RESEARCH PAPER

Antibiotic Resistance of Bacterial Vascular Access Infection in Hemodialysis Patients

Mohamed Fawzy Musallam[1], Mohamed Ahmed Shaarawi Taha[2], Ahmed Yousry Gamil Mahmoud[3*], Mohamed W. Saleh Hasanein[4]

[1] Assistant Professor of Internal Medicine, Faculty of Medicine, Suez University
[2] Professor of Internal Medicine and Nephrology, Faculty of Medicine, Minia University
[3*] M.B.B.Ch (Corresponding Author)
[4] Lecturer of Internal Medicine, Faculty of Medicine, Suez University

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ABSTRACT

Chronic kidney disease (CKD) patients undergoing hemodialysis (HD) are at high risk for vascular access-related infections due to immunosuppression, repeated hospitalizations, and frequent vascular interventions. Catheter-related bloodstream infections (CRBSIs) are the most common, predominantly caused by Staphylococcus aureus, coagulase-negative staphylococci, and Gram-negative bacteria. Infection risk is influenced by vascular access type, catheter insertion site, antibiotic exposure, and healthcare facility practices. CRBSIs are often complicated by biofilm formation, reducing antibiotic susceptibility and necessitating catheter removal or adjunctive therapies such as antibiotic locks or guidewire exchange. Prevention strategies include use of arteriovenous fistulas, strict hand hygiene, contact precautions, topical decolonization, and antibiotic/antiseptic-coated catheters. Antimicrobial resistance (AMR) in HD patients is a growing concern, with multidrug-resistant organisms, including methicillin-resistant S. aureus and carbapenem-resistant Klebsiella pneumoniae, contributing to increased morbidity, mortality, and healthcare costs. AMR arises via intrinsic or acquired mechanisms, including mutations and horizontal gene transfer, often facilitated by mobile genetic elements. Effective management of CRBSIs requires timely empirical antibiotics, guided by local antibiograms, combined with source control and catheter management. Screening, decolonization, and strict infection control are essential to limit colonization and prevent systemic infections.

Keywords: Hemodialysis, Vascular Access Infection, Catheter-related Bacteremia, Antimicrobial Resistance.
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Introduction

CKD constitutes a global public health problem. The escalating incidence of chronic kidney disease is attributable to the growing population of case with diabetes mellitus (DM) and hypertension, which are the principal risk factors for the condition [1].

The infection risk in haemodialysis cases is significant, attributed to compromised immunity and the necessity for recurrent hospitalisations & surgical procedures. Furthermore, haemodialysis entails regular and/or extended exposure to blood through vascular access and the extracorporeal circuit, as well as interactions with other cases throughout the procedure, contact with medical personnel, & the alteration of the dialysis equipment [2].

The pathogenesis of access-related infections in hemodialysis cases typically involves bacterial or fungal colonization of the catheter or fistula site. Common pathogens comprise coagulase-negative staphylococci, Staphylococcus aureus, & gram-negative bacteria. These organisms can enter the bloodstream through breaches in aseptic techniques or through direct contamination of the access site [3].

The clinical presentation of vascular access infections can range from local signs of infection, like erythema, warmth, & tenderness at the access site, to more severe

systemic symptoms like fever, chills, & sepsis. Early diagnosis is critical to avoid the progression of infection, which may necessitate access removal, leading to delays in dialysis treatment. Blood cultures and imaging studies are frequently needed to confirm infection & guide management [4].

This study aimed to evaluate the antibiotic resistance of bacterial vascular access infection in hemodialysis patients.

Hemodialysis (HD)

Hemodialysis is a procedure that eliminates metabolic & toxic waste substances from the body when the kidneys are incapable of functioning properly. The term dialysis originates from the Greek word "dialusis," signifying disintegration, with "dia" meaning through & "lusis" meaning loosening [5].

Hemodialysis is a procedure that utilizes a specialized filter or semi-permeable membrane to facilitate the passage of blood. The filter then eliminates bodily waste, toxic substances, & excess water from the blood. This method purifies the blood, sustains the body's homeostatic environment, & manages normal blood pressure by preserving appropriate balance of electrolyte & fluid [6].

