprofloxacin	-	3	3	6
Cephalexin	-	2	-	2
Colistin	-	-	1	1
Ertapenem	-	2	3	5
Erythromycin	-	-	1	1
Gentamicin	-	4	4	8
Flucloxacillin	-	-	1	1
Imipenem	1	1	3	5
Levofloxacin	-	2	-	2
Nalidixic Acid	-	4	3	7
Nitrofurantoin	-	2	4	6
Norfloxacin	-	2	-	2
Piperacillin Tazobactam	-	2	2	4
Ofloxacin	-	2	1	3
Trimethoprim/ Sulfamethoxazole	-	5	3	8
The **#n** is based on how many antibiotics were used overall to treat *Klebsiella spp.*				

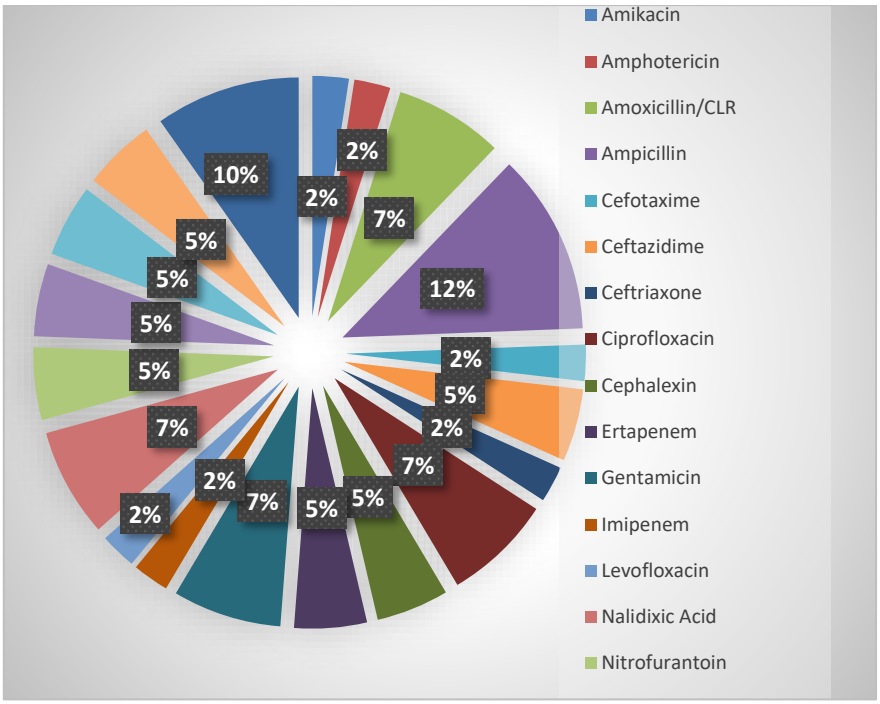

Figure 14:

Antibiotics to which Klebsiella spp.is resistance

When the antibiotic resistance patterns of *K. pneumoniae*. were examined, it was determined that the antibiotic to which it was the most sensitive were gentamicin and nalidixic acid (n=3, in both; Figure 15), and the antibiotic to which it was the most resistant was amoxicillin (n=4, Figure 16). *K. pneumoniae* showed intermediate (I) resistance to nitrofurantoin treatment. Antibiotic resistance patterns of *K. pneumoniae* are shown in (Table 8).

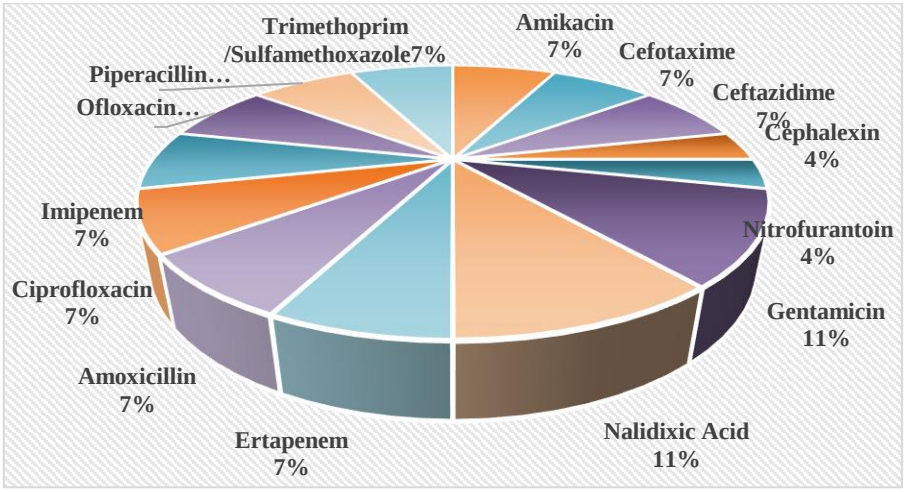

Figure 15:

Antibiotics to which K. pneumoniae is sensitive

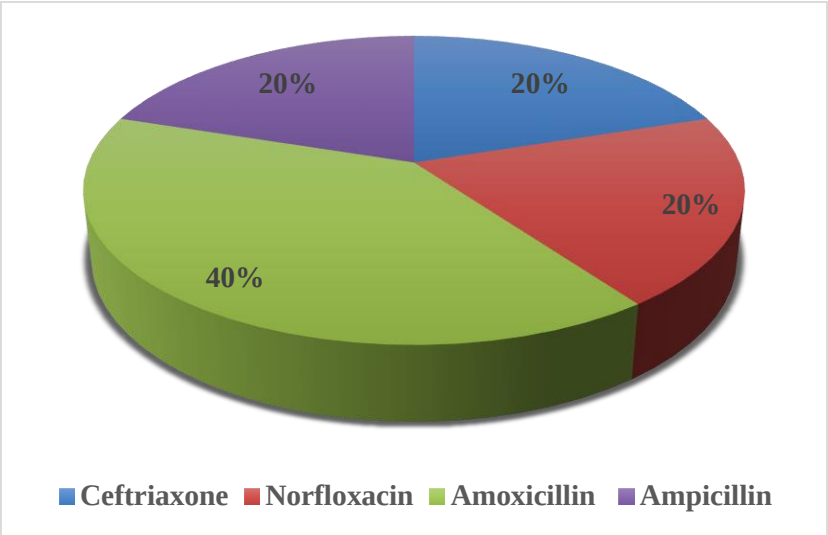

Figure 16:

Antibiotics to which K. pneumoniae is resistance

Table 8

The Antibiotic Resistance Patterns of K. pneumoniae

Antibiotics	**I**	**R**	**S**	**n**
Amikacin	-	-	2	2
Cefotaxime	-	-	2	2
Ceftazidime	-	-	2	2
Cephalexin	-	-	1	1
Ceftriaxone	-	1	-	1
Nitrofurantoin	1	-	1	2
Gentamicin	-	-	3	3
Norfloxacin	-	1	-	1
Nalidixic Acid	-	-	3	3
Ertapenem	-	-	2	2
Amoxicillin	-	2	2	4
Ampicillin	-	1	-	1
Ciprofloxacin	-	-	2	2
Imipenem	-	-	2	2
Ofloxacin	-	-	2	2
Piperacillin Tazobactam	-	-	2	2
Trimethoprim/ Sulfamethoxazole	-	-	2	2

The **#n** is based on how many antibiotics were used overall to treat *K. pneumoniae*.

When the antibiotic resistance patterns of *Pseudomonas spp.* were examined, it was determined that the antibiotic to which it was sensitive were gentamicin, aztreonam, cefepime, ciprofloxacin, imipenem and piperacillin tazobactam (n=1, in all treatment; Figure 17), and it was not resistant to any of the antibiotics used (n=0). Antibiotic resistance patterns of *Pseudomonas spp.* are shown in (Table 9).

