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Medication-related renal toxicity and failure: Clinical perspectives

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Abstract
One important and frequently cause of Acute Kidney Injury (AKI), especially in the patient who are hospitalized and severely ill patient, is drug-induced nephrotoxicity. Because of their crucial function in filtration and excretion, the kidneys are more prone to drug-related harm. The mechanisms of nephrotoxicity, such as immune-mediated interstitial nephritis, hemodynamic changes, and acute tubular necrosis, are thoroughly examined in this study. Direct tubular injury, oxidative stress, inflammation, and altered renal hemodynamics are some of the ways that a variety of pharmacological drugs, such as aminoglycosides, NSAIDs, cisplatin, contrast media, and immunosuppressants, can affect renal function. The article also describes clinical signs, risk factors, and evidence-based management and preventative techniques. To lessen kidney impairment, the focus is on early detection, sensible prescription practices, and therapeutic medication monitoring. Doctors can improve renal outcomes and patient safety by knowing the pathophysiological underpinnings of nephrotoxicity due to those drugs.

Keywords: Drug-induced nephrotoxicity, AKI, nephrotoxic drugs, acute tubular necrosis (ATN), aminoglycosides, cisplatin, contrast-induced nephropathy, antivirals, calcineurin inhibitors, NSAIDS, ACEIS and arbs, vancomycin, methotrexate, sulfonamides and diuretics induced renal toxicity

Introduction
The most common and well known cause of acute kidney injury (AKI), is seen majorly hospitalized and severely ill patients, is drug-induced nephropathy. this is one of the main causes of renal morbidity and mortality globally, with an estimated 60% of all AKI cases in critical care units (ICUs) being related to drugs or their metabolites [1, 2]. Along with longer hospital stays and higher medical expenses, the severity of patien also increases the risk of developing and proceeding of patient to end-stage renal disease (ESRD) or chronic kidney disease (CKD) [3, 4]. Drug-induced nephrotoxicity has a complex etiology. Numerous processes are involved, including changes in intraglomerular hemodynamics, direct tubular toxicity, blockage caused by crystals, oxidative stress, inflammatory reactions, rhabdomyolysis, and thrombotic microangiopathy [5]. Drug-related renal injury is more likely to occur in populations with particularly those with already having pre-existing renal impairment i.e. Glomerural filtration rate (GFR) is <60 mL/min/1.73 m2, heart failure, sepsis, elderly patients, or those with intravascular volume depletion [6, 7].

Pathophysiological mechanisms
A. Acute Tubular Necrosis (ATN)
Apical reuptake in proximal tubular cells: Aminoglycosides are reuptaken through the megalin-cubilin complex into lysosomes, initiating phospholipidosis, mitochondrial damage, reactive oxygen species (ROS) production, and apoptosis [2].

Basolateral secretion accumulation: Drugs like tenofovir and cisplatin enter through organic anion transporters (hOATs) and are removed through efflux transporters (e.g. MRP 2, MRP 4). Accumulation damages mitochondrial DNA, (Table.1) causes apoptosis, and results in tubular damage [2, 8].

B. Hemodynamic and Vascular Effects
NSAID induced afferent arteriole constriction: Through inhibition of COX mediated prostaglandin synthesis, NSAIDs decrease afferent vasodilation and hence renal blood flow and GFR. Risk compounds when taken together with ACE inhibitors or diuretics ("triple whammy")

Table 1: Mechanisms of Drug-Induced Nephrotoxicity

Mechanism	Description	Examples
A. Acute Tubular Necrosis (ATN)	Apical reuptake via megalin-cubilin → lysosomal damage, phospholipidosis, ROS, apoptosis. Basolateral secretion via hOATs → mitoDNA damage, apoptosis.	Aminoglycosides, Tenofovir, Cisplatin
B. Hemodynamic/Vascular Effects	↓ Prostaglandin synthesis → Afferent arteriole constriction → ↓ Renal blood flow & GFR. Exacerbated by ACE inhibitors & diuretics ("triple whammy").	NSAIDs, ACEIs, Diuretics
C. Interstitial Nephritis & Glomerulopathies	Immune-mediated interstitial nephritis or glomerular damage. VEGF blockade, bisphosphonates affect glomeruli.	PPIs, NSAIDs, Antibiotics, VEGF inhibitors, Bisphosphonates

C. Interstitial Nephritis & Glomerulopathies

Some drugs (e.g. PPIs, antibiotics, NSAIDs) cause immune mediated interstitial nephritis or nephrotic syndrome. VEGF inhibitors, bisphosphonates, and immune checkpoint inhibitors often cause glomerular injury [1].

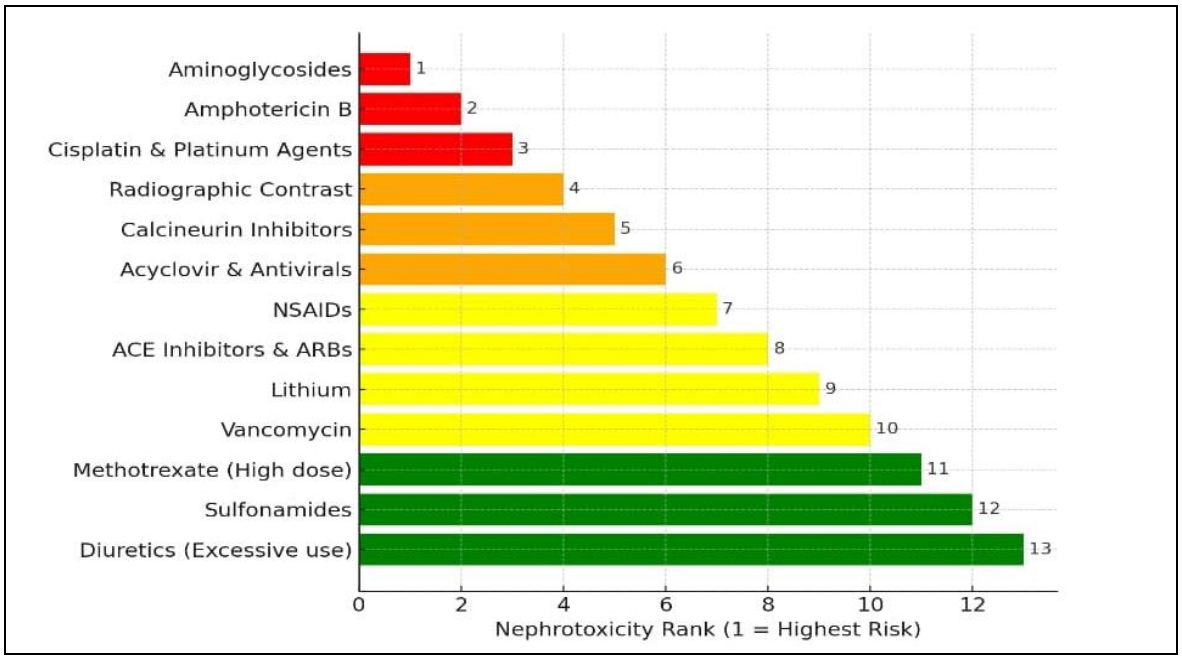

Fig 1: The chart ranks various drug classes based on their risk of nephrotoxicity, from Rank 1 (highest risk) to Rank 13 (lowest risk).