The process of hemodialysis is based on the idea of simple diffusion over a membrane that is only partially permeable. The mechanism of counter current flow enables the blood & dialysate to flow in opposite directions, which results in the establishment of a concentration gradient & a rise in the effectiveness of the dialysis process [7].

Clinical significance & principle

Hemodialysis is a form of inpatient therapy that is administered to cases who are in severe condition and have suffered an acute kidney injury. Generally speaking, HD is typically administered as an outpatient therapy to stable cases who are diagnosed with end-stage renal failure (ESRF). This treatment is carried out in a dialysis outpatient facility, which can be a purpose-built room within a hospital or a clinic that is dedicated solely to providing dialysis services. More rarely, HD is performed at home, where it can be self-initiated and controlled, or it can be performed jointly with the support of a trained assistant, who is typically a member of the family [8].

Counter-current flow enhances dialysis efficiency by maintaining a high concentration gradient across the membrane. Ultrafiltration is achieved by adjusting dialysate hydrostatic pressure, allowing water and some solutes to move across the membrane. Waste products such as urea, creatinine, phosphate, and potassium diffuse into the dialysate, while sodium and chloride concentrations are kept similar to plasma to prevent loss. To correct blood acidosis, dialysate contains a higher concentration of sodium bicarbonate than plasma, and small amounts of glucose may also be added [9].

Technique

Approximately 430,000 patients in the United States undergo hemodialysis, using vascular access via catheters, arteriovenous fistulas (AVFs), or arteriovenous grafts (AVGs). The "fistula first" initiative promotes AVFs due to their reliability, though many patients receive AVGs made of polytetrafluoroethylene connecting an artery and vein [10].During hemodialysis, blood flow ranges from 300–500 mL/min, while dialysate flows countercurrently at 500–800 mL/min. Ultrafiltration is achieved through negative hydrostatic pressure, and dialysis adequacy is commonly assessed using the urea reduction ratio, with an optimal target of 65–70%. Dialysis dosing should be individualized based on fluid removal, electrolyte and acid–base control, and overall metabolic management [9].

Dialysis modality independently influences morbidity, with hemodialysis associated with more severe illness compared to peritoneal dialysis. More frequent hemodialysis (six times weekly) improves blood pressure control, hyperphosphatemia, left ventricular mass, and physical health, but prolonged interdialytic intervals—especially over weekends—are linked to increased heart failure hospitalizations and mortality (Schmidli et al., 2018). Home hemodialysis, typically performed 3–6 times per week for longer sessions, offers lifestyle flexibility but is associated with higher vascular access complications, caregiver burden, and faster loss of residual kidney function. Frequent, prolonged hemodialysis is recommended during pregnancy in end-stage renal disease, while patients with low residual renal function generally require thrice-weekly sessions of at least three hours [11].

Patients with excessive weight gain, poor blood pressure or metabolic control, high ultrafiltration requirements, or difficulty achieving dry weight may benefit from longer or more frequent sessions. Ultrafiltration rates

should be carefully tailored to balance euvolemia, solute clearance, and blood pressure control while minimizing hemodynamic instability and intradialytic symptoms [9].
Dialysis is associated with increased morbidity and mortality and a reduced health-related quality of life (HRQoL), affecting both physical and mental domains. Physical impairment includes fatigue, sleep disorders such as obstructive sleep apnea and restless legs syndrome, and reduced mobility and functional capacity, while mental aspects involve anxiety and depressive symptoms. Intensive hemodialysis has been shown to improve both physical and mental HRQoL scores and significantly shorten post-dialysis recovery time [12].

