ACUTE KIDNEY INJURY {AKI}

- Classification Of AKI
- Approach To Detect The Cause of Acute Kidney Injury
- Workup For Patient With AKI
- Supportive Measures and Treatment Of Complications Of AKI
- Treatment Of Certain Causes Of AKI

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ACUTE KIDNEY INJURY {AKI}

Definition:

Rapid or abrupt decline in the kidney functions over hours to days with retention of nitrogenous waste products (↑Urea & ↑Creatinine) with disturbed electrolytes, Acid base and Fluid homeostasis.

Practically [AKI = rapid rising creatinine over hours to days above baseline]

According to the international [Kidney Disease Improving Global outcome](KDIGO) Foundation

To diagnose AKI, the patient must have one or more criterion of the following:

A) Increase in Serum Creatinine ≥ 0.3 mg/dl within 48 hours

زيادة فى رقم الكرياتينين (٠.٣ او اكتر) فوق ال Baseline

يعنى مثلا ،،

الكرياتينين كان ١.٢ ووصل ١.٨ فى خلال ٤٨ ساعه

1.8 _ 1.2 = 0.6

Means it is > 0.3

AKI <-------- يعنى

B) Increase in serum Creatinine by ≥ 1.5 × baseline (known or have presumed to have occurred within prior 7 days)

زيادة فى رقم الكرياتينين(مره ونص او اكتر) فوق ال baseline

يعنى مثلا ،، الكرياتينين كان ١ ووصل ٢ فى خلال ٧ ايام

١ × ١,٥ = ١,٥ ← زيادة الكريات مره ونص

يعنى نضرب قيمة الكريات فى ١.٥ فى المثال ده الكرياتينين وصل ٢ يعنى اكتر من ١.٥ فى خلال ٧ ايام

يبقى ده

Acute kidney injury {AKI}

C) Urine Volume < 0.5 ml/kg/hr for 6 hours

يعنى مثلا واحد وزنه ١٠٠ كجم ،، يبقى لو كمية البول قلت عن ٣٠٠ مللى فى خلال ٦ ساعات يبقى AKI

0.5 ml/kg/hr

0.5 × 100 = 50 ml/hr

In 6 hours --> 50 × 6 = 300 ml over 6 hrs

ملحوظه هامة :

لايمكن حساب كمية البول بدقه الا بتركيب قسطره بوليه وملاحظه كمية البول بالمللى فى عدد الساعات المطلوبه ،،

اما لو كان المريض محجوز فى المستشفى او العنايه ومركب قسطره بوليه اصلا وبعدين ال creatinine ارتفع وشاكين فى

New onset of AKI

بنشوف القسطره جمعت بول اد ايه فى ٢٤ ساعه اللى فاتت واقسم على ٤ هيدينى كمية البول فى ٦ ساعات ،،

وبعدين احسب

0.5 ml/kg/hr

لمدة ٦ ساعات واقارن ،،

اشوف اللى جابه فى ٦ ساعات اقل فعلا من حسبة

0.5 ml/kg/hr

على مدى ٦ ساعات ولا لا ؟!

لو اقل فعلا يبقى

AKI

Then, you have to do Staging of Acute Kidney Injury {AKI}

➢ افتكر أن أصل المرض كان

Acute renal failure

والتسميه اكتشفوا أنها غير دقيقه لانه ليش فشل كامل ولكنه درجات من القصور المؤقت القابل للعلاج وبالتالى فهو

spectrum

له درجات ،،

شوف درجات ومراحل ال AKI طبقا لمنظمة ال KDIGO العالميه لعلم الكلى

KDIGO classification of AKI

❖ Stage 1

- **Serum Creatinine criteria**

1.5 - 1.9 times of baseline creatinine

Or

≥ 0.3 mg/dl in < 48 hours

وتتحسب زى ما شرحنا فى الامثله السابقه ،،

ببساطه لو الكريات زاد مره ونص او اكتر فوق ال baseline بتاعه بس لم يتجاوز المرتين زياده

2 times of baseline

يبقى stage 1

- **Urine output criteria**

UO < 0.5 ml/kg/hrs for 6 - 12 hrs

وتتحسب زى ما شرحنا فى الامثله السابقه ،،

يعنى لو كان مريض وزنه ١٠٠ كجم وجاب اقل من ٣٠٠ مللى فى مدة ٦ ساعات

واستمر الرقم اقل من ٣٠٠ لحد ١٢ ساعه

يبقى ده stage 1

❖ Stage 2

- **Serum Creatinine Criteria**

2 - 2.9 times of baseline creatinine

وتتحسب زى ما شرحنا فوق

- **Urine Output Criteria**

UO < 0.5 ml/kg/hrs for ≥ 12 hrs

ويتحسب زى ما شرحنا فوق

❖ Stage 3

- **Serum Creatinine Criteria**

≥ 3 times of baseline Creatinine

Or

Increase in serum Creatinine ≥ 4 mg/DL

Or

Initiation of Renal replacement therapy (RRT)

طبعا واضح برضه زى ال

Stage 1 & stage 2

بنفس طريقة الحساب

بس لو المريض دخل فى AKI وكان severe لدرجة انه احتاج dialysis لاى سبب

---> ده برضه بيصنف انه

Stage 3

- **Urine output Criteria**

UO < 0.3 ml/kg/hr for ≥ 24 hrs

Or

Anuria ≥ 12 hrs (< 50 - 100 ml) over ≥ 12 hrs

تحسب زى الامثله السابقه ،،

بس هنا لو المريض ما بيجبش بول خالص تقريبا واللى معناها كمية ضئيله جداا

Anuria = مش انعدام كامل

ودى اقل من ٥٠ الى ١٠٠ مللى بول لمدة ١٢ ساعه او اكتر،، ده يصنف

Stage 3

ملحوظه:

- هناك criteria تانيه لل AKI واحده اسمها RIFLE Criteria ودى الاقدم ،،

والتانيه اسمها AKIN Criteria ودى اتعملت بعد ال RIFLE ،،

- واخيرا اتعملت ال KDIGO ووفقت بين الاتنين فى شكل معايير اسهل واكثر اختصارا

وهيا دى اللى العالم كله حاليا ماشى بيها اعتبارا من سنة ٢٠١٢ لحد النهاردة

What is Acute Kidney disease?

==========

- KDIGO have proposed the term AKD to include not only those with AKI, but also those with
  - GFR <60mL/min/1.73m 2 For <3 months

Or

  - a decrease in GFR by ≥ 35%

Or

  - An increase in SCr by >50% for <3 months.

وده معناه أنه نوع من القصور الحاد فى وظائف الكليتين

ولكنه استمر فتره ولم يتعدى ٣ شهور

مع انخفاض فى قيمة ال

eGFR

اما ال AKI فهو قصور حاد بردو ولكنه حصل اسرع واستمر لفتره أقل وغالبا

Reversible

طبعا نخلى بالنا أن قصور وظائف الكليتين لو عدى عليه اكتر من ٣ شهور يبقى يندرج تحت ال

CKD

APPROACH TO ACUTE KIDNEY INJURY (AKI)

ROAD MAP for AKI

كل ما تحتاجه لمعرفة سبب ونوع ال AKI

Pre-renal causes

Hypoperfusion of the kidney

Low Renal Blood Flow (RBF)

Hypoperfusion of the kidney is either due to one of these

a) Hypovolemia
b) Redistribution of the blood
c) Compartment Syndrome
d) Pump failure" or cardiac causes.

a) Hypovolemia:

- **Hemorrhage** e.g. hematemesis, Hematochezia, Melena, Third space bleeding Like pancreatitis

  Or Trauma (RTA) Road traffic accident.

  ☞ **Clues**
  - History of certain bleeding, RTA
  - Signs of shock (Pallor, cold hands, delayed capillary refill >3 sec, increased thirst, confusion, oliguria, hypotension, tachycardia)

- **Fluid loss:**

  - vomiting (GIT)
  - Diarrhea (GIT)
  - Burn (skin)
  - Diuretics (urinary tract & kidney)

➢ **Dehydration**:

- Decreased water intake
- decreased thirst sensation (elderly)
- Coma / bulbar symptoms
- increased insensible loss as in cases of fever
- DKA / HHS (hyperosmolar hyperglycemic syndrome also known Hyperosmolar Non-ketotic Coma (HONK)

✴ **Clues for Fluid loss & dehydration**

❖ History of one of the above causes

❖ Examination:

- Dry tongue and mucus membranes
- Reduced Skin turgor, absent axillary sweating (dry axilla)
- Orthostatic hypotension, (hypotension & shock in severe fluid loss or dehydration)
- Oliguria
- Low JVP & flat neck veins
- -The most accurate DX: low CVP < 7 or 8

b) Redistribution of the blood

➢ **SEPSIS**

Pooling of blood in the microcirculation + VD ---> impaired kidney perfusion

Clues

❖ History:

-Septic focus (e.g. UTI: dysuria & urinary symptoms)

- Fever, confusion

- Other multi-system affection: e.g cholestasis, ARDS

❖ Examination:

- q SOFA score

(Low BP, Confusion, tachypnea > 20)

Or

- SOFA (multi-organ affection)

❖ To confirm Diagnosis:

- Blood culture, culture from presumed origin of septic focus e.g (urine culture in suspected urosepsis) CRP, procalcitonin, Serum lactate,
- Imaging: e.g. CXR or CT chest in ARDS.

Criterion	Threshold	
	SIRS	qSOFA
Body temperature (°C)	<36 or >38	-
Heart rate (beats/min)	>90	-
While blood cell count (10^3/μL)	<4 or >12	-
Respiratory rate (breaths/min)	>20	≥22
Systolic blood pressure (mmHg)	-	≤100
Glasgow Coma Scale	-	≤13

SIRS: systemic inflammatory response syndrome, qSOFA: quick Sepsis-related Organ Failure Assessment.

➢ **Hepato-renal Syndrome**

Clues :

International Ascitis Club Criteria:

* Creatinine > 1.5 mg/dl.

* Advanced liver disease (ascites jaundice, etc.)

* Absence of shock.

* Absence of hypovolemia as defined as no sustained improvement of renal function (Creatinine decreasing to <1.5) following at least 2 days of diuretic withdrawal (if on diuretics)

✚ Volume expansion by albumin at 1 g/kg/d up to maximum of 100 gm. /day

* No current or recent treatment with nephrotoxic drugs.

