DOI: 10.55522/jmpas.V12I1.4171 ISSN NO. 2320–7418

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Review article

Drug induced nephrotoxicity and associated factors a narrative review

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ABSTRACT

Drugs are a common reason for kidney injury. Antibiotic like gentamicin which is clinically a highly effective drug, is not preferred by physicians primarily because of the renal damage caused by it. Medication-induced renal injury has an intricate mechanism that includes a multitude of elements together with the innate nature of medications, innate patient characteristics that increase the chances of renal damage, and the pharmacokinetics of the drug. A particular drug can produce varied amount of damage in different individuals, which implies that the risk is not same for all. The reason behind this is that, there are different factors which determine the amount of renal damage that occurs due to drugs. In this article, we have reviewed the various elements linked to drug-induced nephrotoxicity.

Keywords: Renal Damage, Reno-Toxins, Kidney Damage, Medicine.

Received - 19-08-2022, Accepted- 04-01-2023

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INTRODUCTION

To some extent, medicines are a common reason for kidney injury. The statistics of medication instigated renal toxicity are presently based on current evidence concentrating on acute kidney injury (AKI). As per reports, about 14 to 26% of adults and 16% of children admitted in the hospital suffer from drug induced kidney damage. Medication-induced kidney damage is much appreciated in the inpatient setting, specifically in the critical care unit [1-2].

Prescription drugs and over-the-counter (OTC) medications in addition to variety of nutraceuticals available at health food shops (nutrients, home remedies, supplements, and alternative medicinal products) can result in kidney damage [3-20]. Different imaging modalities utilized for analytic purposes such as radio imaging contrast media are also connected with nephrotoxicity. Be that as it may, not all subjects presented the different potential nephrotoxins foster kidney illness. In this manner, the nephrotoxicity of medicines, and other ingesting substances is a complex process and involve a sequence of factors. This includes the innate nature of the drug, the various patient attributes and the pharmacokinetics of the drugs [6-9]. This review gives an overview of the various drugs, the mechanism and factors involved behind the drug induced nephrotoxicity.

Elements Associated with Nephrotoxicity

The advancement of medication instigating renal damage can be best perceived by analyzing the elements that add to nephrotoxicity. The structure of the medicine, amount of drug consumed and the metabolic pathway that the drug undergoes are important determining factors of reno-toxicity. Principal patient attributes, for example, pre-existing diseases, hereditary determinants of medication, metabolization and transport, and host genetic factors involved in the immune response, are likewise significant in medication kidney damage [Table 1]. As the kidney process & eliminate (through a filtration process and transfer from peritubular capillaries to the renal tubular lumen) numerous ingested medications, the exchange of these compound with different portions of the nephron might be related to nephrotoxicity [5-9]. For acute renal failure to happen, a blend of the most common three probable determinants are by and large apparent. Generally, more than one factor will be existing.

Table 1: Factors associated with nephrotoxicity

Medication factors	Patient factors
Chemical structure	Pre-existing diseases/Coexisting Diseases
Quantity of exposure	Genotype
Metabolic taking care of	Age
Excretory pathway	Gender

It is the distinctions in the chemical structure of the medication, basic patient attributes, and adaptation in renal

maneuver of the ingested chemical compound that probably demystifies the variableness and diverseness distinguished with medication-prompted nephrotoxicity.

The Medication

Exposure to Reno toxic chemicals leads to kidney damage. The list of such drugs/chemicals is extensive. However, some common nephrotoxic agents are listed in Table 1. These drugs belong to varied categories ranging from antibiotics, analgesics, and immunomodulators. Besides, countless new medicines with obscure nephrotoxic potential endure clinical trials and are therefore delivered into real word settings where they can cause injury to the kidney. This is a reasonable connection with exposure to these new medications in subjects who have coexisting diseases or different attributes that increment nephrotoxic risk that were excluded from experimental studies. In spite of the fact that clinicians recommend by far most possibly nephrotoxic meds, many are likewise accessible as over-the-counter drugs. Radiological contrast media, specifically those administered intravenous/ intra-arterially at higher quantities, are one more possible reason for AKI [21-34].

Furthermore, the Food and Drug Administration (FDA)-endorsed meds, uncontrolled wellsprings of possibly nephrotoxic compounds are integrative medicines, which are broadly accessible at most stores [17-20]. Included are things depicted as natural medicine, herbal products, and nutraceuticals [16]. Another worry is that these items frequently contain various unsafe synthetics or potentially toxins that are not recorded on the product labels. Not remarkably, the substances recorded on the product labels are available in differing quantities from enormous, too little, to even fictitious. Furthermore, in unmediated nephrotoxicity, natural medicines might interact with allopathic medications to build one more likely path of nephrotoxicity. Instances of such unlisted items interact with plant materials containing ephedrine alkaloids and aristolochic acid also natural products debased with nonsteroidal ant inflammatory drugs (phenylbutazone), cadmium, and chromium [Figure 1] [16-20].

Dosage and Duration of Treatment

Higher dose and longer duration usage of specific nephrotoxins will increase the risk for acute renal failure employing over-exposure to the kidney, even in subjects with negligible or no hidden risk. A few medications, for example, the broad-spectrum antibiotics like aminoglycosides, antineoplastic agents like platinum compounds, antifungals like amphotericin B, and polymyxin B, colistin come in this class [22-28].