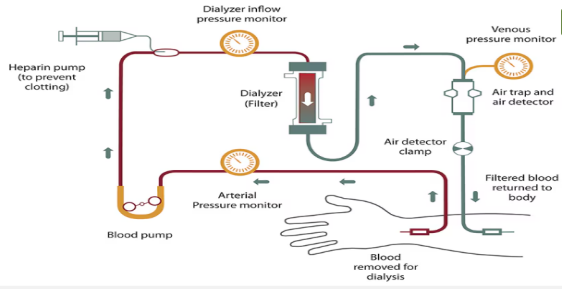

Figure 1: The dialysis machine processes the blood by pumping it through the filter and then returning the blood to the body. In the process of the procedure, the dialysis machine monitors the patient's blood pressure & regulates the flow of blood through the filter, as well as the fluid that is extracted from the body [13].

Indications

Hemodialysis initiation is required for acute illness related to:

- Pericarditis
- Refractory acidosis
- Uremic encephalopathy
- Acute kidney injury
- Hypervolemia causing end-organ complications (e.g., pulmonary swelling)
- Life-threatening hyperkalemia
- Failure to thrive & malnutrition
- Intractable gastrointestinal symptoms
- Peripheral neuropathy
- Asymptomatic patients with a GFR of five to nine mL/min/1.73 m² [14].
- Any toxic ingestion

Cytokine dysregulation and reduced clearance in renal failure contribute to immunosuppression, cardiac depression, vasodilation, hemodynamic instability, and potential end-organ damage, while renal replacement therapy (RRT) enhances cytokine removal in conditions such as sepsis, despite risks including catheter complications, electrolyte disturbances, and intradialytic hypotension. Updated KDOQI 2015 guidelines outline standards for hemodialysis adequacy [15].
Patients reaching CKD stage 4 or requiring early dialysis should receive counseling on kidney failure, available treatment modalities, and conservative management, with involvement of family and caregivers [16].Initiation of maintenance dialysis should be guided by clinical manifestations of renal failure, volume or blood pressure dysregulation, and nutritional decline rather than renal function alone in asymptomatic patients [17].Cardiac indications for dialysis include arrhythmias, uremic pericarditis, fluid overload, and electrolyte imbalances associated with heart failure and renal dysfunction, with potassium, magnesium, and calcium disturbances being common contributors, often exacerbated by medications and impaired renal excretion [9].

Clinical HD outcomes of hemodialysis

Clinical outcomes in hemodialysis (HD) patients include high mortality, cardiovascular disease, vascular access complications, and infections. Mortality rates are markedly elevated compared to the general population, peaking within the first 90–120 days of HD initiation, particularly in those with limited pre-dialysis nephrology care [18].Cardiovascular disease affects nearly two-thirds of HD patients, accounting for ~50% of deaths, with sudden cardiac death being the leading cause. Both traditional (diabetes, hypertension) and non-traditional (left ventricular hypertrophy, electrolyte imbalances) risk factors contribute, yet effective interventions are limited ([19] [20]). Vascular access complications drive over one-third of hospitalizations, with central venous catheters (CVCs) associated with the highest risks of death, infection, and cardiovascular events, influenced by patient- and institution-specific factors[21];[22]). HD patients are also more susceptible to

infections, including access-related bloodstream infections, S. aureus bacteremia, and blood-borne viruses such as HBV and HCV, which increase morbidity and mortality [23].Respiratory infections are common, and vaccination against influenza, pneumococcus, and COVID-19 reduces related mortality [24].

Complications

Hemodialysis (HD) is associated with several acute complications. Intradialytic hypotension, linked to increased mortality and myocardial stunning, presents with dizziness, light-headedness, nausea, and low blood pressure. Management includes Trendelenburg positioning, saline bolus, and ultrafiltration adjustment [25].

Serious emergencies include dialysis disequilibrium syndrome, caused by rapid urea shifts leading to cerebral edema, managed with gradual urea reduction and osmotic agents such as mannitol or elevated sodium dialysate [26].Dialyzer reactions can be type A anaphylactic or type B nonspecific, treated with antihistamines, epinephrine, corticosteroids, or alternative membranes [27]. Acute hemolysis and air embolism are critical events requiring hematologic evaluation, monitoring, oxygen, and sometimes aspiration [13].