* Absence of parenchymal renal disease as defined by proteinuria < 0.5 gm. /day,

No micro-hematuria < 50 RBCs/PHF

And normal renal ultrasound

➢ **Drugs :**(intra-renal vasomotor changes)

- NSAIDs (anti- prostaglandins) --> VC of afferent arterioles

- ACEI particularly in cases of bilateral renal artery Stenosis.

c) Abdominal Compartment Syndrome:

Increase in the intra-abdominal pressure which compresses the renal veins

--> Congestion + ↓cardiac output (CO)

---> ↓RBF

---> Oliguria & AKI (PRE-RENAL)

Clues : ✍

- AKI occurs with certain risk factors

* After Abdominal trauma and after Abdominal Surgical Operations

Or After: sepsis, burn

- In addition to such abovementioned risk factors, the patient will complain of abdominal pain, tenderness, and distention --> acute abdominal Pain

+ Low BP + ↑HR

DX: measurement of intra-abdominal pressure (IAP) ≥ 12 mmHg: diagnostic

d) Pump failure (CHF)

With low COP (chronic & Acute) LV failure: Cardio-renal syndromes

Clues: ✍

- High JVP

- Orthopnea ± PND

- Bilateral LL edema ± Ascites ± Pleural effusion.

- S3 gallop ± Cardiomegaly

- Low BP ± signs of cardiogenic shock in cases of Acute HF

Confirm DX by **ECHO**.

❖ General& Specific Workup

- **To confirm The Diagnosis of pre-renal AKI**
- **To detect the cause**
- **To differentiate between Pre-renal AKI and other causes particularly acute tubular Necrosis (ATN)**

➢ Basics labs including RFTs (BUN & Creatinine) to confirm AKI & CBC to exclude anemia as anemia might be a pointer for Chronicity (CKD)

✔ If BUN/Creatinine ratio > 20/1 --> Points strongly to Pre-renal AKI

➢ U/S abdomen & pelvis for exclusion of Obstruction (hydronephrosis) and to exclude the Chronic kidney disease as Well (poor Cortico-medullary differentiation and Decreased size)

➢ Specific

✴ Urine analysis often normal (bland Urine)

✴ Urinary indices (if available) [[Most Accurate]]

▸ Urine Na < 20 mmol/L

▸ Urine Osmolality > 500 (concentrated urine) بول مركز

▸Fractional excretion of Na (FeNa) < 1% بتحسب عن طريق معادلة ،، ليست اساسيه

▸Fractional excretion of Urea < 35 بتحسب عن طريق معادلة ،، ليست اساسيه

✴ Labs for complications:

- ABG: to detect metabolic acidosis
- ↓PH: ↓HCO3: ↓PaCO2
- Serum K: for ↑K.
- Serum Na: ↓in volume overload.
- Uric acid: could be high.
- Ca: could be low. (Low Ca is more in CKD).
- P: could be high (high P is more in CKD)

Intrinsic Renal Causes:

Either one of the following

a) Vascular
b) Tubular (Acute tubular Necrosis)
c) Interstitial (tubulo-interstitial)
d) Glomerular : RPGN (Crescentic GN)

A. Vascular

Large Vessels

❖ **Cholesterol Embolism (Athero-embolic disease)**

Clues:

- Risk factor: e.g. Cardiac catheterization
- Purple rash on the foot
- Livedo Reticularis (Net like purple rash more often in legs.
- Digital infarction in foot ± gangrene
- Eosinophilia
- Eosinophils in urine

❖ **Thrombosis /Embolism**

♦ **Embolic**:

E.g. AF & prosthetic valve: rare

♦ **Thrombotic**:

☞ **Catastrophic Anti-phospholipid Syndrome**

Clues:

Multi-organ affection: low plts, kidney, liver, arterial /Venous thrombi

+ Abortions in pregnant females.

DX: abovementioned criteria +

Autoantibodies: Lupus Anticoagulant, Anti-Cardiolipin Anti-body, Anti-glycoprotein Abs.

♦ Renal Vein thrombosis

- Occurs on top of Nephrotic Syndrome, particularly Membranous GN.

Clues: ➪

- Known Nephrotic Syndrome (heavy proteinuria > 3 gm.

- Acute loin pain +recent hematuria on top of proteinuria

- Pulmonary Embolism could occur in some cases.

♦ ACEI in Bilateral Renal Artery Stenosis

Clues: ➪

acute deterioration of kidney function after oral intake of ACEI ---> Creatinine ↑ > 30% from the baseline ---> raise the possibility of underlying Renal artery stenosis .

Asymmetry in kidney size on both sides

Occurrence of Flash pulmonary edema

Evidence of other atherosclerotic diseases like CAD and limb ischemia in old patients with presumed renal artery stenosis.

Small Vessels

❖ Malignant HTN:

Clues: ➪

- Diastolic BP often ≥ 120 - 130

- Other Target organ damage {TOD} like

  - Bilateral papilledema on retinoscopy

  - Confusion ± fits (hypertensive encephalopathy).

❖ Thrombotic Microangiopathies (TTP and HUS)

▸ Clues For Thrombotic thrombocytopenic Purpura (TTP)

At least 3 out of 5 criteria (Pentade)

1. Microangiopathic hemolytic anemia (MAHA)
   Evidenced by anemia, ↑LDH, high reticulocytes ≥ 2.5% ± ↑indirect bilirubin
2. Thrombocytopenia.
3. Fever
4. CNS features (Stroke like symptoms in the form of lateralization, confusion and/or fits
5. Renal imapairement (AKI)

DX: Blood film revealing Schistocytes or Fragmented RBCS support the diagnosis

▸Clues for Hemolytic Uremic Syndrome (HUS)

Triad:

1. Thrombocytopenia
2. Renal impairment (Acute kidney Injury) (AKI)
3. Microangiopathic hemolytic anemia (MAHA) as described above

DX: Confirm it by Blood film that reveals Fragmented RBC'S or Schistocytes

❖ Vasculitides

Like **Polyarthritis Nodosa (PAN)**

Clues For PAN

- Hypertension
- Weight loss
- Myalgia, leg pain and/or weakness
- Mononeuropathy or mononeuritis multiplex
- Angiography show aneurysms
- Biopsy show necrotizing vasculitis in medium sized arteries with granulocytes infiltration.
- Testicular tenderness/pain in males
- Livedo Reticularis
- HBV positive (25% of cases)

☞ In addition to acute kidney injury (Creatinine > 1.5)

DX: ACR criteria ≥ 4/10 of the abovementioned items to DX PAN

❖ SCLERODERMA renal crisis

Clues:

➲ Skin features of SCLERODERMA

- Face: Beaked nose, fish's mouth
- Thickened skin in hands with Sclerodactyly, more prominent in Systemic Sclerosis than limited CREST syndrome

➲ **CREST syndrome** abbreviation of Calcinosis cutis + Raynaud's phenomenon + esophageal dysmotility + Sclerodactyly + Telanagiectasia

➲Evidence of Interstitial Lung disease (ILD) in Systemic sclerosis

➲ In addition to AKI

DX: Clinical,

- Autoantibodies can help in DX, but unfortunately they are present only in 30% of cases
- Anti-Scl-70 in systemic sclerosis
- Anti- centromere Antibody in CREST

B. Tubular

(Acute Tubular Necrosis: ATN)

- **ATN** is the most common cause Of AKI and the most important cause as well.
- **ATN:** necrosis (cell death) of tubular cells with sloughing of such cells

  ---> Obstruction of such minute tubules

  ---> Retention of Nitrogenous Waste substances (urea & creatinine)
- **ATN** could be Ischemic or Toxic

➢ Ischemic ATN

- Have the same causes of Pre-renal AKI
- They were discussed before, in details

✴ Neglected or untreated Pre-renal AKI ---> Ischemic ATN

➢ Toxic ATN

✔✔ Toxins could be: Exogenous or Endogenous.

I. Exogenous:

A) Drugs:

- Aminoglycosides: particularly Gentamycin
- Vancomycin
- Amphotericin B (antifungal)
- Other anti-fungal: Foscarnet
- Antivirals drugs like Tenofovir, cidofovir etc.
- Cisplatin (chemotherapy)

Clues: ➮

Take a history asking about such specific drugs.

B) Contrast: (Contrast induced Nephropathy: CIN)

Clues: ➮

- Elevation of Creatinine ± ↓Urine output within 48 -72 hrs after intake of IVContrast
- Examples of contrast: Angiography, coronary angiography, CT with contrast
- Precipitating factors: pre-existing CKD, DM, HTN, use of nephrotoxic drugs, concomitant dehydration.

II. Endogenous:

1) Myoglobin
2) Hemoglobin
3) Bilirubin
4) Uric acid
5) Myeloma casts

1) Myoglobin [Rhabdomyolysis]

Acute muscle damage/injury --> Release of Myoglobin --> tubular injury

Clues:

- Dark Urine (Brown or Dark red): not in All cases
- Some patients C/O Myalgia and tender muscles.
- Features of AKI
- Precipitating factors for Rhabdomyolysis
  - Drugs: Statins ± Fibrates.
  - Illicit Drugs: Cocaine, Amphetamines, heroin, alcohol
  - Viral infection: influenza, Coxsackie viral infection.
  - Electrolytes disturbances E.g. Hypophosphatemia
  - Crush injury.
  - Compartment syndrome.
  - Neuroleptic malignant Syndrome.
  - Malignant Hyperthermia.
  - Serotonin Syndrome.
  - Glycogen Storage disease

DX:

it must be confirmed by the following:

- Serum Creatine Phosphokinase (CPK) if > 5000, it is significant to induce ATN & AKI
- RFT (urea & creatinine)
- Urine analysis: dipstick positive for blood & negative RBCs.

