

Acute Kidney Injury

• Definition Defined by impairment of kidney filtration & excretory functions over days to weeks, resulting in retention of nitrogenous & other waste products.

• Diagnosis Usually a clinical diagnosis, not a structural one.

• Features

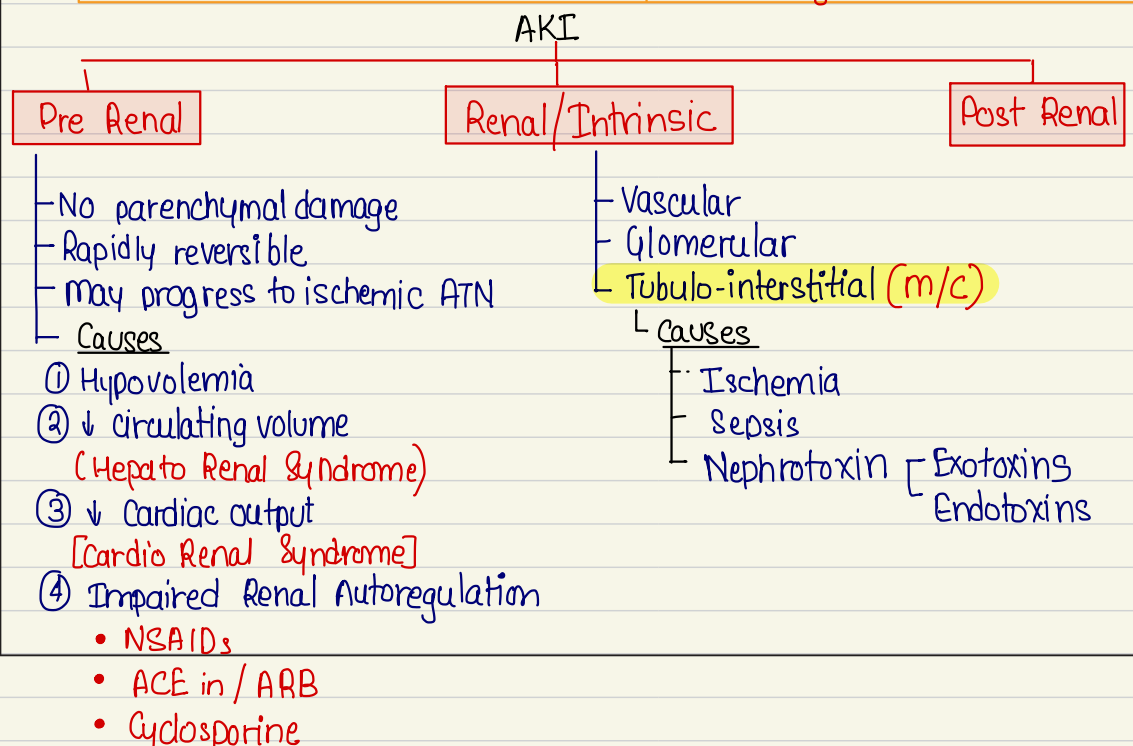
- Increase in Serum Creatinine (SCr) concentration.
 - ↳ ↑ of ≥ 1.5 times baseline (50% or higher) within 7 days
 - ↳ ↑ by ≥ 0.3 mg/dL within 48 hrs.
- Reduction in urine volume.
 - ↳ volume of < 0.5 ml/kg/hr for 6 hrs.

• Criteria

- ① RIFLE classification (Risk ; Injury ; Failure ; Loss ; ESRD)
- ② AKIN classification
- ③ **KDIGO classification** (Kidney disease: Improving Global Outcomes)

Stage	SCr	Urine Output
1	1.5-1.9 x baseline	< 0.5 ml/kg/hr (for 6-12 hrs)
2	2-2.9 x baseline	< 0.5 ml/kg/hr (for 12-24 hrs)
3	3 x baseline [or] > 4 mg/dl	Anuria for 12 hrs. [Anuria = $UO < 100$ ml/day] Oliguria = $UO < 400$ ml/day

• Classification



Prerenal AKI

• Causes

① Hypovolemia / Dehydration

② Drugs

NSAIDs

ACE inhibitors / AARBs

Cyclosporine

} Impair autoregulation

③ Hepato Renal Syndrome

* Type 2 Hepato Renal Syndrome is less severe than type 1.

