

DRUG-INDUCED ACUTE KIDNEY INJURY: INCIDENCE, PATHOPHYSIOLOGICAL MECHANISMS, AND PROGNOSTIC FACTORS – A COMPREHENSIVE REVIEW

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ABSTRACT

Drug-induced acute kidney injury (DI-AKI) is an important and potentially preventable complication of pharmacotherapy, particularly among hospitalized, critically ill, and patients receiving multiple nephrotoxic medications.^[1,2] Drugs can produce acute kidney injury through diverse mechanisms, including renal haemodynamic alterations, direct tubular toxicity, acute tubulointerstitial nephritis, crystal nephropathy, rhabdomyolysis, thrombotic microangiopathy, and immune-mediated renal injury.^[1,3,4] Previous reviews have predominantly focused on individual nephrotoxic drugs, conventional mechanisms, or selected renal biomarkers.^[2-5] The present review aims to provide a more integrated and contemporary assessment by correlating specific drug classes with their mechanisms of renal injury, clinical patterns, risk factors, diagnostic approaches, biomarkers, prevention, and management strategies. Particular attention is given to conventional biomarkers such as serum creatinine and blood urea nitrogen, which may identify renal functional decline relatively late, and to emerging biomarkers including kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL), cystatin C, N-acetyl-β-D-glucosaminidase, clusterin, and osteopontin.^[5-8] Recent evidence also highlights the increasing role of biomarker panels, proteomics, metabolomics, artificial intelligence, and personalized approaches in the early recognition and monitoring of drug-induced renal injury.^[6,7] In addition, newer approaches to defining and classifying DI-AKI may improve the identification of renal injury before substantial functional deterioration occurs.^[8,9] Unlike earlier reviews that primarily describe nephrotoxic agents or individual mechanisms, this review integrates drug-specific injury patterns with emerging biomarkers, risk stratification, pharmacovigilance, and preventive strategies. Such an integrated approach may facilitate earlier recognition, individualized management, and reduction of drug-related renal morbidity.

KEYWORDS: Drug-induced acute kidney injury; DI-AKI; Nephrotoxicity; Drug-induced nephrotoxicity; Acute kidney injury; Renal tubular injury; Acute interstitial nephritis; Nephrotoxic drugs; Biomarkers; Kidney injury molecule-1 (KIM-1); Neutrophil gelatinase-associated lipocalin (NGAL); Cystatin C; Risk factors; Early diagnosis; Pharmacovigilance; Prevention; Renal dysfunction; Precision medicine.

1. INTRODUCTION

Acute kidney injury (AKI) is a sudden decline in renal function characterized by an increase in serum creatinine concentration, reduction in urine output, or both. It represents a major clinical syndrome associated with increased morbidity, mortality, prolonged hospitalization, and healthcare expenditure. According to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, AKI is defined by an increase in serum creatinine ≥ 0.3 mg/dL within 48 hours, an increase in serum creatinine to ≥ 1.5 times baseline within 7 days, or urine output < 0.5 mL/kg/hour for 6 hours. These standardized criteria have improved recognition and classification of AKI severity in clinical practice and research.^[1]

AKI occurs due to a complex interaction of hemodynamic disturbances, renal parenchymal injury, inflammation, oxidative stress, and exposure to nephrotoxic agents. Among the various causes of AKI, drug-induced acute kidney injury (DI-AKI) is a clinically significant and potentially preventable form. A wide range of commonly prescribed medications, including antibiotics, anticancer agents, non-steroidal anti-inflammatory drugs (NSAIDs), renin-angiotensin system inhibitors, immunosuppressants, and radiocontrast agents, have been implicated in renal injury.^[4, 5]

The kidneys are particularly vulnerable to drug toxicity because they receive approximately 20–25% of cardiac output and are responsible for filtration, secretion, and concentration of numerous endogenous and exogenous substances. These physiological characteristics result in high exposure of renal tubular cells to circulating drugs and their metabolites, increasing susceptibility to toxic injury. Furthermore, renal tubular transport mechanisms may accumulate certain drugs intracellularly, resulting in oxidative stress, mitochondrial dysfunction, inflammation, and cellular apoptosis.^[8]