2) Hemoglobin (Hemoglobinuria)

As in cases of intra-vascular hemolysis

Ex:

- Incompatible blood transfusion
- Falciparum Malaria
- G6PD
- Wilson's disease

Clues:

- Jaundice
- Dark urine
- Other features of each hemolytic disease

DX: It must be confirmed by the following:

- Urine analysis (positive for blood, negative for RBCs)
- CBC, bilirubin, reticulocytes%, LDH
- Other specific tests for each hemolytic disease

3) Bilirubin (bilirubin nephropathy)

Occurs in cases of cholestatic (obstructive) jaundice

Ex:

- choledocholithiasis, cholangiocarcinoma
- Cancer head of pancreas
- Medical causes of cholestasis

Clues:

- jaundice ± yellow skin
- itching
- Dark urine
- Features of underlying causes

E.g. - biliary colic in biliary stones

- Weight loss in malignant causes

DX:

- Labs:

  High bilirubin (direct), high Alkaline phosphatase, high GGT

- U/S:

  Dilated intrahepatic biliary radicals in surgical causes

- MRCP or ERCP are needed in some cases

4) Urate (Tumor lysis syndrome: TLS)

Acute Urate Nephropathy

In lymphomas & lymphoid leukemia's, chemotherapy can cause significant lysis of tumor cells resulting in elevation of Uric acid forming Crystals that obstruct the tubules [ATN]

In addition to other electrolytes disturbances, TLS may occur spontaneously

Clues: Cairo - Bishop Criteria

- S.uric acid > 8 mg/dl
- S.potassium > 6 m.mol/l
- S. Phosphate > 4.5 mg/dl
- S. Calcium < 7 mg/dl

➲ To diagnose TLS,

- the patient must has ≥ 2 features between 3 days pre-treatment up to 7 days post-treatment
- In addition to AKI

5) Myeloma Cast Nephropathy:

Formation of casts, composed of mix of Tamm Horsfall protein + light chain immunoglobulins (paraprotein)

Casts --> obstruct the tubules --> ATN

Clues for myeloma

International Working group Criteria for MM:

- Presence of abnormal paraprotein in the blood and/or the urine detected by Protein electrophoresis and/or immunofixation
- Bone marrow examination revealing ≥ 10% plasma cells infiltration
- Evidence of End organ damage in the form of CRAB:
    - C --> high calcium
    - R--> renal impairment
    - A-> Anemia
    - B--> Bone otseolytic lesions (skeletal Survey)

In addition to features of AKI + oliguria

General clues for ATN

- Oliguria + AKI ± volume overload

- Unremarkable urine analysis or granular casts

- Urine indices to differentiate it from Pre-renal AKI

  - ☞ Urine Na > 40
  - ☞ Urine osmolality < 350 mosm/l
  - ☞ Fractional excretion of Na (FeNa >2%)

C. Interstitial (Acute Interstitial Nephritis)

Clues: ☜

- Non-oliguric AKI (most of cases)

- predisposing factors

1) Drugs
   - Antibiotics: Penicillins, Cephalosporin
   - Sulfonamides, Rifamipicin
   - Analgesics
   - Diuretics
   - Allopurinol
   - PPIs
2) Infection: TB, leptospirosis, legionella
3) Autoimmune: Sarcoidosis, Sjogren's syndrome

   Some cases have typical presentation (Fever+ arthralgia+ rash ± flank pain)

DX:

- Urine analysis: WBC's casts
- Eosinophils in urine (Hansel's stain)
- Mild proteinuria often < 1 gm
- Biopsy is sure diagnostic (often not needed)

D. Glomerular (Rapidly Progressive GN)

- Severe form of Nephritic Syndrome
- Rapidly progressive Glomerulo-nephritis (RPGN) occurs as a result of formation of Crescents in the glomeruli resulting in AKI, oliguria in the following conditions:

A] Immune complexes related GN	**B] Pauci-immune GN** (few complexes)
- Post-infectious GN like - Post- streptococcal GN - IgA Nephropathy (Mesangioproliferative GN) - Membranoproliferative (MPGN) or (mesangiocapillary GN) - SLE (stage 3 & 4 lupus nephritis)	- Pulmonary -renal syndromes - Wegener's granulmatosis (GPA) - Churg Strauss Syndrome (EGP) - Microscopic polyangiitis (MPA)
C] Anti-Glomerular basement membrane Ab syndrome (Anti-GBM)	

- **General clues & Dx of RPGN:**

1. Urine containing Active urine Sediment (Dysmorphic RBC's or RBC'S cast)

   ± Proteinuria with variable degrees

   By ACR (albumin creatinine ratio or Protein Creatinine ratio (PCR)

2. Noninvasive Tests for DX
   - ANA & Anti-dsDNA Ab for SLE
   - C3 & C4 in all immune complexes GN like post-infectious , MPGN, SLE
   - HCV Ab & Hbs Ab in suspicious MPGN
   - ANCA in Pauci-immune GN
   - Anti-GBM Ab in suspicious Anti-glomerular basement membrane Syndrome

3. Invasive:

   Biopsy from Kidney with Histopathology (LM) and Immunofluorescence (definitive DX)

Post-renal AKI (Urological causes)

- Either
  - Prostatic cause
  - Bladder outlet obstruction
  - Ureteric causes

Prostatic cause

Most common cause particularly Benign prostatic hyperplasia (BPH) in old patients

Clues:

Obstructive & irritative urinary symptoms

That occurs before

Urgency, dribbling, poor urine stream, hesitancy

Bladder outlet obstruction

E.g. bladder mass

Clues: hematuria, weight loss, old age

Ureteric lesions:

Either

- Bilateral stones with bilateral ureteric obstruction + back pressure + hydronephrosis
- strictures
- Compression from outside by
- Tumors
- LNs (Lymphoma
- Retroperitoneal fibrosis

General work up:

Obstructive uropathy is detected initially by doing US of the abdomen & pelvis

If ----> bilateral back pressure & hydronephrosis ---> Spiral CT urinary tract

--> Then Urology Assessment

QUIZ1: Test your self

- Please mention clues!!

A 72-year-old man is admitted to the ICU with a 3-day history of worsening shortness of breath and edema.

He is found to have pulmonary edema with severe hypoxia requiring intubation and mechanical ventilation.

Medical history is significant for ischemic cardiomyopathy, coronary artery disease, myocardial infarction, hypertension, hyperlipidemia, and benign prostatic hyperplasia.

Medications on admission are aspirin, lisinopril, carvedilol, atorvastatin, and as-needed furosemide.

- **On physical examination**

The patient is afebrile, blood pressure is 92/60 mm Hg, and pulse rate is 112/min.

Estimated central venous pressure is 14 cm H2O.

Diffuse crackles are heard throughout both lung fields.

Cardiovascular examination reveals an S3 gallop.

There is lower extremity edema to the knees.

A dobutamine infusion is started.

A urinary catheter is inserted, and he is given intravenous furosemide with a urine output of 230 mL over the next 4 hours.

- **Laboratory studies:**

Blood urea nitrogen 76 mg/dL

Serum creatinine 3.0 mg/dL (baseline: 1.9 mg/dL)

Serum electrolytes Normal

Urine sodium 64 mEq/L

Fractional excretion of sodium 1.9%

Fractional excretion of urea 8.8%

Urinalysis:

Specific gravity= 1.018

PH= 5.5; protein +1

Erythrocytes = 1-2 /hpf

Leukocytes= 2-4 /hpf

Moderate hyaline and fine granular casts

Which of the following is the most likely diagnosis?

A: Acute interstitial nephritis

B: Acute tubular necrosis

C: Obstructive uropathy

D: Prerenal acute kidney injury

- هيا الحاله دى فيها

Mixed features of **Pre-renal & ATN**

- اللى يركز هيلاقى كده ،،
- وسبب اللخبطه دى هو ال furosemide اللازكس اللى اتاخد فى الحاله ،، وزود الصوديوم فى البول ،،

- BUN / Cr > 20/1 --> pre-renal
- Fractional excretion of urea < 35 % --> suggests pre-renal

While

- Urine Na > 40
- FeNa : 1- 2 suggests ATN but not sure

Most cases of ATN FeNa > 2 %

وده سببه

Diuretic induced

إنما الباقى

Pre-renal

- كمان ال cast بتاعت ال ATN لازم تكون muddy brown granular مش granular عاديه

الاجابه

Pre-renal AKI

الحاله

Not straightforward

لكن كنت عايز اشوف الناس مركزه فى الارقام ولا لا

- دائما لما نعمل ال urinary indices ما تكونش مديين المريض diuretic لأنها هتبوظ الارقام
  لكن القواعد هيا هيا ثابته ما بتتغير
- كمان هو حاططلك prostatic hyperplasia فى الحاله عشان يلخبطك وتفكر فى ال

Obstructive uropathy

- الحالات اللى فى الواقع بتبقى كده فعلا مش

Straightforward

وبالذات المريض إلى عنده

Multiple comorbities

وبياخد ادويه كتير

الحاله وان كانت مش straightforward ولكن بتعلمك تركز اووى فى الارقام وركز فى معطيات الحاله

- This patient has evidence of pulmonary edema due to CHF with underlying ICM and MI requiring mech ventilation --> pump failure --> ↓ Cardiac output --> renal perfusion --> pre-renal AKI
- Neglected Pre-renal may lead to ischemic ATN

- Disturbance in numbers is related to diuretic effect, but unfortunately

BUN/Cr

+

Low Fractional excretion of urea

Points more to pre-renal AKI

- اللى هييجى فى بالك أن ال

ATN leads to volume overload

--> Pulmonary edema

بس فى سياق الحاله مش منطقى ، لان البدايه مشكلة قلب مش مشكلة كلى

QUIZ2: Test your self

- Please mention clues!!

- A 70-year- old hypertensive osteoarthritic female patient with stage three chronic kidney disease presented for follow up. Her medications include: atenolol, enalapril, acetaminophen and low dose aspirin. Six weeks ago she presented with dyspepsia that was treated with omeprazole. Two months ago, her serum creatinine was 1.5 mg/ dl and now it is 3.5mg/dL. Urine analysis: specific gravity 1.009, pH 5, 1+ protein, trace blood, 5-10 leucocytes/hpf, Hansel stain shows > 1 esinophils/ml. Urine protein-creatinine ratio: 0.638 mg/mg creatinine.
- Which of the following is the most likely diagnosis?

A. Acute tubular necrosis.
B. ACEI- induced acute kidney injury.
C. Focal segmental glomerulosclerosis.
D. Interstitial nephritis.
E. Membranous nephropathy.

The answer:

Elevation of Cr over baseline 1.5 --> 3.2 in 2 months is called Acute Kidney Disease rather than AKI

Acute Kidney Disease

- مسمى حديث لقصور حاد فى وظيفة الكليتين ولكن بصورة أبطأ ولا يحدث فى ساعات أو أيام مثل ال AKI ولكنه فى مده لا تتعدى ٣ شهور عشان ما يدخلش فى نطاق ال CKD
- وأسبابه تقريبا نفس أسباب ال AKI

هنا السبب هو ال

Interstitial!! Why!