④ Cardio Renal Syndrome

Ⓐ Type I - Acute Cardiorenal

↳ Acute coronary syndrome → leads to → AKI

Ⓑ Type II - Chronic cardio renal

↳ Chronic cardiac conditions → worsening of kidney function & renal failure.

Ⓒ Type III - Acute Renocardiac

↳ AKI → Acute coronary syndrome

Ⓓ Type IV - Chronic Renocardiac

↳ CKD → chronic cardiac problems

Ⓔ Type V → Systemic

↳ DM / SLE → Cardiac & Renal involvement

• Important points

• Prolonged periods of prerenal azotemia may lead to ischemic injury (ATN).

• Prerenal azotemia involves no parenchymal damage to kidney

• Rapidly reversible once parenchymal blood flow & intraglomerular haemodynamics are restored.

• Mx

• Fluid resuscitation (oral / IV)

• Severe acute blood loss - Packed RBCs.

• Burns, Pancreatitis - Isotonic crystalloids (0.9% NaCl) / Colloids

* Hydroxy ethyl starch increase risk of severe AKI.

Acute Tubulo-Interstitial Disease

• Terms

① Acute Tubular Necrosis (ATN) - Old name for Tubulo-interstitial AKI

② New names

- Acute Tubulo-interstitial nephritis
- Acute Tubular Injury
- Acute Interstitial Nephritis

* Part most susceptible to tubular injury - Pars Recta/
Proximal Straight tubule.

• Causes

① Sepsis (m/c)

② Ischaemia

③ Drugs

④ Contrast

⑤ Snake bite

⑥ Pancreatitis

⑦ Abruptio placenta

⑧ Rhabdomyolysis

⑨ Tumor lysis

⑩ myeloma cast nephropathy / Light chain cast nephropathy

- can progress to renal cortical necrosis (CKD)

Ischemia

- Pre renal azotemia & ischemic AKI represent a continuum of manifestations of renal hypoperfusion.
- Outer medulla of kidneys is one of most hypoxic regions of body.
- Ischemia alone rarely causes severe AKI.

	<u>Prerenal</u>	<u>Intrinsic</u>
<u>Urine exam</u>	Normal	• Albumin - trace to ++ • Casts present - Muddy brown epithelial cast - Eosinophil cast - WBC cast - granular casts (Non specific)
<u>Urine pH</u>	Normal	Alkaline
<u>Blood urea / SCr</u>	>20	<10 (tubule $\rightarrow$ absorbs urea $\rightarrow$ secretes creatinine)
<u>Urine Na⁺ (mEq/L)</u>	<20	>40
<u>Urine creatinine / SCr</u>	>40	<20
<u>Urine osmolality</u>	700-800 mOsm/kg H ₂ O	300 mOsm/kg H ₂ O
<u>FeNa</u>	<1%	>2%

FeNa - Fractional excretion of Na⁺ $\Rightarrow \frac{\text{Urine Na}^+}{\text{Urine Cr}} \times \frac{\text{Plasma Cr}}{\text{Plasma Na}^+} \times 100\%$
 Best parameter
 Normal value: 1-2%

- * ATIN where FeNa < 1% $\rightarrow$
- ① NSAID induced AKI
 - ② Contrast induced AKI
 - ③ Rhabdomyolysis

* FeNa has no value when patient is on diuretics

$\rightarrow$ Fe urea/uric acid is used

- * New markers -
- ① Neutrophil gelatinase associated lipoprotein (NGAL)
 - ② Kidney injury molecule (KIM)
 - ③ Liver fatty acid binding protein.

Sepsis

• Causes

• Most common cause of AKI.

① Post operative sepsis

② Tropical infections [scrub typhus
Leptospirosis

③ Complicated UTI

④ Pneumonia

⑤ spontaneous bacterial peritonitis

⑥ Diabetic foot

* AKI complicates > 50% cases of severe sepsis.

• Post operative AKI causes [sepsis (m/c)
Ischemia

* Ischemia associated AKI is serious complication after major operations involving blood loss & intraoperative hypotension.

* Mostly seen with cardiac surgeries.

