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Drug-Induced Acute Kidney Injury in Children: Mechanisms, Risk Factors, Diagnosis, Prevention, and Management

Dr. Edwin Dias[1], Riya Marya Mathew[2]

[1]Professor and Head, Department of Pediatrics, Director of Research and Publication, Srinivas Institute of Medical Sciences and Research Centre, Mangaluru, India
[2]PharmD Intern, Department of Pharmacy Practice, Srinivas College of Pharmacy, Mangaluru, India

Corresponding Author: Riya Marya Mathew

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ABSTRACT

Drug-induced acute kidney injury (DI-AKI) is a potentially preventable complication of medicine use in children. The risk is influenced by the stage of renal development, age-related differences in drug handling, the child's underlying illness and exposure to several medicines at the same time. This narrative review examines the mechanisms and main causes of DI-AKI in children, together with its risk factors, diagnosis, prevention and management. PubMed and Google Scholar were searched, and relevant guidelines, consensus documents and reference lists were also reviewed. The discussion focuses on pediatric evidence on nephrotoxic medicines, AKI, nephrotoxin stewardship and renal dose adjustment. Reported mechanisms include changes in renal blood flow, direct tubular toxicity, acute interstitial nephritis, crystal deposition, renal vascular effects and urinary obstruction. Medicines commonly associated with kidney injury include aminoglycosides, vancomycin, non-steroidal anti-inflammatory drugs, acyclovir, amphotericin B, calcineurin inhibitors and selected anticancer agents. Assessment generally involves serial serum creatinine measurements, monitoring of urine output, medication review, urinalysis and therapeutic drug monitoring when appropriate. Preventive measures include identifying children at higher risk, avoiding unnecessary nephrotoxin exposure, maintaining adequate fluid status, adjusting doses to kidney function and using structured medication surveillance. When AKI develops, management involves reviewing the suspected medicine, correcting hemodynamic and metabolic disturbances and reassessing other treatments. Newer biomarkers and electronic surveillance may help identify injury earlier, but clinical assessment remains central to care. Close coordination among physicians, pharmacists, nurses and nephrology teams can help prevent avoidable injury and protect kidney health over time.

Keywords: *Drug-induced kidney injury, Acute kidney injury, Children, Nephrotoxicity, Nephrotoxin stewardship*

INTRODUCTION

Acute kidney injury (AKI) is a sudden decline in kidney function that can disrupt the regulation of fluid, electrolytes and acid–base balance. In children, it may occur

during critical illness, infection, dehydration, surgery, cardiac disease, malignancy or treatment with nephrotoxic medicines. Its effects may continue after the acute episode: children who develop AKI can have a higher later risk of chronic kidney disease (CKD), hypertension, recurrent AKI and kidney failure. In the multinational AWARE study, which included 4,683 critically ill children and young adults, 26.9% developed AKI and 11.6% developed severe AKI. Severe AKI was also found to be an independent predictor of 28-day mortality. The study also showed that relying on serum creatinine alone may miss cases detected by urine-output criteria [1].

Drug-induced acute kidney injury (DI-AKI) deserves particular attention because some cases can be prevented through appropriate medicine selection, dosing, monitoring and timely intervention. A systematic review and meta-analysis of 69 studies involving 195,894 children estimated that drug-induced kidney injury (DIKI) occurred in 18.2% of the study population. The pooled incidence was higher among critically ill children than among those who were not critically ill [2]. The estimate reflects DIKI as defined in the included studies and should not be taken as the incidence of DI-AKI alone. Medicines commonly implicated include antimicrobial agents, non-steroidal anti-inflammatory drugs (NSAIDs), antiviral agents, immunosuppressants and anticancer drugs [3].

Children cannot be treated simply as smaller versions of adults when medicines are prescribed. Glomerular filtration, tubular transport, body composition, drug metabolism and renal drug clearance all change during growth. These developmental changes, together with acute illness and the use of multiple medicines, can affect drug exposure and a child's susceptibility to toxicity [4]. Serum creatinine also has limitations as an early indicator of kidney dysfunction in children. Levels vary with age and muscle mass, and may not rise until kidney filtration has already declined.