Other nonspecific complications include nausea, vomiting, headache, back or chest pain, and pruritus, often related to hypotension or early disequilibrium syndrome. Management involves metoclopramide, acetaminophen, or alternative dialyzer membranes. Vascular access dysfunction, especially arteriovenous stenosis, reduces blood flow and increases thrombosis risk. Patients must protect the access site, while healthcare providers monitor for hemorrhage, infection, and occlusion; heparin-related bleeding is managed with protamine sulfate [28].

Electrolyte imbalances such as hyperkalemia, hyponatremia, hypermagnesemia, and hypocalcemia may occur despite dialysis, especially in noncompliant patients [29].Cardiac arrest and sudden cardiac death are more frequent in HD than peritoneal dialysis, particularly in the first two months. Common arrhythmias include ventricular fibrillation, pulseless electrical activity, and asystole. Vascular access procedures may trigger pulmonary edema, arrhythmias, or contrast reactions [28].

Sepsis

Sepsis is a critical medical disorder characterized by significant physiological & metabolic disturbances. The Third International Consensus (Sepsis-3) defines sepsis as "organ dysfunction resulting from a dysregulated host response to infection," highlighting the significant role of both the innate & adaptive immune responses in the manifestation of the clinical syndrome [30].

Timely fluid resuscitation & the prompt delivery of broad-spectrum antibiotics are the only interventions demonstrated to decrease mortality. A critical element is the timely diagnosis & the commencement of causative, supportive, & adjunctive interventions. This indicates that enhancing knowledge of sepsis & advocating for quality improvement activities in sepsis significantly bolster case survival, alongside the advancement of innovative diagnostics & therapies. [31].

Sepsis pathogenesis

Sepsis has long been recognized as a complex condition with challenging diagnosis. Historically, it was thought to result from an excessive inflammatory response to infection, a concept first proposed by William Osler and later emphasized by Lewis Thomas, who suggested that the body’s reaction, rather than the pathogen, drives disease [32].

However, evidence since the 1990s has highlighted the role of immunosuppression in sepsis. Studies indicated that impaired cytokine production and immune dysfunction are associated with poor outcomes, suggesting that immunosuppression may be a primary response rather than merely compensatory. Current theories propose a progression from initial hyperinflammation to subsequent immunosuppression, both of which contribute to sepsis pathophysiology. Hotchkiss et al. described two hypotheses: early mortality results from a “cytokine storm,” whereas late mortality may result from persistent immunosuppression or ongoing innate immune-driven inflammation [33].

Sepsis-3 redefined sepsis as a “dysregulated host response to infection,” replacing the older SIRS-based definition, though the exact mechanisms of dysregulation remain unclear (Feng et al., 2025). Additional emerging concepts include endothelial injury, mitochondrial dysfunction, and cell death via apoptosis, pyroptosis, or ferroptosis, which are still in preclinical research stages. Their therapeutic potential

depends on future studies using well-designed animal models that better replicate clinical sepsis [34].

Management

Survival rates in sepsis have improved over the past four decades, but no targeted molecular therapy exists beyond antibiotics, and trials of biologic agents have largely failed. This summary focuses on acute sepsis management outside critical care settings [35].

Resuscitation

Immediate resuscitation of septic patients mirrors that of non-septic cases. Oxygen should maintain saturations above 95%. Intravenous saline is standard, with a 500 mL bolus over 15 minutes for hypotension, adjusted based on response. Starch-based fluids should be avoided, and albumin is not routinely recommended. Persistent hypotension may require critical care admission and vasopressors, with noradrenaline as first-line therapy [36].

Prompt and appropriate antimicrobial therapy

Rapid administration of antimicrobials targeting likely pathogens improves outcomes, ideally within one hour of admission. Blood cultures should be obtained beforehand to guide subsequent therapy [37].

Accurate fluid balance

Monitor all fluid intake and urine output; urinary catheters may be used when necessary.

Blood glucose

Hyperglycemia should be managed with intravenous insulin to maintain blood glucose below 10 mM; tighter control is contraindicated [38].

