**A review on Antibiotic Resistance in Chronic kidney disease (CKD) Patients undergoing dialysis**

  **Abstract**

Antibiotic resistance is a worldwide health threat, especially within high-risk groups, including chronic kidney disease (CKD) patients who are on dialysis. These patients are at high risk for developing the infections because of altered immunity, frequent contact with healthcare facilities, and invasive procedures and owing to these nosocomial infections these patients suffer from additional challenges. The overuse and misuse of antibiotics in this population additionally increases their risk of multidrug-resistant (MDR) infections, which place notable challenges on clinical management. This review aims to identify the burden and consequences of antibiotic resistance among CKD patients on dialysis, with an emphasis on need for robust infection control measures especially at healthcare setups, targeted surveillance programs, and innovative approaches to mitigate this life threatening antibiotic resistance in CKD patients undergoing dialysis. By addressing these challenges, this review aims to provide a comprehensive understanding of the issue and identify possibilities for improving the health outcomes in these high-risk groups.

**Keywords**: MDR, CKD, High risk, Mitigate, Antibiotics

**Introduction**

The definition of chronic kidney disease is revised several times but CKD is like a syndrome defined as persistent alterations in kidney structure function and both related to individuals health(Aloy et al., 2020). It involves gradual loss of kidney functions and kidney fails to perform its proper functions like filtration and removal of wastes and toxic substances. The glomerular filtration rate (GFR) decreases because the serious effect on the function of kidney. The failure of kidney function is caused by the structural changes include cysts, tumors, malfunctioning, atrophy of nephrons(Santra, Agrawal, Kumar, & Mishra, 2015).

The renal dysfunction can be caused by several factors like hypertension, edema, diabetes, toxic substances signed by increased serum creatinine level or blood urea nitrogen level The Kidney Disease Improving Global Outcomes (KDIGO) initiative classifies an individual as having CKD if abnormalities of kidney structure or function persist for more than 3 months (Eyler & Shvets, 2019). KDIGO describes a classification of severity, defining numerous stages of CKD on the basis of glomerular filtration rate (GFR; either estimated (eGFR) or measured (mGFR)) and the extent of albuminuria (Farag, Garg, Li, & Jain, 2014).GFR and albuminuria are used to classify CKD because GFR is a well-established marker of renal excretory function and albuminuria is an indicator of renal barrier dysfunction (glomerular injury). Both have been found to be reliable predictors of long-term CKD outcomes(Ma et al., 2014). Hence, we can classify on which level a patient of CKD has been reached. Furthermore, the KDIGO categories describe the risk of progression of CKD to kidney failure that is called end-stage renal disease (ESRD). CKD leads too many abnormalities of cardiovascular system and mainly kidney itself lead to the disturbance in the filtration of blood which prove very fatal to all the organs as the level of toxins increased in body(Vilay, 2019). The ckd is the major cause of renal fibrosis renal fibrosis, characterized by tubulointerstitial fibrosis and glomerulosclerosis, is the final manifestation of chronic kidney disease. Renal fibrosis is characterized by an excessive accumulation and deposition of extracellular matrix components (Falcone et al., 2020).

**Pathophysiology leading to CKD**

Nephron loss is one of the leading causes of the CKD. Nephrons are generated in weeks 12–36 of gestation in humans, with a mean of 950,000 nephrons per kidney (with a range of ~200,000 to >2.5 million) (Pea, 2018). No new nephrons can be generated after this period. During growth, the available nephrons can increase in size to accommodate increased renal demands. Furthermore, GFR decreases with age .with the time load the activity of nephron is increased impaired glomerular filtration (Arnold, 2017). Angiotensin II production and mechanistic target of rapamycin (mTOR) signaling maintain persistent podocyte hypertrophy and glomerular hyper filtration and ultimately aggravates podocyte loss and proteinuria. Angiotensin II is a peptide hormone that is part of the renin–angiotensin system (RAS) that drives vasoconstriction and aldosterone secretion (and, therefore, sodium retention and an increase of blood pressure)(Heringa, Floor-Schreudering, De Smet, & Bouvy, 2017). Aldosterone, in turn, directly impairs the glomerular barrier sieving function, possibly by inhibiting expression of the podocyte protein nephron, which is a structural component of the slit diaphragm necessary for maintaining the glomerular filtration barrier53 (Cattaneo, Falcone, Gervasoni, & Marriott, 2022). Angiotensin II possibly also contributes to the deregulated response of progenitor parietal epithelial cells along Bowman’s capsule, generating FSGS lesions instead of replacing lost podocytes54 (Gharbi et al., 2019). This structural remodeling of the glomerulus presents clinically as proteinuria, which is a marker of nephron damage and is predictive of CKD progression (defined as a GFR decline of >5ml/min/1.73m2 per year or sevenfold the normal rate of loss with ageing. Fibrosis. Nephron loss involves nonspecific wound-healing responses that include interstitial fibrosis(Sartelli, 2021). Infiltrating immune cells, albuminuria and, in diabetes, glycosuria, activate proximal tubular epithelial cells, resulting in the secretion of proinflammatory and profibrotic mediators that promote interstitial inflammation and fibrosis57. Interstitial fibrosis seems to drive further nephron injury through the promotion of renal ischaemia57, but as in other organs scar formation might also mechanically stabilize the remaining nephrons58 (Esme, Topeli, Yavuz, & Akova, 2019). The increased tubular transport workload of remnant. In kidney hypo dysplasia, low nephron count and risk of CKD69–71. Aside from CAKUT, ciliopathies, cystic kidney diseases, tubulopathies and podocytopathies can cause CKD68, 70–72. Genetic testing has revealed that ~20% of early-onset CKD (defined as CKD manifesting before 25 years of age) can be attributed to a monogenic cause72 (Miranda et al., 2022). Until recently, monogenic causes of CKD were mostly reported in children or adolescents, but genetic variants also contribute as cofactors to CKD progression in adults .For example, an uromodulin (UMOD) gene variant, present in 17% of the alleles in the general population, is associated with developing CKD73 (Vacaroiu et al., 2022). Another example is gene variants of Apo lipoprotein L1 (APOL1) in African Americans, which confer resistance to Trypanosome brucei infections in sub-Saharan Africa74 but affect endosomal trafficking and autophagic flux(Jamil et al., 2016). In the presence of additional inducers of kidney injury (the nature of which remains unclear), these APOL1 variants promote podocyte loss, glomerulosclerosis, nephron loss and CKD progression75. Obesity. A larger glomerular size in moderately obese patients (Montoya-Urrego, Velasco-Castaño, Quintero Velez, & Jiménez Quiceno, 2023).