This review discusses the mechanisms and clinically important causes of drug-induced AKI in children. It also considers practical approaches to risk assessment, diagnosis, prevention and management, with particular attention to clinical pharmacy and nephrotoxin stewardship.

METHODOLOGY

A narrative literature review was conducted to bring together clinically relevant evidence on drug-induced AKI in children. PubMed and Google Scholar were searched using combinations of the following terms: “drug-induced acute kidney injury,” “drug-induced kidney injury,” “pediatric acute kidney injury,” “children,” “nephrotoxicity,” “nephrotoxic drugs,” “vancomycin,” “aminoglycosides,” “NSAIDs,” “acyclovir,” “cisplatin,” “nephrotoxin stewardship” and “renal dosing.” Reference lists from relevant reviews, consensus documents and guidelines were also checked for additional studies.

Studies and other publications were considered relevant when they addressed drug-induced kidney injury in children or provided clinically useful evidence on its mechanisms, risk factors, diagnosis, prevention, monitoring or management. The review placed particular emphasis on pediatric observational and clinical studies, systematic reviews, consensus statements and guidelines. Earlier publications were included when they offered important mechanistic or clinical information. Findings were grouped according to the main themes of the review: causes, mechanisms, risk factors, diagnosis, prevention and management. A narrative approach was used; no meta-analysis, formal quantitative risk-of-bias assessment or PRISMA-based study-selection process was undertaken.

OVERVIEW AND EPIDEMIOLOGY

DI-AKI includes several forms of kidney injury that may arise directly or indirectly from medicine exposure. Establishing

whether a medicine caused AKI can be difficult. Children who receive nephrotoxic treatment are often seriously ill and may also have sepsis, low circulating volume, hypotension or other factors that can affect kidney function. For this reason, a possible medication-related injury should be assessed in the context of the child's overall clinical condition, rather than being attributed to a medicine on timing alone.

In a 2023 systematic review and meta-analysis, Zhang et al. reported a pooled DIKI incidence of 18.2% across the pediatric populations included in the analysis. The estimates were 19.6% among critically ill children and 16.1% among non-critically ill children. Reported risk factors included longer treatment, admission to intensive care, infection, surgery, CKD and concurrent use of antibacterial, antiviral, diuretic, NSAID or immunosuppressive medicines [2]. As the included studies may have used broader definitions of drug-induced kidney injury, this pooled estimate should not be interpreted as the incidence of DI-AKI alone.

Findings from studies of individual medicines add to this picture. A systematic review of vancomycin-associated AKI included 25 studies and 12,730 children and reported a pooled incidence of 11.8%. Risk factors included the use of other nephrotoxic medicines, higher vancomycin trough concentrations, longer treatment and impaired renal function [5]. In a prospective multicenter study of NSAID-associated AKI, 25 cases were identified; most affected children had volume depletion. Sixty-three percent had received NSAIDs at recommended doses [6]. These results show that a child's clinical condition can contribute to kidney injury even when the medicine has been prescribed within the usual dose range.

PEDIATRIC RENAL SUSCEPTIBILITY

Renal function and drug handling change as a child grows. Glomerular filtration, tubular secretion and reabsorption, renal blood flow and transporter expression all develop with age. In neonates and young infants, immature renal function can slow the elimination of medicines cleared by the kidneys and increase drug exposure. In older children, kidney function may be high relative to body size, while critical illness can cause renal clearance to change quickly [4].

The developing kidney may also respond differently to toxic exposures because nephron maturation and tubular transport are still changing. During critical illness, changes in renal perfusion, inflammation, capillary permeability and drug distribution make drug exposure harder to predict [4]. As a result, children may receive too little or too much medicine if standard doses are used without considering their current kidney function and clinical condition.

Serum creatinine must be interpreted carefully in children. Its production is influenced by muscle mass and growth, and its concentration may rise only after filtration has already fallen. The AWARE study showed that relying on creatinine alone can miss AKI in children with significant oliguria [1]. Urine output, serial creatinine measurements and the child's clinical course should therefore be considered together.