Physicochemical properties of the drug

Medications and primary, and secondary metabolites that are does not dissolve in the urine might cause drug-induced crystal nephropathy intratubular precipitation of exogenously administered medications [29-31].

Table 2: Nephrotoxic medications

Pharmacotherapeutic agents	Active compounds
Aminoglycosides	Gentamicin Tobramycin Amikacin Netilmicin Neomycin Streptomycin Vancomycin
Antiviral	Cidofovir Adefovir Dipivoxil Tenofovir Acyclovir
Antifungal	Amphotericin B
Antibiotic Fluoroquinolones	Colistin Polymyxin B Sulfadiazine Ciprofloxacin
Chemotherapy Alkylating agents Antitumor antibiotic Antimetabolite	
	Ifosfamide
	Mitomycin
	Gemcitabine
Purine analog Platins Interleukin 2 (IL-2)	Methotrexate
	Pentostatin
	Cisplatin
Antiangiogenesis agents	Bevacizumab Ranibizumab Ramucirumab Aflibercept Sorafenib Sunitinib Pazopanib Vandetanib Axitinib
Immunotherapies	Interferon alfa (IFN-α) therapy Chimeric antigen receptor T cells (CAR T) cell therapy
Immunosuppressives	Calcineurin inhibitors Sirolimus Everolimus
Analgesics	
Non-steroidal anti-inflammatory drugs	Naproxen Aspirin
Selective cyclooxygenase-2 (COX-2) inhibitors	
Drugs acting on renin angiotensin system	angiotensin-converting enzyme (ACE inhibitors) / angiotensin II receptor blockers (ARBs)/ renin inhibitors
Sodium-glucose transport protein- 2 (SGLT-2) inhibitors	Canagliflozin Dapagliflozin
Inhalational anesthetic	Methoxyflurane
Anticonvulsant	Zonisamide Topiramate
Lipase inhibitor	Orlistat
Mesalamine	
Miscellaneous	Bee pollen
	Bee propolis
	Chromium Picolinate
	Creatine Monohydrate
	Germanium
	l-Lysine
	Artemisia absinthium (Wormwood Oil)
Adulterants	
	Mefenamic acid
	Dichromate
	Cadmium
Radiological contrast Nonionic contrast media	
	low-osmolality
	High-osmolality
	is osmolar
	Gadolinium-based contrast agents
Environmental toxicants and Heavy metals	Uranium Copper Lead Mercury Cadmium

This activity is upregulated additionally by decreased urinary flow rates, the potential of hydrogen (pH) (depend upon medicine dissociation constant [pKa]), immoderate medication dosing, and higher infusion rates. As well as blocking the urinary stream, the process of crystal formation and formed crystals induced inflammation in the encompassing renal interstitial nephritis. Meds related to drug-induced crystal nephropathy sulfadiazine, acyclovir, triamterene, methotrexate, etc.

Various medicines utilized for intravascular volume replenishments colloid solutions (eg, dextran, colloids derived from amylopectin hydroxyethyl starch) or as transporter molecules (sucrose with iv immunoglobulin preparations, contrast media) are related to osmotic nephrosis. These medications collect inside proximal tubular lysosomes. As a result of their chemical structure, these molecules can't be metabolized, and at last lysosomal impaired function and cellular swelling.

A particular medication characteristic advances the process of nephrotoxicity. The aminoglycosides have a highly positively charged and are cationic in nature. The overall ionic characteristic contributes to both benefits and toxicity. accumulation of these drugs leads to expression of transporter specifically, the endocytosis process formed by megalin and cubilin, these are restricted to proximal convoluted tubule, alters turnover as result leads to phospholipidosis.

Medication Combinations

Prescribing a combination of potent nephrotoxic medications can increment the risk for kidney injury for instance combination of aminoglycosides and platinum anticancer agents, anti-inflammatory drugs, and contrast media. The excretion path in the renal system also shows the possibility of nephrotoxicity. Drugs compete with each other or metabolites for proteins involved in transportation and efflux carriers, which can increase drug levels inside the cells and enhance the possibility of renal damage.

Inherent Drug Nephrotoxicity

Various prescriptions keep up with a higher possibility of causing acute kidney failure based on their natural nephrotoxicity nature. These medications are broad-spectrum antibiotics aminoglycosides, antifungal medication like amphotericin B, and platinum compounds that may cause renal injury with remedial dosages and a short exposure [35-36]. Inside Intracellular lysosomes accumulation of positively charged polycationic mycin drugs causes tubular lysosomal injury, which is related to phospholipid layer injury, the imbalance between production and buildup of oxygen reactive species (ROS), and mitochondrial derangements. This advances proximal convoluted tubule cell apoptosis and putrefaction with clinical indications, for example, a proximal tubulopathy or acute or chronic kidney injury [35-36].

Liposomal formulations (example, liposomal amphotericin B) less significantly, cause AKI or CKD by distorting renal tubular cell membrane and enhancing penetrability to a positively charged ions, which bring about impaired function of renal tubules because of cellular swelling / impaired function [37]. As a general rule, the lipid/liposomal pharmaceutical formulations are less toxic to the nephron. The polypeptide antibiotics polymyxin, and colistin, are exceptionally nephrotoxic with an extremely attenuated therapeutic range. toxicity is associated with their D-amino substance and fatty acid, which increments cell membrane penetrability and permits cation. This impact prompts renal tubular cell enlargement and lysis with acute kidney injury advancement.