**Treatment of CKD**

CKD is a major public health problem nowadays with great expenses. Over the past some decades it became one of the prevailing problem because of poor lifestyle, hypertension and exposure of toxic substances (Khwaja, El Kossi, Floege, & El Nahas, 2007). First of all the treatment of ckd involves changes in life style which keeps us active and healthy and maintains the health of nephrons and kidney. The food which is good for kidney include fish, root vegetables, beans ,seeds, whole grains, herbs and eggs along with pomegranate and avocado(Levin et al., 2008). Exercise and morning walk is a good source of health update. Then medicine therapy is also an important factor to get control diabetes, hypertension and high cholesterol levels. Then if the CKD is getting worse we have two options of treatment including dialysis which may be necessary in end stage kidney failure and kidney transplant. The dialysis can be done by two ways ne is hemodialysis and peritoneal dialysis(Davison et al., 2019).

Aliskiren, a renin inhibitor, was emerged as a highly promising treatment for chronic kidney disease (CKD), demonstrating a substantial reduction in albuminuria compared to a placebo in patients with type 2 diabetes and nephropathy who were also receiving losartan therapy(Ruiz-Ortega, Lamas, & Ortiz, 2022). However, recent findings from a trial investigating aliskiren in combination with RAS inhibitors in individuals with type 2 diabetes and renal impairment have dampened the initial optimism surrounding this novel drug. Managing high blood pressure is crucial for preventing and slowing the progression of chronic kidney disease (CKD)(Wanner & Tonelli, 2014). Blood pressure control remains essential at all stages of CKD and serves as the foundation of renal and cardiovascular protective therapy. Agents that block the renin-angiotensin-aldosterone system (RAAS), such as ACE inhibitors (ACEi) and angiotensin receptor blockers (ARB), are the first-line treatment, given their proven ability to lower albuminuria and provide Reno protection(Chen, Knicely, & Grams, 2019).

RAAS plays a significant role in the progressive loss of organ function in CKD patients. Numerous randomized controlled trials and meta-analyses have demonstrated that RAAS inhibition protects both renal and cardiovascular health(Arici, 2014). This has led to the hypothesis that intensified RAAS blockade could offer enhanced protection against major adverse renal and cardiovascular outcomes. Following this approach, combinations such as ACEi and ARB or ACEi/ARB with direct renin inhibitors (DRIs) have been explored. Dual therapy has shown greater efficacy than monotherapy in reducing urinary albumin excretion and blood pressure(Vassalotti et al., 2016). The Reno protective effects of RAAS inhibitors have been validated across diverse types of renal diseases, including diabetic nephropathy, hypertensive nephrosclerosis, and non-diabetic nephropathies. Since lowering albuminuria slows the progression of renal function loss, it should be considered a distinct therapeutic target in CKD management. Additionally, lipid-lowering treatments have demonstrated cardiovascular benefits in CKD patients, further supporting a comprehensive approach to protecting kidney and cardiovascular health(Koncicki, Unruh, & Schell, 2017).