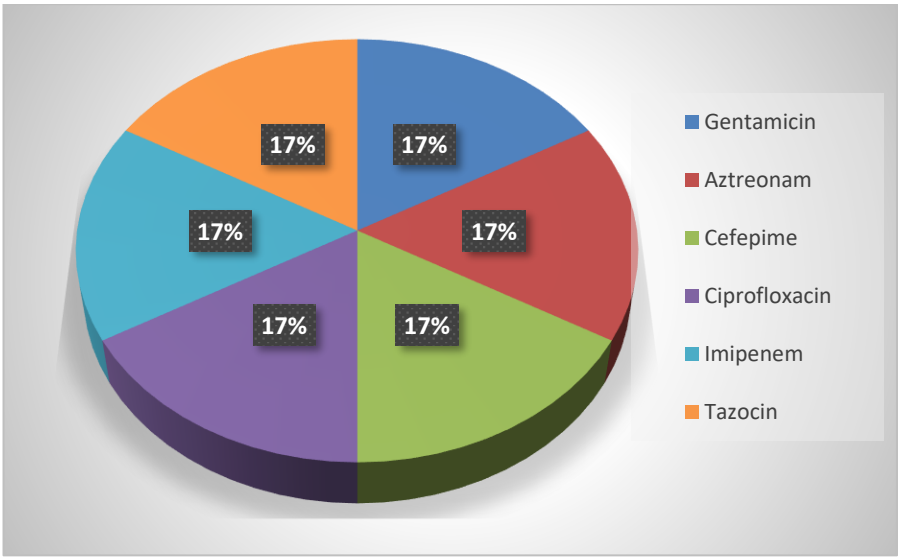

Figure 17:

Antibiotics to which Pseudomonas spp. is sensitive

Table 9

The Antibiotic Resistance Patterns of Pseudomonas spp.

Antibiotics	**R**	**S**	**n**
Gentamicin	-	1	1
Aztreonam	-	1	1
Cefepime	-	1	1
Ciprofloxacin	-	1	1
Imipenem	-	1	1
Piperacillin Tazobactam	-	1	1

The **#n** is based on how many antibiotics were used overall to treat *Pseudomonas spp.*

When the antibiotic resistance patterns of *P. aeruginosa* were examined, it was determined that the antibiotic to which it was the most sensitive were gentamicin, ciprofloxacin and piperacillin tazobactam (n=2, in both; Figure 18), and the antibiotic to which it was the most resistant were cefotaxime, ceftazidime and imipenem (n=1, Figure 19). *P. aeruginosa* showed intermediate (I) resistance to ofloxacin treatment.

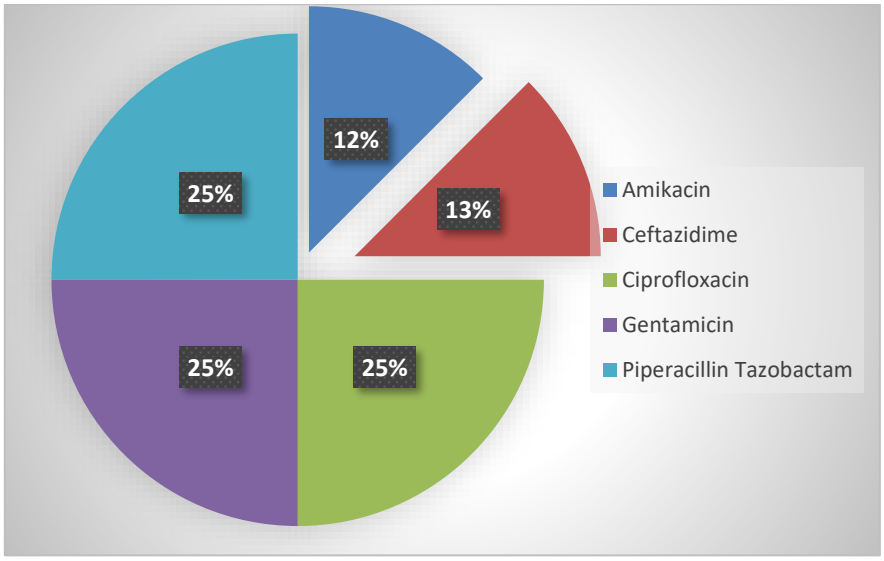

Figure 18:

Antibiotics to which P. aeruginosa is sensitive

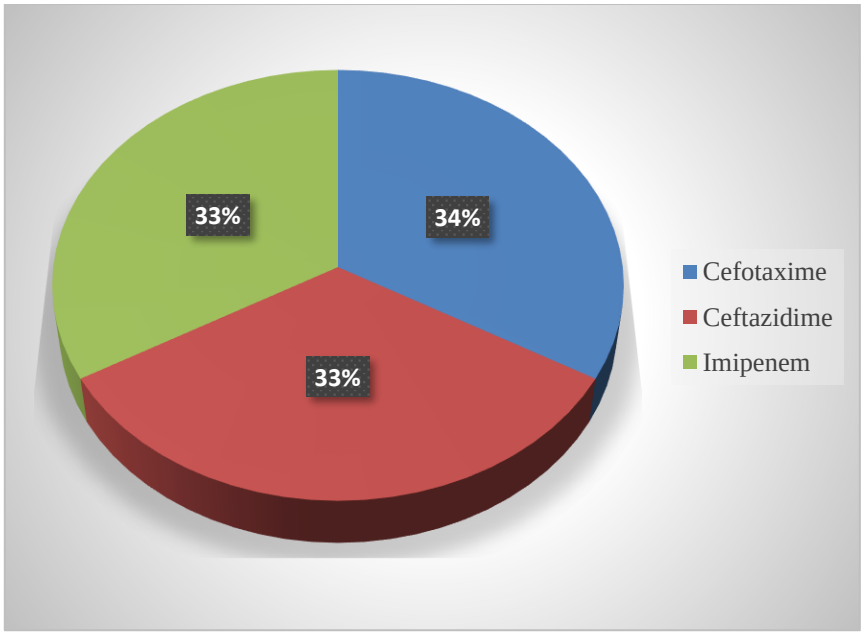

Figure 19:

Antibiotics to which P. aeruginosa is resistance

Antibiotic resistance patterns of *P. aeruginosa* are shown in (Table 10).

Table 10

The Antibiotic Resistance Patterns of P. aeruginosa

Antibiotics	**I**	**R**	**S**	**n**
Amikacin	-		1	
Cefotaxime	-	1	-	1
Ceftazidime	-	1	1	2
Ciprofloxacin	-	-	2	2
Gentamicin	-	-	2	2
Imipenem	-	1	-	1
Piperacillin Tazobactam	-	-	2	2
Ofloxacin	1	-	-	1

The **#n** is based on how many antibiotics were used overall to treat *P. aeruginosa.*

When the antibiotic resistance patterns of *Streptococcus spp.* were examined, it was determined that it was sensitive to vancomycin and teicoplanin and resistant to gentamicin. Antibiotic resistance patterns of *Streptococcus spp.* are shown in (Table 11).

Table 11

The Antibiotic Resistance Patterns of Streptococcus spp.

Antibiotics	**R**	**S**	**n**
Vancomycin	-	1	1
Gentamicin	1	-	1
Teicoplanin	-	1	1

The **#n** is based on how many antibiotics were used overall to treat *Streptococcus spp.*

When the antibiotic resistance patterns of *S. aureus* were examined, it was determined that the antibiotic to which it was the most sensitive were teicoplanin and vancomycin (n=5, Figure 20), and the antibiotic to which it was the most resistant were fusidic acid and penicillin G (n=2, Figure 21). *S. aureus* showed intermediate (I) resistance to erythromycin, cefazolin and cloxacillin treatments. Antibiotic resistance patterns of *S. aureus* are shown in (Table 12).

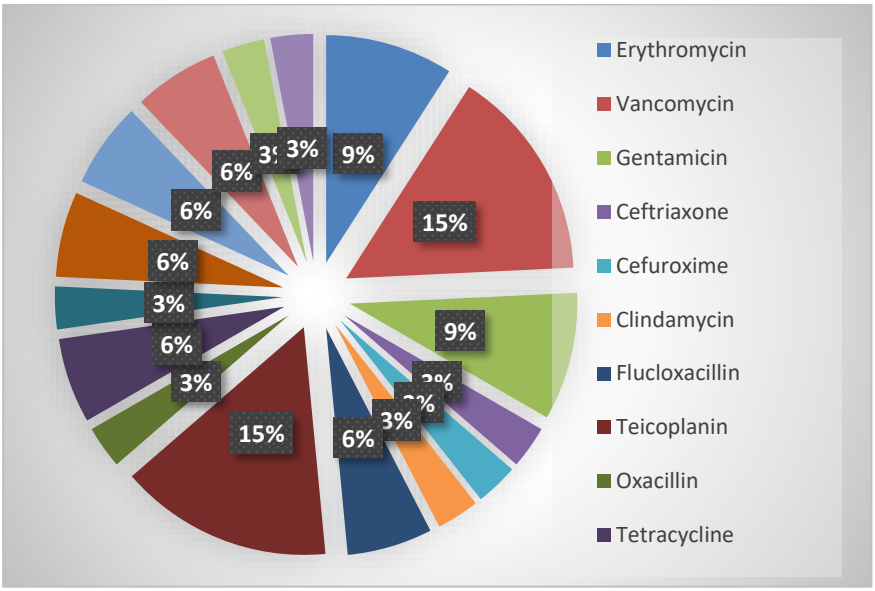

Figure 20:

Antibiotics to which S. aureus is sensitive

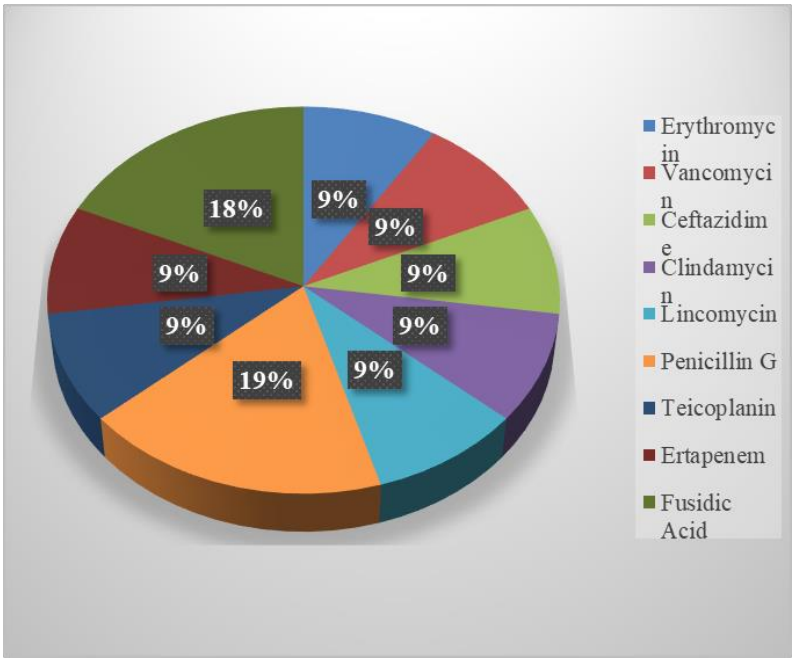

Figure 21:

Antibiotics to which S. aureus is resistance

Table 12

The Antibiotic Resistance Patterns of S. aureus

Antibiotics	**I**	**R**	**S**	**n**
Erythromycin	1	1	3	5
Vancomycin	-	1	5	6
Gentamicin	-	-	3	3
Cefazolin	1	-	-	1
Cloxacillin	1	-	-	1
Ceftriaxone	-	-	1	1
Cefuroxime	-	-	1	1
Ceftazidime	-	1	-	1
Clindamycin	-	1	1	2
Flucloxacillin	-	-	2	2
Lincomycin	-	1	-	1
Penicillin G	-	2	-	2
Teicoplanin	-	1	5	6
Oxacillin	-	-	1	1
Tetracycline	-	-	2	2
Ertapenem	-	1	-	1
Fusidic Acid	-	2	-	2
Gentamicin	-	-	1	1
Linezolid	-	-	2	2
Moxifloxacin	-	-	2	2
Rifampicin	-	-	2	2
Tigecycline	-	-	1	1
Trimethoprim/ Sulfamethoxazole	-	-	1	1

The **#n** is based on how many antibiotics were used overall to treat *S. aureus.*

When the antibiotic resistance patterns of *MRSA* were examined, it was determined that the antibiotic to which it was the most sensitive were gentamicin and teicoplanin (n=4, Figure 22), and the antibiotic to which it was the most resistant was erythromycin (n=3, Figure 23). *MRSA* showed intermediate (I) resistance to vancomycin treatment. Antibiotic resistance patterns of *MRSA* are shown in (Table 13).

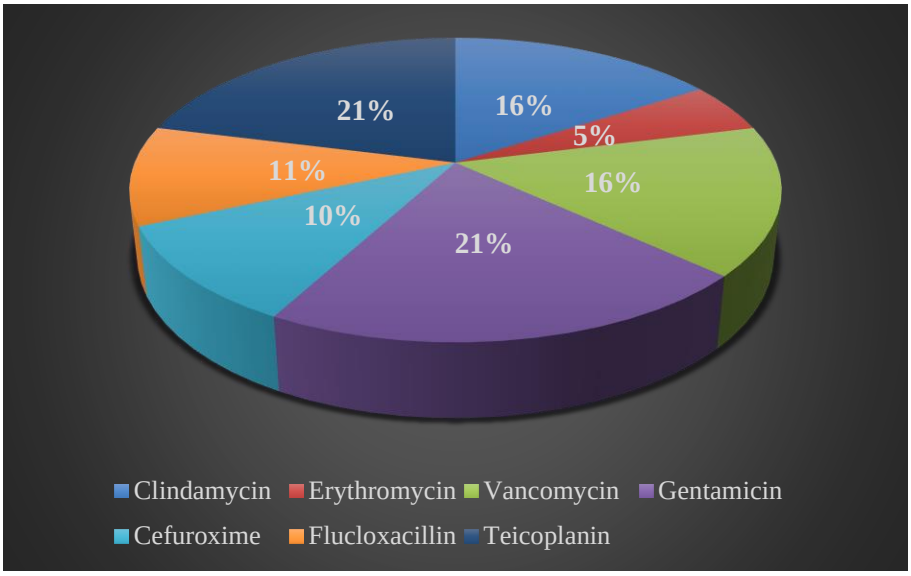

Figure 22:

Antibiotics to which MRSA is sensitive

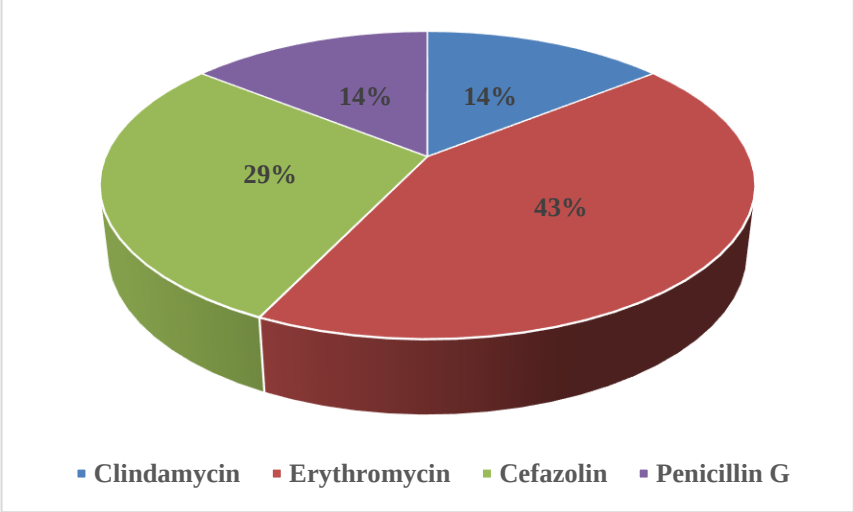

Figure 23:

Antibiotics to which MRSA is resistance

Table 13

The Antibiotic Resistance Patterns of MRSA

Antibiotics	**I**	**R**	**S**	**n**
Clindamycin	-	1	3	4
Erythtomycin	-	3	1	4
Vancomycin	1	-	3	4
Gentamicin	-	-	4	4
Cefuroxime	-	-	2	2
Flucloxacillin	-	-	2	2
Teicoplanin	-	-	4	4
Cefazolin	-	2	-	2
Penicillin G	-	1	-	1

The **#n** is based on how many antibiotics were used overall to treat *MRSA.*

When the antibiotic resistance patterns of *E. coli* were examined, it was determined that the antibiotic to which it was the most sensitive were amikacin and imipenem (n=5, Figure 24), and the antibiotic to which it was the most resistant were ampicillin and ciprofloxacin (n=4, Figure 25).