- History of drugs (PPI) which is newly taken by the patient on top of Old CKD (acute on top of Chronic)
- Hansel stain in urine: positive
- Tubular PROTEINURIA < 1g
- Relative Low specific gravity

The answer:

D: INTERSTITIAL NEPHRITIS

هنشرح الموضوع وحده وحده

Q1: How to recognize AKI simply?!

Acute or sudden new rise of serum creatinine over the baseline

How

1) Creat ↑ ≥ 0.3 over the last creatinine within 48 hrs

- **Example:**

Patient with normal creatinine that was done 2 days ago and was 0.9 mg/day

Today creat 1.8

1.8 - 0.9 = 0.9

يعنى اكتر من ٠.٣ ولو تابعته كل يوم هتلاقيه بيعلى عن اليوم اللى قبله لو ما اتعالجش أو ما اتعرفش سببه

Or

2) Creat ↑ مره ونص over the last measures Cr within 1 week

Example:

Patient with creat 2 since 1 week, today his Cr: 3.7

3.7 ÷ 2 = 1.85

1.85 > 1.5

- يبقى كده بردو AKI ولو تابعته يوميا هتلاقيه بيعلى كل يوم عن اليوم اللى قبله لو ما اتعالجش وما اتعرفش سببه وكل ما يعلى يبقى ده مؤشر لقصور وظيفة الكليتين وبالتالى هتظهر أعراض اشد مع زيادة الرقم وتكون أقل والرقم قليل

نسيبنا من criteria بتاعت ال urine output لو مستصعبنها

****

النقطه التانيه

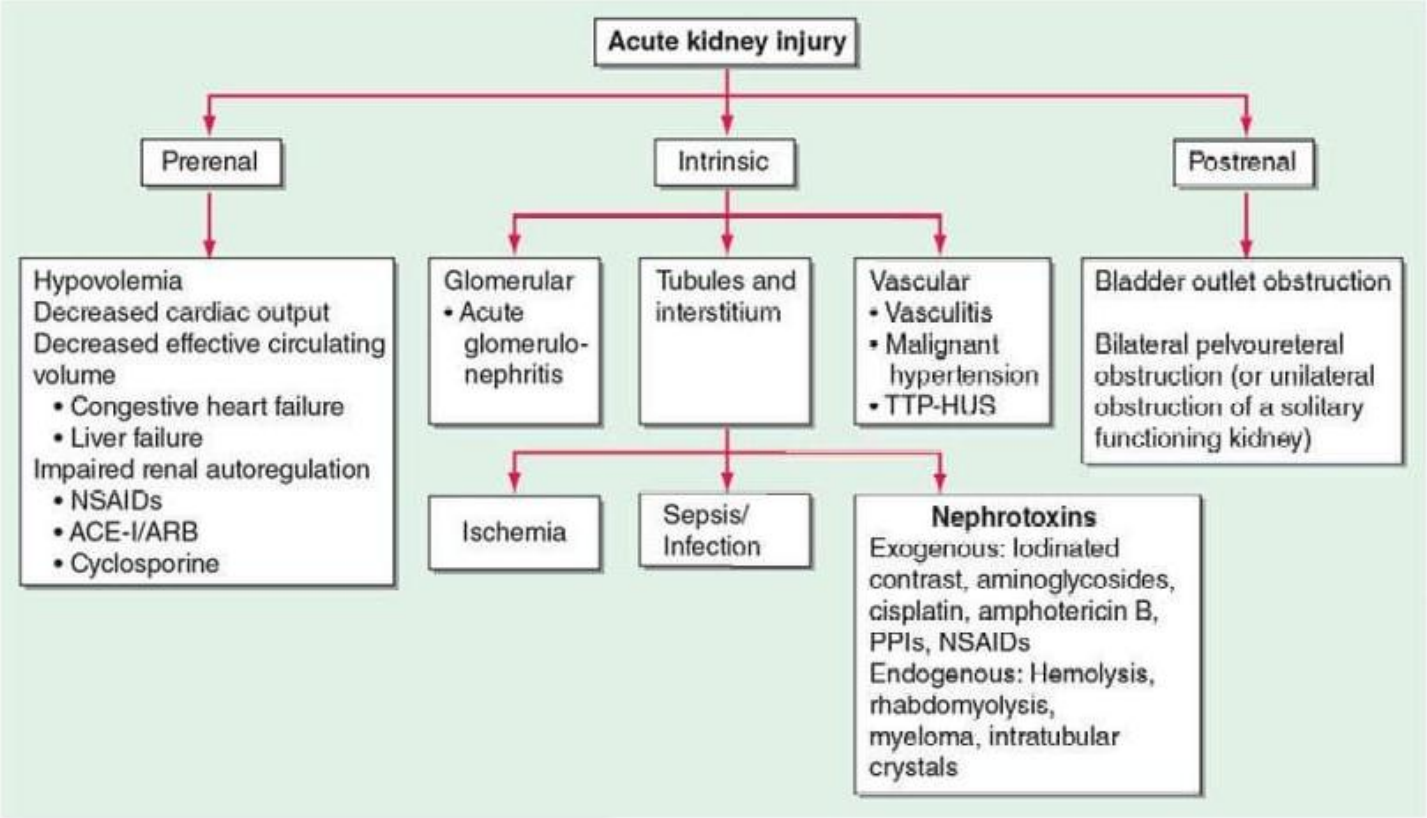
CAUSE OF AKI

هاعرفه ازاى وهاعمله ايه ؟

عشان ما نتلخبطش ونقول الموضوع كان مليان معلومات وكله دخل فى بعضه

نعرف الخريطه والعناوين الرئيسيه الاول ونحط البيانات تحتها

دى الخريطه بكل بساطه

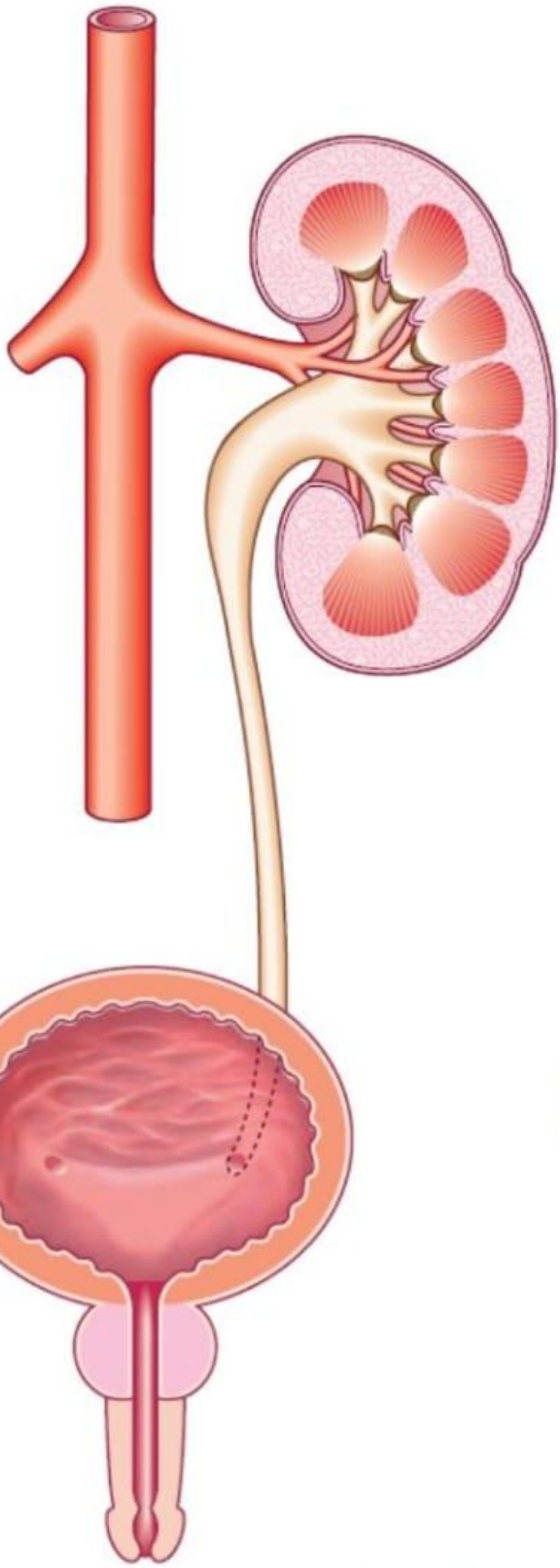


المشكله أما أنها

- Pre-renal = problem in blood supply of the kidneys
- Intrinsic Renal = problem in kidney tissue
- Post-renal = problem in urinary tract

ابتداءا من ال

Ureter down to bladder



PRE-RENAL

Impaired perfusion:
- Cardiac failure
- Sepsis
- Blood loss
- Dehydration
- Vascular occlusion

RENAL

Glomerulonephritis
Small-vessel vasculitis
Acute tubular necrosis
- Drugs
- Toxins
- Prolonged hypotension

Interstitial nephritis
- Drugs
- Toxins
- Inflammatory disease
- Infection

POST-RENAL

Urinary calculi
Retroperitoneal fibrosis
Benign prostatic enlargement
Prostate cancer
Cervical cancer
Urethral stricture/valves
Meatal stenosis/phimosis

Causes of acute kidney injury.

Pre-renal Azotemia or AKI

Low blood supply to the kidneys!!

What are the possibilities?

- الكليتين الطبيعى أنهم محتاجين ٢٠ ٪ من كل ال blood ،، وعشان اقلل الكميه دى عندى احتمال من ٣
  - اما أن حجم الدم أو السوائل تقل

أو

  - حجم الدم/السوائل ثابت أو زايد نتيجة ضعف المضخه(عضلة القلب)

أو

  - حجم الدم/السوايل ثابت لكن فى مرض عمل سوء توزيع للسوائل والدم وحرم الكليتين من حصتها فى الدم

- hypovolemia
- Normal volume or ↑ volume but with low Cardiac output
- Normal volume but with pathological redistribution of the blood that deprive kidneys from 20 % of COP

1) HYPOVOLEMIA

دى معناها اما فقدان سوائل بس من غير مكونات الدم أو فقدان الدم نفسه بسوايله

I. Loss of fluids = dehydration

Causes?