The nephrotoxicity ranking of drugs places aminoglycosides (Rank 1) like gentamicin and amikacin at the top due to their accumulation in proximal tubular cells causing acute tubular necrosis via mitochondrial dysfunction and reactive oxygen species (ROS) generation [1]. Amphotericin B (Rank 2), especially in its conventional deoxycholate form, induces renal vasoconstriction, hypokalemia, and distal tubular acidosis [3, 4, 6]. Cisplatin and other platinum agents (Rank 3) cause dose-dependent nephrotoxicity through DNA adduct formation and oxidative stress [9]. Radiographic contrast agents (Rank 4) especially in patients with pre-existing kidney disease or diabetes causes Contrast-induced nephropathy [4]. Calcineurin inhibitors (Rank 5) such as cyclosporine and tacrolimus impair renal perfusion and promote chronic interstitial fibrosis and arteriolopathy [10]. Other drugs mentioned in (Table.2) and (fig.1)

List of drugs induced nephrotoxicity

Table 2: Nephrotoxicity Risk Ranking of Drugs

rank	Class of drugs	examples
1	Aminoglycosides	Gentamycin, Amikacin, Tobramycin
2	Amphotericin B	Amphotericin B (Deoxycholate form)
3	Cisplatin & Platinum Chemotherapy Agents	Cisplatin, Carboplatin, Oxaliplatin
4	Radiographic Contrast Agents	lohexol, Iodixanol
5	Calcineurin Inhibitors	Cyclosporine, Tacrolimus
6	Antiviral Drugs	Acyclovir, Tenofovir, cidofovir, Foscarnate
7	Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	Diclofenac,Ibuprofen, Naproxen, Indomathacin
8	ACEIs & ARBs	Enalapril, Lisinopril, Losartan, Telmisartan
9	Lithium	Lithium Carbonate
10	Vancomycin	Vancomycin
11	Methotrexate	Methotrexate
12	Sulphonamides	Sulfamethaxazole, Sulfadiazine
13	Diuretics	Furosemide, Hydrochlorothiazide, Bumetanide

Aminoglycosides

E.g., gentamicin, amikacin, tobramycin are Gram-negative-bactericidal antibiotics and are usually nephrotoxic, particularly with more than 5-7 days of therapy. These drugs get filtered at the glomerulus and within proximal tubular cells become concentrated, leading to oxidative damage, mitochondrial damage, and non-oliguric acute tubular necrosis (ATN) (fig.2). Risk factors are high dose, long-term therapy, age, underlying renal impairment, dehydration, and concurrent nephrotoxic agents.

Nephrotoxicity can be characterized by clinically with a slow peak increase in serum creatinine, mild proteinuria, and electrolyte disturbances such as hypomagnesemia or hypokalemia. Treatment consists of immediate discontinuation, hydration, correction of electrolytes, and avoidance of subsequent nephrotoxins, with dialysis reserved for fulminant cases. Prevention involves once-daily dosing, therapeutic drug monitoring, short treatment course, and proper hydration [3, 4].

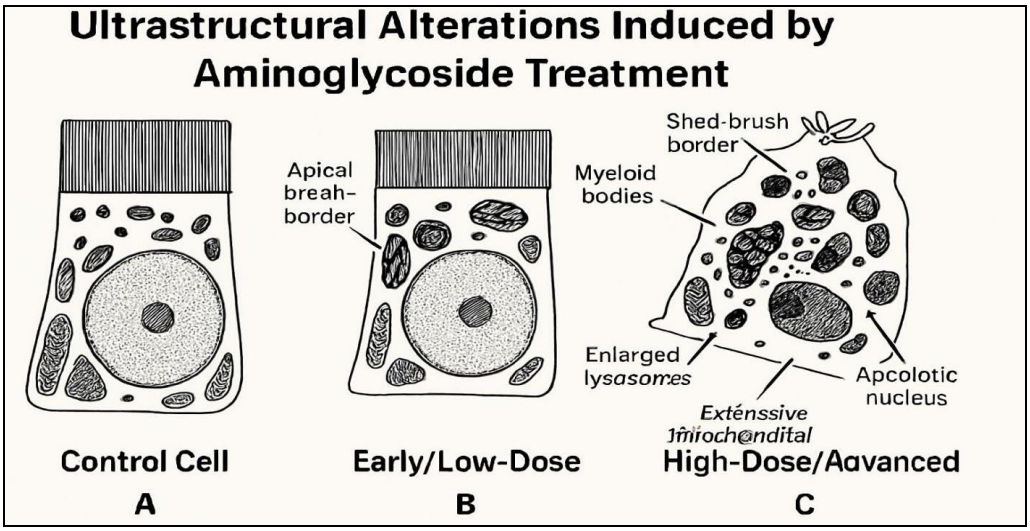

Fig 2: Ultrastructural changes in proximal tubular cells during aminoglycoside exposure.(A) Control cell: ormal ultrastructure.(B)Early/low dose: Lysosomal enlargement from fusion of pre existing structure with polar lipid accumulation forming concentric myelin like (myeloid) bodies: other organelles largely intact.(C) High dose/ advanced dose exposure: Lysosomal rupture with cytoplasmic release of myeloid bodies, mitochondrial swelling, dilated endoplasmic reticulum, lose of brush-border microvilli, membrane discontinuities, and apoptotic nuclei. Changes may occur independently across cells

Amphotericin B

Amphotericin B is a pan-antifungal that can usually cause dose-related nephrotoxicity due to direct tubular cell damage and vasoconstriction of the afferent arterioles, causing renal vasoconstriction, electrolyte loss, and non-oliguric acute kidney injury (AKI) (fig.3). Risk is increased by high cumulative doses, extended therapy, underlying renal disease, and concomitant nephrotoxic agents. Clinical manifestations include increasing serum creatinine, hypokalemia, and hypomagnesemia. Prevention is with lipid formulations, slow administration, good hydration, and electrolyte checking [3, 4, 6].