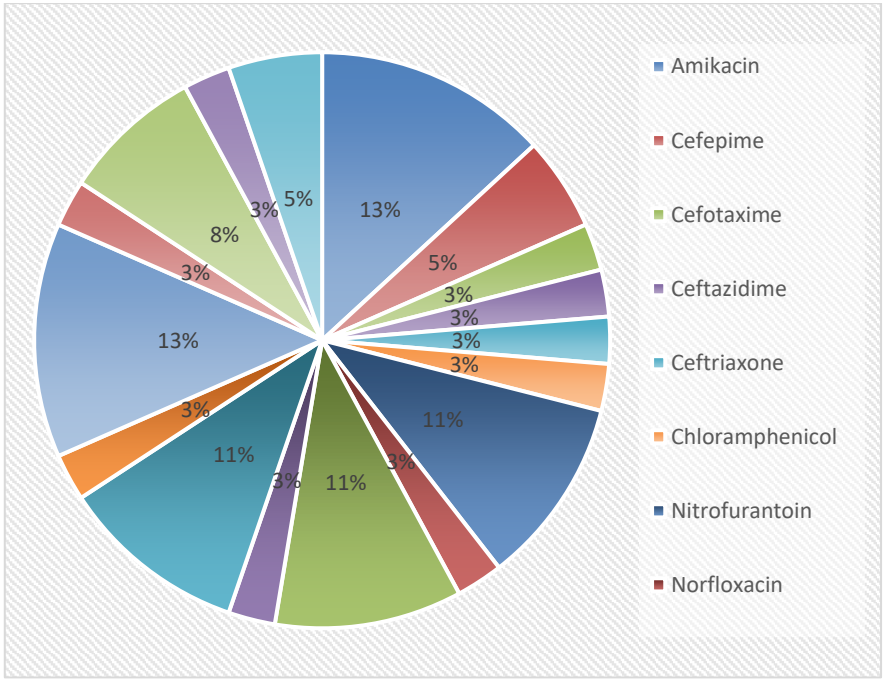

Figure 24:

Antibiotics to which E. coli is sensitive

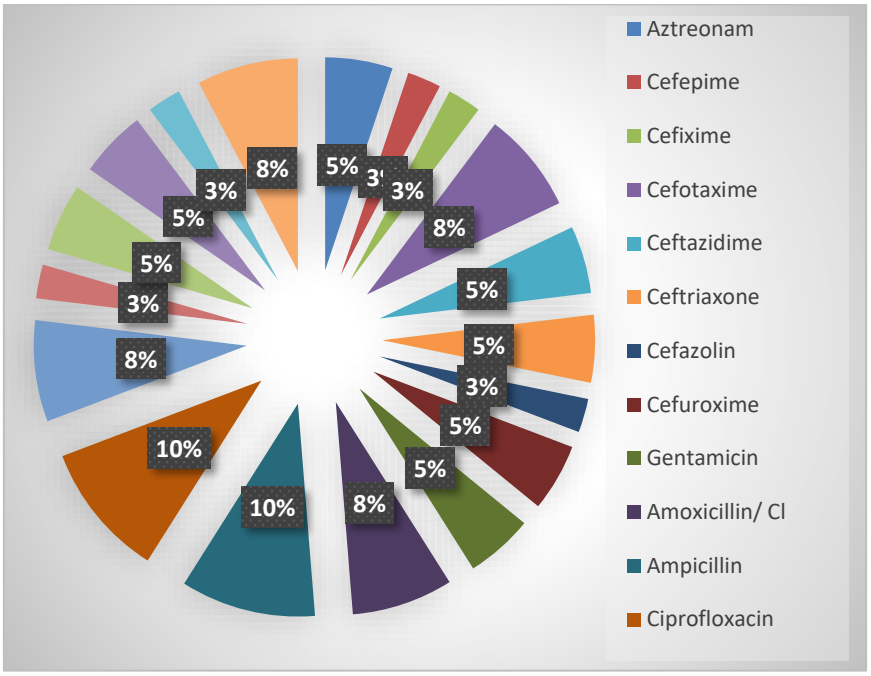

Figure 25:

Antibiotics to which E. coli is resistance

E. coli showed intermediate (I) resistance to nitrofurantoin treatment. Antibiotic resistance patterns of *E. coli* are shown in (Table 14).

Table 14

The Antibiotic Resistance Patterns of E. coli

Antibiotics	**I**	**R**	**S**	**n**
Amikacin	-	-	5	5
Aztreonam	-	2	-	2
Cefepime	-	1	2	3
Cefixime	-	1	-	1
Cefotaxime	-	3	1	4
Ceftazidime	-	2	1	3
Ceftriaxone	-	2	1	3
Cefazolin	-	1	-	1
Chloramphenicol	-	-	1	1
Cefuroxime	-	2	-	2
Nitrofurantoin	1	-	4	5
Norfloxacin	-	-	1	1
Gentamicin	-	2	4	6
Nalidixic Acid	-	-	1	1
Ertapenem	-	-	4	4
Amoxicillin	-	3	1	4
Ampicillin	-	4	-	4
Ciprofloxacin	-	4	-	4
Imipenem	-	-	5	5
Ofloxacin	-	3	-	3
Meropenem	-	-	1	1
Moxifloxacin	-	1	-	1
Levofloxacin	-	2	-	2
Piperacillin Tazobactam	-	2	3	5
Tetracycline	-	1	-	1
Tigecycline	-	-	1	1
Trimethoprim/ Sulfamethoxazole	-	3	2	5

The **#n** is based on how many antibiotics were used overall to treat *E. coli.*

When the antibiotic resistance patterns of *Serratia spp.* were examined, it was determined that the antibiotic to which it was sensitive were nitrofurantoin, ertapenem, imipenem, piperacillin tazobactam and trimethoprim/ sulfamethoxazole (n=1, Figure 26), and the antibiotic to which it was resistant were cefotaxime, ceftazidime, gentamicin, nalidixic acid, amoxicillin, and ciprofloxacin (n=1, Figure 27). *Serratia spp.* showed intermediate (I) resistance to amikacin treatment. Antibiotic resistance patterns of *Serratia spp.*are shown in (Table 15).

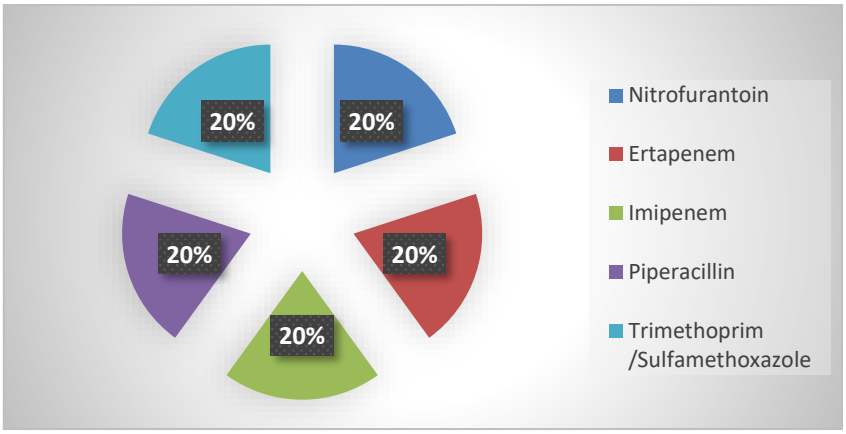

Figure 26:

Antibiotics to which Serratia spp. is sensitive

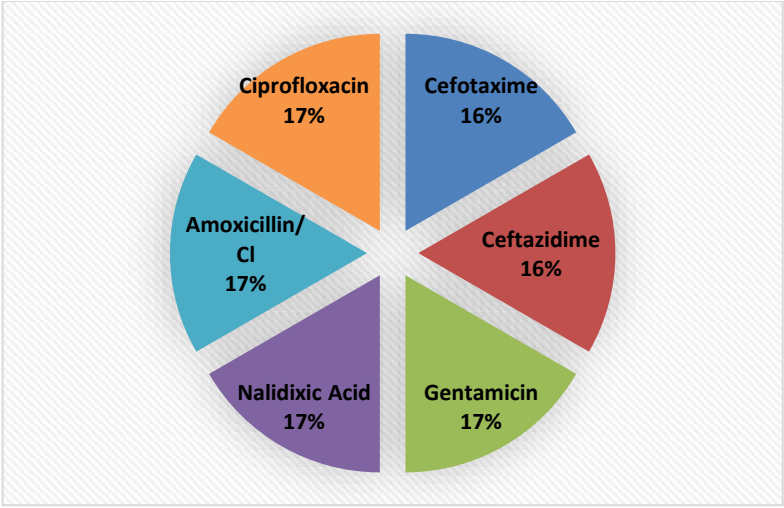

Figure 27:

Antibiotics to which Serratia spp. is resistance

Table 15

The Antibiotic Resistance Patterns of Serratia spp.

Antibiotics	**I**	**R**	**S**	**n**
Amikacin	1	-	-	1
Cefotaxime	-	1	-	1
Ceftazidime	-	1	-	1
Nitrofurantoin	-	-	1	1
Gentamicin	-	1	-	1
Nalidixic Acid	-	1	-	1
Ertapenem	-	-	1	1
Amoxicillin	-	1	-	1
Ciprofloxacin	-	1	-	1
Imipenem	-	-	1	1
Piperacillin Tazobactam	-	-	1	1
Trimethoprim/ Sulfamethoxazole	-	-	1	1

The **#n** is based on how many antibiotics were used overall to treat *Serratia spp*.