Drug-induced AKI represents an important challenge in hospitalized patients, particularly among critically ill individuals where multiple risk factors such as sepsis, hypotension, advanced age, and polypharmacy coexist. Recognition of nephrotoxic medications and early implementation of preventive strategies are essential components of patient safety and clinical pharmacy practice.^[10]

The diagnosis of DI-AKI is often challenging because conventional biomarkers such as serum creatinine increase only after substantial loss of renal function has occurred. Therefore, identification of novel biomarkers, improved risk assessment tools, and pharmacist-led medication monitoring programs are gaining importance in reducing the incidence and severity of drug-related kidney injury.^[11, 12]

2. Incidence and Clinical Burden of Drug-Induced Acute Kidney Injury

2.1 Global Incidence of Acute Kidney Injury

Acute kidney injury is recognized as a global public health problem affecting millions of patients annually. The incidence of AKI varies depending on the clinical setting, patient population, diagnostic criteria, and underlying disease conditions. Large epidemiological studies have demonstrated that AKI occurs in approximately 10–15% of hospitalized patients and may affect more than 50% of patients admitted to intensive care units (ICUs).^[13, 15]

A multinational meta-analysis by Susantitaphong et al. reported that approximately one in five adults and one in three children develop AKI during hospitalization, highlighting the widespread occurrence of this condition across healthcare

settings. The incidence is particularly high among critically ill patients due to exposure to multiple insults including infection, shock, surgery, and nephrotoxic medications.^[14]

In critically ill patients, AKI is associated with increased mortality, longer ICU stays, higher healthcare costs, and greater risk of progression to chronic kidney disease (CKD). The severity of AKI directly correlates with clinical outcomes, with patients requiring renal replacement therapy having significantly increased mortality compared with patients with mild kidney injury.^[15,17]

2.2 Incidence of Drug-Induced AKI

Drug-induced AKI accounts for a substantial proportion of hospital-acquired kidney injury. The reported incidence varies between 14–26% among hospitalized adults and may be higher in ICU settings due to increased exposure to multiple nephrotoxic agents. The actual incidence may be underestimated because medication-related renal injury is often multifactorial and may occur along with other causes such as sepsis, dehydration, and hemodynamic instability.^[4, 10]

Antimicrobial agents represent one of the most common causes of drug-related AKI. Drugs such as aminoglycosides, vancomycin, amphotericin B, and certain antiviral agents can cause direct tubular toxicity or immune-mediated renal injury. The increasing use of broad-spectrum antibiotics in critically ill patients has contributed to the continued clinical importance of antimicrobial-associated nephrotoxicity.^[7]

Anticancer therapies, particularly platinum-containing compounds such as cisplatin, are also major contributors to DI-AKI. Cisplatin-induced nephrotoxicity occurs due to accumulation of the drug in renal tubular cells, oxidative stress generation, DNA damage, mitochondrial injury, inflammation, and apoptosis. Despite advances in hydration protocols and preventive strategies, cisplatin-associated AKI remains a major dose-limiting adverse effect in oncology practice.^[6]

Contrast-associated acute kidney injury (CA-AKI) is another important medication-related renal complication occurring after administration of iodinated contrast media during diagnostic and interventional procedures. Although the incidence varies according to patient characteristics, individuals with chronic kidney disease, diabetes mellitus, heart failure, and advanced age are at increased risk.^[19]

2.3 Clinical Burden and Consequences of Drug-Induced AKI

Drug-induced AKI contributes significantly to patient morbidity and mortality. Even mild elevations in serum creatinine are associated with adverse outcomes, including prolonged hospitalization, increased risk of cardiovascular events, progression to CKD, and increased healthcare resource utilization.^[1,13]