Inhibiting sodium-glucose transport has emerged as a novel approach to achieving glycemic control. Sodium-glucose co-transporter 2 (SGLT-2) inhibitors work by reversibly blocking the SGLT-2 protein found in the proximal tubule of the kidney(D’Alessandro et al., 2016). Under normal physiological conditions, this transporter facilitates the nearly complete reabsorption of glucose to maintain appropriate glucose levels. By inhibiting SGLT-2, these drugs enhance urinary glucose excretion while reducing fasting plasma glucose and HbA1c levels. Emerging evidence highlights the critical role of vitamin D in maintaining renal and cardiovascular health(Shah, Kalantar-Zadeh, & Kopple, 2015). Individuals with chronic kidney disease (CKD) tend to have lower vitamin D levels compared to healthy individuals. Observational studies have shown that CKD patients treated with vitamin D receptor activators experience improved survival outcomes compared to those who remain untreated. One proposed mechanism behind the antiproteinuric effects of vitamin D receptor agonists, such as paricalcitol, is their ability to inhibit renin activity(de Boer et al., 2020). Additionally, new drugs are being developed to slow the progression of renal disease by targeting pathways downstream of proteinuria. For instance, pirfenidone, a TGF-β inhibitor, has demonstrated potential in reducing renal function decline. However, its safety profile is a concern, especially in diabetic patients, due to a high rate of treatment discontinuation in studies(Nakayama, Kabayama, & Miyazaki, 2024).

High blood pressure and albuminuria, key risk factors for cardiovascular and renal complications, are closely linked to low-grade inflammation. Growing evidence highlights the role of inflammation in CKD progression, offering potential new targets for treatment. One such anti-inflammatory agent, bindarit, inhibits monocyte chemo attractant protein-1 (MCP-1) and has shown promise in slowing renal disease progression and improving survival in murine lupus models(Levin et al., 2024). (1,3) The endothelin system is persistently activated in nephropathy, with endothelin binding to ETA receptors causing vasoconstriction, sodium retention, podocyte dysfunction, and subsequent glomerular damage, proteinuria, and renal decline. Blocking ETA receptors presents a potential strategy to reduce renal complications. Additionally, endothelin's interaction with tubular proteins may contribute to renal fibrosis(Elkeraie et al., 2024). Monocyte chemo attractant protein-1 (MCP-1), a powerful cytokine, is crucial in triggering and maintaining chronic inflammation in renal tissues. It stimulates the activation of monocytes, macrophages, and other pro-inflammatory cytokines. Evidence suggests that inhibiting MCP-1 can lower albuminuria and enhance long-term renal function(Samal et al., 2024).

**Dialysis**

Dialysis is the process of removing waste and excess water from the blood, serving as an artificial substitute for kidney function, particularly in cases of renal failure. While dialysis cannot fully replicate the kidneys' functions, it partially manages them through diffusion and ultrafiltration(Himmelfarb, Vanholder, Mehrotra, & Tonelli, 2020). This procedure becomes necessary in chronic renal failure (CRF) when the glomerular filtration rate drops below 15 ml/min/1.73m². Dialysis can be performed through two methods: hemodialysis, which uses a machine or artificial kidney-like device, and peritoneal dialysis, which employs the peritoneal membrane as a filter(Cozzolino et al., 2018). The core mechanism of dialysis involves the diffusion of solutes across a semipermeable membrane. Metabolic waste products like urea and creatinine move down their concentration gradients from the blood into the dialysate. However, patients undergoing dialysis, especially during the first three months of hemodialysis, face a high mortality rate(P. K.-T. Li et al., 2017). Hypotension, often caused by ultrafiltration-induced volume depletion, is the most common complication during dialysis. Other adverse effects include hypersensitivity reactions, ranging from mild itching and hive to severe anaphylactic shock. These reactions may result from allergies to ethylene oxide, used for sterilizing the dialyzer, or from sensitivity to certain membrane materials like polyacrylonitrile. Notably, polyacrylonitrile-related reactions are more common in patients using angiotensin-converting enzyme (ACE) inhibitors(Bello et al., 2022).

When prescribing for dialysis patients, it is crucial to determine whether a drug undergoes renal clearance and if dose adjustments are necessary. Adjustments can involve lowering the dose, extending the dosing interval, or combining both strategies. The key factors influencing dose modification in dialysis patients are the drug’s renal clearance and therapeutic index(Neves, Sesso, Thomé, Lugon, & Nascimento, 2021). Dialysis patients experience extracorporeal clearance of small molecules, including many medications. Hemodialysis, being intermittent, can lead to relatively rapid drug clearance, posing challenges, particularly for once-daily medications like antibiotics. In contrast, peritoneal dialysis offers slower and steadier clearance, making timing less critical. Pain management in dialysis patients is often inadequate(N. Chen et al., 2019). Paracetamol is the preferred simple analgesic due to its safety and lack of dose adjustment requirements. Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided despite reduced nephrotoxicity concerns, as they can cause sodium retention, hypertension, and gastrointestinal side effects. For severe pain, hydromorphone is recommended as it is 5–7 times more potent than morphine, requiring low starting doses (0.5–1 mg orally every 6 hours)(Htay et al., 2018). Antibiotics frequently require dose adjustments for dialysis patients. Significant dose reductions are necessary for quinolones, sulfamethoxazole-trimethoprim, glycopeptides, and aminoglycosides. Cephalosporins and penicillins, having broader therapeutic indices, vary in their adjustment needs. For diabetic patients on dialysis, reduced insulin clearance increases the risk of hypoglycemia with insulin and insulin secretagogues (sulfonylureas). Gliclazide and glipizide are the preferred sulfonylureas because of their short half-lives and lack of active metabolites(Masakane et al., 2015).

