# MEDICINE

## 432 Team

17

# Acute Kidney Injury


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**COLOR GUIDE:** • Females' Notes • Males' Notes • Important • Additional

# Objectives

1. Define AKI
2. Know the epidemiology of AKI
3. Know the etiology of AKI
4. Manage AKI
5. Diagnose AKI
6. Treat AKI

## General Notes:

- Important kidney functions: waste excretion, electrolyte balance & fluid balance & blood pressure maintenance (acid base balance, erythropoietin , vitamin D)
- Normal urine output: 0.8-2 liter/day
- Fractional excretion of Sodium (FENa): Percentage of Sodium filtered by the kidney that is excreted in urine. Normal < 1%
- Oliguria: <400 ml or CC urine output in 24 hours
- Anuria: <100 ml urine output in 24 hours or (no urine output)

## What is Acute Kidney Injury (AKI)? (There is lots of definitions for AKI)

- A sudden decrease in kidney function over a period of hours to days (days to weeks, Kumar)
- Results in failure to: (you will see **high urea and creatinine** .. by the way urea and creatinine are not toxic they are just markers and they depends on the severity of the disease )
    - Excrete nitrogen waste products
    - Maintain fluid electrolyte balance
- Clinically defined as:
    - In accordance to serum creatinine increase from baseline:
        - Absolute increase by 0.3mg/dl (26.4µmol/L) (bellow 0.3 is not significant)
        - 50% increase from baseline
    - Urine output <0.5ml/hour for 6 hours
- Stages of Acute Kidney Injury:

| Stage | Creatinine | Urine Ourput |
|---|---|---|
| **Stage I** | 1.5-2 times baseline (it is important to know the baseline)<br>**Or**<br>0.3mg/dl increase | <0.5ml/kg/h for more than 6 hours |
| **Stage II** | 2-3 times baseline | <0.5ml/kg/h for more than 12 hours |
| **Stage III** | More than 3 times baseline<br>**Or**<br>0.5mg/dl increase if baseline>4mg/dl<br>**Or**<br>Any renal replacement therapy is given | <0.3 ml/kg/h for more than 24 hours<br>**Or**<br>Anuria for more than 12 hours |

## Epidemiology: how common is AKI?

- 5% of all hospitalized patients
- 35% of ICU patients (it is more sever because patients are sick they usually came with hypotension, sepsis, septic shock plus we gave them nephro toxic medications. most of them have multi organ failure which will lead to increase mortality as well)

- Mortality rates:
  - 75-90% in patients with sepsis
  - 35-45% in patients without sepsis ( not in the ICU )
  - The doctor mentioned a study about percentages of mortality in AKI patients compared to others.
  - even if they did not die usually they do not go back to baseline, some will develop ESRD some will have chronic kidney disease

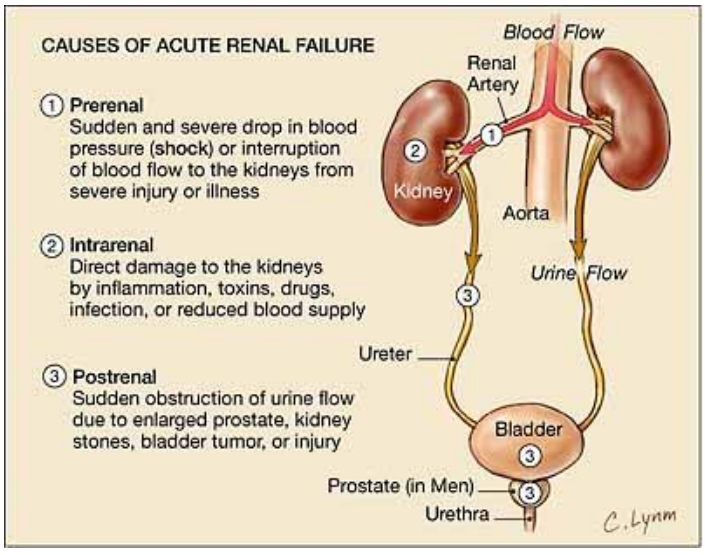
## Clinical and Biochemical features of AKI:

- Hyperkalemia
- Hyponatremia
- Hypocalcemia
- Metabolic acidosis
- Pulmonary edema
- Hypertension
- Hyperphosphatemia
- Uremia, which causes:
  - Anorexia
  - Vomiting
  - Nausea
  - Pruritus

## Etiology of Acute Kidney Injury:

Can be classified according to the cause into three types:

- Pre-Renal
- Renal
- Post-Renal




## (Anything above the kidneys)

Due to impaired perfusion of the kidneys with blood either from hypovolemia or hypotension (cardiac): like in septic shock and vasodilation.