When the antibiotic resistance patterns of *E. cloacae* were examined, it was determined that the antibiotic to which it was sensitive were amikacin, ciprofloxacin, gentamicin, ertapenem, imipenem and trimethoprim/ sulfamethoxazole (n=3, Figure 28), and the antibiotic to which it was resistant was amoxicillin (n=3, Figure 29). *E. cloacae* showed intermediate (I) resistance to nitrofurantoin treatment. Antibiotic resistance patterns of *E. cloacae* are shown in (Table 16).

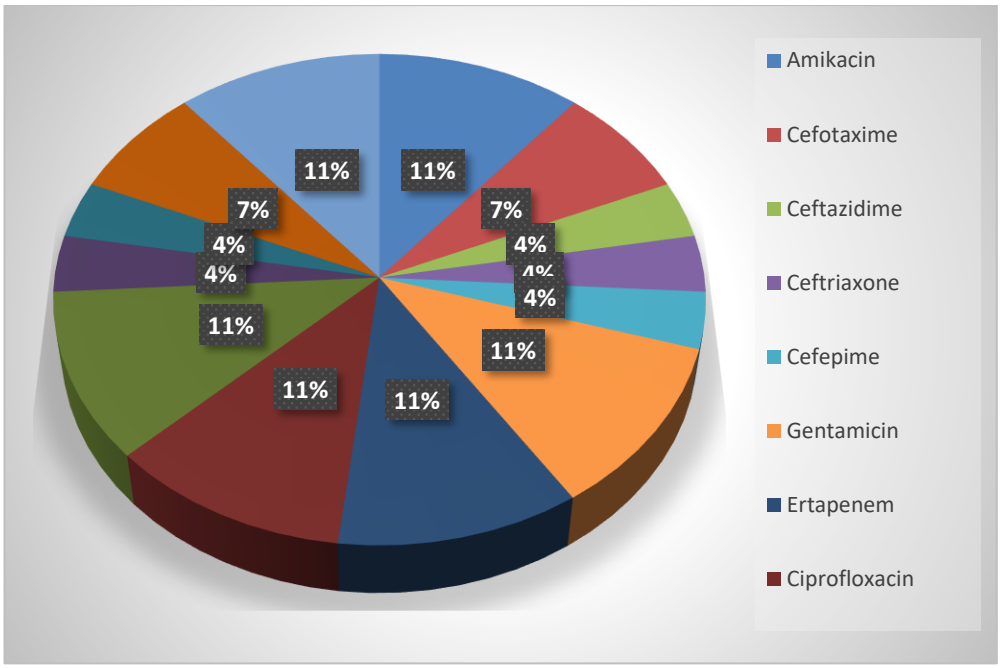

Figure 28:

Antibiotics to which E. cloacae is sensitive

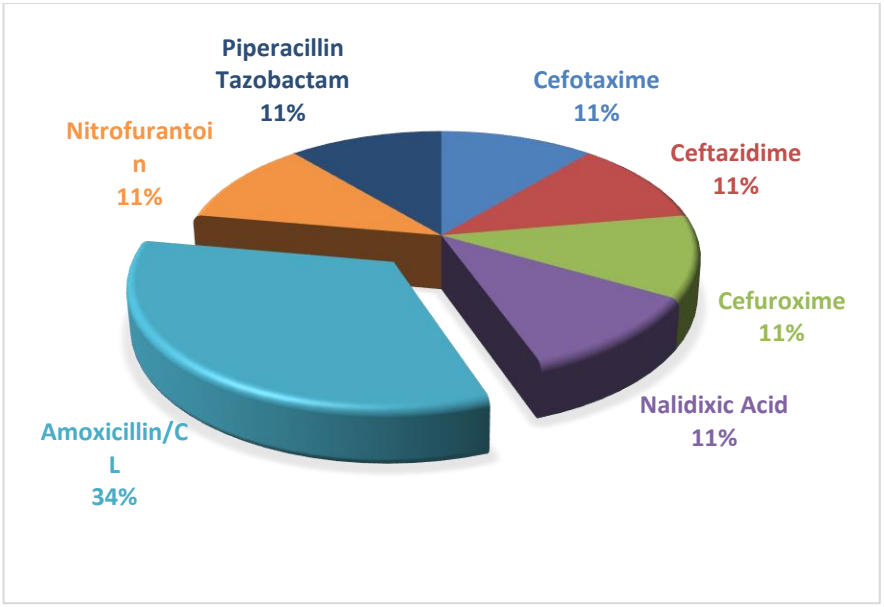

Figure 29:

Antibiotics to which E. cloacae is resistance

Table 16

The Antibiotic Resistance Patterns of E. cloacae

Antibiotics	**I**	**R**	**S**	**n**
Amikacin	-	-	3	3
Cefotaxime	-	1	2	3
Ceftazidime	-	1	1	2
Cefuroxime	-	1	-	1
Ceftriaxone	-	-	1	1
Cefepime	-	-	1	1
Gentamicin	-	-	3	3
Nalidixic Acid	-	1	-	1
Ertapenem	-	-	3	3
Amoxicillin	-	3	-	3
Ciprofloxacin	-	-	3	3
Imipenem	-	-	3	3
Meropenem	-	-	1	1
Nitrofurantoin	1	1	-	2
Ofloxacin	-	-	1	1
Piperacillin Tazobactam	-	1	2	3
Trimethoprim/ Sulfamethoxazole	-	-	3	3

The **#n** is based on how many antibiotics were used overall to treat *E. cloacae*

When the antibiotics resistance patterns of *S. epidermidis* was examined, it was determined that antibiotic to which it was sensitive were amoxicillin and cefuroxime (n=1). *S. epidermidis* showed intermediate (I) resistance to amoxicillin and cefuroxime treatments. Antibiotic resistance patterns of *S. epidermidis* are shown in (Table 17).

Table 17

The Antibiotic Resistance Patterns of S. epidermidis

Antibiotics	**R**	**S**	**n**
Amikacin	-	1	1
Ceftazidime	-	1	1
Cefuroxime	1	-	1
Ceftriaxone	-	1	1
Cefepime	-	1	1
Gentamicin	-	1	1
Ertapenem	-	1	1
Amoxicillin	1	-	1
Ciprofloxacin	-	1	1
Imipenem	-	1	1
Meropenem	-	1	1
Nitrofurantoin	-	1	1
Piperacillin Tazobactam	-	1	1
Trimethoprim/ Sulfamethoxazole	-	1	1

The **#n** is based on how many antibiotics were used overall to treat *S. epidermidis.*

When the antibiotic resistance patterns of *M. morganii* were examined, it was determined that the antibiotic to which it was sensitive were amikacin, cefotaxime, ceftazidime, ertapenem, imipenem and piperacillin tazobactam (n=1), and the antibiotic to which it was resistant were nitrofurantoin, gentamicin, nalidixic acid, amoxicillin, ampicillin, ciprofloxacin, ofloxacin and trimethoprim/ sulfamethoxazole (n=1). *M. morganii* showed intermediate (I) resistance to nitrofurantoin treatment. Antibiotic resistance patterns of *M. morganii* are shown in (Table 18).

Table 18

The Antibiotic Resistance Patterns of M. morganii

Antibiotics	**R**	**S**	**n**
Amikacin	-	1	1
Cefotaxime	-	1	1
Ceftazidime	-	1	1
Nitrofurantoin	1	-	1
Gentamicin	1	-	1
Nalidixic Acid	1	-	1
Ertapenem	-	1	1
Amoxicillin	1	-	1
Ampicillin	1	-	1
Ciprofloxacin	1	-	1
Imipenem	-	1	1
Ofloxacin	1	-	1
Piperacillin Tazobactam	-	1	1
Trimethoprim/ Sulfamethoxazole	1	-	1

The **#n** is based on how many antibiotics were used overall to treat *M. morganii*.

When the antibiotic resistance patterns of *A. baumannii* were examined, it was determined that the antibiotic to which it was sensitive were colistin and trimethoprim/ sulfamethoxazole (n=1), and the antibiotic to which it was resistant were cefotaxime, ciprofloxacin, gentamicin, imipenem and piperacillin tazobactam (n=1). Antibiotic resistance patterns of *A. baumannii* are shown in (Table 19).