Patients who develop DI-AKI frequently require additional monitoring, adjustment or discontinuation of medications, fluid management, electrolyte correction, and occasionally renal replacement therapy. These interventions increase hospital costs and may delay administration of essential therapies, particularly in patients receiving antimicrobial or anticancer treatment.^[5]

The burden of DI-AKI is amplified by the presence of multiple risk factors such as advanced age, pre-existing renal impairment, diabetes mellitus, cardiovascular disease, dehydration, and concurrent use of multiple nephrotoxic

medications. Elderly patients demonstrate increased susceptibility because of age-related reduction in renal reserve, altered drug pharmacokinetics, and increased prevalence of comorbid illnesses.^[18]

Polypharmacy is a major contributor to DI-AKI, particularly among hospitalized and critically ill patients. The simultaneous administration of multiple nephrotoxic drugs may result in additive or synergistic renal injury. Clinical pharmacy interventions, including medication review, dose adjustment according to renal function, therapeutic drug monitoring, and avoidance of unnecessary nephrotoxic combinations, have demonstrated effectiveness in reducing medication-associated AKI.^[10,16]

3. Pathophysiological Mechanisms of Drug-Induced Acute Kidney Injury

Drug-induced AKI occurs through multiple mechanisms involving renal hemodynamic alterations, direct tubular toxicity, immune-mediated injury, crystal deposition, and inflammatory pathways. Understanding these mechanisms is essential for prevention, early diagnosis, and management of nephrotoxic drug reactions.^[4]

3.1 Hemodynamic Alterations

Renal perfusion is maintained through a delicate balance between afferent and efferent arteriolar resistance. Certain drugs alter renal blood flow and glomerular filtration pressure, resulting in functional AKI without direct structural damage.

Non-steroidal anti-inflammatory drugs inhibit cyclooxygenase enzymes, reducing prostaglandin synthesis. Since prostaglandins maintain afferent arteriole vasodilation, their inhibition causes renal vasoconstriction, decreased renal blood flow, and reduction in glomerular filtration rate (GFR).^[5]

Similarly, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers reduce efferent arteriolar constriction by inhibiting angiotensin II activity. Although beneficial in many cardiovascular and renal diseases, these drugs may precipitate AKI in patients with reduced renal perfusion, dehydration, or renal artery stenosis.^[4]

3.2 Direct Tubular Toxicity

The renal tubular epithelium is a major target for nephrotoxic drugs due to active transport mechanisms and high metabolic activity. Drugs may accumulate within tubular cells and induce cellular injury through oxidative stress, mitochondrial dysfunction, ATP depletion, and apoptosis.^[4]

Aminoglycosides enter proximal tubular cells through megalin-mediated endocytosis and accumulate within lysosomes, causing membrane disruption and tubular epithelial injury. Similarly, cisplatin accumulates in renal tubular cells through organic cation transporters and produces reactive oxygen species, mitochondrial damage, and inflammatory responses.^[6,7]

Tubular toxicity may result in acute tubular necrosis (ATN), which is one of the most common histological patterns observed in drug-induced AKI. Recovery depends on the severity of injury, elimination of the causative drug, and regeneration capacity of tubular epithelial cells.^[4]

3.3 Immune-Mediated Renal Injury

Several medications cause AKI through immune-mediated mechanisms, particularly acute interstitial nephritis (AIN). Drug exposure can trigger an immune response characterized by infiltration of inflammatory cells including lymphocytes, eosinophils, and plasma cells within the renal interstitium.^[5]

Common drugs associated with AIN include antibiotics, proton pump inhibitors, NSAIDs, and certain diuretics. Clinical manifestations may include fever, rash, eosinophilia, and renal dysfunction; however, many cases present without classical symptoms, making diagnosis difficult.^[7]

3.4 Oxidative Stress and Mitochondrial Dysfunction

Oxidative stress is a central mechanism involved in many forms of drug-induced renal injury. Nephrotoxic drugs increase production of reactive oxygen species (ROS), leading to lipid peroxidation, protein oxidation, DNA damage, and activation of apoptotic pathways.^[6]