- Volume depletion: ( severe dehydration)
  - Renal losses (diuretics, polyuria)
  - GI losses (vomiting, diarrhea)
  - Cutaneous losses (burns, Stevens-Johnson syndrome)
  - Hemorrhage
  - Pancreatitis
- Decreased cardiac output:
  - Heart failure
  - Pulmonary embolus
  - Acute myocardial infarction
  - Severe valvular heart disease
  - Abdominal compartment syndrome (tense ascites)
- NSAIDS and ACE-inhibitors increase the tendency of developing AKI because they impair the renal auto-regulation process
- Urinary Na & Osmolality:
  - Urinary Na<10
  - Osmolality > 300 high because the kidneys are trying to absorb sodium and water and the urine will be DARK
  - Fractional excretion of Na <1%

***Note(s):***

*431:*
*Pre-renal failure urine analysis is normal plus hyaline casts (casts with no content)*

***Note(s):***

***Management:***
*Treat the underlying cause if he is dehydrated give fluids if he is bleeding give blood and wait for them to improve*

***Note(s):***

**How does patient with pre renal present:**

Hypotension

Tachycardia (depends on the severity)

Dehydration

Jvp is not raised or propyly low

Oliguria – anuria

The kidneys here is normal


(The problem will be in the kidneys "glomeruli – tubules – interstitial ")

Usually due to **acute tubular necrosis**. (Affecting the tubules) Other causes include **acute tubulointerstitial nephritis** (affecting the interstitial), **acute glomerular injuries** (affecting the glomeruli), vascular diseases, accelerated hypertension & cholesterol emboli.

## Acute Tubular Necrosis:

- **Causes**
  - **Ischemia**:
    - Cases of prolonged pre-renal state
    - More vulnerable to ischemia in cases of cholestatic jaundice and other ischemic factors
    - Occlusion of renal arteries: septicemia causing disseminated intravascular coagulation, pregnancy complications such as placental rupture, pre-eclampsia & eclampsia

***Note(s):***

*431:*
*Prolonged pre- renal state (Hypotension) will affect tubules causing ATN. Tubular cells will be sloughed away and accumulated in the tubules causing obstruction and resulting in Muddy brown urine which contains these tubular cells. "Muddy brown casts"*

  - **Toxicity:**
    - Heme pigment: rhabdomyolysis, intravascular hemolysis
      - Muscle injury (rhabdo) might result in the occlusion of renal tubules by myoglobin & hemoglobin casts
    - Crystals: tumor lysis syndrome, seizures, ethylene glycol poisoning, megadose vitamin C, acyclovir, indinavir, methotrexate
    - Drugs: Heroin, aminoglycosides (gentamycin), lithium, amphotericin B, pentamidine, cisplatin, ifosfamide, radiocontrast agents

***Note(s):***

*normally the glomeruli filters blood and send the fluid to the tubules and it will absorb it **but in patients with ATN** there is tubulo-glomerular feedback once they die they will send signals to the glomerular not to filter so the patients does not bleed and die from loss of fluids.*

***Note(s):***

*In ATN you will see muddy brown cast or granular cast (because the tubules are sloughed off) زي الموية مع الطين*
*With low specific gravity. And the urine will be dilute (low osmolality and the Na is high because there is no absorption*

***Note(s):***

***Management:***
*Give them blood and maintain their volume status by giving them IV fluid.*
*If they develop fluid overload or hyperkalemia or metabolic acidosis we will start dialysis tell the kidney re generate.*
*The prognosis is good but make sure he is not hypotensive and not nephrotoxic medication,*

- Pathogenesis:

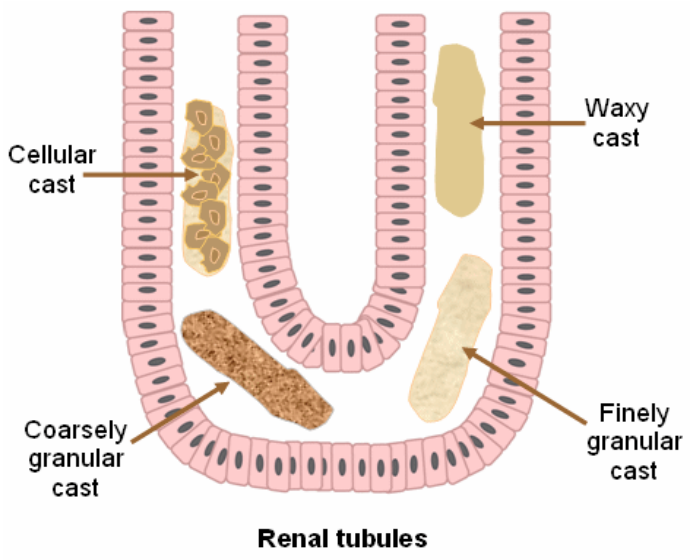
Factors involved in the development of acute tubular necrosis:

- Intra-renal microvascular vasoconstriction:
  - Vasoconstriction is increased in response to: adenosine, thromboxane $A_2$, leukotrienes & sympathetic activity
  - Vasodilation is impaired due to reduced sensitivity in response to:
    - $PGE_2$, acetylcholine & bradykinin
    - Endothelial and vascular smooth muscle damage
  - Leukocyte endothelial adhesion causing vascular obstruction and inflammation
- Tubular cell injury: either by apoptosis or necrosis due to ischemia

Ischemic tubular damage causes reduced GFR by:

- Glomerular contraction: as a reflex due to increased solute delivery to the macula densa, owing to the impaired absorption of the proximal tubules.
- 'Back-leak' of filtrate: in proximal tubules due to loss of tubular cell function
- Obstruction of the tubule: by debris shed from ischemic tubular cells

## Renal Cast Formation




## Acute Tubulointerstitial Nephritis:

Can be caused by drug hypersensitivity, infections, systemic diseases or idiopathic causes.

- **Characteristics:**
  - Acute creatinine elevation
  - Polyuria & polydipsia

***Note(s):***

*You will see WBCs and WBCs cast.*

- Malaise & nausea
- Proteinuria
- Pyuria
- Hematuria
- Maculopapular rash (drug induced)
- Eosinophiluria (drug induced)

- **Drug induced:**
  - 70% of cases, mostly due to hypersensitivity to NSAIDs or penicillins. Other drugs include: acid suppressors omeprazole, cimetidine, phenytoin & furosemide and cephalosporins
  - Present with:
    - Fever
    - Eosinophilia & eosinophiluria
    - Arthralgia
    - Rashes
    - Histology: intense interstitial cellular infiltrate
  - **Treatment:**
    - Withdrawal of causative drug
    - May require dialysis
    - Most patients recover but some may be left with significant interstitial fibrosis & CKD
- **Infections:**
  - Direct infiltration such as CMV, leptospirosis & candidiasis
  - Reactive to systemic infections such as diphtheria, Hantavirus & streptococcal infections
- **Systemic Diseases:**
  - Immunologic reactions: Systemic Lupus Erythematosus, sarcoidosis, Wegener's granulomatosis & Sjorgen's syndrome
  - Metabolic diseases: urate nephropathy, oxalate nephropathy & hypercalcemic nephropathy
  - Neoplastic diseases
- **Idiopathic**

***Note(s):***

***Management:***
*Drug induced > stop the medication*
*Systemic disease > give steroids*

## Glomerular Causes:

- Goodpasture Syndrome(Anti-glomerular basement membrane disease)
- Anti–neutrophil cytoplasmic antibody-associated glomerulonephritis (ANCA-associated GN) (Wegener granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis)
- Immune complex GN (lupus, postinfectious, cryoglobulinemia, primary membranoproliferative glomerulonephritis)
- Acute Glomerulonephritis:

***Note(s):***

*In glomerulonephritis you will see RBCs cast*

- Hematuria with RBC casts
- Proteinuria
- Hypertension
- Edema
- Can occur post streptococcal infection
- Associated with ANCA & GBM
- Renal biopsy and serology to confirm
- high creatinine

## Post-Renal Causes

## (Related to ureter urinary bladder and urethra)

Which are mainly obstructions: it should be bilateral obstruction to develop AKI or unilateral if the patient has one kidney

- **Ureteric obstruction**
  - Stone disease,
  - Tumor
  - Fibrosis
  - Ligation during pelvic surgery
- **Bladder neck obstruction:**
  - Benign prostatic hypertrophy (BPH)
  - Cancer of the prostate
  - Neurogenic bladder
  - Drugs (Tricyclic antidepressants, ganglion blockers)
  - Bladder tumor
  - Stone disease
  - Hemorrhage/clot
- **Urethral obstruction:**
  - Due to enlarged BPH (most common)
  - Strictures
  - Tumors

***Note(s):***

*Bilateral obstruction causes AKI. If only one is obstructed, the other, if healthy, can compensate.*

***Note(s):***

*Neurogenic Bladder: Inability to pass urine due to CNS damage. Seen in spinal cord injuries. Managed by Foley Catheter to empty the bladder*

***Note(s):***

*Usually the kidneys and the urine here is normal even if it is low. Sometimes you will find RBCs if it is trauma or stones. For the diagnosis JVP and blood pressure will be normal, most of them came with* ***Anuria*** if they have complete obstruction. We will diagnose it with ultrasound you will see hydronephrosis "the kidneys are swallown. And we will treat it by relieving the obstruction

## Contrast Nephropathy:

- Acute deterioration in renal function, sometimes life-threatening, commencing < **24 - 48 hrs** after administration of IV radiographic contrast media (in 30-40% of the patients the creatinine will go up and then it will peak and at the end it will improve)
- Possibly by causing vasoconstriction and toxic effect on renal tubules
- Effect is dose dependent
- Non-oliguric
- FENa <1%
- Risk factors:
  - Pre-existing renal impairment
  - Old age
  - Use of high-osmolality ionic contrast media and repetitive dosing in short time periods
  - Diabetes mellitus
  - Myeloma
  - hypertensive
- Prevention:
  - Provide hydration with free oral fluids plus IV isotonic saline during procedure
  - N-acetylecystein 600 BID pre/post procedure
  - Avoid nephrotoxic drugs
  - If the risks are high, consider alternative methods of imaging

## Rhabdomyolysis:

- Increase in serum CK (above 10,000)
- Blood positive urine dipstick, with no RBC on microscopy
- Pigmented granular casts
- Common after trauma, burns, seizures, limb ischemia
- Treatment is supportive care with IV fluids

***Note(s):***

*Muscle breakdown releases myoglobin which accumulates in the tubules and creates casts that obstruct normal fluid flow*

## Atheroembolic AKI:

- Associated with emboli fragments of atherosclerotic plaque from arteries or aorta
- Diagnosed by history (previous CVA, or emboli, limb ischemia) they will have pulse less lower limp * look for gangrene *
  - Eosinophiluria & peripheral eosinophilia
  - Low serum C3 & C4 (but the creatinine will go up after **ONE WEEK)**
- Commonly occurs after intravascular procedures or cannulation or cardiac cath

## Diagnosis of AKI:

- Blood urea nitrogen and serum creatinine

***Note(s):***

*To differentiate between contrast and atheroembolic AKI the contrast nephropathy symptoms will appear after **24 – 48 hrs** but in atheroembolic AKI after **One week***

- CBC, peripheral smear, and serology
- Urinalysis
  - Unremarkable in pre and post renal causes
  - Differentiates ATN, AIN & AGN:
    - Muddy brown casts in ATN
    - WBC casts in AIN
    - RBC casts in AGN

    Very Important!!
  - Urinary indices:
    - Fractional Excretion of Na (FENa) = $\frac{UNa \times PCr}{PNa \times UCr} \times 100$
    - Pre-Renal: FENa <1%
    - Renal: FENa >1%.
      - May be low in contrast nephropathy, AGN & Myoglobin induced ATN
  - Hansel stain for Eosinophils
- Urine electrolytes
- Ultrasound kidneys
- Serology: ANA,ANCA, Anti DNA, HBV, HCV, Anti GBM, cryoglobulin, CK, urinary Myoglobin