Table 19

The Antibiotic Resistance Patterns of A. baumannii

Antibiotics	**R**	**S**	**n**
Cefotaxime	1	-	1
Gentamicin	1	-	1
Colistin	-	1	1
Ciprofloxacin	1	-	1
Imipenem	1	-	1
Piperacillin Tazobactam	1	-	1
Trimethoprim/ Sulfamethoxazole	-	1	1

The **#n** is based on how many antibiotics were used overall to treat *A. baumannii*

When the antibiotic resistance patterns of *C. freundii* were examined, it was determined that the antibiotic to which it was sensitive were amikacin and imipenem (n=2, Figure 30), and the antibiotic to which it was resistant were amoxicillin, aztreonam, ceftazidime and piperacillin tazobactam (n=1, Figure 31).

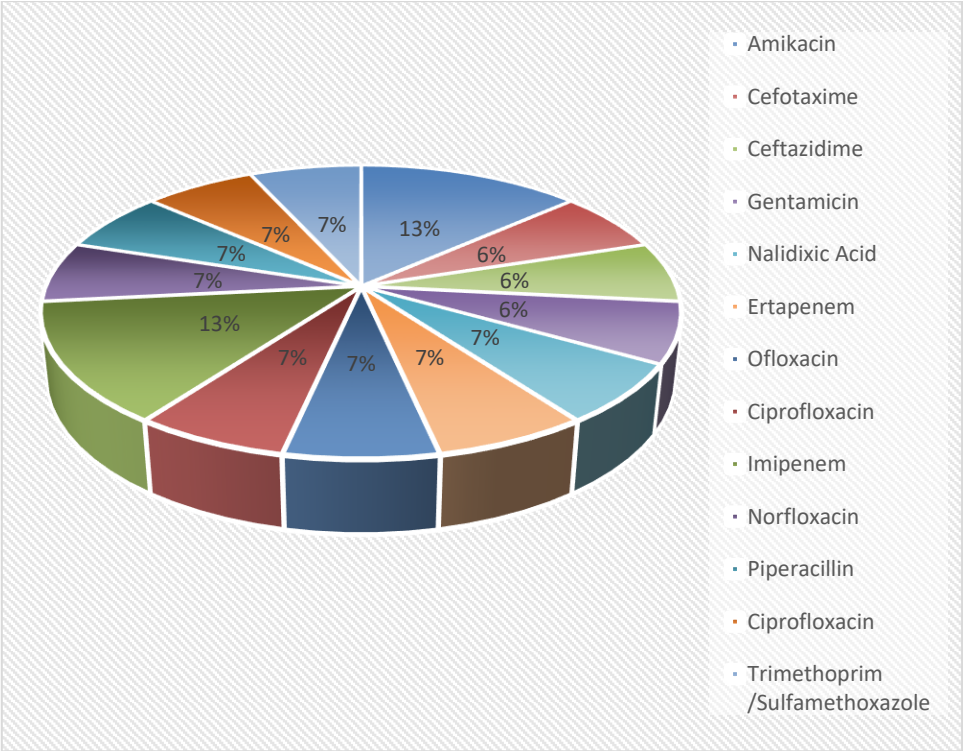

Figure 30:

Antibiotics to which C. freundii is sensitive

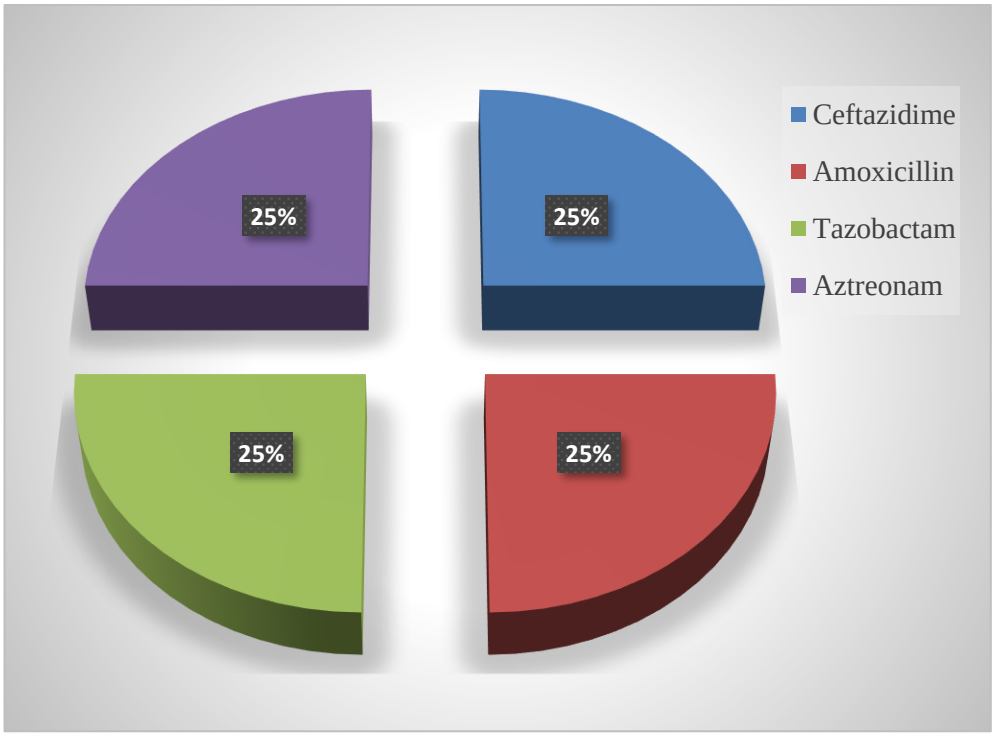

Figure 31:

Antibiotics to which C. freundii is resistance

Antibiotic resistance patterns of *C. freundii* are shown in (Table 20).

Table 20

The Antibiotic Resistance Patterns of C. freundii

Antibiotics	**R**	**S**	**n**
Amikacin	-	2	2
Ceftazidime	1	-	1
Cefotaxime	-	1	1
Ceftazidime	-	1	1
Gentamicin	-	1	1
Nalidixic Acid	-	1	1
Ertapenem	-	1	1
Amoxicillin	1	-	1
Ofloxacin	-	1	1
Ciprofloxacin	-	1	1
Imipenem	-	2	2
Norfloxacin	-	1	1
Piperacillin Tazobactam	1	1	2
Aztreonam	1	-	1
Ciprofloxacin	-	1	1
Trimethoprim/ Sulfamethoxazole	-	1	1

The **#n** is based on how many antibiotics were used overall to treat *C. freundii*.

4.5. Infection Distribution

When the origins of infection in HD patients were examined, it was determined that 4 (6.5%) patients had hospital-acquired infections, 20 (32.5%) patients had community-acquired infections, and no causative agents were found in 38 (61.3%) patients (Figure 32).

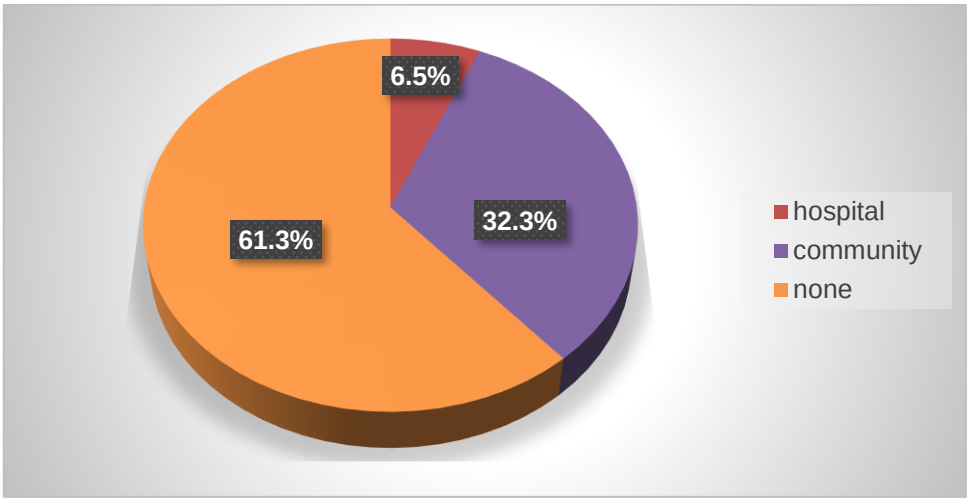

Figure 32:

Distribution According to The Origins of Infection in HD Patients

When HCV, Hepatitis B surface antigen (HBsAg), Hepatitis B antigen (HB-core), anti-HIV and HIV-RNA serology results are evaluated in HD patients, the following results were obtained: HBsAg was positive in 5 (8.1%), HCV was positive in 11(17.7%), and HB-core was positive in 7 (11.3%) HD patients. One HD patient (1.6%) was identified as negative for anti-HIV and HIV-RNA. Distribution of Hemodialysis Patients according to HBV, HCV and HIV Serology is given in (Table 21).