Source control

Identifying and treating the source of infection is essential. This may involve imaging, drainage of effusions, debridement of infected tissue, or surgery for abscesses. In ~25% of cases, no source is identified, but timely intervention remains critical [35].

Infections in Patients Undergoing Hemodialysis

Infection is a major cause of morbidity and mortality among hemodialysis patients, ranking as the second leading cause of death globally and the foremost cause during the first year of dialysis in Japan. It accounts for roughly 30% of hospitalizations in the U.S. Hemodialysis patients are particularly susceptible to bloodstream infections (BSIs) due to impaired immunity, comorbidities, malnutrition, and repeated vascular access interventions, with central venous catheters posing the highest risk compared to arteriovenous grafts or fistulas. Chronic dialysis patients are also vulnerable to multidrug-resistant nosocomial pathogens, primarily Gram-positive bacteria, but Gram-negative infections remain a critical concern given limited therapeutic options, contributing to increased morbidity, mortality, and healthcare costs [39].

Definitions of Catheter-related bacteremia

Catheter-related bacteremia is characterized by a positive blood culture from the catheter, with or without a corresponding positive peripheral blood culture, accompanied by systemic infection symptoms and the absence of an alternative infection source [40]

Incidence of bacteremia in hemodialysis patients

The occurrence of bacteremia in hemodialysis cases is significantly greater compared to in the general population. Community-based cohort research in Denmark revealed that the frequency of bacteremia was 13.7 per 100 person-years among hemodialysis cases, compared to 0.53 per 100 person-years in the general population [41].

In the Dialysis Outcomes & Practice Patterns Study (DOPPS), the adjusted relative risks of mortality were 2.84 for Europe & 3.78 for the United States in comparison to Japan, although it was hypothesized that this discrepancy may be due to the non-participation of all dialysis facilities in Japan in the research. The infection-related mortality rate in Japan was approximately eighteen percent, surpassing that of North America & aligning with figures from Europe & Australia/New Zealand in the DOPPS. Alternative reasons of death might influence the disparity in death rates. [42].

Etiology

Bloodstream infections (BSIs) in hemodialysis patients are predominantly caused by Gram-positive bacteria, with *Staphylococcus aureus* and *Staphylococcus epidermidis* being the most frequently isolated pathogens, consistent with prior studies [21].

BSIs can be classified as exogenous, arising from contaminated dialysis fluids or equipment, or endogenous, originating from bacteria on or within the patient. Exogenous infections are often linked to lapses in dialyzer reprocessing, contaminated water, or tainted prescription vials [43]. Endogenous infections are particularly common in catheterized patients, with bacteria entering via extra-luminal (skin-related) or intra-luminal (hub-related) pathways, often involving

adhesion to host proteins or catheter surfaces (*S. aureus* binds fibrinogen, coagulase-negative staphylococci attach directly) [44].

A major challenge in catheter-associated infections is biofilm formation within the catheter lumen, which renders bacteria 100–1,000 times less susceptible to antibiotics and increases resistance to antimicrobial measures. As a result, catheter removal is often the only effective intervention, emphasizing the importance of preventing colonization [45].

Risk Factors

Dialysis patients are highly susceptible to infections due to immunosuppression, repeated vascular access, and factors such as diabetes, low albumin, and low hemoglobin, which further increase the risk of bacteremia and compromise infection-related survival [46]

Hospital Exposure

Hospitalization is common among hemodialysis patients, with 1.88 hospitalizations per patient-year, and recent hospital stays are linked to increased multidrug-resistant organism (MDRO) prevalence, including MRSA and VRE. This may result from in-hospital acquisition or reflect greater illness severity, with evidence supporting patient-to-patient transmission in hospital settings [47].

Dialysis Facility Exposure

MDRO transmission can also occur within dialysis facilities via direct or indirect contact with contaminated environments, equipment, or healthcare workers. MRSA carriage among staff ranges from 2.8–11.6%, though their role in transmission is unclear. Environmental contamination with VRE and MDR bacteria is prevalent on chairs, machines, and healthcare worker gowns, highlighting the facility as a potential source of MDRO exposure [48].