## Management of AKI:

- Supportive therapy until recovery
- Maintain fluid and electrolyte balance
- Sodium & Potassium dietary restrictions
- Avoid further renal damage (don't give drugs that impair renal function)
- Emergency measures:
  - Pulmonary edema: diuresis
  - Sepsis: should be addressed immediately
  - Hyperkalemia:
    - Causes cardiac arrhythmias (life threatening)
    - Managed by:
      - Calcium gluconate (protect myocardium)
      - Insulin units + 50ml 50% glucose (drive $K^+$ into cells)
      - Diuresis
      - Dialysis
- Dialysis & hemofiltration indications (renal replacement therapy):
  - Uremia symptoms
  - Uremia complications (put in notes)
  - Pulmonary edema
  - Severe acidosis
  - Hyperkalemia that is resistant to other treatments
  - Removal of drugs that caused AKI

# Cases from 431 File:

**Case 1:**

75 years old female, known to have DM II and HTN Presented with nausea, vomiting and diarrhea for days, Medication: Insulin, lisinopril, and her Serum Creatinine 205. On history, there's no evidence of previous high creatinine or chronic renal disease. Diagnosis?

A: The patient has Acute Kidney Injury due to pre-renal cause which is volume depletion (diarrhea, vomiting). We treat her by IV fluids, if left untreated for a long time, it might lead to acute tubular necrosis. Also patient has DM2 and HTN so she is at high risk of chronic kidney disease as well.

What do you expect to find in urine analysis?

A:

- Urine analysis: normal with possible hyaline casts
- Urine Na<10 (low)
- Osmolality >300 (high)
- FE Na<1%
- Possible proteinuria due to diabetes `

Treatment plan?

A:

- Rehydration
- Avoid nephrotoxic medication
- Monitor kidney functions

**Case 2:**

16 yr, Saudi male. Quadraplegic due to car accident. Creatinine increased from 32 to 201 in a few days. Urine output is 2L/day. No history of vomiting or diarrhea, no new medications. BP 123/73, pulse 78/min. Diagnosis?

A: It's an AKI (sudden increase in creatinine). Normal BP & no volume loss => not pre-renal (also, car accident is not recent => not rhabdomyolysis). No new medication & history has no suggestions of renal causes => not renal. However, he has a damaged spinal cord => neurogenic bladder. Use Foley catheter as management.

**Case 3:**

25 yr, Saudi male sustained a road traffic accident this morning & admitted to ER. Hypotensive & required 6 units of blood transfusion Urine output has significantly decreased <10cc. Serum creatinine 285umol/L. Dark Urine. Urine Na >10. Osmolality <350. Bicarbonate 21. Cl 99, K 4.7 Diagnosis?

A: AKI due to acute tubular necrosis caused by shock (he was hypotensive and lost a lot of blood in the accident which is why he needed the transfusion). Give him blood and fluids to restore BP and monitor the patient.

The next day, he underwent respiratory distress and was intubated. BP is 120/78. No urine for the last 3 hours. Creatinine is 499umol/L. Bicarbonate 12. K 6.3. What happened?

A: He developed pulmonary edema. Large amounts of fluids were given to him, but he can't get rid of them due to AKI. Bicarbonate is low => acidosis. Creatinine increased. Management plan is to put him on dialyze him (until he recovers).

## SUMMARY

General characteristics

1. AKI may be oliguric, anuric, or nonoliguric. Severe AKI may occur without a reduction in urine output (nonoliguric AKI).
2. Weight gain and edema are the most common clinical findings in patients with AKI. This is due to a positive water and sodium (Na+) balance.

Prognosis

3. a. More than 80% of the patients in whom AKI develops recover completely. However, the prognosis varies widely depending on the severity of renal failure and the presence of comorbid conditions.
4. The most common cause of death is infection followed by cardiorespiratory complications.

Complications

5. ECF volume expansion and resulting pulmonary edema—treat with a diuretic (furosemide).
6. Infection (a common and serious complication of AKI).

***432 Medicine Team Leaders***

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