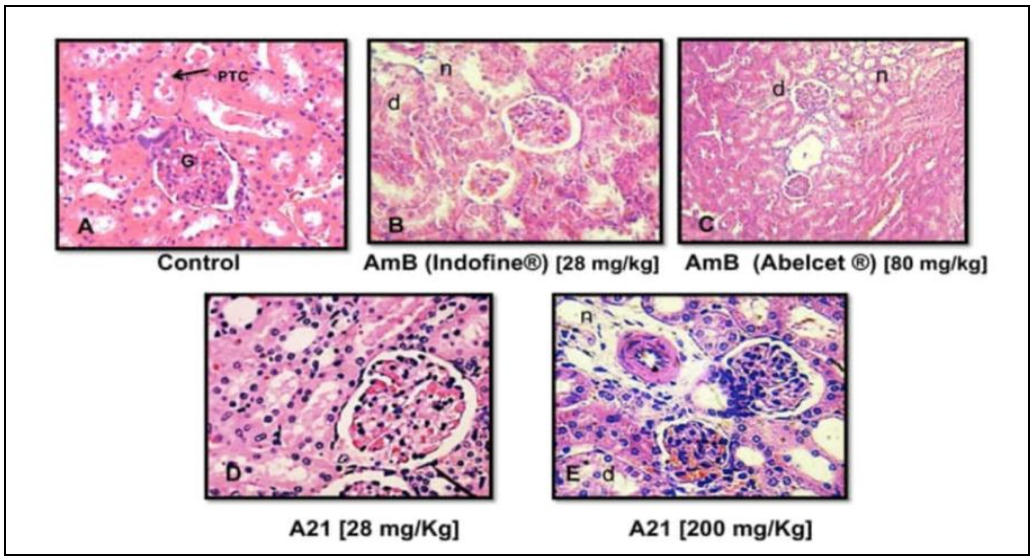

Fig 3: Histopathological kidney changes in Balb-C mice after teatment. (A) Control: Normal tubules following 2 weeks of daily IP sodium deoxycholate (B)AB(DMSO,28 mg/kg): Dilated degenerative tubules(d) with exfoliated necrotic epithelium and necrotic tubules(n). (C) Amb(Abelcet®,80mg/kg). (D) A21 (28mg/kg): fewer necrotic/degenerative lesions with occational regenerative epithelium and protein casts. (E) A21 (200 mg/kg): dilated degenrative tubules(d) comtaining exfoliated necroti cells, necrotic tubules(n), and inflammatory cells. (ic). G=Glomerulus; PT= Proximal Tubles: TD= Distal Tubule: IP= intraperitoneal [7].

Cisplatin & platinum chemotherapeutic agents

Cisplatin and the other platinum-containing chemotherapeutic agents (carboplatin, oxaliplatin) are all well characterized for their dose-related nephrotoxicity, of which cisplatin is the most toxic. The main mechanism is uptake in proximal tubular epithelial cells through organic cation transporters, resulting in oxidative stress, mitochondrial damage, and DNA damage, which result in tubular cell apoptosis and necrosis (fig.4). Cisplatin also initiates inflammatory cytokine release and renal vasoconstriction, additionally decreasing renal perfusion. Clinically, it presents as acute kidney injury (AKI), electrolyte imbalance (hypomagnesemia, hypokalemia), and occasionally chronic kidney disease following repeated treatment cycles. Carboplatin is less toxic to the kidney, whereas oxaliplatin is infrequently associated with major renal damage. Hydration regimens and dose modifications are preventive measures of prime importance [8].

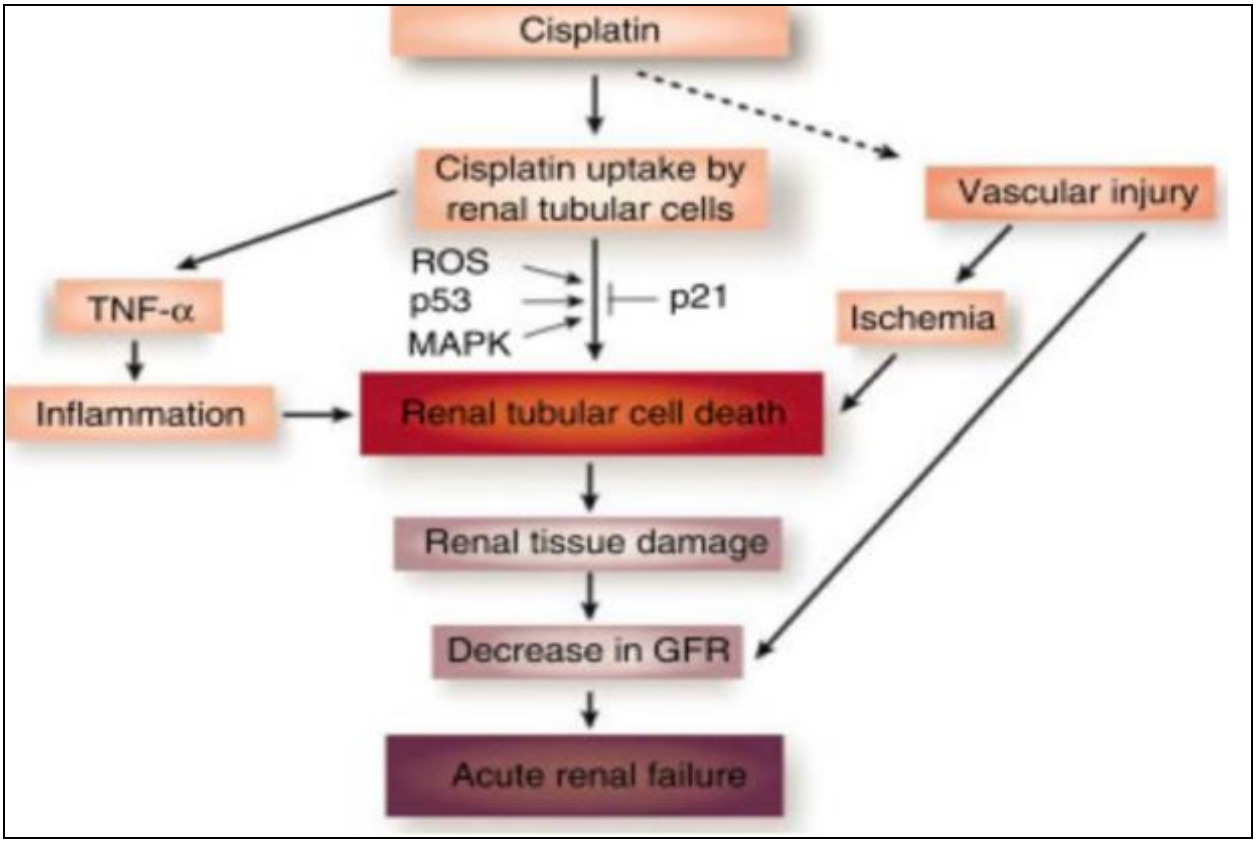

Fig 4: Overview of the pathophysiological events in cisplatin nephrotoxicity [9].

Radio graphic contrast media

Radio graphic contrast media can cause and even directly induce contrast-induced nephropathy (CIN) or acute kidney injury which most probably develops within 24-72 hours of exposure. The pathogenesis includes renal vasoconstriction that results in ischemia and direct tubular toxicity. The risk factors involve pre-existing chronic kidney disease, diabetes mellitus, dehydration, high contrast volume, and concomitant Nephrotoxins. Clinically, CIN will show gradual increase in serum creatinine and reduced amount of urine output, typically non-oliguric, and wil start to improving within 7-14 days in mild cases. Prevention is based on proper intravenous hydration, utilization of low- or iso-osmolar contrast media, restriction of contrast dose, and avoidance of nephrotoxic medications during the procedure. Therapy is mostly supportive, as no proven therapy is available [3, 4, 6].