- Vomiting
- Diarrhea
- Severe burn
- Dehydration from overdiuresis or in elderly due to impaired thirst sensation

II. Loss of blood = hemorrhage

How?

- Bleeding orifices
  - GIT --> hematemesis
    --> Melena & hematochezia
  - Lungs --> massive hemoptysis
- Massive vaginal bleeding
- Internal massive bleeding like hemorrhagic pancreatitis or surgical trauma

2) Low Cardiac Output

بتحصل اما

a) Acute (all shock states)

Including cardiogenic shock & acute heart failure

b) Congestive heart failure with impaired Systolic function (low Ejection fraction)

خلى بالك حالات

Acute heart failure & CHF

بيكون فيهم

Volume overload

Lungs: pulmonary edema

High JVP etc.

3) Pathological Redistribution Of The Blood

- الاحتمال الأخير أن السوائل حجمها مش كبير ولكن حصل إعادة توزيعها بشكل مرضى

- Sepsis

Bacterial infection leads to release of chemical mediators such IL1causes systemic VD

--> Multi organ affection

ومن ضمن الاعضاء دى ال kidneys

Or

- Advanced liver cirrhosis with failure --> ↓ albumin

+

Accumulation of systemic vasodilators

Albumin is responsible for maintence of effective circulatory volume

وبالتالى فى الحالة دى

Blood supplies to kidneys will ↓

والمرض ده اسمه

Hepatorenal syndrome

- باقى نوع بيعمل Pre-renal هو

Abdominal compartment syndrome

وده مشكله جراحيه وفكرتها بردو أن المشكله الجراحيه فى البطن ايا كان سببها علت الضغط جوا البطن وده قلل ال

Blood supply to the kidneys

طب هتفرق ازاى بين كل سبب والتانى ؟

==========

Clinical &Labs

I. CLINICAL

- All Hypovolemia cases will be known from history
  - Vomiting, Diarhora etc
  - Dehydration, DKA etc
  - Hemorrhage
- All of them have signs of hypovolemia

انا ذكرتها فى الموضوع فوق بالتفصيل في صفحة ٥ & ٦

- Cardiac causes has
  - History of cardiac problem
  - Signs of heart failure + volume overload
- Shock states
  - Signs of shock
  - Septic, cardiogenic, hypovolemic, obstructive and anaphylactic shock

وطبعا العيان بيكون محجوز فى العنايه

- Sepsis
  - Septic focus

  Like UTI often with fever

+

  - Q SOFA
  - Low BP

±

Tachypnea

±

Confusion

+

Multi-organ affection

Multi-organ affection

يعنى ممكن تلاقى مع ال

AKI

- Liver injury (↑ ALT/AST/bilirubin)
- Leukocytosis / low platelets
- High PT high PTT

±

- Lung affection (ARDS)

N.B1: Hepatorenal syndrome

دى لا تحدث إلا فى مريض تليف كبدي متأخر يعنى عنده

Ascites & jaundice

أو

فشل كبدى حاد

وانا حاطط المعايير التشخيصية بتاعتها فى الموضوع فوق

ولازم نستبعد الأسباب الأخرى زى ال

Dehydration & drugs

لان مريض الكبد معرض للاتنين

II. LABORATORY

In Pre-renal AKI

الكلى بتتاثر وظيفتها نتيجة حرمانها من ال

Blood

ونتيجه لكده بترتفع ال

Waste products

زى ال

BUN & Cr

زى اى سبب اخر

- لكن خلى بالك بالرغم أن البول قليل لان كفاءة الكليتين قلت إلا أنه بول سليم!!

يعنى ايه ؟

Urine which is bland and free of anything except hyaline casts (ودى عادى)

ايه تانى

The kidneys are still able to concentrate the urine

طب دى وظيفة مين ؟ !! وظيفة ال

Tubules

- هنا وظيفة ال tubules ما زالت سليمة وبالتالى البول وان كان قليل بس هينزل مركز وال Osmolality بتاعته عاليه نسبيا
- وكمان ال tubules هتقدر تعمل

Good reabsorption of Na and urea

- وبالتالى لو قيسنا ال Na فى البول وحسبنا مؤشر ال excretion بتاعه هو واليوريا هيطلعوا قليلين ومش عاليين والعلماء استغلوا الحقيقه دى وقالك نعمل

Urinary indices to confirm the diagnosis of Pre-renal cause

- Urine Na
- FeNa (Fractional excretion of Na) وبتتحسب بمعادلة
- FeUrea وبتتحسب بمعادلة

- مش كده وبس القدرة على المحافظة على ال

Nitrogenous wastes products

غالبا هترفع مستوى ال

Urea & BUN in blood

لانهم قلوا فى البول

- المحصلة

Urine Na < 20

FeNa < 1%

FeUrea < 350

BUN/creatinine > 20/1 (normally BUN/Cr < 20/1)

- دى الجزئيه اللى شرحناها وبسطناها

Pre-renal causes

تقدر ترجع لها بالتفصيل من صفحة (9 – 5)

Intrinsic AKI

➢ لو رجعنا لل Algorithm بتاع ال AKI هتلاقى السبب التانى فى ال AKI هو ال

Intrinsic Renal Causes

- Intrinsic AKI = damage to kidney tissue

Kidney tissue

احنا شرحنا بالتفصيل قبل كده وشرحنا وظيفته هو حاجه من ٤

Tubules

Glomeruli

Interstitium

Vessels (intra-renal) vessels

(Tubules + Glomeruli = Nephron)

اى خلل أو تلف نتيجة مرض ما بيؤثر على كل جزء منهم بيعمل

AKI

ناخد اول واحد فيهم

- **ATN (Acute tubular necrosis)**

➢ **ازاى بيحصل ؟!**

- بيحصل لو حصل موت فى الخلايا الموجوده على جدار ال!! tubules
- وده بيحصل نتيجه سبب من اتنين أما أنه حصل

I. Ischemic to tubules

وده امتداد لل

Pre-renal AKI

لو ما اتعالجش

Or

II. Toxic injury to tubules

- In ATN , tubular cells will undergo necrosis , and inflammation will occur in association with necrosis of cells

Necrosis of tubular cells

هيعمل حاجتين

١) جزء من الخلايا الميته هيحصلها shedding وهتنزل فى ال lumen بتاع ال tubules

وهذا سيؤدى إلى درجه من درجات ال

Tubular obstruction

٢) الجزء التانى هيتحد مع مكونات موجود فى ال filtrate ويعمل ما يسمى بال

CASTS

وال casts هنا نوعها

Muddy brown granular casts

ودى بردو هتؤدى إلى انسداد فى ال tubules

أو هتزود ال

Tubular obstruction

(خلايا الالتهاب ستساهم فى تكوين الcasts)

٣) انسداد ال tubules نتيجة ال

Damaged tubular epithelial cells And Tubular casts

هيؤدى إلى وقف سريان ال infiltrate

وتتقفل السكه وبالتالى يقل البول الخارج من الكليتين

٤) إلى جانب ارتفاع فى الضغط بداخل تجويف ال tubules

ويضطر السوائل المتراكمة اللى اسمها ال filtrate

بأنه يتسرب من الغشاء الخارجى المغطى لل tubular cells ويخرج بره فى ال interstitium

والعمليه دى اسمها

Tubular backleak

Tubular backleak
↓
Decreased GFR
+
Oliguria

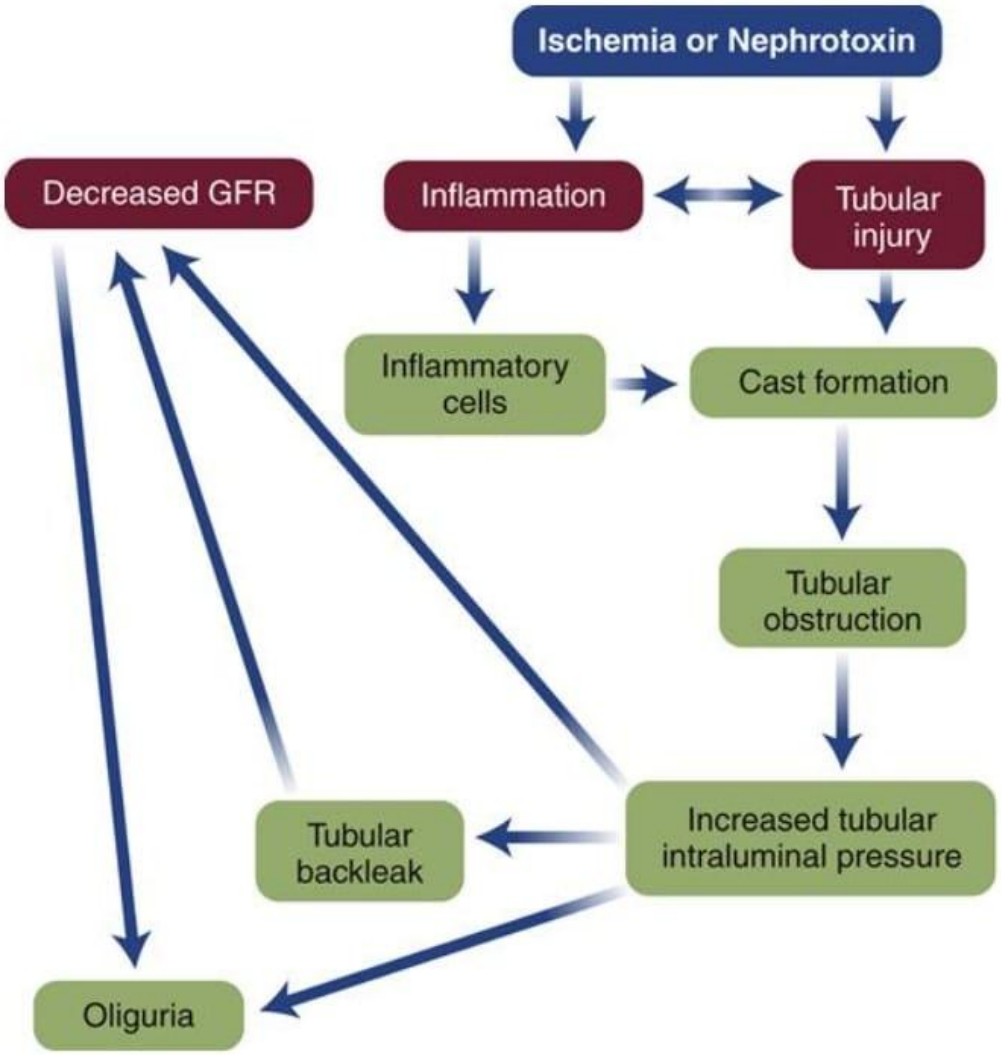


FIGURE 28-1 Pathogenesis of acute tubular necrosis.