Mitochondrial dysfunction contributes significantly to tubular cell injury by reducing ATP production and impairing cellular repair mechanisms. This mechanism is particularly important in cisplatin-induced nephrotoxicity and other forms of toxic acute tubular injury.^[6]

3.5 Crystal-Induced Nephropathy

Certain medications or their metabolites have low solubility and may precipitate within renal tubules, causing obstruction and inflammation. Crystal-induced AKI has been reported with drugs such as acyclovir, sulfonamides, methotrexate, and some antiretroviral agents.^[5]

Adequate hydration, dose adjustment, and monitoring of renal function are important preventive strategies for minimizing crystal-associated renal injury.

3.6 Inflammation and Cellular Apoptosis

Drug-induced renal injury activates inflammatory pathways involving cytokines, chemokines, and immune cells. These inflammatory responses amplify tubular injury and delay recovery. Activation of pathways such as nuclear factor-kappa B (NF- κ B) contributes to inflammatory mediator release and progression of kidney damage.^[4]

Apoptosis and necrosis of renal tubular epithelial cells further worsen renal dysfunction. The extent of cellular injury determines the severity of AKI and influences long-term renal outcomes.^[5]

4. Major Drug Classes Associated with Acute Kidney Injury (AKI)

Drug-induced acute kidney injury (DI-AKI) represents a significant proportion of hospital-acquired AKI cases and may occur through multiple mechanisms including direct tubular toxicity, immune-mediated interstitial inflammation, hemodynamic alterations, crystal deposition, and obstruction. More than 200 medications have been reported to cause renal injury, and the risk increases with polypharmacy, critical illness, and pre-existing renal impairment. Recognition of high-risk medications is essential for prevention and early intervention by healthcare professionals, especially clinical pharmacists involved in medication monitoring.^[4,5,10]

Table 1: Major Drug Classes Associated with Drug-Induced Acute Kidney Injury^[4,5,7,8,20-25]

S.No	Drug Class	Commonly Implicated Drugs	Mechanism of Kidney Injury
1	Antimicrobial Agents	Aminoglycosides (Gentamicin, Amikacin), Vancomycin, Amphotericin B, Acyclovir, Sulfonamides	Direct tubular epithelial toxicity, oxidative stress, mitochondrial injury, immune-mediated interstitial nephritis, crystal precipitation
2	β -Lactam Antibiotics	Methicillin, Piperacillin–Tazobactam, Cephalosporins	Immune-mediated hypersensitivity causing inflammatory infiltration of renal interstitium
3	Non-Steroidal Anti-inflammatory Drugs (NSAIDs)	Ibuprofen, Diclofenac, Naproxen, Indomethacin	Cyclooxygenase inhibition reduces prostaglandin synthesis causing afferent arteriolar vasoconstriction and reduced renal blood flow
4	Renin–Angiotensin System Inhibitors	ACE inhibitors (Enalapril, Ramipril), ARBs (Losartan, Valsartan)	Reduced efferent arteriolar constriction leading to decreased glomerular filtration pressure
5	Diuretics	Furosemide, Hydrochlorothiazide, Spironolactone	Volume depletion, electrolyte disturbances, reduced renal perfusion
6	Antineoplastic Drugs	Cisplatin, Methotrexate, Ifosfamide, Gemcitabine	Tubular toxicity, oxidative stress, DNA damage, mitochondrial dysfunction
7	Contrast Media	Iodinated contrast agents used in angiography and imaging	Renal vasoconstriction, oxidative stress, direct tubular epithelial injury
8	Calcineurin Inhibitors	Cyclosporine, Tacrolimus	Renal vasoconstriction, endothelial dysfunction, chronic arteriolar injury
9	Proton Pump Inhibitors (PPIs)	Omeprazole, Pantoprazole, Esomeprazole	Immune-mediated hypersensitivity causing acute interstitial nephritis
10	Antiviral Drugs	Tenofovir, Indinavir, Acyclovir	Tubular mitochondrial toxicity, crystal precipitation
11	Immunosuppressive Agents	Sirolimus, Everolimus	Endothelial injury, altered renal hemodynamics
12	Antiepileptic Drugs	Phenytoin, Carbamazepine	Hypersensitivity reactions causing interstitial nephritis
13	Herbal and Alternative Medicines	Aristolochic acid-containing products, herbal supplements	Direct tubular toxicity, fibrosis, contamination with nephrotoxic substances