**Kidney Failure**

Chronic kidney disease (CKD) involves the gradual decline of kidney function, eventually progressing to chronic kidney failure (CKF), which is traditionally classified as mild, moderate, or severe(Tangri et al., 2011). A global consensus now categorizes CKF into five stages based on glomerular filtration rate (GFR) and signs of kidney damage. Stage 5 represents complete kidney failure, where the kidneys can no longer maintain homeostasis, leading to a metabolic state incompatible with life. While dialysis helps reduce metabolite accumulation, it can deplete critical metabolic regulators and induce chronic inflammation, contributing to secondary complications such as atherosclerosis, cardiovascular disease, malnutrition, anemia, and renal bone disease(Ortiz et al., 2014). These issues significantly worsen the prognosis and quality of life for CKF patients while increasing treatment costs. Early diagnosis and effective management of CKD, including its complications, can improve patient outcomes. Treatment strategies include maintaining consistent blood pressure control, preventing malnutrition, anemia, and hyperparathyroidism, and addressing metabolic disorders. Preservation of kidney function can be supported through non-pharmacological measures like dietary and lifestyle modifications, alongside CKD-specific pharmacological treatments(Grams et al., 2016). Medications that modulate intrarenal hemodynamics, such as renin-angiotensin-aldosterone system (RAAS) inhibitors and SGLT2 inhibitors, help protect kidney function by reducing intraglomerular pressure independently of blood pressure and glucose control. Additionally, newer agents like non-steroidal mineralocorticoid receptor antagonists may offer kidney protection through anti-inflammatory and antifibrotic effects(Hallan & Orth, 2011).

**Nosocomial infections**

Nosocomial infections, also called hospital-acquired infections or HAIs, are those infections the patients acquire during their stay in a health care facility which at admission time were neither present nor incubating. The typical presentation of these infections occurs after 48 hours following admission but may occur even after discharge when related to hospitalization(Kollef, Torres, Shorr, Martin-Loeches, & Micek, 2021). Criteria for nosocomial infection definition are broad and tend to focus on identifying infections attributable to healthcare interventions or the hospital environment. Nosocomial infections have significant implications in public health because they rank high among the factors contributing to increased morbidity, mortality, and healthcare costs worldwide(Khan, Ahmad, & Mehboob, 2015). Such infections also target patients whose underlying conditions require prolonged hospital stays and inserted invasive medical devices. The problem of nosocomial infections contributes to antimicrobial resistance issues, which is a factor that complicates treatment and challenges infection control measures. For instance, the SDNI has shown that the definitions cannot be standardized since differences would impact surveillance, reporting, and management practices. Such nosocomial infections are a real cause to make constant efforts in finding ways to develop effective prevention, control, and surveillance programs that will improve patient safety and healthcare outcomes(Edwardson & Cairns, 2019).

 Nosocomial infections are a significant challenge to the healthcare systems in many regions of the world since their rates vary with different regions, healthcare settings, and populations. A nosocomial infection hits millions of patients every year; however, the critical care area, or ICU, becomes a specific hotspot due to critical patient conditions and the repeated use of invasive devices(Khan, Baig, & Mehboob, 2017). Nosocomial infections formed significant percentages of cases in ICUs, which include ventilator-associated pneumonia, bloodstream infection, and catheter-associated urinary tract infection. Studies on Italian ICUs reported infection rates as high as 20%, mainly attributed to the length of time that patients have to spend in the hospitals, this includes mechanical ventilation, and their immunity is compromised. Nosocomial infections, in general, have an overall prevalence between 5% to 15%, depending on the healthcare infrastructure, infection control practices, and the resources available(Trubiano & Padiglione, 2015).

Specific pathogens are associated with these infections, including such bacterial agents like Escherichia coli, Staphylococcus aureus and Klebsiella pneumonia. Fungal pathogens, especially Candida species, are very much linked to current reports; such infections have particularly been seen in immunocompromised patients and also on admission into high-risk ICU settings(Ramasethu, 2017). Nosocomial fungal infections have mainly brought about diagnostic and therapeutic challenges because of high mortality rates. Regional differences in nosocomial infections are associated with disparities in surveillance and reporting and healthcare resource utilization. Nosocomial infections have, undoubtedly, been linked with resistance to antimicrobial agents in all regions, further complicating their treatment, thus vindicating the requirement for strict infection control policies(Y. Li et al., 2017).