MECHANISMS OF DRUG-INDUCED KIDNEY INJURY

Hemodynamic injury

Some medicines reduce renal blood flow or interfere with the mechanisms that help maintain glomerular filtration. NSAIDs inhibit prostaglandin synthesis and can cause constriction of the afferent arteriole, particularly in children who are volume depleted. Medicines that affect systemic or intrarenal hemodynamics may pose a greater risk in children with dehydration, sepsis or pre-existing renal impairment [3,6].

Direct tubular toxicity

Aminoglycosides accumulate in proximal tubular epithelial cells, where they can cause cellular damage, oxidative stress and

impaired tubular function [7]. Vancomycin has also been associated with oxidative stress, mitochondrial injury and tubular damage; the risk is influenced by drug exposure and the use of other nephrotoxic medicines [5]. Amphotericin B can affect tubular membrane permeability and cause renal vasoconstriction [8]. Calcineurin inhibitors may also reduce renal blood flow and contribute to acute or chronic tubular injury [9].

Acute interstitial nephritis

Beta-lactam antibiotics, NSAIDs and several other medicines can trigger immune-mediated acute interstitial nephritis. Findings may include a rise in serum creatinine, pyuria, hematuria, rash or fever. However, the classic combination of fever, rash and eosinophilia is often not present. Diagnosis is based on the clinical assessment and, in selected cases, kidney biopsy [3].

Crystal nephropathy

Some medicines, or the metabolites formed from them, can crystallize within the renal tubules. Intravenous acyclovir is a recognized cause of crystal-associated AKI, particularly when drug exposure is high or hydration is inadequate [10]. High-dose methotrexate can also precipitate in the tubules, especially when urine is acidic and drug concentrations are elevated [3].

Glomerular and vascular injury

Calcineurin inhibitors can affect renal vascular function and contribute to vasoconstriction and kidney injury [9].

Obstructive injury

Some antimicrobial medicines can precipitate in the renal tubules when urinary drug concentrations become sufficiently high, leading to crystal formation and tubular obstruction [8]. Reduced urine flow and inadequate hydration may increase this risk. Imaging may be considered when clinical findings suggest urinary tract obstruction.

MAJOR NEPHROTOXIC DRUGS IN CHILDREN

Antimicrobials

Aminoglycosides such as gentamicin, tobramycin and amikacin can injure the proximal renal tubules. The risk is greater with prolonged treatment, repeated courses, high drug exposure or the concurrent use of other nephrotoxic medicines [7]. These drugs are cleared mainly by the kidneys and their toxicity is related to exposure. Dosing and therapeutic drug monitoring should therefore take account of the child's renal function and the relevant treatment protocol. Extended-interval dosing may be suitable for selected patient groups.

Vancomycin is prescribed in pediatric patients for serious infections involving susceptible Gram-positive bacteria. In children, the risk of vancomycin-associated AKI is affected by cumulative exposure, trough concentration, treatment duration, critical illness and the use of other nephrotoxic medicines [5]. Where validated and practical, exposure-guided monitoring using area-under-the-curve methods can help maintain efficacy while limiting toxicity.

Acyclovir can cause crystal-associated AKI, particularly when given intravenously. In a retrospective study of 472 children who received intravenous acyclovir, 6.8% developed AKI. Older age, higher doses, longer treatment and concurrent nephrotoxic medicines were associated with greater risk [10]. Adequate hydration and appropriate dose selection are therefore important during treatment.

Amphotericin B can cause renal vasoconstriction, tubular dysfunction, electrolyte disturbances and a reduction in glomerular filtration. Lipid formulations generally have a more favorable renal safety profile than conventional amphotericin B, but kidney function and electrolytes still need to be monitored [8].

NSAIDs

NSAIDs are frequently prescribed to children for pain and fever. By inhibiting

prostaglandin synthesis, they can reduce renal perfusion, especially in children with dehydration, sepsis, underlying kidney disease or exposure to other nephrotoxic medicines [6]. The prospective pediatric study discussed above identified cases after short courses of treatment, including in children who had received recommended doses while volume depleted [6].