Calcineurin inhibitors

Calcineurin inhibitors, e.g: Cyclosporine and Tacrolimus have significant causes of both Acute as well as chronic nephrotoxicity in transplant and autoimmune disease patients. Their mechanism is primarily dose-dependent vasoconstriction of efferent and afferent arterioles through increased endothelin and reduced nitric oxide and prostaglandins, which results in decreased renal blood flow and reduced GFR. Chronic injury results in tubulointerstitial fibrosis and arteriolar hyalinosis, in part through activation of profibrotic cytokines such as TGF β. Acute toxicity is reflected as reversible serum creatinine rises, whereas chronic toxicity results in irreversible structural kidney injury. The nephrotoxic potential is increased with increased drug concentration, concomitant nephrotoxins, and existing kidney disease; judicious therapeutic drug monitoring and minimization are necessary [10].

Antiviral drugs

Some antiviral agents, particularly acyclovir, foscarnet, cidofovir, and tenofovir, induce drug-induced nephropathy through precipitation of crystals, direct tubular toxicity, or mitochondrial damage. Acyclovir and cidofovir can cause intratubular crystals to form and result in obstructive nephropathy, and tenofovir causes proximal tubular damage and ATN (fig.5 & 6). The risk factors are dehydration, high dose, renal impairment, and concurrent nephrotoxicity. Treatment includes adequate hydration, dose reduction according to renal function, and withdrawal of the causative agent, and the majority of cases are reversible if it is identified early [3, 4, 6].

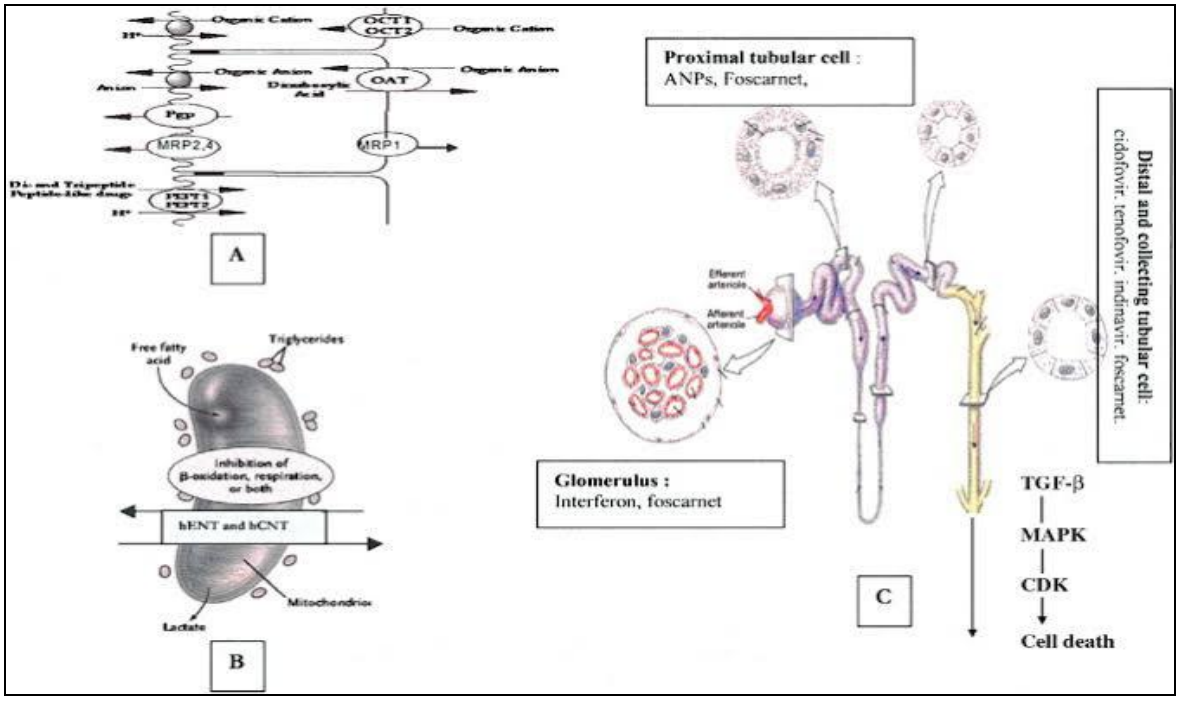

Fig 5: Antiviral drug- induced nephrotoxic may involve three principal mechanisms: **(A)** Transporter- mediated injury- altered expression or competitive inhibition of Renal transporter (e.g., hOATs, MRP2, MRP4) can impair drug excretion, leading to proximal tubular accumulation and toxicity as seen with acyclic nucleotide phosphonates, often presenting as tubular acidosis. **(B)** MAPK Pathway activation- stimulation of the mitogen - activated protein kinase cascade may disrupt epithelial barrier function in renal tubules, initiating, signaling events that culminate in apoptosis. **(C)** Mitochondria dysfunction - direct inhibition of respiratory chain enzymes or binding to mitochondrial DNA impairs fatty acid oxidation and ATP production, causing oxidative stress, lactic acidosis, and microvesisular steatosis. nucleoside reverse transcriptase ihibitors are class examples, and pre-existing mitochondrial injury may predispose patients to Tenofovir- induced tubular damage [11].