Nosocomial infections remain one of the biggest challenges to global healthcare, for prevalence rates in regions and healthcare settings leave much to be desired. A systematic review and meta-analysis about the world prevalence of nosocomial infections indicated a general pooled prevalence of 15.5% and influences are brought under a limelight patient care; the rates depend on factors such as the strength of healthcare infrastructure, infection control practice, and socioeconomic conditions of the region(Xia, Gao, & Tang, 2016). Specific studies demonstrate national and institutional differences that add emphasis to the complexity of the concern. For instance, in Switzerland, it was documented that the nosocomial infections prevalence among four university hospitals stands at 11.6% in which urinary tract infections were reported as the most frequent one. The prevalence rates in Norway during 2002 and 2003 were reported to be at 5.1% and 6.0%, respectively, and this rate had been significantly lower than the global averages because of strict infection control measures(Du et al., 2021). In developing countries, the burden is usually significantly higher because of the scarceness of resources for infection prevention and control. For instance, a prevalence rate of 9.1% was reported in Thailand indicating a need to improve hospital hygiene practices and surveillance systems. In fact, earlier studies have pointed out the discrepancy between incidence and prevalence, indicating the need to distinguish accurate methodologies to evaluate the occurrence of nosocomial infections(Mbim, Mboto, & Agbo, 2016).

Nosocomial infections commonly referred to as hospital-acquired infections (HAIs), can be broadly categorized in a variety of ways: by site of infection, causative pathogen, healthcare intervention involved, or by more sophisticated predictive methods. The most common method of categorization is by site-based and includes UTIs, SSIs, respiratory infections such as ventilator-associated pneumonia (VAP), BSIs, gastrointestinal infections such as Clostridioides difficile, and skin or soft tissue infections(Mbim et al., 2016). Invasive treatments in the intensive care setting are often at the heart of device-associated infections, such as catheter-associated urinary tract infections (CAUTIs), central line-associated bloodstream infections (CLABSIs), and procedure-related infections(Busl, 2017). Pathogen-based classification places infections into various categories based on the type of microorganism causing the infection. Bacterial infections are the most common, primarily caused by Escherichia coli, Staphylococcus aureus (including MRSA), and Klebsiella pneumoniae. Fungal infections, mainly Candida species, are also rising, particularly in immunocompromised patients. Viral pathogens, including norovirus and respiratory syncytial virus (RSV), are also common pathogens, especially in neonatal and pediatrics(Liu & Dickter, 2020).
Modern trends in classification use advances made in artificial intelligence. Systems like neural networks and case-based reasoning relate clinical and lab values to predict and classify infection types, improving the chances of detecting infections and adjusting treatment appropriately. Predictive models can offer early detection of nosocomial infections, as well as predict the treatment outcome, showing great promise in improving patient management(Bardi et al., 2021). Nosocomial infections can be temporally classified into early-onset infections, that are acquired within the first 4-5 days after admission, typically from community-acquired pathogens, and late-onset infections, that occur thereafter, usually involving MDR organisms, making treatment more difficult. This multi-dimensional classification helps healthcare professionals identify risk factors, develop appropriate diagnostic methods, and apply targeted prevention and treatment(Zhou et al., 2020).

Nosocomial infections arise due to a convergence of microbial virulence, patient susceptibility, and healthcare interventions in the pathogenesis. The typical pathogens implicated in nosocomial infections include Staphylococcus aureus, Clostridioides difficile, Candida species, and gram-negative bacilli, including Escherichia coli and Klebsiella pneumoniae, which eventually lead to infection via adhesion to host tissues, biofilm production on medical devices, or production of toxins or enzymes degrading the host's defenses(Pezhman, Fatemeh, Amir, Mahboobeh, & Mohammad, 2021). Biofilms are very important because they protect pathogens from the host immune system and antimicrobial agents, making it difficult to treat infections. Nosocomial pneumonia is one such type of pathogenesis. VAP is caused due to the prolonged mechanical ventilation of patients that disrupts the mucous membrane and allows healthcare-associated pathogens to colonize the lower respiratory tract(Dasgupta, Das, Chawan, & Hazra, 2015). Direct entry into the lungs is often facilitated by the use of endotracheal tubes, typically causing extreme inflammation and infection. Moreover, overuse or misuse of broad-spectrum antibiotics may alter the patient's microbiome, thereby predisposing them to opportunistic pathogens such as Candida and Clostridioides difficile(Salmanzadeh et al., 2015).

Nosocomial infections arise from both patient vulnerabilities and healthcare interventions in collaboration with environmental factors. Immunosuppression, age extremes, and comorbidities such as diabetes and chronic respiratory conditions raise patient susceptibility to infections. Healthcare-related risks include invasive devices such as catheters, ventilators, and central lines that bypass the body's natural barriers and surgical procedures, particularly prolonged or complex ones, that predispose to infections(Grasselli et al., 2017). Overcrowding, non-adequate equipment sterilization, and low adherence to hand hygiene are environmental factors that increase transmission risks. In addition, antimicrobial resistance, which results from improper use of antibiotics, has created resistant microorganisms such as MRSA and VRE, making the treatment cycle complicated(Behnke et al., 2017).