Anticancer agents

Cisplatin is an important cause of kidney toxicity in children. It can injure renal tubules, increase magnesium loss, disturb electrolyte balance and reduce GFR. In a multicenter prospective cohort of 159 children treated with cisplatin, 46% developed AKI during treatment and 35% experienced severe electrolyte abnormalities [11]. Because renal changes may continue after treatment ends, follow-up is important.

Ifosfamide can cause proximal tubular dysfunction and Fanconi-like abnormalities [12]. High-dose methotrexate may lead to crystal nephropathy and delayed drug clearance [3]. Tumor lysis syndrome can cause uric acid and calcium-phosphate deposition, resulting in severe AKI [13]. In this setting, kidney injury is related to metabolic changes associated with treatment rather than to direct drug toxicity alone.

Immunosuppressants and other drugs

Calcineurin inhibitors, including cyclosporine and tacrolimus, can cause dose-related vasoconstriction and tubular or vascular injury [9]. Diuretics are not generally considered primary nephrotoxins, but inappropriate use can lead to volume depletion and make a child more susceptible to AKI.

Table 1. Major drug classes associated with pediatric drug-induced acute kidney injury

Drug/class	Major mechanism	Important risk factors	Key preventive/monitoring measures	Reference
Aminoglycosides	Proximal tubular toxicity	Prolonged therapy, high exposure, concomitant nephrotoxins	Renal function monitoring; therapeutic drug monitoring; dose/interval adjustment	[7]
Vancomycin	Tubular/oxidative injury	High exposure, prolonged therapy, ICU illness, nephrotoxins	Exposure-guided monitoring; serial creatinine; review concomitant nephrotoxins	[5]
NSAIDs	Reduced renal perfusion	Dehydration, sepsis, CKD, concomitant nephrotoxins	Avoid in dehydrated/high-risk children; hydration; renal monitoring	[6]
Acyclovir	Crystal nephropathy	IV therapy, high dose, dehydration, nephrotoxins	Hydration; dose adjustment; renal monitoring	[10]
Amphotericin B	Vasoconstriction and tubular injury	Conventional formulation, prolonged therapy	Renal/electrolyte monitoring; consider less nephrotoxic formulation when appropriate	[8]
Cisplatin	Tubular injury and electrolyte wasting	Cumulative dose, repeated cycles, baseline risk	Hydration; electrolyte monitoring; renal function surveillance	[11]
Ifosfamide	Proximal tubular injury	Cumulative exposure, repeated therapy	Renal/electrolyte monitoring; dose adjustment	[12]
Calcineurin inhibitors	Renal vasoconstriction and vascular/tubular injury	High exposure, interacting drugs, CKD	Therapeutic drug monitoring; renal function and blood pressure monitoring	[9]

RISK FACTORS

Risk factors for DI-AKI can be grouped into patient-related, disease-related and treatment-related factors. Neonates and infants may be more vulnerable because their renal function is still developing. Risk

is also increased in children with pre-existing CKD, structural urinary tract abnormalities, a history of AKI or reduced baseline GFR. Dehydration and poor oral intake are important considerations because even relatively small changes in fluid balance can reduce renal perfusion in children.

Sepsis, shock, hypotension, mechanical ventilation and major surgery can reduce renal perfusion or increase inflammatory injury. Children with malignancy face additional risks related to chemotherapy, tumor lysis, infection and repeated exposure to nephrotoxic medicines. ICU admission has consistently been associated with a higher risk of DIKI [2]. Treatment-related risks include high cumulative exposure, prolonged therapy, multiple nephrotoxic medicines, drug interactions, inappropriate dosing and failure to adjust treatment as kidney function changes. Risk often reflects the combined effect of several factors rather than one medicine alone. A structured medication review should therefore consider the child's total nephrotoxic burden.

CLINICAL MANIFESTATIONS

DI-AKI may cause few obvious symptoms in its early stages. Reduced urine output is an important warning sign, although some children continue to produce urine. Other possible features include edema, hypertension, fluid overload, nausea, fatigue, altered mental status and symptoms caused by electrolyte or acid–base disturbances. Hematuria, proteinuria, pyuria or urinary crystals may help point to the underlying type of injury.