طب هل المرض ده عباره عن مرحله واحده ؟

الحقيقه ان المرض ده بيمر ب ٣ مراحل

1) Prodromal Phase

ودى مرحله تمهيديه فى الساعات الأولى من ال

Tubular injury

وبيكون البول لسه كميته ما قلتش أو قلت شويه مع ارتفاع فى

وظائف الكلى بس الحاله العامه ما زالت مستقرة

2) Oliguric Phase

ودى أشد مرحله لان ال

Tubular obstruction

بيكون حصل خلاص ووظائف الكلى كلها اختلت تقريبا

- Oliguria
- Volume overloads ± pulmonary edema
- Hyperkalemia
- Metabolic acidosis
- Azotemia or may develop Uremia in severe cases

ودى مدتها ايام ،، وغير متوقع امتى هتتحسن!!

لان المرحله دى مفيش وسيله علاجيه تقدر تفتح ال tubules

المقفوله دى ،،

العلاج كله Supportive

3) Post-Oliguric Phase (diuretic phase)

ودى بيحصل فيها إعادة فتح ال

Obstructed tubules

ولكن مع نزول كميات كبيره من البول نوعا ما بعد ال Oliguria

وبيحصل معاها

hypovolemia from fluid loss

ودى تعتبر مؤشر لل

Recovery of tubules

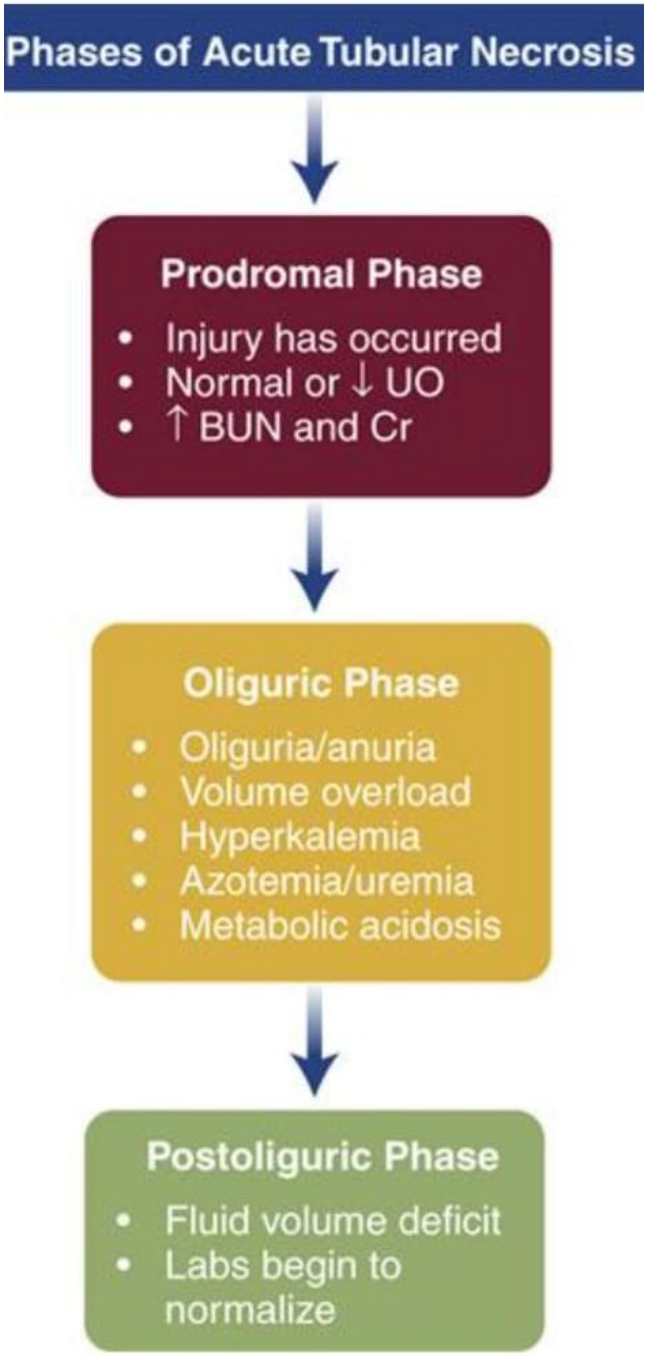


FIGURE 28-2 Phases of acute tubular necrosis and primary clinical issues. *BUN,* Blood urea nitrogen; *Cr,* creatinine; *UO,* urine output.

طب ايه الفرق بقى بين ال

Pre-renal AKI & ATN

مش الاتنين بيعملوا AKI وخلاص

- وان كان الاتنين بيعملوا AKI ولكن لاحظنا أن فى ال

Pre-renal AKI

Kidney tissue are intact, particularly the tubules and their function so, the concentration ability of the kidney is preserved

- إنما فى ال

ATN = tubular injury

وده معناه

Loss of tubular function.So, despite that Urine coming from kidneys is little in amount (oiguria), the urine is dilute, and the concentration ability of the kidneys is lost

والنتيجه

- Low urine osmolality < 350
- Loss of Na in urine (Na > 40)
- FeNa ≥ 2%
- FeUrea > 50 %

Distinguishing Prerenal azotemia and ATN

Parameter	Prerenal AKI	Acute Tubular Necrosis
Urinary sediment	Normal/Hyaline casts	Epithelial cell casts
Urine specific gravity	>1.020	<1.020
Urine sodium (mmol/L)	<20	>40
FE_{Na}	<1%	>2%
FE_{urea}	<35%	>50%
Urine osmolality (mOsmol/kg H_2O)	>500	<350

Casts طبعا بالنسبه لل

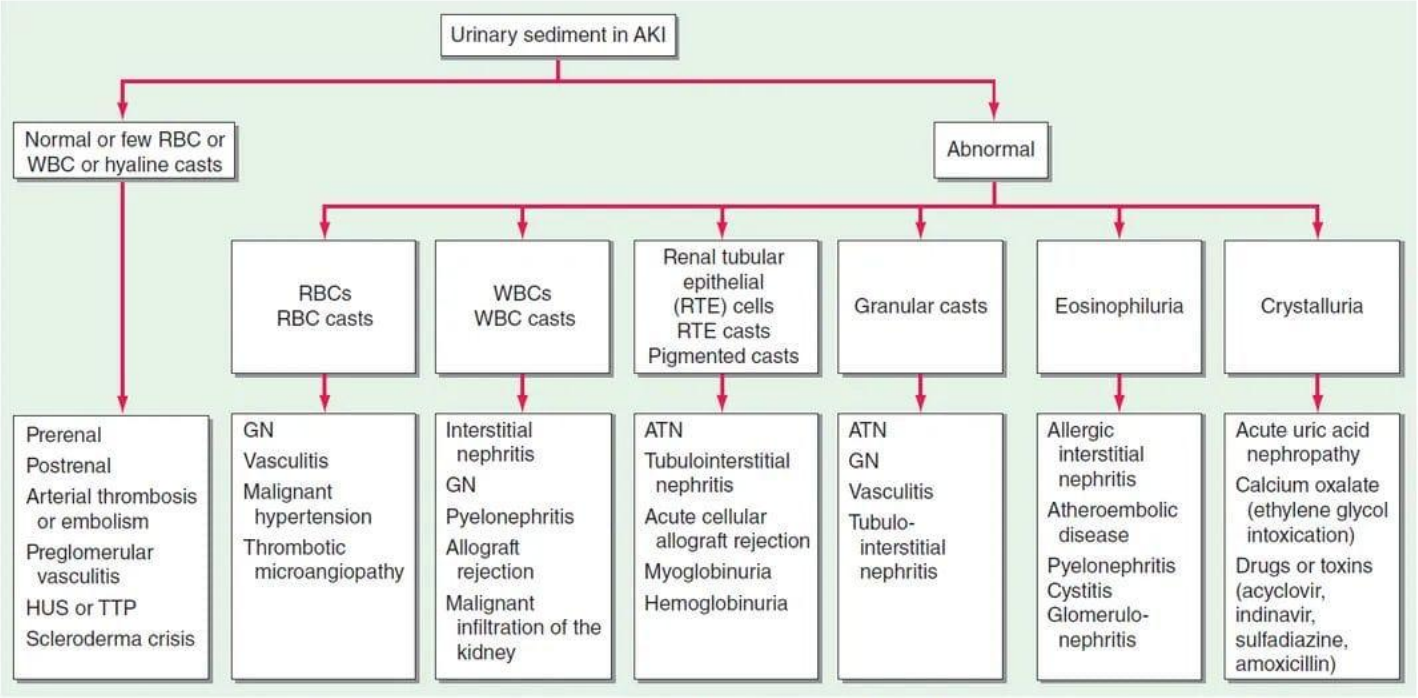
- ATN is characterized by casts in urine because of the pathophysiology of tubular obstruction that it is caused by Tubular epithelial cells

واسمها

Muddy brown granular casts

- While pre-renal AKI , if there are casts , they will be usual casts that are frequently found in the urine without disease and might be formed in concentrated urine due to dehydration and impaired perfusion in the kidneys

They are called Hyaline casts



Interpretation of urinary sediment findings in acute kidney injury (AKI). ATN, acute tubular necrosis; GN, glomerulonephritis; HUS, hemolytic-uremic syndrome; RBCs, red blood cells; RTE, renal tubular epithelial; TTP, thrombotic thrombocytopenic purpura; WBCs, white blood cells. *(Adapted from L Yang, JV Bonventre: Diagnosis and clinical evaluation of acute kidney injury. In Comprehensive Nephrology, 4th ed. J Floege et al [eds]. Philadelphia, Elsevier, 2010.)*

Source: Harrison's Principles of Internal Medicine (19th Ed)