Risk Factors for Establishment of Colonization or Development of Infection following Exposure to MDROs

Antibiotic Exposure: Frequent antibiotic use in dialysis patients, particularly those with transient central venous catheters, increases MDRO colonization and infection risk (Atta et al., 2001).

Type of Vascular Access: Central venous catheters (CVCs) carry a 12–57 times higher infection risk than fistulas, increasing susceptibility to MDROs due to more frequent hospitalizations and antibiotic exposure [49].

Role of Vascular Access as a Risk Factor for Infections in Hemodialysis: Non-AVF access, including CVCs and arteriovenous shunts, is the primary source of infections, with AVFs showing the lowest infection rates [50].

Site of Catheter Insertion: Catheter placement influences infection risk; subclavian sites are preferred over internal jugular or femoral veins to reduce infection and thrombosis risk, while femoral catheters may be considered in specific pediatric cases [51].

The mechanism of infection in hemodialysis catheters.

Bloodstream infections from intravascular devices occur via four main routes: skin insertion site invasion, catheter hub contamination, hematogenous spread, or infusion of contaminated fluids, with the first two being the most significant [52].Skin and hub contamination involve the patient's flora and exogenous flora from healthcare workers, with coagulase-negative staphylococci and *Staphylococcus aureus* predominating from the skin, and nosocomial pathogens entering via the hub [53].

Biofilm formation occurs within 24 hours of catheter insertion. Short-term devices (<10 days), such as peripheral IVs and uncuffed central lines, are mainly colonized on the external surface. In long-term devices (>30 days), like tunneled central lines, PICCs, and subcutaneous ports, intraluminal colonization predominates. These distinctions inform preventive strategies for catheter-related infections[53].

Diagnosis of Catheter-related blood stream infection (CRBSI)

Catheter-related bloodstream infections (CRBSIs) in dialysis patients may present with localized signs, subclinical bacteremia or fungaemia, or vascular access thrombosis and dysfunction, with diagnostic confirmation requiring blood cultures from peripheral veins, catheter tips, or both, while 111Scintigraphy can aid in subtle cases. Prevention strategies include regular surveillance for *S. aureus* with intranasal mupirocin, prioritizing autologous arteriovenous fistulas over catheters or grafts, strict hand hygiene and contact precautions to prevent pathogen transmission, judicious antibiotic use to reduce resistance, and targeted antimicrobial prophylaxis, particularly single-dose vancomycin in MRSA-colonized patients [54].

Antibiotic lock for hemodialysis catheter

Antibiotic locks using agents such as minocycline, gentamicin, cefotaxime, and vancomycin, as well as antiseptics like taurolidine and citrate, have been shown to significantly reduce CRBSI in hemodialysis catheters, though efficacy varies by agent [55]. Despite this, CDC guidelines do not recommend routine use of antibiotic locks, limiting them to patients with long-term catheters who experience recurrent CRBSIs despite strict aseptic practices, due to risks of toxicity, allergic reactions, and antimicrobial resistance[51].

Table 1: Antibiotic concentrations applied in locks. [56]

	Dosage (milligram per milliliters)	Heparin or saline, international unit per milliliters
Vancomycin	2.5	2500 or 5000
Vancomycin	2.0	10
Vancomycin	5.0	0 or 5000
Ceftazidime	0.5	100
Cefazolin	5.0	2500 or 5000
Ciprofloxacin	0.2	5000
Gentamicin	1.0	2500
Ampicillin	10.0	10 or 5000
70% ethanol		0

Topical antibiotics

Topical antibiotics, such as mupirocin and polysporin triple antibiotic ointments, applied to catheter exit sites significantly reduce CRBSI in hemodialysis patients. Polysporin reduced bacteremia risk by 60% and mortality by 78%, while mupirocin decreased CRBSI incidence by 85%. However, rapid emergence of resistant *S. aureus* and coagulase-negative staphylococci has been reported, and CDC guidelines recommend topical antibiotic use only in hemodialysis patients [57].

Antibiotics/antiseptics coated catheters

Catheters coated or impregnated with antibiotics or antiseptics have shown potential in reducing catheter-associated bacteremia [41].