Important Drug-Specific Nephrotoxicities

1. Aminoglycoside-Induced AKI

Aminoglycosides remain important causes of drug-induced AKI, particularly in hospitalized and critically ill patients. These drugs accumulate in proximal tubular epithelial cells through megalin-mediated uptake, resulting in lysosomal dysfunction, oxidative stress, and cellular necrosis. The renal injury usually presents as non-oliguric acute tubular necrosis after several days of therapy. Risk increases with prolonged treatment duration, high cumulative dose, advanced age, and concomitant nephrotoxic drugs.^[7,20]

2. Vancomycin-Associated AKI

Vancomycin-induced nephrotoxicity has gained clinical importance due to increasing use against resistant Gram-positive infections. Proposed mechanisms include oxidative injury, mitochondrial dysfunction, and cast formation within renal tubules. High trough concentrations, prolonged therapy, intensive care admission, and concurrent nephrotoxic medications significantly increase AKI risk. Therapeutic drug monitoring and area-under-the-curve guided dosing are recommended approaches to minimize toxicity.^[7,21]

3. Cisplatin Nephrotoxicity

Cisplatin is one of the most nephrotoxic anticancer drugs. Approximately one-third of patients receiving cisplatin develop renal toxicity due to accumulation in proximal tubular cells, generation of reactive oxygen species, inflammatory cytokine activation, and apoptosis. Clinical manifestations include acute tubular necrosis, electrolyte abnormalities, and reduced glomerular filtration rate. Adequate hydration, dose modification, and nephroprotective strategies are essential for prevention.^[6, 22]

4. Contrast-Associated Acute Kidney Injury

Contrast-associated AKI occurs after administration of iodinated contrast agents and is associated with increased hospitalization and mortality. The pathogenesis involves renal vasoconstriction, medullary hypoxia, oxidative stress, and direct tubular epithelial injury. Patients with chronic kidney disease, diabetes mellitus, dehydration, heart failure, and advanced age are at higher risk.^[19, 23]

5. Risk Factors, Biomarkers, and Diagnostic Approach of Drug-Induced AKI

5.1 Risk Factors for Drug-Induced Acute Kidney Injury

Drug-induced AKI occurs due to interaction between patient susceptibility factors and exposure to nephrotoxic medications. Identification of risk factors before initiation of therapy allows clinicians to implement preventive strategies and reduce renal complications.^[10, 13]

Table 2: Risk Factors Associated with Drug-Induced AKI.^[10,13,15,18]

Category	Risk Factors	Explanation
Patient-related factors	Advanced age (>65 years), chronic kidney disease, diabetes mellitus, hypertension, cardiovascular disease	Reduced renal reserve increases susceptibility to nephrotoxic injury
Clinical conditions	Sepsis, hypotension, dehydration, shock, heart failure	Reduced renal perfusion enhances drug toxicity
Medication-related factors	High dose, prolonged duration, multiple nephrotoxic drugs, inappropriate dosing	Increases cumulative renal exposure
Intensive care factors	Mechanical ventilation, vasopressor use, critical illness	Associated with systemic inflammation and renal ischemia
Laboratory abnormalities	Elevated baseline serum creatinine, electrolyte imbalance	Indicates reduced renal function
Genetic susceptibility	Variations affecting drug transporters and metabolism	May influence individual susceptibility
Procedural factors	Exposure to contrast media, cardiac surgery	Causes additional renal stress

5.2 Biomarkers for Early Detection of Drug-Induced AKI

Traditional markers such as serum creatinine and blood urea nitrogen detect AKI only after significant reduction in renal function. Emerging biomarkers can identify kidney injury earlier, allowing timely discontinuation or modification of nephrotoxic medications.^[11]