راجع ال casts فى ال Chapter السابق

بالنسبه لأسباب ال ATN

قد تكون

I. Ischemic

ودى هيا نفس أسباب ال

Pre-renal

Or

II. Toxic

Toxins may be

Exogenous **or** Endogenous

- **Exogenous**

  ادويه هتخفظ اسمائها **+** صبغة (contrast)

- **Endogenous**

  Toxis that are produced inside the body then they induces toxic injury to tubules

  3 of them are pigments

  - Myoglobin
  - Hemoglobin
  - Bilirubin

  والاتنين التانيين مرضين من أمراض الدم

I. Multiple myeloma

Myeloma casts (cause of ATN)

II. Tumour lysis syndrome

Uric acid nephropathy **+** AKI + Electrolytes disturbances

طبعا تفاصيل ال**ATN** تقدر ترجع لها من صفحة (18 – 13)

نقاط هاامة واسئله هاامة للتعامل مع مريض ال AKI

==========

❖ Questions

1) **What's the story?**

ايه اللى حصل وايه قصتك ،،

خد هستورى بشكل منظم ومحترف وركز فى كل كلمه عشان بتفرق فى التشخيص والعلاج

2) **What's the potassium?** اوعى تنساه

3) **What's the patient's volume and haemodynamic status?**

Are they dehydrated, overloaded, or about right? How do you know? مهم جداا

4) **Is there anything else of note on clinical examination?** خلى بالك

5) **What's the patient's acid – base status?**

اوعى تنسى الABG

6) **What drugs has the patient been on?**

مهم فى حالات ال ATN والAIN

7) **What did the urine dipstick show?** مهم جدا

8) **Has the patient had a renal ultrasound?** مهم جداا

9) **Is the patient passing urine? How much?** مهم جداا

10) **Do you have any record of a previous eGFR/serum creatinine?**

مهم لتأكيد أنه AKI مشCKD

11) **What comorbidity does the patient have?**

سؤال روتينى مهم

Common Risk Factors For AKI:

Inherent risk factors:

- Age >75 years
- Chronic Kidney Disease (eGFR < 60 ml/min/1.73m2)
- Previous episode of AKI
- Heart failure
- Liver disease
- Atherosclerotic peripheral vascular disease
- Diabetes mellitus

Exposure risk factors:

- Sepsis
- Toxins
  - Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
  - Aminoglyclosides
  - Gentamicin
  - Iodinated intravenous/intra-arterial contrast
- Hypotension/Hypovolaemia

Risk factors & severity of risk in Contrast Nephropathy

Patients at risk for contrast nephropathy include those with

A) Estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m2, who also have proteinuria (defined as albuminuria >300 mg/day which corresponds to proteinuria >500 mg/day), diabetes, or other comorbidities including heart failure, liver failure, or multiple myeloma.

B) Patients are also at risk who have eGFR <45 mL/min/1.73 m2, even in the absence of proteinuria, diabetes, or other comorbidities.

C) Patients who have eGFR <45 mL/min/1.73 m2 and have proteinuria and diabetes or other comorbidities

D) Patients with eGFR <30 mL/min/1.73 m2 should be considered at highest risk.

❖ ايه هو ال workup اللى هاعمله لمريض AKI ؟

قبل ما تعمله هتسال نفسك اهم سؤال هو ال

Renal insufficiency

ده Acute يعنى ماشى مع ال AKI ولا gradual يعنى ماشى مع الCKD

راجع الموضوع ده لانه تم شرحه سابقا

Workup

I. Basic Investigations

1) CBC (anemia supports the chronicity)

   Low platelets with anemia may support possibility of TMA (HUS & TTP)

   Also multiple myeloma

2) RFTs (confirm the renal insufficiency)
   - ↑ Urea/BUN and ↑ Creatinine
   - BUN/Creatinine ratio ≥ 20: 1 supports the diagnosis of Pre-renal cause
3) LFTs (useful in Hepatorenal syndrome) and sepsis
4) Coagulation profile (Useful in Hepatorenal syndrome in advance CLD)

II. Basic metabolic panel including

- Na
- K (searching for ↑ K)
- Ca (searching for ↓ Ca)
- P (searching for ↑ P)
- Uric acid (searching for ↑ Uric acid)
- ABG (searching for metabolic acidosis)

III. Urine analysis

Searching for casts & sediments & proteinuria & hematuria (see before)

Ex:

- Bland urine & hyaline casts in pre-renal AKI
- Muddy brown granular gasts in ATN
- Active sediment (dysmorphic RBCs/RBC's casts ± proteinuria) in acute GN

ملحوظه هاامة :

فى حالة ال

Acute GN (severe nephritic syndrome or RPGN (crescentic)

هتعمل ال

The following Workup

- ANA, ANCA
- Anti-GBM Ab
- C3, C4, C3 Nephritic factor
- ASOT
- Viral markers (HCV Ab & HBs Ag)
- Serum Cryoglobulins if the rash is present

IV. Urinary indices (to differentiate between ATN and Pre-renal AKI)

- Urine Na, Urine Osmolality
- Fractional excretion of Na (FeNa), Fractional excretion of Urea

V. U/S abdomen (comment on Kidney size and echogenicity)

Also it diagnose obstructive uropathy (bilateral back pressure & prostatic hypertrophy)

VI. Renal biopsy

Indicated in certain suspected cases only

- suspected RPGN (crescentic GN)

- Unexplained AKI particularly if suspicious acute interstitial nephritis (selected cases)

VII. Other investigations

According to the history & exam

Such as ECG, ECHO, CXR, septic screen, etc.

VIII. Recent biomarkers in AKI

منذ عدة سنوات اكتشف العلماء دلالات كيميائيه بتشخص ال AKIفى الساعات الأولى حتى قبل ارتفاع الكرياتينين وأمثلتهم

- Kidney Injury molecule 1 KIM1
- Interleukin 18
- NGAL

وهما غالبا مش متوفرين فى المعامل ولا يضيفوا قيمه كبيره للتشخيص

نقطه هاامه جداااا :

☞ **Please Don't Estimate GFR in Cases of AKI**.

Why?!

☞ The serum creatinine will not accurately reflect the glomerular filtration rate (GFR) in patients who are not in steady state.

☞ Thus, among patients who have just developed AKI and in whom the serum creatinine is actively increasing, the estimated GFR (eGFR), based upon the serum creatinine, will overestimate the actual GFR.

☞ Conversely, among patients who are recovering from AKI, the eGFR may underestimate the actual GFR. In order to address this non-steady state phenomena of serum creatinine

ما تحسبش eGFR فى AKI الا عشان تظبيط جرعات الادويه وعن طريق معادلة

CKD-EPI 2021

مع أن الرقم اللى هيطلع مش دقيق ،، بس هيبقى رقم تقريبى

****

❖ ما هى خطورة ومضاعفات ال AKI ؟

==========

✪ **The major complications of AKI include**

- volume overload
- hyperkalemia
- metabolic acidosis
- mental status changes

✪ **Other minor complications of AKI**

- Hypocalcemia (less common)
- Hyperphosphatemia (less common)
- Hyperuricemia (less common)
- hypermagnesemia (rare)

ملحوظه :

☞ These minor complications are common in chronic kidney disease in comparison to AKI and they will be discussed in CKD topic later on.

اخيرا ،، ازاى تعالج مريض ال AKI ؟

TREATMENT

I. Supportive Measures and Treatment of Complications of Aki

✪ At ER

- ABC approach (Airway, breathing, circulation)
- Then -- > Admission at ICU

✪ At ICU

العلاج ٣ خطوات اساسيه

الخطوه الاولى

هل هناك مضاعفات خطيره لدى مريض ال AKI ولا لا؟

ولو وجدت باعرفها وبعالجها . ودى بتندرج تحت ال

General supportive measures

الخطوه الثانيه

هل يوجد سبب واضح لل AKI ؟!

واذا وجد ،، هل له علاج خاصه به بالاضافه لل

Supportive measures

وطبعا لو وجد لازم نضيف العلاج

ولو ليه prevention ،، بادى العيان ال

Preventive measures

لمنع حدوث الAKI

الخطوه الثالثه

هل المريض محتاج

Other supportive measures like

Dialysis or not and also nutrition

❖ **First of all,**

You should assess for major complications & life threatening issues in AKI

❖ **Immediate therapy**

The management of life-threatening fluid and electrolyte abnormalities due to AKI should be started immediately.

❖ **Complications of AKI include the following:**

- Fluid overload
- Hyperkalemia (serum potassium >6 mEq/L) or a rapidly increasing serum potassium
- Signs of uremia, such as pericarditis, or an otherwise unexplained decline in mental status
- Severe metabolic acidosis (pH <7.2)

N.B: Patients with any of these complications despite appropriate medical therapy generally require urgent dialysis

✪ VOLUME ISSUES

بتقيم مريض ال AKI وتشوفه

Hypovolemic

euvolemic ولا

hypervolemiacولا

☞ Ex for hypovolemia (pre-renal AKI due to volume depletion)

☞ Ex for hypervolemia [(ATN as an intrinsic cause of AKI and acute GN (RPGN)]

⇨ An assessment of volume status is performed in all patients who present with AKI since correction of volume depletion or volume overload (especially when associated with worsening cardiac output) may reverse AKI)

1. Volume depletion: pre-renal AKI only

Unless contraindicated, the patient with a clinical history consistent with fluid loss (such as vomiting and diarrhea), a physical examination consistent with hypovolemia (hypotension and tachycardia), and/or oliguria should be administered intravenous fluid therapy.

المحاليل المناسبه لتصليح ال hypovolemia فى مريض ال (Pre-renal AKI)

- Fluids of choice are **crystalloids**

Crystalloid solutions, such as isotonic saline, are preferred for initial therapy since studies have shown that colloid solutions provide no additional benefit

محلول الملح هو المفضل

- The overall goal of fluid therapy is to increase cardiac output and improve tissue oxygenation in patients who are preload dependent or volume responsive.
- Potassium-containing crystalloid solutions, such as lactated Ringer's solution, should be used with caution since the kidney may not be able to excrete potassium and hyperkalemia may result.

يفضل عدم استخدام الرينجر لاكتات

- The amount of Crystalloids (such as Saline) that are needed beginning with 1 to 3 liters of fluid with rate of 75 to 100 mL per hour with careful and repeated clinical assessment to assess the patient's response to this therapy. In some cases, additional fluid therapy may be necessary (e.g., severe burns, acute pancreatitis).