Nosocomial infections are dramatically complicated by the problem of AMR, endangering the efficacy of treatment, engendering increased morbidity and mortality, and increasing healthcare cost. Infections with multi-drug resistant organisms are particularly difficult to treat owing to the fact that most of the organisms within critical care settings possess vulnerabilities that are readily exposed(Suleyman & Alangaden, 2016). Significant resistance has been reported among the nosocomial isolates in the study conducted at a teaching hospital in Goa. Even pathogens such as Escherichia coli and Klebsiella pneumoniae were found to be resistant against third-generation cephalosporins and aminoglycosides, which are primarily used for their treatment. Likewise, gram-negative bacteria, such as Pseudomonas aeruginosa and Acinetobacter baumannii, are also usually resistant to multiple classes of antibiotics, including carbapenems, thereby posing problems in the treatment of infections caused by such pathogens(Mancini et al., 2016).

Factors include large-scale misuse and overuse of broad spectrum antibiotics in critical care units, and this applies particularly to gram-negative bacilli, which have mechanisms, such as the production of beta-lactamase and efflux pumps, that make them resistant to antimicrobial action. There is a report of the same pattern as being similar to human disease through a review on AMR in veterinary critical care, and it also raises an interdisciplinary implication towards human and animal health. The impact of AMR in the nosocomial environment is profound: nosocomially-acquired antibiotic-resistant organisms spread in a hospital and into the environment, facilitating outbreaks. There consequently becomes a need for stewardship programs that promote judicious use of antibiotics, infection control measures, and follow-up of resistance patterns at all times to change the treatment regimen(Ghashghaee et al., 2018).

Nosocomial infections are a big clinical and economic burden and have often resulted in longer hospital stays, more morbidity and mortality. Most infections related to implantable biomaterials like central venous catheters and urinary catheters are complicated by bloodstream infections and catheter associated urinary tract infections. These infections prolong recovery and increase healthcare costs on account of extended treatment and more interventions that may be needed.
One of the most difficult nosocomial pathogens is Gram-positive bacteremia, primarily caused by Staphylococcus aureus and Enterococcus species. Of particular concern is the development of resistant strains, such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE), associated with potentially life-threatening delays in treatment and increased mortality(Abbasi, Aftab, & Chua, 2020). The confounding effect of superimposed antimicrobial resistance complicates treatment and makes it harder to manage infections and leads to poor outcomes. New interests have emerged with the reevaluation of older antibiotics, such as polymyxins and fosfomycin, to combat MDR bacterial infections. These agents are repurposed to counter the problem of resistance, especially when new antibiotics fail because of severe resistance mechanisms(Schweiger, Trevino, & Marschall, 2015). Careful selection, proper dosing, and suitable duration of antibiotic treatments help reduce resistance and protect the effectiveness of existing medications. Antibiotics are used in the treatment of nosocomial infections, and the choice is based on the pathogens, the anatomic site involved, and local trends in resistance. In general, for severe gram-negative infections such as Klebsiella pneumoniae and Pseudomonas aeruginosa, carbapenems, third-generation cephalosporins, and fluoroquinolones are used. For gram-positive pathogens, including methicillin-resistant Staphylococcus aureus (MRSA), vancomycin and linezolid are mainly used zinc(Ishigami & Matsushita, 2019).
However, excessive use of these antibiotics has increased resistance, especially within the intensive care area, where such infections are common, including those related to ventilator-associated pneumonia and bloodstream infections. It is evident from studies such as the national prevalence survey conducted in Germany that beta-lactams and glycopeptides are utilized predominantly in hospitals, which reflects their use in nosocomial infections. Ensuring the use of antibiotics is optimized through stewardship programs will ensure efficacy and not allow the emergence of multidrug-resistant organisms(Starzyk-Łuszcz, Zielonka, Jakubik, & Życińska, 2017).

The use of antibacterial in nosocomial infections does not lack challenges on the clinical and operational fronts. Poor use of antimicrobial therapy is one of the concerns, including inappropriate choice, dosing, or timing, often resulting in bad outcomes for patients, long hospital stays, and higher mortality rates. Multidrug-resistant pathogens such as Klebsiella pneumoniae and Acinetobacter baumannii make effective treatment even harder, as standard antibiotics are often ineffective against these strains(Bajaj et al., 2019).

Developing countries have other challenges such as limited access to appropriate antibiotics, poor infection control measures, and insufficient surveillance systems. These are responsible for the overuse or misuse of antibiotics, hence potentiating resistance patterns. Resource constraints often prevent antimicrobial stewardship programs from being implemented(Alscher, Erley, & Kuhlmann, 2019). Such programs play an important role in guiding rational antibiotic use and resisting resistance. Indeed, such challenges can only be met by a multifaceted approach through better diagnostic capabilities, access to antibiotics, and infection prevention strategies. Using antibiotics wisely in nosocomial infections is key to better patient outcomes and preventing antimicrobial resistance. It starts with starting the right empirical therapy, using broad spectrum antibiotics guided by local resistance patterns and site of infection which can then be de-escalated with pathogen specific info. Early and appropriate therapy reduces mortality and limits resistant organisms. Infection control and antimicrobial stewardship programs are also important. These programs involve proper use of antibiotics, resistance monitoring, and compliance to treatment guidelines. In hospital institutional commitment to these approaches can prevent spread of multidrug resistant bacteria which is now global. Consolidation of both approaches will make available antibacterial work but consumption is minimized(Rteil et al., 2020).