The signs of AKI are often nonspecific, so the medication history and timing of events are important. If creatinine rises after a nephrotoxic medicine is started, clinicians should also consider other possible or contributing causes, including sepsis, dehydration, obstruction, glomerulonephritis and thrombotic microangiopathy.

DIAGNOSIS AND MONITORING

AKI should be diagnosed and staged using accepted criteria, primarily the KDIGO framework [14]. Serum creatinine and urine output remain central to the assessment, although both have limitations. Whenever possible, a baseline creatinine should be established, and subsequent results should be interpreted as a trend rather than as isolated values.

Routine laboratory testing generally includes serum electrolytes, urea and bicarbonate, with additional tests selected according to the child's clinical condition. Urinalysis may provide clues to tubular, interstitial or glomerular injury. Renal ultrasound is useful when obstruction, structural disease or another diagnosis is suspected.

Therapeutic drug monitoring is particularly useful for medicines with a narrow therapeutic range or toxicity related to drug exposure, including aminoglycosides and vancomycin. The dose and dosing interval should be reviewed whenever renal function changes.

Emerging biomarkers

Researchers are evaluating biomarkers that may identify kidney stress or injury before serum creatinine increases. Cystatin C is less dependent on muscle mass and may provide additional information. Other markers studied in children with AKI include urinary neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), interleukin-18 (IL-18), liver-type fatty acid-binding protein (L-FABP), and the combination of tissue inhibitor of metalloproteinases-2 and insulin-like growth factor-binding protein 7 (TIMP-2/IGFBP7) [15,16]. A systematic review found that several biomarkers may have useful predictive performance, although differences in study populations and diagnostic cut-offs limit their use in routine practice [15]. Pediatric studies have also examined TIMP-2/IGFBP7; further work is needed to determine how well it distinguishes functional changes from intrinsic kidney injury [17].

Table 2. KDIGO staging of acute kidney injury in children

Stage	Serum creatinine criteria	Urine output criteria
Stage 1	Increase ≥0.3 mg/dL within 48 h or increase to 1.5–1.9 times baseline within 7 days	<0.5 mL/kg/h for 6–12 h
Stage 2	Increase to 2.0–2.9 times baseline	<0.5 mL/kg/h for ≥12 h
Stage 3	Increase to ≥3 times baseline, or increase in serum creatinine to ≥4.0 mg/dL, or initiation of kidney replacement therapy, or, in patients younger than 18 years, decrease in eGFR to <35 mL/min/1.73 m².	<0.3 mL/kg/h for ≥24 h or anuria ≥12 h

PREVENTION

Pre-treatment risk assessment

Prevention remains the most effective way to reduce drug-induced AKI. Before starting a potentially nephrotoxic medicine, clinicians should review the child's baseline kidney function, hydration, comorbidities and other medicines that may affect the kidneys. The indication, dose, route and planned duration of treatment should also be considered.

Avoid unnecessary nephrotoxin exposure

If two treatments are expected to be similarly effective, a less nephrotoxic option may be preferable. However, avoiding a medicine should not compromise the effective treatment of a serious infection or another important condition. The aim is to reduce avoidable risk while ensuring that the child receives appropriate treatment.

Maintain adequate hydration and perfusion

Fluid status should be assessed and corrected when needed. Children who are dehydrated and receive NSAIDs or nephrotoxic antimicrobials are particularly vulnerable to kidney injury. In high-risk oncology protocols, appropriate hydration and electrolyte replacement are important parts of prevention.

Dose and interval adjustment

Doses of medicines eliminated by the kidneys should be adjusted according to current renal function and the child's clinical condition. Kidney function can change quickly during AKI, so a dose that was appropriate the previous day may no longer be suitable. Doses should be reassessed after important changes in creatinine, urine output, fluid status or overall clinical condition.

Therapeutic drug monitoring

Therapeutic drug monitoring can help limit excessive exposure to medicines with a narrow therapeutic range. Vancomycin monitoring should be based on drug exposure when appropriate, while aminoglycoside monitoring should follow the selected dosing regimen and local protocol.

Serial monitoring

Children at high risk need a planned monitoring schedule rather than testing only after a problem is suspected. The frequency of monitoring should reflect the number and type of nephrotoxic medicines, duration of treatment, baseline kidney function and severity of the acute illness.