Drugs like cidofovir and tenofovir utilize the organic anion transporter to enter the renal cell and they primary cause mitochondrial injury which is evidenced by distortions in the mitochondrial structure and formation of cristae and tangles. Tenofovir, commonly causes proximal tubulopathy and acute kidney injury [8], [26], [38].

Drugs that act on the vascular endothelial growth factor (VEGF) pathway causes kidney damage by a different mechanism. Reduction in VEGF levels leads to loss of glomerular cell fenestrations and microvascular thrombosis and microangiopathy. These lead to ischemia and infarction resulting in kidney damage [36]. By slowing down nearby elective supplement pathway controllers, these medications may likewise initiate supplement pathways and increment the risk for thrombotic microangiopathy [32.

Medication instigated inflammation

Immune mediated kidney damage is another mechanism of drug induced nephrotoxicity. Through different components (haptens/prehaptens, prohaptens, antigen-antibody complex formation), drugs can advance the inflammatory infiltrate in the kidney interstitium prompting AKI as well as different urinary irregularities like increased levels of protein in the urine, pyuria, and hematuria [34-36]. Drugs causing immune medicated interstitial damage include quinolones, ondansetron, aspirin and allopurinol. Onco-immunotherapies like monoclonal antibodies causes acute interstitial nephritis (AIN) through the actuation of T cells [34-36].

Medication-Induced Cast Nephropathy

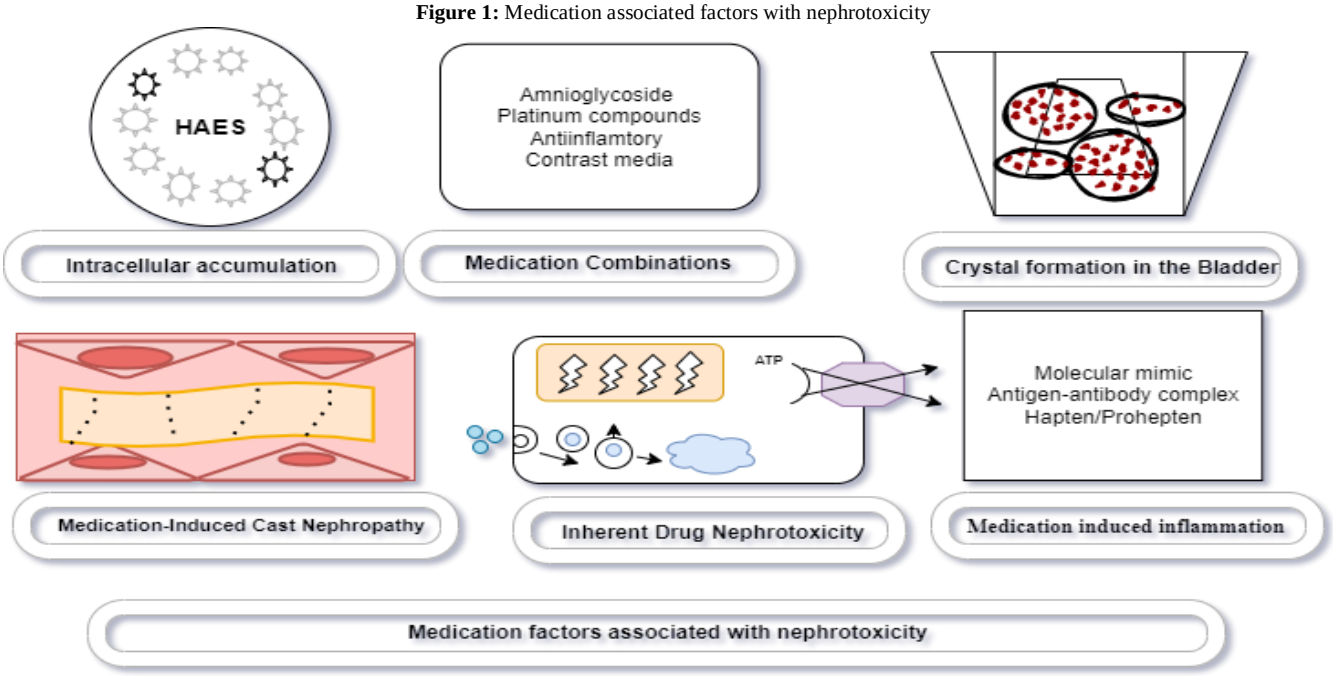
The solidification of protein in the renal tubule. Mechanism of glycopeptide antibiotic like vancomycin induced cast nephropathy, nano spheric vancomycin totals entrap with uromodulin in the tubules to form the cast. The medication's plasma concentration is the most remarkable component prompting this medication-induced cast nephropathy.

The patient factors

There are various subject-explicit elements that advance the risk for medicine-actuated nephrotoxicity. Certain fundamental factors for nephrotoxicity might be nonmodifiable, for example, more advanced age and female gender, which are related to

diminished body mass and decreased water content that can prompt overabundance of drug doses [6-9]. A "serum creatinine" in these subjects may be a lower filtration rate. Females and the aged have lower serum albumin levels bringing about decreased plasma protein binding and expanded free medication concentration that can be toxic to nephrons [35-37]. Notwithstanding these variables, the old have an expanded inclination to vasoconstriction from over-the-top coursing angiotensin II and endothelin levels and have more elevated levels of oxidatively changed biomarkers [29]. These variables join to increment subject exposure to an overabundance of medication concentration and nephrotoxic risk [figure 2].