Contact Precautions

Infection control measures aim to reduce pathogen transmission via horizontal interventions (hand hygiene, environmental cleaning) or vertical interventions targeting specific pathogens, such as contact precautions for MDRO-colonized patients. Contact precautions involve gowns, gloves, and spatial separation. However, healthcare worker attire is often contaminated during dialysis care, and the effectiveness of contact precautions in this setting is limited by open layouts and patient interactions. Some reports indicate reduced MDRO transmission following implementation, but lack control groups, limiting assessment of true impact [58].

Decolonization

Decolonization therapy in hemodialysis patients, primarily targeting *S. aureus*, uses topical agents (intranasal mupirocin, chlorhexidine washes), systemic antibiotics, or a combination to reduce nasal carriage, with most studies focusing on MSSA and showing substantial but often transient reductions **(Calfee, 2013)**. Empirical treatment of suspected vascular access infections should begin after obtaining blood and pus cultures, typically with vancomycin plus an anti-Gram-negative agent, and be adjusted based on antibiogram results. Vancomycin remains standard for MRSA, while linezolid or quinupristin/dalfopristin can treat VRE, VISA, and MRSA. Treatment duration is generally at least four weeks for *S. aureus* and three weeks for other pathogens. Management of infected synthetic grafts usually requires removal due to relapse risk, whereas autologous arteriovenous fistulas may be treated conservatively. In select cases, parenteral antibiotics, subtotal graft excision, or vacuum-assisted therapy can preserve access while treating infection [59].

Treatment of catheter related bacteremia

The management of catheter-related bloodstream infections (CRBSI) in hemodialysis patients involves systemic antibiotics and addressing the infection source, with catheter removal considered essential [56]. Empirical therapy typically includes vancomycin plus coverage for Gram-negative rods, guided by local antibiograms. When vascular access is limited, catheters may be retained with antibiotic lock therapy or guidewire exchange. Meta-analyses show higher cure rates with antibiotic locks or guidewire exchange compared to systemic antibiotics alone, particularly for *S. aureus* infections, where guidewire exchange is most effective[60]. Guidelines recommend systemic antibiotics and catheter removal for infections caused by *S. aureus*, *P. aeruginosa*, or *Candida*, reserving guidewire

exchange only when no alternative access site is available [41].

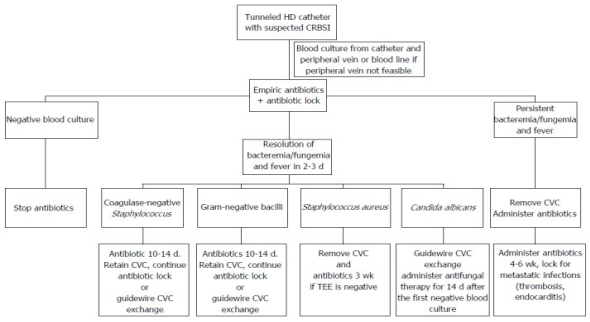

Figure 2: Catheter-related blood stream infection among patients who are having hemodialysis with tunneled catheters. TEE: Trans esophageal echocardiograph; CRBSI: Catheter-related blood stream infection; CVC: Central venous catheter; HD: Hemodialysis. [41]

Patterns of microbial resistance in bloodstream infections of hemodialysis patients

Antimicrobial resistance, though a natural phenomenon, has become a major public health threat due to factors such as excessive antibiotic use, poor hygiene, inadequate infection control, environmental contamination, and use in agriculture [61]. Initially thought manageable with new drugs like methicillin and vancomycin, bacteria have since evolved diverse resistance mechanisms, prompting the WHO in 2017 to classify twelve high-risk bacterial families into critical, high, and medium priority based on the need for new antibiotics. Critical-priority pathogens—including *Pseudomonas*, *Acinetobacter*, and multidrug-resistant Enterobacteriaceae—cause severe infections in hospitals and device-dependent patients, while high-priority bacteria like *Enterococcus faecium* and *Staphylococcus aureus* show resistance to key antibiotics, and medium-priority organisms such as *Streptococcus pneumoniae* remain mostly treatable with existing therapies [62].