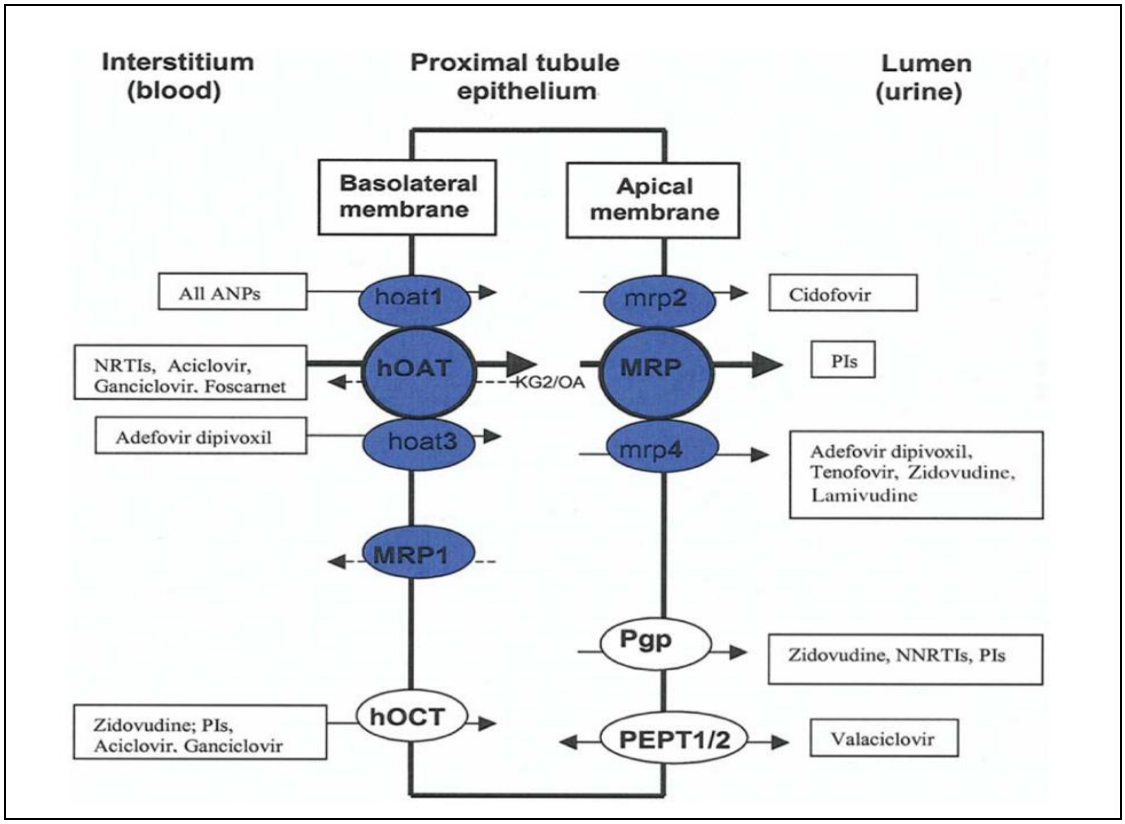

Fig 6: Antiviral drugs are actively excreted by the kidney via specialized transport systems inthe proximal tubules. Organic anions (eg., NRTIs, ANPs) enter tubular cells from blood across the basolateral membrane via the sodium dependent OAT1 transporter, using a ketoglutarate exchange and Na+/dicarboxylate cotransport. Once inside, they can disrupt cell processes and are secreted into the tubular lumen through apical membrane transporters, including MRP for active efflux. Organic cations (eg., certain antivirals) enter via OCTs at the basolateral side and exit into the lumen through P-glycoprotein. This process, while eliminating drugs, can contribute to proximal tubular injury [11].

Non steroidal anti inflammatory drugs

NSAIDs (eg., ibuprofen, diclofenac, naproxen, and indomethacin) causes Acute kidney injury, especially in the elderly or volume-depleted or chronic patients.The most frequent mechanism is COX 1/COX 2 inhibition, which lowers renal prostaglandin (PGE_2/PGI_2) production, affecting afferent arteriolar vasodilation and consequently decreasing GFR and renal perfusion. The secondary mechanism is acute interstitial nephritis (AIN), (fig.7) commonly immune mediated, that occurs with nephrotic-range proteinuria; interestingly, ~80% of NSAID related AIN are due to drugs such as ibuprofen or naproxen. Although frank nephrotoxicity is uncommon in normal individuals, risk increases exponentially in susceptible individuals, and large cumulative exposure leads to progression of chronic kidney disease [12, 13].

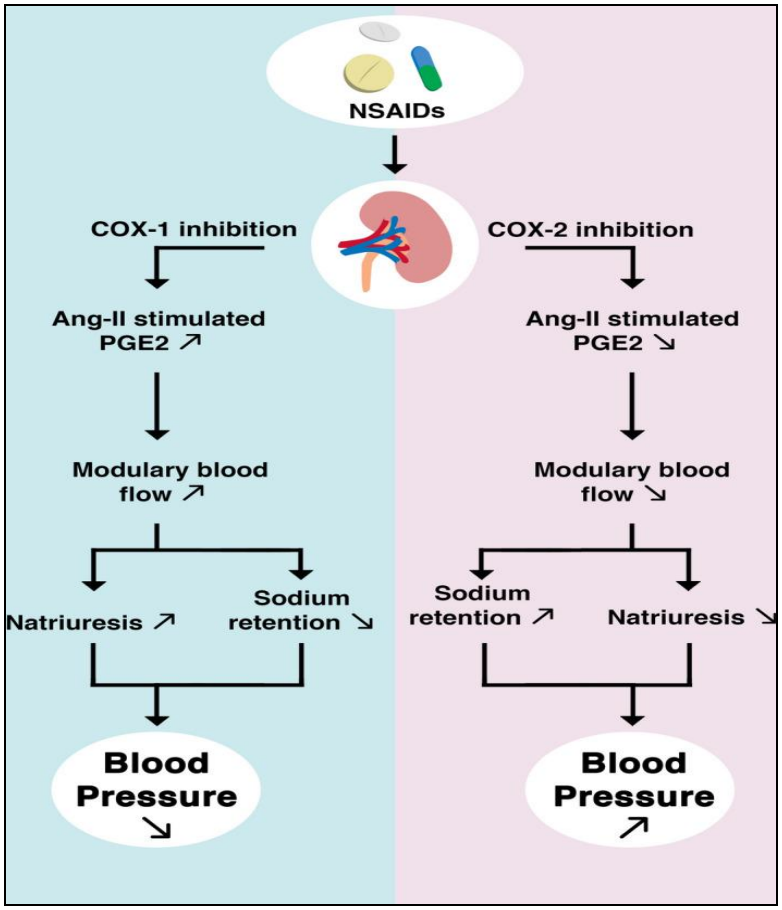

Fig 7: Mechanism of NSAIDs on COX-1 and COX-2 Receptors. [13]

ACE Inhibitors & ARBs

ACE inhibitors lower intraglomerular pressure which inhibits the of angiotesin I to convert into angiotensin II, which otherwise constricts the efferent arteriole. In patients with conditions reliant on angiotensin II-induced efferent vasoconstriction—bilateral renal artery stenosis, heart failure, hypovolemia, or advanced CKD—this will leads to profound drop in glomerular filtration rate and trigger AKI. The effect is usually reversible on withdrawal, and in the majority of patients without such risk factors, ACE inhibitors are renoprotective in the long run use by preventing glomerular HTN and proteinuria. Hyperkalemia is a frequent concomitant adverse effect secondary to decreased aldosterone secretion [14].

Angiotensin Receptor Blockers (ARBs) (e.g., Losartan, Telmisartan)

ARBs binds to the angiotensin -II type 1 receptor and blocks the action of angiotensin-II. Similar to ACE inhibitors, ARBs cause dilation of the efferent arteriole, decreasing intraglomerular pressure, which in volume-depleted patients, bilateral renal artery stenosis, (fig.8) or advanced heart failure can be detrimental and cause AKI. They do not have the bradykinin-related cough and angioedema associated with ACE inhibitors. In the long run, ARBs provide renoprotective benefits by lowering proteinuria and delaying CKD progression, but necessitate attention to serum creatinine and potassium levels, especially in high-risk groups or with other nephrotoxins [15, 16].