Figure 1: Medication associated factors with nephrotoxicity



* HAES, hydroxyethyl starch.

Genetic Makeup/Genotype

Following unmodifiable risk elements is the patient's hidden genotype. The job of pharmacogenetics/ pharmacogenomics as a clarification for the heterogeneous individual reaction to medications (insufficient dosing, restorative dosing, and excessive dosing) reflect hereditary factor and supports the requirement for "customized" or " P4 medicine " medication. Accordingly, basic host inheritance can advance the possibility of the renal system to possible nephrotoxins [26-35]. Some literatures recommend that biochemical pathway, carrier proteins, and medication carrier protein vary between individuals because of the genetic makeup. A few proteins that include the hepatic cytochrome superfamily- P450 chemical framework have genetic polymorphisms that are related to decreased drug metabolization and ensuing vital organ damage (harmfulness). Since the kidney additionally has CYP450 compounds that partake in medication digestion, it isn't actually to be expected that genetic polymorphisms inclining toward diminished drug digestion could increment nephrotoxic risk.

Polymorphisms of gene coding proteins associated with the digestion and resulting renal excretion of medications as well as the restoration mechanisms after medication-induced injury are connected with different degrees of medication responsiveness. Polymorphisms in gene coding ERCC1, a critical compound in the deoxyribonucleic acid restoration pathway by which renal cells fix platinum-compound induced Double-strand breaks (DSBs), might be related to renal toxicity [39]. Genetic variation in cytosolic Glutathione-S transferase (GSTs), which typically act as a protective agent to cellular macromolecules from reactive electrophiles, for example, cisplatin, increment the risk for renal toxicity with exposure to this medication [40].

Null mutation or leaky mutations in apical secretory carriers that diminish medication efflux to the renal system, and transformations in kinases that direct medication transporter proteins, can impede medication disposal and advance nephron toxicity by lifting intracellular medication concentration [23-29]. It is plausible that subject's contrast in the capacity and regulation of receptors, channels, transporter protein, and carrier protein that direct the digestion and excretion of medications by the renal system. The classic example of mutation affecting nephrotoxicity with drugs is seen with tenofovir. Subjects with HIV getting tenofovir who were affected by Fanconi condition were noted to have snips SNPs: 1249 G→ A snips in the gene encoding the multidrug-resistant (MDR) protein-2 efflux carrier, which is involved with efflux of tenofovir. HIV patients who didn't have the mutation did not get Fanconi's syndrome [38].

Hereditary modifications in a subject's infection-resistant framework may likewise upgrade the risk for medication-induced renal toxicity employing provocative injury. The regulated medication or its metabolite might form the addition of two or more distinct molecules that alter their actual structure, which upgrades

their immunogenic reaction. Diverse responding reaction to medications and exogenous compounds exists, with one model being the elevated hypersensitive reaction of certain people as contrasted to others. Thusly, contrasts in natural host defense reaction genes can incline a patient toward fostering an unfavorably susceptible response to a medication. The variation of immunogenicity has been exhibited in individuals whose foster medication prompted acute interstitial nephritis, which seems, to be a T-cell-mediated process [37]. Consequently, the easiness of allergic reaction in the renal and the related advancement of acute interstitial nephritis reflect one more type of medication renal toxicity.

Coexisting Diseases

Pre-existing kidney injuries acute or chronic in nature are additionally significant risk elements for renal toxicity. The decrease in filtration rate and transfer of materials from peritubular capillaries to the renal tubular lumen of OA, organic anion; OC, organic cation; etc. (and drugs) increment the risk for medication co-related kidney impairment. GFR decrease can likewise bring about exorbitant medication dosing for prescriptions eliminated by the renal system, expanded medication exposure in diminished working nephrons and ischemic conditioned renal tubule cells, and stronger imbalance between production and accumulation of oxygen reactive species (ROS) damage reaction to different meds by the kidney. Furthermore, expanded transfer of materials from peritubular capillaries to the renal tubular lumen of medications that are eliminated by both glomerular filtration and tubular secretion might upgrade tubular damage [6-9].

Different sorts of comorbid and altered renal function may likewise build the nephrotoxicity impacts of medications. Nephrotic disorder and cirrhosis upgrade nephrotoxicity risk through various mechanistic that incorporate changed renal blood perfusion from diminished viable circling blood volume, reduced albumin levels, can lead to increased plasma levels of the drug [35-38]. Obstructive jaundice is additionally poisonous to specific medications, for example, the aminoglycosides, through modified hemodynamics, for example, the diminished volume of blood delivered to the kidneys per unit time and direct harmful impacts of bile salts on the renal tubular epithelium [27]. Excessive vomiting, diarrhea, use of diuretics or conditions like congestive heart failure which can restrict fluids entering the kidneys, greatly enhance the risk of drug induced renal damage. At last, decreased renal blood perfusion upgrades nephrotoxicity in medications eliminated through the kidneys by encouraging medication overdosing, expanding plasma concentration inside renal tubules in medications reabsorbed by the PCT, and improving medication/metabolite crystal formation inside distal lumens in the setting of the languid urinary flow of insoluble medications [35-38].