Drug induced AKI

① Drug causing Dose dependant tubular injury

a) Antimicrobials

- **Aminoglycosides** [Proximal injury
Non oliguric AKI
Hypomagnesemia may be present]
- **Amphotericin B** [↑ tubuloglomerular feedback ; direct tubular toxicity
Polyuria, Hypomagnesemia, Hypocalcemia
Nongap Metabolic acidosis]
- Adefovir

b) Other drugs

- Cisplatin
- Cyclophosphamide
- Ethylene glycol
- Salicylates

② Drugs causing dose dependent intratubular obstruction (oliguric)

- Methotrexate
- Indinavir
- Triamterene
- Acyclovir
- Sulphonamide

③ Drugs causing dose Independent type IV Hypersensitivity [AKI secondary to Acute Interstitial Nephritis]

- β lactum antibiotics (Penicillins, Cephalosporins)
- Rifampicin
- NSAID
- Sulphonamides
- Anticonvulsants
- Allopurinol
- These drugs may be used in Renal failure, withdraw if AKI is seen.

* Vancomycin - May be associated with AKI when used in high doses in combination with other nephrotoxic drugs.

* Ifosfamide - Manifests as Type II RTA (Fanconi's Syndrome), polyuria, hypokalemia

NSAID Induced Kidney Injury

• <u>Mechanisms</u>	① Pre Renal AKI ② Acute interstitial nephritis by type III hypersensitivity.
• <u>Features</u>	• Oliguria • $f_eNa < 1\%$. • Reversible AKI • Hyperkalemia
• <u>Mx</u>	Discontinue the use of NSAIDs

Analgesic Nephropathy

- Use of combination of Phenacetin - Aspirin - Caffeine

medullary Hypoxia

Papillary necrosis with interstitial fibrosis

- More common in females.
- Disease of historical relevance.
- Shows papillary calcification on CT.
- Slowly progressive renal failure [CTID]
- Increased risk of uroepithelial malignancy

Contrast induced AKI

• <u>Risk factors</u>	① Use of Iodinated contrasts (High Osmolar contrasts) ② Diabetic Nephropathy.
• <u>Clinical Course</u>	① Rise in Scr 24-48 hrs following exposure ② Peak within 3-5 days ③ Resolves within 1 week (7-10 days)
• <u>Pathology</u>	① Hypoxia of outer renal medulla due to occlusion of small vessels ② Direct cytotoxic damage to tubules by generation of free radicals. ③ Transient tubule obstruction with precipitated contrast material.
• <u>Histopathology</u>	Vacuolar changes in PCT. ✱ $FeNa < 1\%$
• <u>Prevention</u>	① Fluids - 1hr before contrast exposure & for 3-6 hrs afterwards. ↳ Isotonic Saline (1ml/kg/hr) ✱ Upto 150 ml/hr is recommended for 1st 6 hrs post exposure. Use of low volume low osmolar contrast materials (LOCM)
• <u>Mx</u>	Good prognosis; Resolves spontaneously in 7-10 days. Drug used- N-acetyl Cysteine

✱ Nephrogenic Systemic Fibrosis / Nephrogenic Fibrosing dermatopathy -

↳ Used of Gadolinium based contrast
↳ $GFR < 30 \text{ ml/min.}$

Tumor Lysis Syndrome

	• Also known as Uric Acid Nephropathy
• <u>Cause</u>	• High count leukemia [CML (m/c)] • Lymphoma
• <u>Features</u>	• Oliguric AKI due to intratubular obstruction • Hyperkalemia • Hyperphosphatemia • Hypocalcemia • Hypermagnesemia • Serum & Urine uric acid ↑ • SCr increases very rapidly
• <u>Rx</u>	Haemodialysis / Rasburicase
• <u>Prevention</u>	• Aggressive Hydration → 4-6 L/day • Alkalinise urine by NaHCO_3. • Reduce cell counts by giving Hydroxyurea. • Start Allopurinol • Means to lower LDH (Risk factor)