Table 3: Important Biomarkers for Early AKI Detection^[11,12,24]

Biomarker	Source	Clinical Significance
Serum Creatinine	Muscle metabolism	Conventional marker but delayed rise after renal injury
Blood Urea Nitrogen (BUN)	Protein metabolism	Indicates impaired renal clearance but lacks specificity
NGAL (Neutrophil Gelatinase-Associated Lipocalin)	Injured tubular epithelial cells	Early marker of tubular injury within hours
Kidney Injury Molecule-1 (KIM-1)	Proximal tubular cells	Detects ischemic and toxic tubular injury

IL-18	Renal tubular cells	Marker of inflammatory renal injury
NAG (N-acetyl- β -D-glucosaminidase)	Lysosomes of proximal tubules	Indicates tubular damage
Cystatin C	All nucleated cells	Sensitive marker of reduced filtration
TIMP-2 $\times$ IGFBP7	Tubular cells	Detects cell-cycle arrest and predicts AKI risk
Urinary Albumin	Glomerular barrier	Indicates renal structural damage

5.3 Diagnostic Approach of Drug-Induced AKI

The diagnosis of drug-induced AKI requires systematic evaluation of medication history, clinical presentation, laboratory findings, and exclusion of other causes of renal dysfunction. Early recognition of the offending medication is essential to prevent progression.^[1,2]

Diagnostic Steps

1. Clinical Assessment

Detailed medication history including:

- Recent initiation of drugs
- Dose escalation
- Over-the-counter medications
- Herbal preparations
- Exposure to multiple nephrotoxic agents

2. Laboratory Evaluation

Important investigations include:

- Serum creatinine
- Blood urea nitrogen
- Estimated glomerular filtration rate (eGFR)
- Serum electrolytes
- Urinalysis
- Urine microscopy
- Urinary biomarkers

3. Imaging Studies

Renal ultrasound is performed to exclude:

- Urinary obstruction
- Structural abnormalities
- Renal stones

4. Kidney Biopsy

Kidney biopsy may be considered when diagnosis remains uncertain, particularly in suspected acute interstitial nephritis, glomerular diseases, and unusual drug reactions.^[1,2,25]

6. Prevention Strategies for Drug-Induced Acute Kidney Injury

Drug-induced acute kidney injury (DI-AKI) is a potentially preventable adverse drug reaction. Prevention primarily depends on early identification of high-risk patients, avoidance or modification of nephrotoxic medications, appropriate dose adjustment, and continuous monitoring of renal function. Since many nephrotoxic insults are reversible when recognized early, preventive strategies play a critical role in reducing AKI-associated morbidity, mortality, and healthcare costs.^[1,2]

6.1 Identification of Patients at High Risk

Risk assessment is the first step in preventing drug-induced AKI. Patients with advanced age, pre-existing chronic kidney disease (CKD), diabetes mellitus, heart failure, liver disease, dehydration, sepsis, hypotension, and exposure to multiple nephrotoxic drugs have increased susceptibility to renal injury. Elderly patients are particularly vulnerable due to reduced renal reserve, altered drug pharmacokinetics, and increased prevalence of comorbidities.^[8,18]

Before initiating potentially nephrotoxic medications, baseline evaluation of serum creatinine, estimated glomerular filtration rate (eGFR), electrolyte status, volume status, and concurrent medication profile should be performed. Identification of high-risk individuals allows clinicians to select safer alternatives or implement intensive monitoring protocols.^[10]

6.2 Rational Use of Nephrotoxic Medications

Avoidance of unnecessary nephrotoxic drugs is one of the most effective approaches for preventing DI-AKI. Clinicians should carefully evaluate the risk–benefit ratio before prescribing medications such as aminoglycosides, vancomycin, cisplatin, non-steroidal anti-inflammatory drugs (NSAIDs), calcineurin inhibitors, and radiographic contrast agents.^[4,5]