The Mechanisms by Which Antimicrobial Resistance Is Steadily Increasing?

Antimicrobial resistance (AMR) is a natural process in which microorganisms become unresponsive to previously effective antibiotics, complicating treatment and increasing the risk of severe infections and mortality [63]. AMR can be intrinsic, where bacterial species naturally resist certain antibiotic classes (e.g., *E. coli* to vancomycin, *Pseudomonas aeruginosa* to ampicillin and early-generation cephalosporins), or acquired through mutations or DNA transfer [64].Acquired resistance spreads vertically to progeny or horizontally via transformation, transduction, and conjugation, enabling bacteria to rapidly share resistance genes within and between species [65].

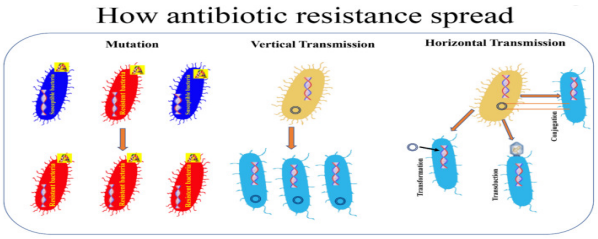

Figure 3: How antibiotic resistance spread. Bacterial resistance towards antibiotics may be natural, or acquired via horizontal or vertical transmission. A: antibiotic. [64]

How Bacteria Acquire Resistance

The fast spread of antimicrobial resistance in bacterial populations cannot be ascribed to a singular mechanism. It frequently arises from intricate procedures. Consequently, it is essential to subdivide antibiotics into groups according to their different mechanisms of action prior to examining the variables influencing resistance to these molecules. This review focuses on the classes of antibiotics most directly associated with the occurrence of antibiotic resistance. [66]

Table 2: Mode of action & resistance mechanisms of antibiotics. [67]

Antimicrobial Groups	Mechanism of Action	Resistance Mechanism
β-Lactams Penicillins	Suppress cell wall production	Beta-lactamase production Penicillinase

Cephalosporins Carbapenems		Cephalosporinase Carbapenemase
β-Lactamase inhibitors	Block the activity of beta-lactamase enzymes	Extended-spectrum beta-lactamase (ESBL)
Aminoglycosides, Chloramphenicol Macrolides, Tetracyclines	Suppress ribosome assembly through binding to the bacterial 30S or 50S (Suppress synthesis protein)	Multifactorial (enzymatic modification, target location modification & efflux pumps)
Fluoroquinolone	Suppress DNA replication	Multifactorial (efflux pumps, target-site gene mutations & modifying enzyme)
Sulfonamides & trimethoprim	Suppress metabolism of folic a`	Horizontal spread of resistance genes, mediated via plasmids &transposons, expressing drug-insensitive variants of the target enzymes.

Resistance genes on mobile elements allow bacteria to spread quickly, such as colistin resistance via ISKpn25 modifying the *mgrB* gene, often alongside plasmid-borne carbapenemases like KPC. This creates strains resistant to both carbapenems and colistin[68]. In hemodialysis patients, colonization with multidrug-resistant organisms (MDR) greatly increases the risk of systemic infections with limited treatment options, raising morbidity and mortality two- to five-fold compared to susceptible strains. Preventing colonization and infection is critical, including screening and decolonization at nasal and catheter sites [69].

In Ethiopia, both Gram-positive and Gram-negative bacteria show high antimicrobial resistance, with 47–72% of isolates being multidrug-resistant. *S. aureus* showed 87.6% resistance to penicillin and 61.1% to oxacillin, while *K. pneumoniae* showed 61.1% resistance to trimethoprim-sulfamethoxazole and 53.7% to meropenem. Carbapenem-resistant *K. pneumoniae*, reaching 63.6% in Spain, is especially concerning due to limited treatment options and potential gene transfer, highlighting the need for infection prevention and antimicrobial stewardship [70].

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