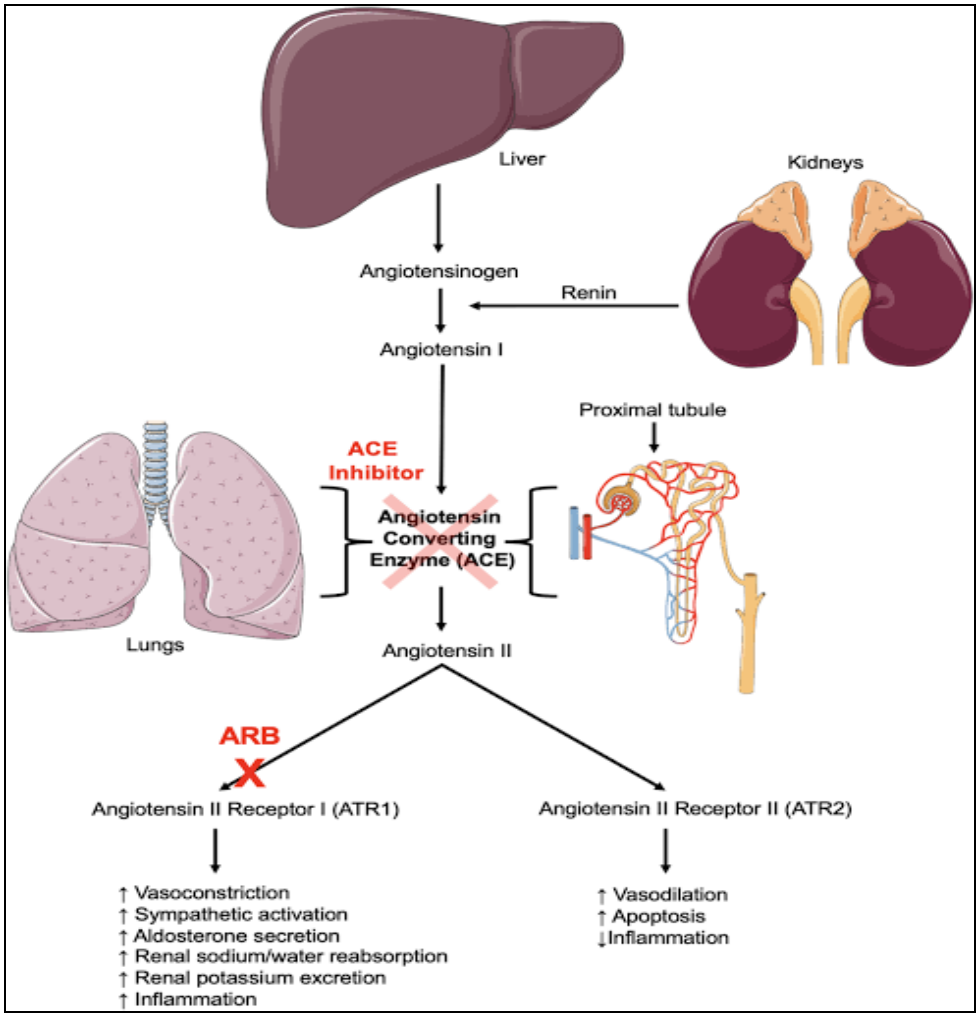

Fig 8: Mechanisms of action of ACE inhibitors/ARB [16].

Lithium

Lithium, a common medication for bipolar disease, can induce both acute and chronic nephrotoxicity. Chronic tubulointerstitial nephritis is the most frequent chronic effect, which can progress to slow GFR decline and ultimate chronic kidney disease after prolonged exposure over years. Lithium penetrates into renal tubular cells by epithelial Na+ channels (ENaC) which are present in collecting duct, causing cellular damage, concentrating defect, and nephrogenic diabetes insipidus in as many as 40% of chronic users. Reversible AKI results from overdose or volume depletion, but chronic exposure results in irreversible structural damage with cortical and medullary fibrosis. Risk is enhanced by high serum levels of lithium, long-term therapy (>10 years), co-administration of nephrotoxins, and recurrent lithium toxicity. Preventive measures involve scrupulous monitoring of serum levels, dose reduction, and dehydration avoidance [17].

Vancomycin

Vancomycin, a glycopeptide antibiotic for which MRSA and other resistant Gram-positive infections are the main indications, is dose-dependent nephrotoxicity, particularly at high trough levels (>15-20 mg/L), extended therapy (>7 days), or with other nephrotoxins (most notably piperacillin-tazobactam) (fig.9). The mechanism is primarily through oxidative stress and thus directly damage of tubular epithelial cells takes place. resulting in acute tubular necrosis. Vancomycin can also cause acute interstitial nephritis by immune-mediated mechanisms. Clinically, nephrotoxicity manifests as increasing serum creatinine and decreased urine output, usually reversible with prompt drug cessation. There is increased risk in severely ill patients, those with underlying CKD, obesity, or concomitant aminoglycoside therapy. Therapeutic drug monitoring and avoiding unnecessary extended courses are important prevention strategies [18].

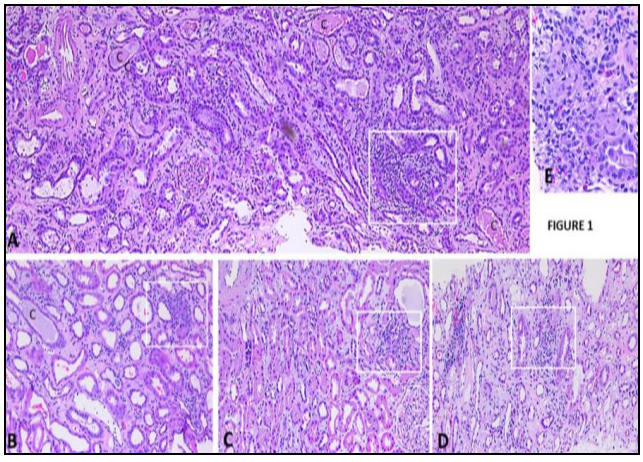

Fig 9: Tubule-interstitial inflammation seen in patients with Vancomycin Nephrotoxicity, Different types of inflammatory response seen in the vicinity of distal tubules with vancomycin casts in both cortex and also at region away from tubules with casts [1].

Methotrexate

Methotrexate, an immunosuppressant and antimetabolite, a folate antagonists used as an immunosuppressant and anti cancer agent induces nephrotoxicity by deposition of methotrexate and methotrexate metabolites present in the renal tubules leading to crystal-induced tubular injury and resulting in acute kidney injury\ (fig.10). Risk is increased with high-dose therapy, dehydration, acidic urine, and baseline renal insufficiency [19, 20]. Clinically manifested by increasing serum creatinine and oliguria, prevention consists of proper hydration, alkalinization of urine, and leucovorin rescue [10, 11]. Prevention involves aggressive IV Hydration, alkalinization (eg: sodium bicarbonate) and leucovorin rescue while glucarpidase is used in cases of severe toxicity with renal dysfunction [21, 22].