**Antibiotic Resistance**

Antimicrobial resistance (AMR) is one of the top global public health and development threats. It is estimated that bacterial AMR was directly responsible for 1.27 million global deaths in 2019 and contributed to 4.95 million deaths. The misuse and overuse of antimicrobials in humans, animals and plants are the main drivers in the development of drug-resistant pathogens. AMR affects countries in all regions and at all income levels(Frieri, Kumar, & Boutin, 2017). Its drivers and consequences are exacerbated by poverty and inequality, and low- and middle-income countries are most affected. MR affects countries in all regions and at all income levels. Its drivers and consequences are exacerbated by poverty and inequality, and low- and middle-income countries are most affected. AMR puts many of the gains of modern medicine at risk. It makes infections harder to treat and makes other medical procedures and treatments – such as surgery, caesarean sections and cancer chemotherapy much riskier(MacGowan & Macnaughton, 2017). The world faces an antibiotics pipeline and access crisis. There is an inadequate research and development pipeline in the face of rising levels of resistance, and urgent need for additional measures to ensure equitable access to new and existing vaccines, diagnostics and medicines. In addition to death and disability, AMR has significant economic costs. The World Bank estimates that AMR could result in US$ 1 trillion additional healthcare costs by 2050, and US$ 1 trillion to US$ 3.4 trillion gross domestic product (GDP) losses per year by 2030. Priorities to address AMR in human health include preventing all infections, which may result in inappropriate use of antimicrobials; ensuring universal access to quality diagnosis and appropriate treatment of infections; and strategic information and innovation, for example surveillance of AMR and antimicrobial consumption/use, and research and development for novel vaccines, diagnostics and medicines(Larsson & Flach, 2022; Lin et al., 2015).

Antimicrobials including antibiotics, antivirals, antifungals, and antiparasitics – are medicines used to prevent and treat infectious diseases in humans, animals and plants. Antimicrobial Resistance (AMR) occurs when bacteria, viruses, fungi and parasites no longer respond to antimicrobial medicines. As a result of drug resistance, antibiotics and other antimicrobial medicines become ineffective and infections become difficult or impossible to treat, increasing the risk of disease spread, severe illness, disability and death.AMR is a natural process that happens over time through genetic changes in pathogens. Its emergence and spread is accelerated by human activity, mainly the misuse and overuse of antimicrobials to treat, prevent or control infections in humans, animals and plants(MacLean & San Millan, 2019).

The rapid emergence of resistant bacteria is occurring worldwide, endangering the efficacy of antibiotics, which have transformed medicine and saved millions of lives. Many decades after the first patients were treated with antibiotics; bacterial infections have again become a threat. The antibiotic resistance crisis has been attributed to the overuse and misuse of these medications, as well as a lack of new drug development by the pharmaceutical industry due to reduced economic incentives and challenging regulatory requirements(Yelin & Kishony, 2018). The Centers for Disease Control and Prevention (CDC) has classified a number of bacteria as presenting urgent, serious, and concerning threats, many of which are already responsible for placing a substantial clinical and financial burden on the U.S. health care system, patients, and their families. Coordinated efforts to implement new policies, renew research efforts, and pursue steps to manage the crisis are greatly needed(Darby et al., 2023).

The prevalence of antimicrobial resistance among many common bacterial pathogens is increasing. The emergence and global dissemination of these antibiotic-resistant bacteria (ARB) is fuelled by antibiotic selection pressure, inter-organism transmission of resistance determinants, suboptimal infection prevention practices and increasing ease and frequency of international travel, among other factors. Patients with chronic kidney disease, particularly those with end-stage renal disease who require dialysis and/or kidney transplantation, have some of the highest rates of colonization and infection with ARB worldwide(Friedman, Temkin, & Carmeli, 2016). This ARB includes methicillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus spp. and several multidrug-resistant Gram-negative organisms. Antimicrobial resistance limits treatment options and increases the risk of infection-related morbidity and mortality. Several new antibiotic agents with activity against some of the most common ARB have been developed, but resistance to these agents is already emerging and highlights the dire need for new treatment options as well as consistent implementation and improvement of basic infection prevention practices. Clinicians involved in the care of patients with renal disease must be familiar with the local epidemiology of ARB, remain vigilant for the emergence of novel resistance patterns and adhere strictly to practices proven to prevent transmission of ARB and other pathogens(Aslam et al., 2018; Landecker, 2016).

The antimicrobials work in a variety of ways, the main ones being the inhibition of bacterial wall synthesis (penicillins, glycopeptides, carbapenems, and cephalosporins), the inhibition of DNA replication or transcription (quinolones, rifampicin), the impairment of bacterial ribosomes and protein synthesis (macrolides, linezolid, dalfopristin, tetracyclines, and aminoglycosides), the disruption of metabolic pathways (sulfonamides and trimethoprim), or the disruption of the cytoplasmic membrane (polymyxin and daptomycin)(Ventola, 2015).