Metabolic abnormalities

Various metabolic irregularities can likewise enhance the risk for nephrotoxicity to certain medications. For instance, electrolyte issues like low blood potassium, magnesium, and calcium levels increment the renal toxicity related to the mycin drugs [6-9], [35-38], Serious calcium influx through voltage-gated calcium channels prompts afferent arteriolar vasoconstriction and sodium loss. Extracellular fluid depletion due to low sodium levels, disturbs prerenal physiology, and increases the risk of nephrotoxic medication-associated injury. Metabolic irregularities that modify urine pH increment the possibility of tubular crystal formation with specific medications [29-31], . metabolic acidosis or alkalosis might diminish or increment pH. Acidic urine pH [<5.5] increments tubular crystal formation with medications like a metabolite of sulfadiazine, 'N-acetylsulfadiazine. Alkaline urine [>pH.6.0] increments crystal precipitation inside tubular lumens from medications like ciprofloxacin [21], [29-31]. Also, medications, for example, 'acetazolamide' alkalinizes the urine by inhibiting carbonic anhydrase resulting in calcium-phosphate stones inside renal tubules [30,31].

The Kidney

Kidneys receives a significant amount of the cardiac output resulting in direct exposure to a high plasma concentration of drugs. In contrast, certain parts of the nephron, like the loop of henle has a hypoxic environment which is required for solute absorption through the Na^+-K^+-ATPase-driven transporter [18,23,36-38]. Such adverse environment enhances the risk of reno- toxicity due to various drugs. The mechanisms by which kidney handles the drugs and toxins determine the damage caused to the renal tissue (Figure 3).

Drug Metabolization

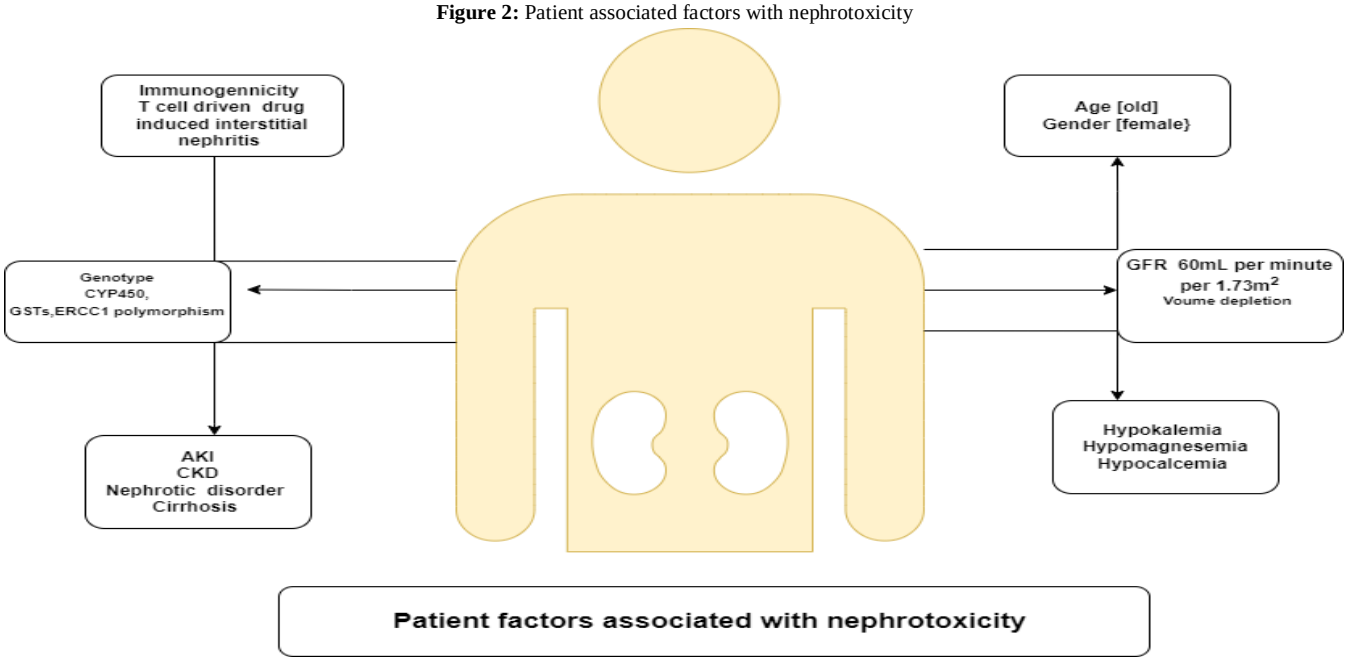
In addition to liver metabolism, various medications go through biochemical modification by kidney catalyst frameworks, including the CYP450 and flavin-containing monooxygenases protein family [21,26,32,37]. This prompts the likely development of reno toxic metabolites and receptive reactive oxygen species as seen with the mycin drugs, platinum compounds, and a few different drugs. These results of biochemical modification might swing the equilibrium for oxidative stress, which surpasses regular cell reinforcements and increments renal damage employing double-strand breaks, DNA alkylation or oxidation, oxidative degradation of lipids, and protein damage [34].