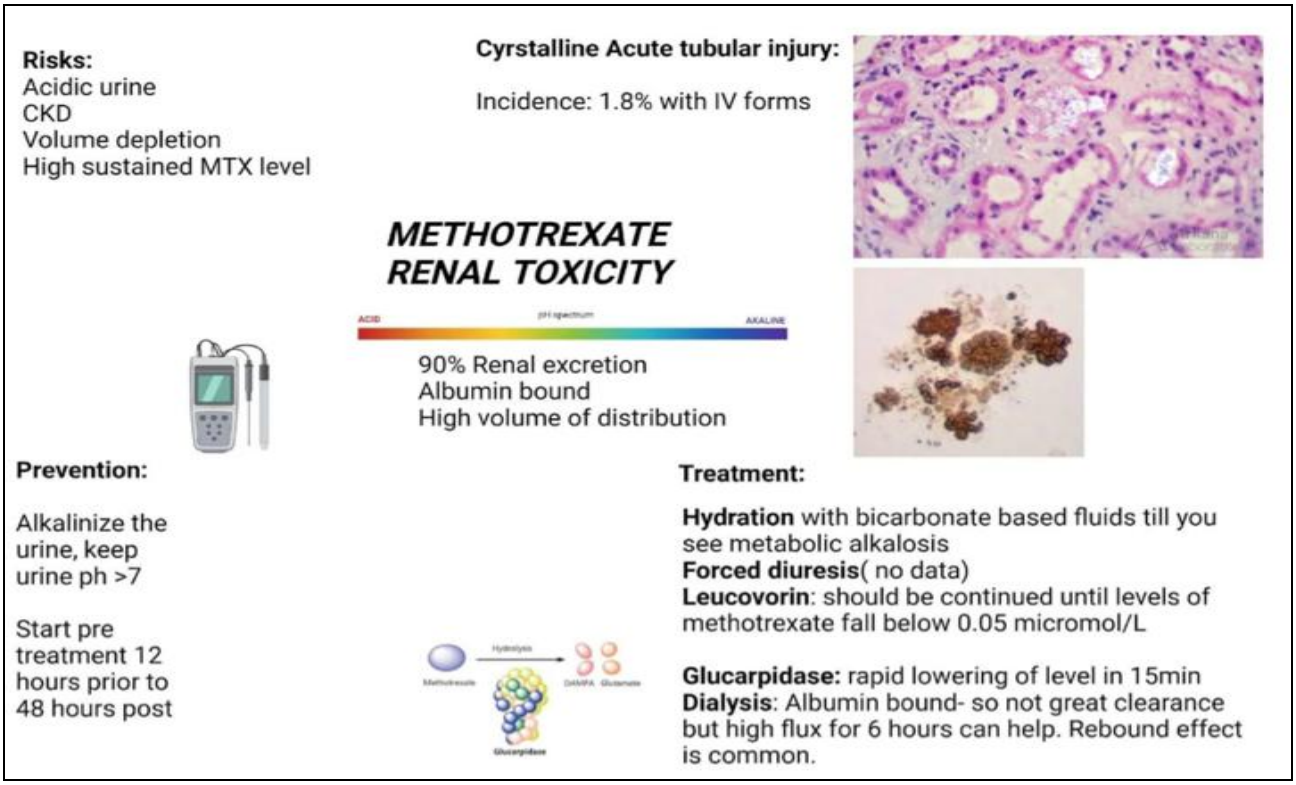

Fig 10: Methotrexate induced renal toxicity

Sulphonamides

e.g., sulfamethoxazole induces drug-induced nephropathy mainly through crystal-induced tubular obstruction and acute interstitial nephritis (AIN). Risk factors are dehydration, acidic urine, and high dose. Clinically, patients can present with flank pain, hematuria, pyuria, or increasing serum creatinine. Treatment consists of stopping the drug, adequate hydration, and urine alkalinization, with severe AIN needing corticosteroids [3, 6, 23] Sulfonamides, particularly older or less soluble agents like sulfadiazine, may cause nephrotoxicity by forming crystalls in renal tubules, resulting in crystal-induced acute kidney injury [24]. This occurs more commonly in acidic urine, where the drug is less soluble, promoting crystal formation and tubular obstruction [25]. Clinical features include flank pain, hematuria, oliguria, and a rise in serum creatinine. [26] Risk factors include volume depletion, high doses, acidic urine, and pre-existing kidney disease [27]. Management involves discontinuation of the drug, hydration, urine alkalinization, and in severe cases, dialysis [28]. Prevention includes using more soluble sulfonamides, ensuring adequate hydration, and maintaining alkaline urine pH during therapy (fig.11) [29].

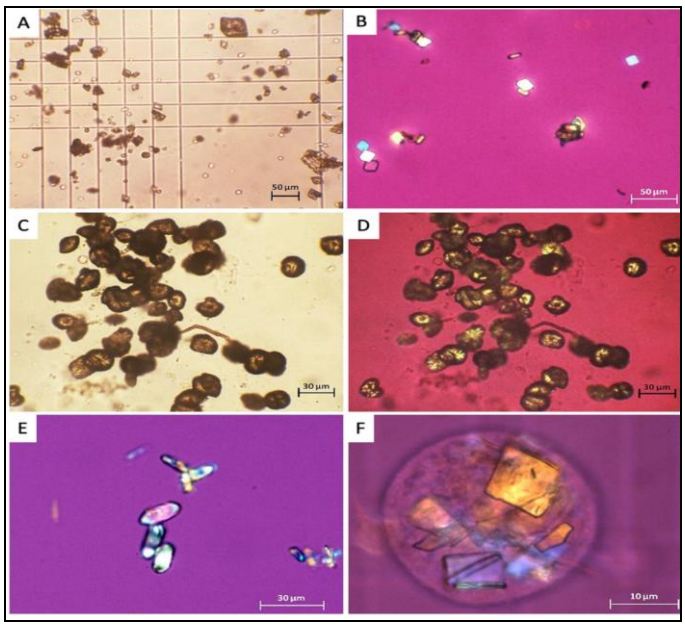

Fig 11: Representative N-Acetyl-Sulfamethoxazole (NASM) crystals in urine. (A) - (B): lozenges/parallelepipeds [bright field (A) and polarized light (B)]; (C) - (D): spheroids/ "shocks of wheat" shapes [bright field (C) and polarized light (D)]; (E) ovals mimicking calcium oxalate monohydrate; (F) crystals inside a possible macrophage [29].

Diuretics

Diuretics such as loop diuretics furosemide, thiazides, and potassium-sparing agents can cause nephropathy primarily through volume depletion and prerenal azotemia and less frequently through interstitial nephritis or electrolyte imbalance. Hypovolemia, hypokalemia, and hyponatremia with hypovolemia caused by loop and thiazide diuretics predispose to AKI. Potassium-sparing diuretics cause hyperkalemia, particularly in CKD patients. Treatment consists of dose reduction, hydration, and discontinuation in case of AKI [3, 6].