190 individuals received a total of 495 antibiotic prescriptions. Antibiotics were administered to 51.6% of patients without renal dosage modifications. Fluoroquinolones were the most suitably adjusted class, whilst penicillins were the most improperly dosed (39.8%). The most commonly prescribed medication (30.6%) without renal dosage modification was piperacillin/tazobactam. According to the fitted multivariable-adjusted logistic models, there were statistically significant correlations between unadjusted antibiotic dosage and respiratory infections (OR 1.301, CI 95% 1.327–1.915) and multimorbidity (OR 1.183, CI 95% 1.358–2.081)(Chinemerem Nwobodo et al., 2022).

About 10% of people worldwide suffer from chronic kidney disease (CKD) [12]. The progression is shown by a glomerular filtration rate (GFR) < 60 mL/min/1.73 m2, which indicates a loss of function maintained for ≥ 3 months. Cardiovascular illness and chronic kidney disease (CKD) are intimately related; in CKD patients, cardiovascular mortality might be up to 15 times greater than in the general population. The number of individuals with stage 3 CKD (CKD3) is unknown because they are self-sufficient and infrequently seek the advice of a nephrology professional, making management of this condition very challenging. Increased microbial resistance or tolerance to arsenic, cadmium, mercury, and lead in tap water is a potential consequence of daily exposure (Ostermann et al.,2016). Through co-selection, the presence of metals also increases antibiotic resistance. Cross-resistance, in which a single resistance mechanism confers resistance to multiple components simultaneously, such as the cadmium efflux pump that can expel beta-lactam antibiotics, or co-resistance phenomena, in which two or more resistance genes are in the same genetic element and regulated by the same promoter, can result in co-selection(Martens & Demain, 2017).

**Possible Interventions**

In the treatment of patients with chronic kidney disease (CKD), cooperation between pharmacists and doctors may enhance the quality of medication dosage schedules that need to be modified based on renal function(Jit et al., 2020). Goal to show that a pharmacist's involvement in a CKD patient monitoring program enhances the patients' renal function.People with chronic kidney disease (CKD) are often advised to make dietary adjustments based on non-randomized research in CKD and randomized evidence in the general population that suggests specific healthy eating patterns may reduce mortality and prevent cardiovascular events(Rather, Kim, Bajpai, & Park, 2017). Dietary changes have been identified by renal disease patients as a significant therapeutic uncertainty.We located 17 studies that examined the potential health benefits of dietary modifications or guidance for 1639 individuals with chronic renal disease. Men and women with moderate to severe renal disease were included in the studies. Diets included consuming more fruits and vegetables, more fish and poultry, more nuts and olive oil, some more cereals and legumes (like beans), and less salt, sweets, and red meat. We specifically examined three outcomes: quality of life, risk of advanced renal disease needing dialysis, and risk of mortality(Bassetti, Tschudin-Sutter, Egli, & Osthoff, 2022). A total of four studies involved kidney transplant recipients, while three studies involved dialysis patients.After combining the available studies, it was uncertain whether making healthy diet changes prevented heart complications as most studies did not measure these. Diet changes may improve life quality. We did see that some risk factors for future disease, such as blood pressure and cholesterol, were lower following diet counseling or healthier eating(Roca et al., 2015).

Major depressive disorder is common in dialysis patients with end-stage kidney disease (ESKD). Depression has been identified by dialysis patients as a crucial clinical outcome in nephrology trials. For patients on long-term dialysis, we have a moderate level of confidence that cognitive behavioral therapy, physical activity, and relaxation techniques likely reduce depressive symptoms(Sabtu, Enoch, & Brown, 2015). While we don't know if acupressure, phone support, or meditation has any effect, counseling may help reduce the symptoms of depression. We discovered evidence with a moderate level of assurance that CBT improves dialysis patients' quality of life. Psychosocial treatments' effects on major depression and suicide risk were not measured in studies, and it's unclear if they had any bearing on anxiety, hospitalizations, or dialysis treatment withdrawal. Treatment-related adverse effects are often unpredictable(Manaia, Macedo, Fatta-Kassinos, & Nunes, 2016).

**Conclusion**

Antibiotic resistance in CKD patients as those undergoing dialysis is a significant global health concern due to frequent antibiotics use along with altered pharmacokinetic state and compromised immune health. The patients on dialysis are on higher risks of multi drug resistant infections and which are leading cause of increased morbidity, mortality and healthcare cost. Addressing this issue requires a multifaceted approach as optimized antibiotic stewardship in CKD patients, fostering development of rapid diagnostic tools and enhancing the infection control measures in these dialysis units. Additionally ongoing research into alternative therapeutic strategies as the bacteriophage therapy and immunomodulatory treatments as these hold promise for the mitigation of antibiotic resistance. Collaborative efforts including clinicians, researchers and improve overall outcomes for CKD patients undergoing dialysis.

**Conflict of interest:**

There is no conflict of interest.

**Acknowledgment:**

None

**Disclaimer (Artificial intelligence)**

**Option 1:**

**Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.**

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**Details of the AI usage are given below:**

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**2.**

**3.**

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