Medication elimination pathway

Medications are eliminated by both GFR and renal tubular secretion. A significant number of renal failures happens with the elimination of medications through the active transport in proximal convoluted tubules [13,23,28,31,]. Renal tubular cell reabsorbs most of the nephrotoxic medications through the various transporters resulting in kidney damage. From the lumen, apical uptake of

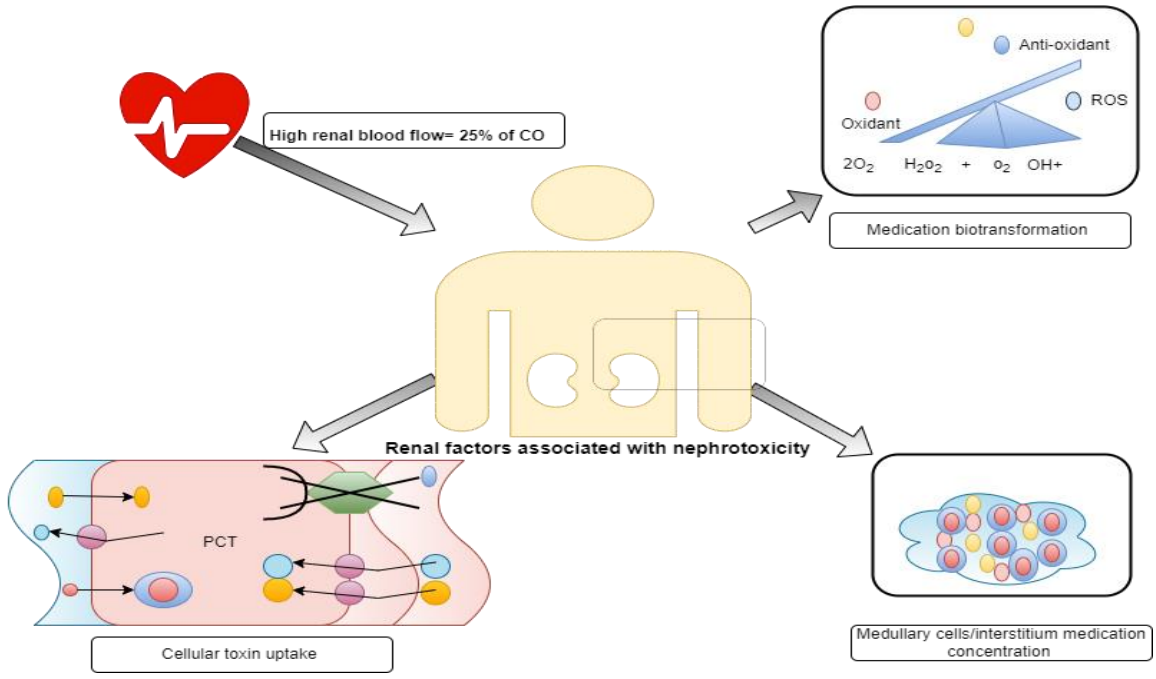
medications happens through endocytosis/pinocytosis and other transporter mechanisms [32-34]. Examples of drugs utilizing this pathway include aminoglycosides, metals, and various complex sugars and starches. Aminoglycosides, after endocytic receptor (megalin/cubilin) uptake, move into the lysosomes and damage the lysosomes by formation of myeloid bodies [6], [34]. This uptake pathway prompts the collection of a basic grouping of aminoglycoside inside cells, which sets off a physical issue overflow prompting cell injury and demise.

Figure 2: Patient associated factors with nephrotoxicity



* GSTs, Glutathione-S transferase (GSTs); ERCC1, excision repair cross complementation group1; AKI, acute kidney injury; CKD, chronic kidney disease; GFR, glomerular filtration rate.

Figure 3: Renal factor associated with nephrotoxicity



*CO, cardiac output, ROS; reactive oxygen species;

Drugs such as hydroxyethyl starch, contrast media, sucrose are taken by the proximal tubular cells through pinocytosis. After pinocytosis, these drugs are stored in the tubular cell lysosomes and they cause tubular cell damage. [34-35].

In addition to apical take-up of medications, there is another pathway through which the proximal renal tubules are exposed to medications. It is through the basolateral transport through the peritubular vessels. After the passage of possibly nephrotoxic medications by the peritubular vessels, they move into proximal renal tubules with the help of a group of dynamic solute carriers. These incorporate the anionic transporter for negatively charged medications and the human natural cation carriers (hOCT) for positively charged medications [6], [26], [40]. Endogenously created anionic and cationic substances, as well as exogenously given

medications, go through these pathways. Exemplary instances of possibly renotoxic medications using these carrier pathways are the non-cyclic nucleotide phosphonates, tenofovir, utilizes anionic transporters, and cisplatin, which utilizes cationic transporters [6], [26], [28-34], [37]. The medications enter through the proximal tubular cell, then move through the intercellular spaces and finally exits with the aid of carrier proteins located apically. Due to transport of the drugs through the proximal tubular cells and accumulation due to reduced activity of the efflux proteins, these cells are at higher risk of toxic damage. Reasons of the reduced efflux include mutations or competition for apical secretory carriers [6], [9], [26], [38]. Accumulation of the toxins in these tubular cells results in cell death (Figure 5). Reduced glomerular filtration results in increased tubular drug secretion resulting in enhanced exposure of the tubular cells to the drug. Presence of other risk factors along with this, accentuates renal damage.