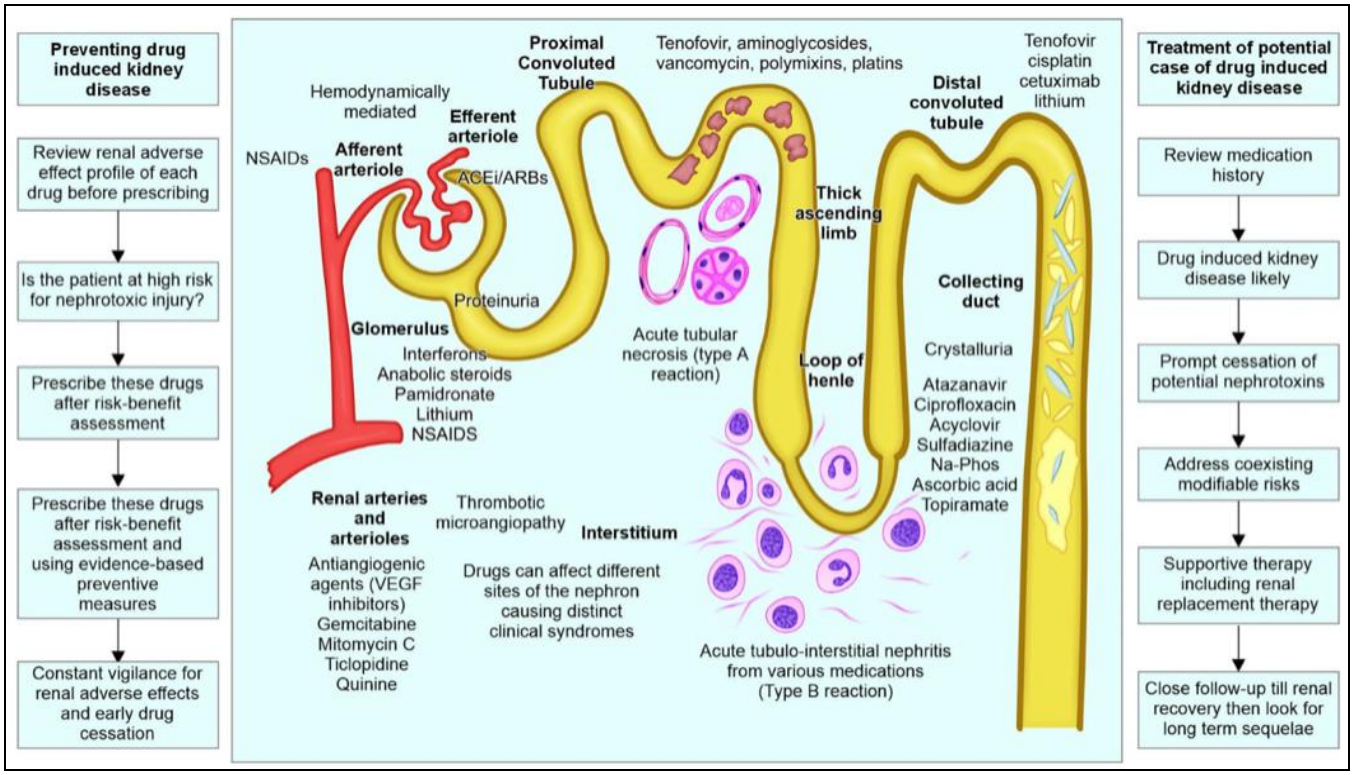

Fig 12: General approach to DIKD [30]

Discussion

Drug Indian nephrotoxicity is a significant cause of acute kidney injury (a k i) close and chronic kidney damage particularly in hospitalised patient. Multiple pharmacological classes contribute to renal injury through diverse mechanisms. Aminoglycosides (Gentamicin, Amikacin, Tobramycin) accumulate in proximal tubular epithelial cells generating oxidative stress and acute tubular necrosis (ATN); risk increases with prolonged therapy, high doses, and concurrent nephrotoxins [5]. Amphotericin B causes doss -related tubular damage and afferent arteriolar vasoconstriction, leading to electrolyte loss and AKI [6]. Cisplatin and other platinum agents induce mitochondrial damage, DNA cross-linking, oxidative stress, while radiographic contrast agents cause Contrast-induced nephropathy (CIN) through vasoconstriction and direct tubular toxicity. Calcineurin inhibitors (cyclosporine, tacrolimus) produce reversible vasoconstriction acutely and chronic tubulointerstitial fibrosis with prolonged use [10]. Antivirals such as Acyclovir, Cidofovir, and Tenofovir cause crystal induced obstruction or mitochondrial injury [11]. NSAIDS impair renal prostaglandin synthesis, reducing afferent arteriolar dilation and renal perfusion, sometimes precipitating immune-mediated acute interstitial nephritis (AIN). ACE Inhibitors and ARBS lower intra glomerular pressure by dilating efferent arterioles, beneficial in many cases but potentially harmful in bilateral renal artery stenosis, severe hypotension or dehydration [14]. Lithium can cause chronic tubulo-interstitial nephritis and nephrogenic diabetes insipidus, especially with long term therapy. Vancomycin may produce dose-dependent oxidative tubular injury and AIN, especially at high levels or in combination with other nephrotoxins. Methotrexate and Sulphonamides precipitation in renal tubules as crystals, resulting obstruction and tubular damage, particularly in acidic urine [21, 22]. Diuretics may cause pre renal AKI via volume depletion, with potassium sparring agents increasing hyperkalemia risk (fig.12) [30].

Management

Management of drug-induced nephrotoxicity focuses on the early identification and discontinuation or dose adjustment of the offending agent. Maintaining adequate hydration to preserve renal perfusion is critical, especially in high-risk patients. Management also includes correction of electrolyte disturbances, close renal function monitoring, and use of therapeutic drug monitoring (TDM) for nephrotoxic agents like aminoglycosides and vancomycin [1]. In certain cases, urine alkalization is beneficial for preventing crystalluria with drugs like methotrexate or sulfonamides [19]. For contrast-induced nephropathy, N-acetylcysteine and sodium bicarbonate infusion are preventive measures [31]. Additionally, avoiding harmful combinations such as NSAIDs, ACE inhibitors, and diuretics known as the “triple whammy” is essential [32]. In severe or rapidly progressing renal dysfunction, early nephrology consultation is strongly advised and plant based antioxidant diet with less potassium is usually advised by some researchers [33, 34].

Conclusion

Drug Induced Nephrotoxicity remains a preventable yet prevalent cause of renal impairment with implications for morbidity healthcare cause and long terms outcomes. a wide range of drugs including anti microbials, chemotherapeutics, immunosuppressants, anti-viral agents, anti inflammatory agents, cardiovascular agents and diuretics can cause renal injury through mechanism such as altered hemodynamics direct tubular toxicity oxidative stress and immune mediated inflammation. Effective prevention requires risk stratification before initiating potentially nephrotic drugs, patient specific dose adjustments and therapeutic drug monitoring when applicable. Ensuring adequate hydration, avoiding concurrent nephrotoxins, and employing protective measures such as urine alkalinization or antioxidant therapy can reduce risk. Once nephrotoxicity is suspected, immediate withdrawal or modification of therapy, supportive renal care, and correction of electrolyte and acid base disturbances are essential. In case is where drug continuation is unavoidable, dose reduction, prolong dozing intervals, and adjunctive protective agents should be considered. Ultimately, interdisciplinary collaboration among prescribers, pharmacists, and nephrologists is vital to balance therapeutic efficacy with renal safety. By integrating preventive protocols, early detections strategies and evidence base management has healthcare providers can minimise the burden of drug induced nephrotoxicity and preserve renal function in vulnerable patient populations.

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