Table 21

HBV, HCV and HIV Serologies of Hemodialysis Patients

HBsAg	**N**	**%**
+	5	8.1
-	57	91.9
Anti-HCV	**N**	**%**
+	11	17.7
-	51	82.3
HB-core	**N**	**%**
+	7	11.3
-	21	33.9
Anti-HIV	**N**	**%**
	0	0

CHAPTER V

Discussion

Patients who get hemodialysis on a regular way are at an increased risk of infection. As a result of uremia, patients with chronic renal failure become more susceptible to infectious agents due to defects in cellular immunity, neutrophil function, and complement activation (Vanholder and Ringoir, 1992). Infection is a common complication and the leading cause of death in hemodialysis patients. Patients who need HD due to chronic renal failure can easily become infected from external environments in addition to disorders in the immune system. Since vascular procedures are applied for a long time in patients receiving hemodialysis with other patients in the hemodialysis unit, it is possible to add infectious agents even in units with good infection control. Among the factors that play a role in the transfer of infectious agents in the HD unit are the surrounding surfaces, contaminated equipment, consumables, injectable drugs used, contaminated hemodialysis device, and especially with poorly washed hands of healthcare personnel could be responsible direct or indirect transmission from patient to patient (USRDS 2016). In the USA Renal Data System, hospitalization and death records of hemodialysis patients over a seven-year period, all septicemia records as well as secondary diagnosis codes, hemodialysis catheter-induced infection (18%), decubitus ulcer (6%), urinary tract infections (5%), pneumonia (5%), gangrene (3%), endocarditis (2%), and cellulitis and diabetic foot infection (1%) (Powe et.al 1999).

Hospitalization is quite common among HD patients. The rate of recurrent hospitalizations for HD patients in the United States is 1.7 per year (USRDS 2015). Microorganism growth was detected in 21 of the 62 patients included in the study, representing an incidence of 33.9%. 41 culture samples were obtained from 21 (33.9%) of 62 HD patients due to infection. While there was no growth in blood, urine and catheter culture samples in 15 (36.5%) of 41 samples cultured (monitored) in the microbiology laboratory, growth was observed in 26 (63.5%) samples. In a study including 269 HD patients, infection was found in 162 patients (60.2%) (Shepshelovich et.al., 2017).

According to our results, the most common bacteria was *MRSA* (24.5%), followed by *Klebsiella spp*. (19.5%) and *E. coli* (17.1%). In the study of Sahli et al.,

the most common bacteria were found to be *MRSA* (36.4%), *K. pneumoniaea* (33.3%) and *E. coli* (8.3%) (Sahli et.al., 2017).

In HD patients, Gr (+) is among the most common causative microorganisms when bacteremia develops. According to studies, HD patients had a higher risk of methicillin-resistant Staphylococcus aureus infection. *E. coli, Klebsiella spp.* and *Enterobacter spp.* are Gr (-) organisms frequently isolated from blood samples (Loo et al., 2015, Aslam et al., 2014). In comparison to the general population, the incidence of *S. aureus* was relatively increased in HD patients, and the rate of *E. coli* was relatively decrease (Alfandari S et.al 2017). Although it is unclear whether the rate of resistant bacteria in HD patients is higher than in the general population, it has been shown to be higher in studies. In a single-center report conducted in Brazil in 2010-2013, 38.5% of *S. aureus* were *MRSA*, while the percentage of methicillin resistance was found to be 31.0% in surveillance data from Brazil in 2005-2008 (Fram et al., 2015, Gales et al., 2009).

The UK national surveillance report showed that the risk of *MRSA* bacteremia for dialysis patients is approximately 8 times higher in HD patients using catheters than in the general population (Fluck et al., 2009). When a total of 144 episodes of catheter-related infection from 118 patients followed in a HD center were evaluated; *MRSA* and *MSSA* were responsible for 64.2% (68/106) of Gr (+) infections. Methicillin-resistant *S. aureus* was isolated in 18.9% (20/106) of blood cultures (Loo et al., 2015). In our study, the frequency of *MRSA* was found to be 24.5%. If we look at the relationships between the studies mentioned above and our study, it is seen that similar results are obtained.

Although Gr (+) bacteria are frequently detected in cultures of HD patients, Gr (-) bacteria can also be detected. However, in studies conducted in other centers, differences can be detected in the most common Gr (-) microorganism species. In our study, *Klebsiella spp*. (19.5%) and *E. coli* (17.1%). *E. cloacae* (10.3%) ranked first. In the study of Murray et al., (2015) the main organisms were *E. coli* (49.5%), *Enterobacter spp.* (13.1%), *Klebsiella spp*. (11.1%), Proteus mirabilis (6.1%), and *P. aeruginosa* (5.1%). In the study of Loo et al., the most frequently detected Gr (-) microorganism was *Pseudomonas spp.* In the same study, respectively, *Enterobacter spp*., *A. baumannii* and *Klebsiella spp*. are included. Today, the frequency of detection of Gr (-) bacteria in blood cultures is increasing, and they deserve special attention considering the increase in antibiotic resistance rates (Girndt, 2015). While rates of

MRSA have remained stable or are beginning to decline, at least in many countries in Europe, multiresistant Gr (-) are on the rise (Weist et al., 2016). In patients who are not on dialysis but have chronic renal disease, the risk of bloodstream infection increases due to suppression of the immune system. Gr (-) bloodstream infections, although catheter-related, usually originate from soft tissue, foot ulcer infection, urinary tract, and intra-abdominal focus. These issues should be kept in mind when making the assessment. Bloodstream infections detected in HD patients were also detected in our study. However, since compliance with the rules of rational antibiotic use is different in countries, although *staphylococci* are frequently detected as in Gr (+), the microorganism that ranks first in Gr (-) bacteria can change.

HD patients are more likely to become chronic carriers after acute HBV infection. In addition, the risk of developing chronic liver disease in HD patients who are HBV carriers is high, and many patients lose the chance of kidney transplantation. As a result; Detection, prevention and treatment of HBV infections in HD patients are very important. In our study, HBsAg positivity was found to be 8.1%. All HBsAg negative patients were protected with hepatitis vaccine. In a study conducted in 1990, the frequency of HBsAg was found to be 9.9% in the general population in Jordan (Toukan et al., 1990).

In Jordan, hepatitis B vaccine was included in the childhood immunization program in 1995. With the vaccination program, the frequency of hepatitis has been reduced to 2.4% within three decades (Nusair et.al, 2020). The frequency of HBsAg, which was found to be 8.1% in our study, is compatible with the general population, considering the age group of the patients.

Hepatitis B and C virus co-infection is a common clinical condition (Sheen et al., 1992). In patients with chronic liver disease, the HBV-DNA positivity is higher due to HCV than those due to non-HCV causes (Cacciola et., 1999). Although its clinical significance is not well understood, it has been reported that patients with chronic hepatitis C are more common to have an occult HBV infection (Khattab et al., 2005). On the other hand, there are studies suggesting that the presence of HCV suppresses HBV replication (Khattab et al., 2005). Altindiş et al., determined the rate of latent hepatitis B as 12.4% in HD patients and 27.5% in HD patients with anti-HCV positive. In contrast, Goral et al., reported the rate of occult hepatitis B as 0% in 50 patients with HBsAg negative and anti-HCV positive chronic HD (Goral et al., 2006). The presence of occult hepatitis, hepatitis B and hepatitis C relationship with hepatitis

markers were not investigated in HD patients included in the study. Among the HD patients included in the study, the number of HCV-positive patients was 11, so an evaluation of the interaction of HCV and occult HBV could not be made with these data. Important studies are also carried out in organ transplant patients regarding the clinical consequences of occult HBV infection. The risk of HBV transmission after transplantation from donors with occult HBV infection is between 25–94%. In addition, it has been suggested that occult HBV infection causes mild chronic damage to the liver in some patients (Blackberg and Kidd-Ljunggren, 2006). Considering the contagious characteristics of HD patients, transmission of the virus to HBV-negative patients via dialysis seems inevitable. This will create an important risk that may increase morbidity and mortality in HD patients whose quality of life has decreased significantly due to chronic renal failure. Since the key test in the diagnosis of latent hepatitis B infection is the detection of HBV-DNA, standardization of the technique and method used is very important. In patients applying to dialysis units, at least during the first application, viral DNA research with a PCR-based method may be beneficial in terms of preventing future health problems. The need for more comprehensive studies on this subject continues.