CONCLUSION

Drugs are the commonest cause of kidney injuries. The renal damage is an intricate process which is dependent on numerous factors. These factors are primarily related to the patient, the inherent nature of the drug and its pharmacokinetics.

Conflict of interest: NIL

REFERENCES

1. Mehta RL, Pascual MT, Soroko S, et al, 2004. Spectrum of acute renal failure in the intensive care unit: the PICARD experience. Kidney international. 66(4), Pages - 1613-1621, DOI: 10.1111/j.1523-1755.2004.00927.x.
2. Uchino S, Kellum JA, Bellomo R, et al, 2005. Acute renal failure in critically ill patients: a multinational, multicenter study. The Journal of the American Medical Association. 294(7), Pages - 813-818, DOI: 10.1001/jama.294.7.813.
3. Perazella MA, 2012. Drug use and nephrotoxicity in the intensive care unit. Kidney international. 81(12), Pages -1172-1178, DOI: 10.1038/ki.2010.475.
4. Markowitz GS, Perazella MA, 2005. Drug-induced renal failure: a focus on tubulointerstitial disease. Clinica chimica acta. 351(1-2), Pages -31-47, DOI: 10.1016/j.cccn.2004.09.005.
5. Perazella M, 2005. Drug-induced nephropathy: an update. Expert opinion on drug safety. 4(4), Pages -689-706, DOI: 10.1517/14740338.4.4.689.
6. Perazella MA, 2003. Drug-induced renal failure: Update on new medications and unique mechanisms of nephrotoxicity. The American Journal of the Medical Sciences. 325, Pages -349–362, DOI: 10.1097/00000441-200306000-00006.
7. Perazella MA, 1999. Crystal-induced acute renal failure. The American Journal of Medicine. 106(4), Pages -459-465, DOI: 10.1016/s0002-9343(99)00041-8.
8. Gambaro G, Perazella MA, 2003. Adverse renal effects of anti-inflammatory agents: evaluation of selective and nonselective cyclooxygenase inhibitors. Journal of internal medicine. 253(6), Pages -643-652, DOI: 10.1046/j.1365-2796.2003.01146.x.
9. Isnard Bagnis C, 2004. Herbs and the kidney. The American Journal of Kidney Diseases. 44 Pages -1-1, DOI: 10.1053/j.ajkd.2004.02.009.
10. Blowey DL, 2005. Nephrotoxicity of over-the-counter analgesics, natural medicines, and illicit drugs. Adolescent Medicine Clinics. 16(1), Pages -31-43. DOI: 10.1016/j.admecli.2004.10.001.
11. Perazella MA, Reilly RF, 2011. Imaging patients with kidney disease: how do we approach contrast-related toxicity? The American journal of the Medical Sciences. 341(3), Pages -215-221, DOI: 10.1097/MAJ.0b013e3181f016e6.
12. Rougier F, Ducher M, Maurin M, et al, 2003. Aminoglycoside dosages and nephrotoxicity. Clinical pharmacokinetics. 42(5), Pages -493-500.
13. Perazella MA, 2010. Tenofovir-induced kidney disease: an acquired renal tubular mitochondriopathy. Kidney International. 78(11), Pages -1060-1063, DOI: 10.1038/ki.2010.344.
14. Perazella MA, Izzedine H, 2015. New drug toxicities in the onco-nephrology world. Kidney international. 87(5), Pages - 909-917, DOI: 10.1038/ki.2015.30.
15. Stratta P, Lazzarich E, Canavese C et al, 2007. Ciprofloxacin crystal nephropathy. American journal of kidney diseases. 50(2), Pages -330-335, DOI: 10.1053/j.ajkd.2007.05.014.
16. Vega D, Maalouf NM, Sakhaee K, 2007. Increased propensity for calcium phosphate kidney stones with topiramate use. Expert opinion on drug safety. 6(5), Pages -547-557, DOI: 10.1517/14740338.6.5.547.
17. Orbach H, Tishler M, Shoenfeld Y, et al, 2004. Intravenous immunoglobulin and the kidney—a two-edged sword. InSeminars in arthritis and rheumatism. 34(3), Pages -593-601). WB Saunders, DOI: 10.1016/j.semarthrit.2004.06.003.
18. Nagai J, Takano M, 2004. Molecular aspects of renal handling of aminoglycosides and strategies for preventing the nephrotoxicity. Drug metabolism and pharmacokinetics. 19(3), Pages -159-170, DOI: 10.2133/dmpk.19.159.
19. Evenepoel P, 2004. Acute toxic renal failure. Best Practice & Research Clinical Anaesthesiology.18(1), Pages -37-52.
20. Luther MK, Timbrook TT, Caffrey AR, et al, 2018. Vancomycin plus piperacillin-tazobactam and acute kidney injury in adults: a systematic review and meta-analysis. Critical care medicine. 46(1), Pages -12-20, DOI: 10.1097/CCM.0000000000002769.
21. Alexander BD, Wingard JR, 2005. Study of renal safety in amphotericin B lipid complex–treated patients. Clinical infectious diseases.40(6), Pages -S414-421, DOI: 10.1086/429335.
22. Markowitz GS, Fine PL, Stack JI, Kunis CL, et al, 2003. Toxic acute tubular necrosis following treatment with zoledronate (Zometa). Kidney international. 64(1), Pages -281-289, DOI: 10.1046/j.1523-1755.2003.00071.x.
23. Izzedine H, Launay-Vacher V, Deray G, 2005. Antiviral drug-induced nephrotoxicity. American journal of kidney diseases. 45(5), Pages -804-817, DOI: 10.1053/j.ajkd.2005.02.010.
24. Yang JC, Haworth L, Sherry RM, Hwu P, Schwartzentruber DJ, et al, 2003. A randomized trial of bevacizumab, an anti–vascular endothelial growth factor antibody, for metastatic renal cancer.