NEPHROTOXIN STEWARDSHIP

Nephrotoxin stewardship aims to reduce preventable kidney injury through coordinated medication-safety practices. One pediatric example is the Nephrotoxic Injury Negated by Just-in-time Action (NINJA) program. During its multicenter quality-improvement implementation, hospitalized children with high nephrotoxin exposure were identified, daily serum creatinine monitoring was prompted and alternative medicines were considered. The program was associated with a sustained 23.8% reduction in rates of nephrotoxin-associated AKI [18].

A nephrotoxin stewardship pathway may include automated identification of children receiving selected nephrotoxic medicines, review of whether each medicine is still needed, renal-dose alerts, monitoring

recommendations and referral to a pharmacist or nephrology team when appropriate. Hospitals without electronic surveillance can use standardized medication-review checklists and scheduled laboratory testing instead.

MANAGEMENT

Modification of the offending regimen

When DI-AKI is suspected, the first step is to assess whether the suspected medicine can be stopped, replaced or given at a lower dose. Other possible causes of AKI should be investigated at the same time. Management should follow the general principles of supportive AKI care. All medicines eliminated by the kidneys need to be reviewed, as reduced renal clearance during AKI can lead to further drug accumulation.

Correction of hemodynamic abnormalities

Any existing hypovolemia should be corrected, while unnecessary fluid administration should be avoided. Children with shock may need vasoactive support. Fluid therapy should be tailored to the child's perfusion, urine output, cumulative fluid balance and cardiopulmonary status.

Electrolyte and acid-base management

Hyperkalemia, metabolic acidosis, hyperphosphatemia, hypocalcemia and fluid overload should be treated according to their severity and cause. Medicines that may worsen electrolyte disturbances should be reviewed and, where appropriate, stopped or replaced.

Kidney replacement therapy

Kidney replacement therapy (KRT) may be needed for refractory hyperkalemia, severe metabolic acidosis, pulmonary edema or fluid overload, symptomatic uremia, or certain toxin-related indications. The decision should reflect the child's overall clinical condition rather than a creatinine value in isolation. Current approaches to pediatric AKI emphasize timely, individualized kidney support and appropriate medicine dosing during KRT [19].

ROLE OF THE CLINICAL PHARMACIST

Clinical pharmacists can support safe medicine use at every stage of treatment. Before therapy begins, they can identify nephrotoxic medicines, review baseline kidney function, suggest alternatives and help establish a monitoring plan. During treatment, they can assess renal dose adjustments, therapeutic drug monitoring, cumulative exposure and drug interactions. If AKI develops, pharmacists can help identify medicines that need to be withheld or adjusted and reduce the risk of further drug-related harm.

Pharmacist-led surveillance for nephrotoxic medicines can also strengthen hospital stewardship programs. Electronic alerts and structured medication-review pathways are particularly helpful when children receive several nephrotoxic medicines at the same time. Regular communication across the care team is important because preventing and managing drug-induced AKI requires input from more than one professional group.

LONG-TERM FOLLOW-UP AND FUTURE DIRECTIONS

Recovery from an episode of AKI does not always mean that kidney function has returned completely to normal. Long-term pediatric studies show that children who survive AKI may remain at increased risk of CKD, hypertension, recurrent AKI and kidney failure. In a large Ontario cohort, 18% of children who had experienced AKI developed a major adverse kidney event during a median follow-up of 9.7 years, compared with 5% of matched hospitalized children without AKI [20].

Children treated with nephrotoxic anticancer medicines may need particularly careful follow-up. Kidney dysfunction and electrolyte abnormalities can persist after cisplatin treatment, and prospective pediatric data support continued monitoring

after therapy [11]. Follow-up should be tailored to the child and may include blood pressure measurement, serum creatinine/eGFR, urinalysis and assessment for proteinuria.

Areas for future research include earlier injury biomarkers, electronic surveillance for nephrotoxic exposure, model-informed precision dosing and clinical decision-support systems. Pediatric pharmacology is moving toward individualized dosing based on changing renal function and measured drug exposure rather than relying only on fixed population-based regimens [4]. These approaches are promising, but they need to be validated in a wider range of pediatric populations before they become routine practice.