When nephrotoxic drugs are clinically essential, strategies such as using the lowest effective dose, limiting treatment duration, avoiding combination nephrotoxins, and selecting alternative agents with lower renal toxicity should be considered. For example, aminoglycosides should be reserved for appropriate indications, and therapeutic drug monitoring should be used to maintain safe plasma concentrations.^[20]

6.3 Dose Optimization and Therapeutic Drug Monitoring

Renal impairment significantly affects drug elimination, increasing the risk of drug accumulation and toxicity. Appropriate dose adjustment according to renal function is essential for medications primarily eliminated by the kidneys. The use of eGFR or creatinine clearance-based dosing recommendations helps prevent excessive drug exposure.^[2]

Therapeutic drug monitoring (TDM) is particularly important for drugs with a narrow therapeutic index, including vancomycin, aminoglycosides, and certain immunosuppressive agents. Monitoring serum drug concentrations enables individualized dosing and reduces nephrotoxic risk while maintaining therapeutic effectiveness.^[7,21]

6.4 Prevention of Contrast-Associated Acute Kidney Injury

Contrast-associated acute kidney injury (CA-AKI) remains a significant concern among hospitalized patients undergoing diagnostic and interventional procedures. Prevention strategies include assessment of renal function before contrast administration, minimizing contrast volume, avoiding repeated contrast exposure within a short interval, and ensuring adequate hydration.^[19]

Intravenous isotonic saline hydration remains the most consistently recommended preventive intervention. Additional strategies include discontinuation of unnecessary nephrotoxic medications before procedures and careful monitoring of renal parameters after contrast exposure, particularly in high-risk patients.^[23]

6.5 Prevention of Antimicrobial-Induced AKI

Antimicrobial agents represent one of the most common causes of hospital-associated DI-AKI. Vancomycin-associated nephrotoxicity is influenced by high trough concentrations, prolonged therapy, concomitant nephrotoxic drugs, and patient-specific risk factors. Appropriate antimicrobial selection, antimicrobial stewardship programs, and therapeutic monitoring can significantly reduce AKI occurrence.^[7,21]

For aminoglycosides, extended interval dosing, pharmacokinetic monitoring, and limiting unnecessary exposure are recommended approaches. Combination therapy involving multiple nephrotoxic antimicrobials should be avoided whenever clinically feasible.^[20]

6.6 Hydration and Maintenance of Renal Perfusion

Maintenance of adequate renal perfusion is an important preventive measure because reduced renal blood flow increases susceptibility to drug-induced tubular injury. Avoidance of dehydration, correction of hypotension, appropriate fluid management, and early treatment of sepsis are essential components of AKI prevention.^[1,24]

Patients receiving nephrotoxic chemotherapy, antimicrobial therapy, or contrast procedures should receive individualized fluid management plans to maintain optimal intravascular volume without causing fluid overload.^[6]

6.7 Implementation of Nephrotoxicity Prevention Programs

Hospital-based nephrotoxicity prevention programs involving physicians, pharmacists, nurses, and laboratory personnel have demonstrated reductions in medication-associated AKI. Such programs include electronic alerts, medication review systems, renal function monitoring protocols, and pharmacist-driven interventions.^[16]

Clinical decision support systems integrated into hospital information systems can identify patients receiving multiple nephrotoxic medications and recommend appropriate monitoring or alternative therapies.^[10]

7. Role of Clinical Pharmacists in Prevention and Management of Drug-Induced AKI

Clinical pharmacists play a vital role in preventing medication-related kidney injury through medication review, renal dose adjustment, therapeutic monitoring, patient education, and interdisciplinary collaboration. With expanding roles in healthcare systems, pharmacists contribute significantly to improving medication safety and patient outcomes.^[10]

7.1 Medication Review and Identification of Nephrotoxic Drugs

Clinical pharmacists should routinely evaluate patient medication profiles to identify nephrotoxic agents, unnecessary drug combinations, potential drug interactions, and inappropriate dosing. Early identification of nephrotoxic exposure allows timely intervention before irreversible renal damage occurs.^[5]