New England Journal of Medicine. 349(5), Pages -427-434, DOI: 10.1056/NEJMoa021491.

25. Sugimoto H, Hamano Y, Charytan D, Cosgrove D, et al, 2003. Neutralization of circulating vascular endothelial growth factor (VEGF) by anti-VEGF antibodies and soluble VEGF receptor 1 (sFlt-1) induces proteinuria. Journal of Biological Chemistry. 278(15), Pages -12605-12608, DOI: 10.1074/jbc.C300012200.

26. Keir LS, Firth R, Aponik L, et al, 2017. VEGF regulates local inhibitory complement proteins in the eye and kidney. The Journal of clinical investigation. 127(1), Pages -199-214, DOI: 10.1172/JCI86418.

27. Spanou Z, Keller M, Britschgi M, et al, 2006. Involvement of drug-specific T cells in acute drug-induced interstitial nephritis. Journal of the American Society of Nephrology. 17(10), Pages -2919-2927, DOI: 10.1681/ASN.2006050418.

28. Krishnan N, Perazella MA, 2015. Drug-induced acute interstitial nephritis: pathology, pathogenesis, and treatment. Iranian journal of kidney diseases. 9(1), Pages -3-13.

29. Cortazar FB, Marrone KA, Troxell ML, et al, 2016. Clinicopathological features of acute kidney injury associated with immune checkpoint inhibitors. Kidney international. 90(3), Pages -638-647. DOI: 10.1016/j.kint.2016.04.008.

30. Luque Y, Louis K, Jouanneau C, et al, 2017. Vancomycin-associated cast nephropathy. Journal of the American Society of Nephrology. 28(6), Pages -1723-1728, DOI: 10.1016/j.ekir.2021.04.035.

31. Ciarimboli G, Koepsell H, Iordanova M, et al. 2005. Individual PKC-phosphorylation sites in organic cation transporter 1 determine substrate selectivity and transport regulation. Journal of the American Society of Nephrology. 16(6), Pages -1562-1570, DOI: 10.1681/ASN.2004040256.

32. Ulrich CM, Bigler J, Potter JD, et al, 2006. Non-steroidal anti-inflammatory drugs for cancer prevention: promise, perils and pharmacogenetics. Nature Reviews Cancer. 6(2), Pages -130-140, DOI: 10.1038/nrc1801.

33. Awdishu L, Nievergelt CM, Davenport A, et al, 2016. Rationale and design of the genetic contribution to Drug Induced Renal Injury (DIRECT) study. Kidney international reports.1(4), Pages -288-298, DOI: 10.1016/j.ekir.2016.08.010.

34. Suk R, Gurubhagavatula S, Park S, et al, 2005. Polymorphisms in ERCC1 and grade 3 or 4 toxicity in non–small cell lung cancer patients. Clinical Cancer Research. 11(4), Pages -1534-1538, DOI: 10.1158/1078-0432.CCR-04-1953.

35. Izzedine H, Hulot JS, Villard E, et al, 2006. Association between ABCC2 gene haplotypes and tenofovir-induced proximal tubulopathy. The Journal of infectious diseases. 194(11), Pages -1481-1491, DOI: 10.1086/508546.

36. Aleksa K, Matsell D, Krausz K, et al, 2005. Cytochrome P450 3A and 2B6 in the developing kidney: implications for ifosfamide nephrotoxicity. Pediatric Nephrology. 20(7), Pages -872-885, DOI: 10.1007/s00467-004-1807-3.

37. Enomoto A, Endou H, 2005. Roles of organic anion transporters (OATs) and a urate transporter (URAT1) in the pathophysiology of human disease. Clinical and experimental nephrology. 9(3), Pages -195-205, DOI: 10.1007/s10157-005-0368-5.

38. Lang F, 2005. Regulating renal drug elimination? Journal of the American Society of Nephrology. 16(6), Pages -1535-1536, DOI: 10.1681/ASN.2005030311.

39. Alexander BD, Wingard JR, 2005. Study of renal safety in amphotericin B lipid complex–treated patients. Clinical infectious diseases. 40(Suppl 6), Pages -S414-S421, DOI: 10.1086/429335

40. Swayamprabha Sahoo, Jatindra Nath Mohanty, Tapas Ranjan Behera, Rajesh Kumar Lenka, Saurjya Ranjan Das, 2022. Global concern of antimicrobial effectiveness and resistance Combat strategies. The Journal of Medical Pharmaceutical And Allied Sciences V 11 – I 3, Pages – 4827 – 4832.

How to cite this article

Nagalakshmi N, Manju V., Basavaraj Poojar, Ravi K. Sori, Amrita Parida, 2023. Drug induced nephrotoxicity and associated factors a narrative review. Journal of medical pharmaceutical and allied sciences, V 12 - I 1, Pages - 5563 – 5570. DOI: 10.55522/jmpas.V12I1. 4171.