DISCUSSION

Drug-induced AKI in children is shaped by the interaction between medicine exposure, developmental renal physiology and the child's underlying illness. The high incidence reported in pediatric studies highlights the need for prevention strategies rather than waiting until serum creatinine has increased before taking action [2].

The available evidence shows that the clinical context strongly influences the risk of nephrotoxicity. A medicine may be tolerated by a well-hydrated child with normal kidney function but contribute to injury during dehydration, sepsis or shock. Total exposure also matters. Children in intensive care and oncology settings may receive several nephrotoxic medicines, making it difficult to identify one drug as the sole cause of AKI. Monitoring also has limitations: serum creatinine may rise late and is affected by muscle mass, while reduced urine output can be overlooked if it is not measured consistently [1].

Hospital-based prevention can be strengthened through structured programs. The NINJA initiative, for example, uses exposure surveillance, scheduled monitoring and medication review to reduce nephrotoxin-associated AKI [18]. Similar pathways can be adapted to local resources, with clinical pharmacists helping to review medicines and monitor doses.

AKI should also be viewed in terms of a child's longer-term kidney health. Children who recover from an episode may remain at risk of CKD, hypertension and further AKI. Discharge planning should therefore include an appropriate follow-up plan, particularly after severe or recurrent episodes [20].

This review has several limitations. As a narrative review, it draws on literature selected for clinical relevance rather than studies identified through a prespecified systematic process with formal risk-of-bias assessment. Pediatric studies of DI-AKI also differ in their definitions, populations, medicines and monitoring approaches, making incidence estimates difficult to compare directly. Evidence for newer biomarkers and precision-dosing strategies is still developing. Despite these limitations, the literature consistently points to the value of early risk assessment, medication review, renal monitoring and prevention involving the wider clinical team.

QUALITY IMPROVEMENT AND IMPLEMENTATION

Preventing drug-induced AKI in children calls for a planned approach to medication safety, rather than waiting until kidney injury becomes apparent. Hospitals can start by identifying medicines with important nephrotoxic potential and recognizing children who may be at higher risk because of dehydration, critical illness, pre-existing kidney disease or exposure to several nephrotoxic medicines. Locally approved nephrotoxin lists, clear requirements for renal monitoring and agreed criteria for medication review when kidney function changes can help make practice more consistent. Electronic prescribing systems can support this work through renal-dose alerts, warnings about duplicate nephrotoxin exposure and prompts for laboratory monitoring. Where electronic surveillance is not available, medication-review checklists, pharmacist-led review and predefined monitoring protocols offer practical

alternatives. The NINJA program showed that structured surveillance of nephrotoxin exposure, combined with clinical review, can reduce nephrotoxin-associated AKI in hospitalized children [18]. Implementation should involve physicians, clinical pharmacists, nurses and nephrology teams where appropriate. Useful quality indicators include timely serum creatinine monitoring, appropriate renal dose adjustment, reduced unnecessary concurrent nephrotoxin exposure and the incidence of nephrotoxin-associated AKI. Regular review of these measures can identify gaps and guide improvement. In settings with limited resources, the same principles can be applied through simple checklists, pharmacist-led surveillance and clear criteria for escalation.

CONCLUSION

Drug-induced AKI is an important and potentially preventable complication in children. Its development reflects the interaction between nephrotoxic drug exposure and factors such as developmental renal physiology, dehydration, critical illness, underlying kidney disease and concurrent nephrotoxins. Early recognition requires serial assessment of serum creatinine and urine output together with careful medication review and therapeutic drug monitoring when indicated.

Prevention should focus on avoiding unnecessary nephrotoxic exposure, maintaining adequate hydration and renal perfusion, adjusting doses to current kidney function and implementing structured nephrotoxin stewardship. Clinical pharmacists have an important role in medication review, dose optimization, monitoring and prevention. Future research should strengthen pediatric evidence for early biomarkers, precision dosing, electronic surveillance and long-term follow-up. Because significant pediatric AKI may have consequences beyond the acute episode, appropriate renal follow-up should form part of comprehensive care.

Declaration by Authors

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