Common pharmacist interventions include discontinuation of unnecessary NSAIDs, adjustment of antimicrobial doses, monitoring of vancomycin concentrations, and prevention of nephrotoxic drug combinations.^[7]

7.2 Renal Dose Adjustment

Dose optimization based on renal function is a major responsibility of clinical pharmacists. Drugs eliminated through kidneys require appropriate dose modification during AKI to prevent accumulation and toxicity. Pharmacists should calculate creatinine clearance, interpret renal laboratory values, and recommend individualized dosing regimens.^[2]

7.3 Therapeutic Drug Monitoring

Clinical pharmacists are actively involved in therapeutic drug monitoring programs for nephrotoxic medications such as vancomycin, aminoglycosides, and immunosuppressants. Monitoring drug concentrations helps maintain efficacy while minimizing renal toxicity.^[21]

7.4 Patient Education and Counseling

Patient counseling is essential for preventing community-associated drug-induced kidney injury. Pharmacists should educate patients regarding avoidance of unnecessary over-the-counter NSAID use, adequate hydration, medication adherence, and recognition of symptoms suggestive of renal dysfunction.^[25]

7.5 Pharmacovigilance and Reporting

Clinical pharmacists contribute to pharmacovigilance activities by identifying, documenting, and reporting nephrotoxic adverse drug reactions. Systematic reporting improves understanding of drug safety profiles and supports preventive strategies within healthcare institutions.^[5]

8. Prognostic Factors and Outcomes of Drug-Induced AKI

The prognosis of drug-induced AKI depends on the severity of renal injury, patient characteristics, underlying diseases, and timing of intervention. Although many cases are reversible after withdrawal of the offending drug, severe AKI may progress to chronic kidney disease, prolonged hospitalization, or death.^[24]

8.1 Severity of AKI

The severity classification of AKI according to KDIGO criteria is strongly associated with clinical outcomes. Patients with stage 2 or stage 3 AKI have significantly higher risks of mortality, prolonged intensive care admission, and renal replacement therapy compared with patients having mild AKI.^[1]

8.2 Patient-Related Prognostic Factors

Advanced age, CKD, cardiovascular disease, diabetes mellitus, sepsis, and multi-organ failure are important predictors of poor outcomes following AKI. Elderly patients often experience incomplete renal recovery due to reduced renal reserve and increased susceptibility to additional renal insults.^[13,18]

8.3 Duration of AKI and Renal Recovery

The duration of kidney injury is an important determinant of prognosis. Persistent AKI is associated with increased risk of CKD progression and long-term cardiovascular complications. Early diagnosis and discontinuation of the causative drug improve the likelihood of renal recovery.^[24]

8.4 Need for Renal Replacement Therapy

Patients with severe DI-AKI may require dialysis or continuous renal replacement therapy (CRRT). Requirement of renal replacement therapy is associated with increased mortality and indicates severe renal dysfunction. Early recognition and appropriate supportive management may reduce progression to dialysis-dependent kidney failure.^[3]

9. CONCLUSION

Drug-induced acute kidney injury represents a major healthcare challenge due to its high incidence, multiple mechanisms, and association with adverse clinical outcomes. Nephrotoxic medications including antimicrobials, anticancer drugs, contrast agents, and immunosuppressive therapies remain important contributors to AKI development. Early identification of risk factors, rational prescribing practices, renal dose optimization, therapeutic monitoring, and implementation of preventive strategies are essential for reducing the burden of DI-AKI.^[4,24]

Clinical pharmacists play an indispensable role in multidisciplinary AKI prevention programs by optimizing drug therapy, monitoring nephrotoxic medications, educating patients, and promoting medication safety. Integration of pharmacist-led interventions, electronic monitoring systems, and biomarker-based early detection strategies may further improve patient outcomes.^[10,16]

Future advances in AKI management will depend on improved predictive biomarkers, personalized pharmacotherapy, and collaborative healthcare approaches aimed at preventing avoidable kidney injury and improving long-term renal health.^[11,12]

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