The risk of exposure to HCV infection increases due to medical conditions that require frequent injections or blood transfusions. People with diseases such as hemodialysis, thalassemia, and hemophilia are considered as risky groups. In a study examining risky groups in Jordan, the prevalence of HCV was found to be 9.2% (WHO 2020). It is accepted that hepatitis C is a transmission route in HD units due to percutaneous injuries and inadequacy in healthcare-related practices. There is no need to use a separate device for hepatitis C positive patients. Although anti-HCV was found to be 9.2% in risk groups, this rate was found to be 17.7% in our study. These findings are an indication of insufficient adherence to optimal infection control procedures. The high rate of anti-HCV during healthcare continues to be a problem.

CHAPTER VI

Conclusion and Recommendations

This study was conducted retrospectively. Therefore, the deficiencies in the analyzed data can be listed as follows. It is seen that HBV-DNA and HCV-RNA have not been checked in patients with HBsAg and anti-HCV positivity. Data are not sufficient for occult hepatitis diagnoses.

Also, the study was conducted in one center and did not include all regions and the population. therefore, the deficiencies in sample size in our study may affect the demographic features.

If standard infection control measures are followed while patient follow-up in hemodialysis units, the frequency of bacterial and viral infections can be reduced.

A better understanding of these interconnections may help us to develop both preventive and therapeutic strategies for infectious diseases with a global health impact. And we recommend that further studies should be conducted to look for risk factors associated with infection and for ways to control the risk factors in terms of determining disease course and appropriate treatment.

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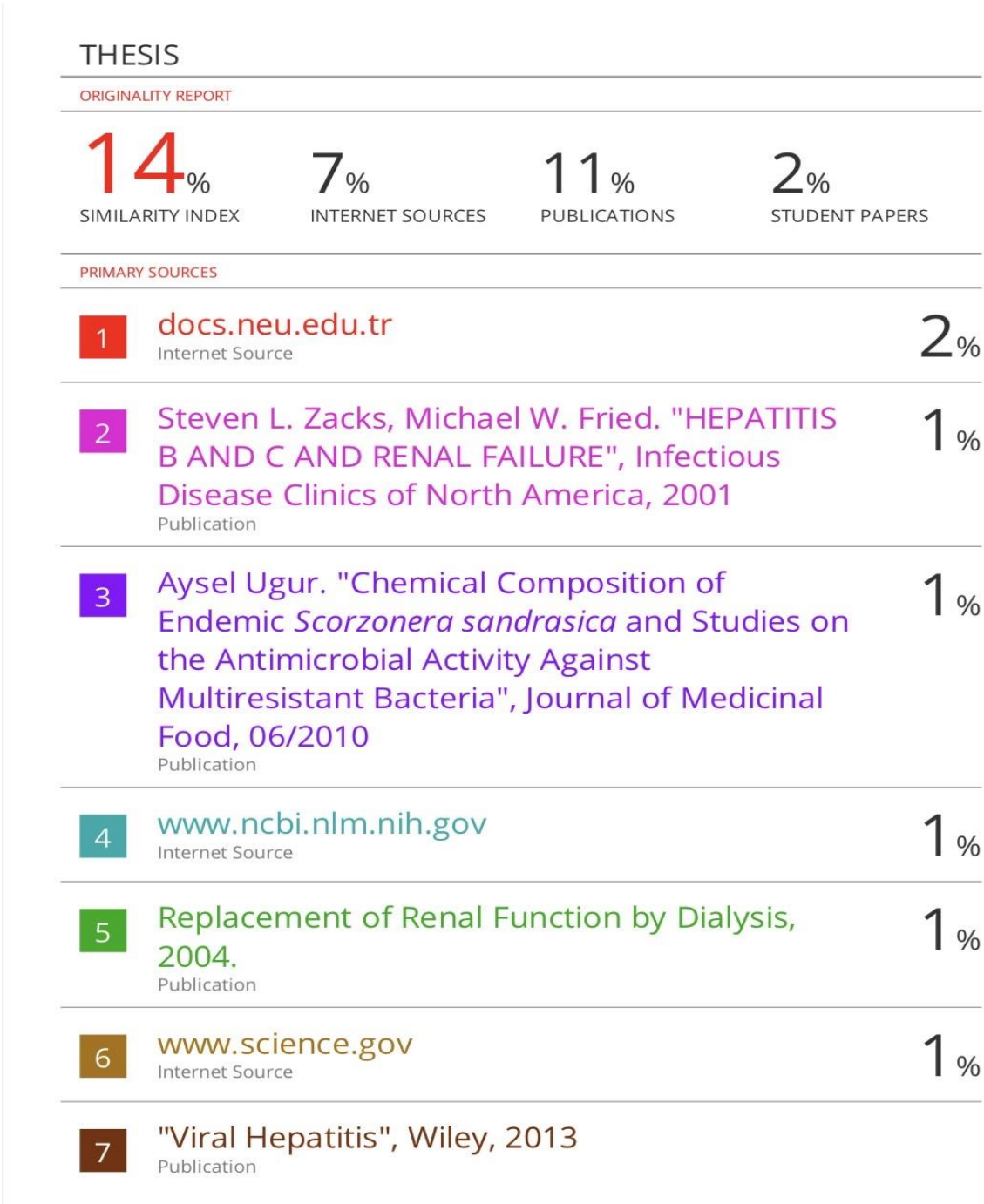
APPENDICES

Appendix A

Turnitin Similarity Report



THESIS

ORIGINALITY REPORT

14%	7%	11%	2%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	docs.neu.edu.tr Internet Source	2%
2	Steven L. Zacks, Michael W. Fried. "HEPATITIS B AND C AND RENAL FAILURE", Infectious Disease Clinics of North America, 2001 Publication	1%
3	Aysel Ugur. "Chemical Composition of Endemic *Scorzonera sandrasica* and Studies on the Antimicrobial Activity Against Multiresistant Bacteria", Journal of Medicinal Food, 06/2010 Publication	1%
4	www.ncbi.nlm.nih.gov Internet Source	1%
5	Replacement of Renal Function by Dialysis, 2004. Publication	1%
6	www.science.gov Internet Source	1%
7	"Viral Hepatitis", Wiley, 2013 Publication	

Ethical Approval

YAKIN DOĞU ÜNİVERSİTESİ
BİLİMSEL ARAŞTIRMALAR ETİK KURULU

ARAŞTIRMA PROJESİ DEĞERLENDİRME RAPORU

Toplantı Tarihi :30.06.2022
Toplantı No :2022/104
Proje No :1576

Yakın Doğu Üniversitesi Tıp Fakültesi öğretim üyelerinden Doç. Dr. Ayşe Arıkan'ın sorumlu araştırmacısı olduğu, YDU/2022/104-1576 proje numaralı ve **"Investigation of the Prevalence and Risk Factors of Bacterial and Viral Infections in Hemodialysis Patients in Jordan"** başlıklı proje önerisi kurulumuzca değerlendirilmiş olup, etik olarak uygun bulunmuştur.

Prof. Dr. Şanda Çalı
Yakın Doğu Üniversitesi
Bilimsel Araştırmalar Etik Kurulu Başkanı

Kurul Üyesi	Toplantıya Katılım	Karar
	Katıldı(✓)/ Katılmadı(X)	*Onay(✓)/ Ret(X)*
Prof. Dr. Tamer Yılmaz	✓	✓
Prof. Dr. Şahan Saygı	✓	✓
Prof. Dr. Nurhan Bayraktar	✓	✓
Prof. Dr. Mehmet Özmenoğlu	✓	✓
Prof. Dr. İlker Etikan	✓	✓
Doç. Dr. Mehtap Tınazlı	*X*	*X*
Doç. Dr. Nilüfer Galip Çelik	✓	✓
Doç. Dr. Emil Mammadov	✓	✓
Doç. Dr. Ali Cenk Özay	✓	✓

Curriculum Vitae

1. PERSONAL INFORMATION

NAME, SURNAME: **DATE of BIRTH and PLACE:**	RAZAN ABDELAZIZ ABDALLAH KHATER 11 Aug 1995 / Jordan - Aqaba
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2. EDUCATION

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3. ACADEMIC EXPERIENCE

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4. FIELD OF INTERESTS

FIELDS OF INTERESTS	KEY WORDS
Medical Microbiology	Chronic kidney disease, Hemodialysis, Bloodstream infection, Hepatitis, MRSA.