Rhabdomyolysis

	• Haem pigment nephropathy ┌ Rhabdomyolysis └ Haemolysis
• <u>Mechanisms</u>	① Direct tubular injury Pigmented granular casts → Precipitate in tubules ↓ Oliguric Renal failure ② Haem pigments └ Renal vasoconstriction → $F_{eNa} < 1\%$
• <u>Causes</u>	① Trauma ┌ Crush Injury └ Electric shock ② Seizure ③ Exertion ④ Toxins ┌ Alcohol ├ Cocaine ├ Amphetamine └ Heroin ⑤ Drugs ┌ Fibrates ├ Statins ├ Zidovudine └ Theophylline ⑥ Electrolyte imbalance ┌ Hypokalemia └ Hypophosphatemia ⑦ Infections ┌ Leptospirosis ├ Influenza └ Coxsackie virus ⑧ Hypothyroidism ⑨ Poliomyelitis ⑩ Dermatomyositis

✱✱ Recurrent - McArdle's disease (Type II Glycogen Storage disorder)

• Features

- Muscle Pain
- High coloured urine
- Hyperkalemia
- Hyperphosphatemia; Hypocalcemia
- Hypermagnesemia
- Scr very high
- High Anion gap metabolic acidosis

• Dx

Creatinine Phosphokinase → starts increasing after 2 hrs
↓
Peak in 24 hrs

• mx

- Large amounts of fluids
- Alkalinise urine



Fails



Haemodialysis

Miscellaneous

- Snake bite
- Pancreatitis
- Abruptio placenta

— can lead to **Renal Cortical Necrosis**

↓
Classic Coagulative Necrosis
+ Preserved architecture
+ loss of viable structures
+ Karyorrhexis

- IOC- CT → Non enhancing cortex & Normal medulla

↓
Reverse Rim Sign

* Oliguric AKI seen

Non Oliguric AKI

- Seen in
- ① Nephrogenic diabetes insipidus
 - ② Tubulointerstitial disease (if tubules not blocked)
 - ③ Aminoglycoside & Cisplatin toxicity

Atheroembolic Renal Disease

• <u>Aetiology</u>	Seen in patients with extensive atherosclerosis after ① An endovascular intervention (OR) ② Anticoagulation (OR) ③ Spontaneously
• <u>Presentation</u>	• Subacute Renal failure > Rapidly progressive Renal failure. • Livedo reticularis - mottle discolouration of skin (Lower limbs) • Hollen horst plaques - Yellow plaque on Retina
• <u>Kidney Biopsy</u>	Birefringent biconvex cholesterol crystals with biconcave clefts within lumen of small vessels.
• <u>Dx</u>	• ↑ LDH ++ • ↑ CK/CPK • Eosinophilia • ESR, CRP, WBC, Amylase ↑ • Biopsy
• <u>Imp points</u>	Risk for ESRD - minimal • ACE inhibitors useful → contraindicated if b/l Renal artery stenosis • Anticoagulants → Risk factor

Complications of AKI

① <u>Uremia</u>	- Uremic pericarditis - Uremic bleeding
② <u>Volume abnormalities</u>	- Hypovolemia - Fluid Resuscitation - Hypervolemia - Salt & water restriction - Diuretics - Ultrafiltration
③ <u>Electrolyte Imbalance</u>	- Hyponatremia - Restriction of free water intake - Minimize hypotonic IV solⁿ. - Hypertonic saline rarely needed in AKI. - Hyperkalemia - Restriction of dietary potassium - Loop diuretics - Insulin (10 units) & glucose (50ml of 50% dextrose) ↳ promotes entry of K⁺ intracellularly - Calcium gluconate / Calcium Chloride (1g) ↳ Stabilize myocardium - Hyperphosphatemia - Restriction of dietary phosphate - Phosphate binding agents - Hypocalcemia → CaCO₃ / Ca Gluconate if symptomatic - Hypermagnesemia - Hyperuricemia → Rx required only in Tumor lysis syndrome
④ <u>Metabolic Acidosis</u>	Sodium bicarbonate (if pH < 7.2)
⑤ <u>Cardiac Complications</u>	- Arrhythmias (Hyperkalemia) - Pericarditis - Pericardial effusion.
⑥ <u>Malnutrition</u>	Due to Hypercatabolic state Seen in AKI.

Management of AKI

- ① Optimisation of Systemic & Renal Haemodynamics
 - Volume resuscitation
 - Judicious use of vasopressors
- ② Elimination of nephrotoxic agents.
- ③ Management of complications.
- ④ Initiate Renal Replacement Therapy when indicated.