طريقه اخرى

- ⇨ If hypovolaemic, give bolus fluids (e.g. 250–500 mL) until volume replete with regular review of response.
- ⇨ If the patient is euvolaemic clinically, give maintenenance fluids (estimated output plus 500 mL) and set daily fluid target.

ملحوظه : من الافضل والأدق استخدام ال

Dynamic tests for detection of hypovolemia (passive leg raising test)

لان ال CVP قد تكون insensitive and inaccurate فى حالات كتيررر

N.B: Aggressive volume repletion should be avoided as excessive volume expansion may lead to pulmonary congestion, especially in septic patients.

2. Hypervolemia (Volume Overload)

⇨ Hypervolemia may be present in the patient with AKI in such situations

⇦احتمالات ال hypervolemia فى مريض ال AKI

A) Upon initial evaluation (as in the cases of ATN and Acute Glomerulonephritis)

B) Excessive fluid administration in the setting of impaired ability to excrete sodium and water. This is especially true for patients with sepsis who commonly receive aggressive intravenous fluid resuscitation.

⇨ Diuretics may be used to relieve hypervolemia among patients with AKI.

- **Loop diuretics** are the preferred agents as they provide a greater natriuretic effect than thiazide diuretics.
- Loop diuretic as Frusemide (Lasix 40 amp)

Starting dose

- We often start with 40 to 80 mg of intravenous furosemide (Lasix)
- The dose of loop diuretics can be titrated upward to assess for responsiveness, and a thiazide diuretic can be added to augment diuresis
- If there is minimal response to high-dose loop diuretics (>80 to 120 mg of furosemide) combined with a thiazide diuretic, then dialysis/ultrafiltration should be considered.

⇦ فى حالة عدم الاستجابه المبدئيه للازكس على جرعة أقصاها ١٢٠مج (٣ أمبولات ٤٠ مج) ،،

يجب وضع المريض على ماكينة الغسيل الكلوى حالا

⇦هناك طريقه اخرى للازكس⬇⬇⬇

In severe cases of volume overload, furosemide may be given as a bolus (200 mg) followed by an intravenous drip (10–40 mg/h), with or without a thiazide diuretic.

Harrison Textbook ودى مصدرها

⇦ خلى بالك مهم جداااا

- If diuretics are used to treat volume overload, then the patient should be regularly assessed to see if urine output responds. If there is no increase in urine output, then alternative therapies such as dialysis/UF should be initiated.
- Refractory Volume overloads ➔ **Urgent Hemodialysis**

  HD with Ultrafiltration UF modality in HD machine....

✪ TREATMENT OF METABOLIC ACIDOSIS

⇨ Commonly used treatments for metabolic acidosis include ↴↴↴

A) Dialysis

B) Bicarbonate administration.

⇨ Among patients with AKI, the choice of therapy depends upon the absence or presence of volume overload and the underlying cause and severity of the acidosis...

طب امتى المريض يغسل وامتى ياخد bicarb؟

⇨ Dialysis is preferred to the administration of bicarbonate among patients who are volume overloaded because bicarbonate administration results in a large sodium load that may cause or contribute to volume overload.

Even among patients who are not volume overloaded on exam, bicarbonate may cause volume overload among patients who are oliguric or anuric and should be used cautiously.

⇨ We dialyze patients with severe oligo-anuric AKI who are volume overloaded and have severe metabolic acidosis (a pH <7.2) regardless of the cause of acidosis...

⇨ **Bicarbonate may be administered instead of dialysis in the following settings:**

A) Severe organic acidosis (pH <7.2 mEq/L) while awaiting dialysis or in patients in whom the cause of AKI is readily reversible (such as prerenal AKI due to volume depletion or obstruction).

B) Intravenous bicarbonate may also be indicated among patients with AKI due to rhabdomyolysis in order to prevent further renal injury (i.e., ATN), providing other indications for dialysis are not present and the patient is not volume overloaded.

جرعة ال HCO3 كام ؟

لايوجد كلام متفق عليه لتحديد جرعة ال HCO3 ،، وهناك مدرستين !!

⇨ If there is established moderate to severe metabolic acidosis with PH < 7.25 in the abscence of volume overload You can use either

- **This formula:**

  HCO3 (mEq) required = 0.5 x weight (kg) x [24 - serum HCO3 (mEq/L)].

Or

- **This dose :**

  Moderate metabolic acidosis: 50 to 150 mEq sodium bicarbonate diluted in 1 L of D5W to be intravenously infused at a rate of 1 to 1.5 L/hour during the first hour.

  Target PH ≥ 7.2 - 7.25

⇨ Refractory Metabolic Acidosis ➔ **Urgent Hemodialysis**

✪ Treatment of Hyperkalemia

1) **If serum K : 5.5 - 5.9**
   - Just avoidance of medications that increase the K level like ACEi and ARBs
   - Also diet control (avoid food containing k like bananas

+

- Lab monitoring

2) **If serum K : 6 - 6.4**

- You must do ECG searching for ECG changes related to hyperkalemia
  (Tall peaked T, wide QRS, prolonged PR interval and heart block)
- If there are any ECG changes particularly Tall peaked T Wave (the commonest)
  ➔ Give Anti-hyperkalemic measures

3) **If serum K ≥ 6.5** with or without ECG changes
   ➔ Give Anti-hyperkalemic measures

What Are The Anti-Hyperkalemic Measures?

1) First medication that should be taken at once is IV calcium gluconate or Calcium chloride (2 ampoules slow IV infusion or better with 50 - 100 ml saline)

Why calcium?

-> To stabilize the heart in order to ameliorate the cardiac toxicity and to prevent Cardiac arrest

2) Measures that induce K shift from intravascular component to intracellular component.

A) **Glucose/insulin**

For every 25 gm. Glucose, you should give 10 units regular insulin

- 10 units insulin (Actrapid) for

- 100 ml glucose 25%

Or

- 250 ml glucose 10%

Or

- 500 ml glucose 5%

- Monitor Glucose regularly

B) **Inhaled Beta-Agonists**

جلسة فاركولين salbutamol

C) **IV NaHCO3** particularly if associated with moderate to severe metabolic acidosis (without volume overload) See before

3) medication that remove K out of the blood and the body (diuretics) see before

4) medication that prevent K from absorption by binding to it(k resin)

Sodium Polystyrene Sulfonate (SPS)

Trade name: ***Resinokaten*** 454 g powder

Dose: 15 - 60 gm (15 gm = 4 teaspoons)

Intially give 4 teaspoons once

Maximum dose: 4 teaspoons four times daily

This medication is reserved for cases with recurrent or persistent hyperkalemia

⇨ Acute hyperkalemia that is refractory to Anti-hyperkalemic measures

--> **Urgent Hemodialysis**

✪ Uremic encephalopathy

- Manifestations of this syndrome vary from mild symptoms (eg, lassitude, fatigue) to severe signs (eg, seizures, coma).
- Severity and progression depend on the rate of decline in renal function; thus, symptoms are usually worse in patients with acute kidney injury
- Prompt identification of uremia as the cause of encephalopathy is essential because symptoms are readily reversible following initiation of dialysis.
- Uremic encephalopathy --> **Urgent Hemodialysis**

****

II. Treatment of certain causes of AKI

Rule:

Treatment of any cause of AKI requires both supportive measures that were discussed above

+

Specific treatment related to the cause

❖ Abdominal comparemt syndrome

Surgical consultation + supportive therapy

❖ Hepatorenal syndrome

The definitive treatment of the hepatorenal syndrome is liver transplantation.

★ Bridge therapies that have shown promise include terlipressin (a vasopressin analog), with albumin.

Or, when terlipressin is not available, combination therapy with octreotide (a somatostatin analog) and midodrine (an α1- adrenergic agonist), in combination with intravenous albumin (25–50 g, maximum 100 g/d)

❖ Contrast Nephropathy

==========

➢ **For all at-risk patients, we use the following preventive measures**:

- the use of iodixanol or nonionic low-osmolal agents, such as iopamidol or ioversol, is recommended rather than iohexol

  The use of high-osmolal agents (1400 to 1800 mosmol/kg) is not recommended
- We should use lower doses of contrast and avoid repetitive, closely spaced studies (e.g. <48 hours apart)
- We should avoid volume depletion and non-steroidal anti-inflammatory drugs (NSAIDs).

➢ **For patients at highest risk, defined as**

- Those who have eGFR <45 mL/min/1.73 m2, proteinuria, and diabetes or other comorbidities
- all patients with eGFR <30 mL/min/1.73 m2, in the absence of contraindications to volume expansion,

- We should give intravenous fluids prior to and continued for several hours after contrast administration.

Dose of saline

We give 1 mL/kg/hour saline for 6 to 12 hours preprocedure, intraprocedure, and for 6 to 12 hours postprocedure.

ملحوظة :

طبقا الجايدلاينز العالميه ، لا فائده من استخدام ال

Acetylcysteine

و هناك فايده ضئيله جدا من استخدام ال bicarb

لمنع حدوث ال

Contrast nephropathy

★ If Contrast nephropathy occurs it will be treated by supportive measures as ATN

(see general measures)

❖ AKI due to Acute GN & vasculitides

AKI due to acute glomerulonephritis or vasculitis may respond to immunosuppressive agents

(steroids + steroid sparing drugs)

and/or

plasmapheresis

❖ Acute interstitial nephritis (DRUG INDUCED)

- Allergic interstitial nephritis due to medications requires discontinuation of the offending agent.
- Glucocorticoids have been used but not tested in randomized trials, steroids might be used in cases where AKI persists or worsens despite discontinuation of the suspected medication

❖ AKI due Scleroderma (SCLERODERMA RENAL CRISIS)

AKI due to scleroderma (scleroderma renal crisis) should be treated with ACE inhibitors

❖ TTP

Idiopathic TTP is a medical emergency and shouldbe treated promptly with plasma exchange

❖ Rhabdomyolysis

- Early and aggressive volume repletion is mandatory in patients with rhabdomyolysis, who may initially require 10 L of fluid per day.
- Alkaline fluids (e.g. 75 mmol/L sodium bicarbonate added to 0.45% saline) may be beneficial in preventing tubular injury and cast formation, but carry the risk of worsening hypocalcaemia.
- Diuretics may be used if fluid repletion is adequate but unsuccessful in achieving urinary flow rates of 200–300 mL/h.
- There is no specific therapy for established AKI in rhabdomyolysis, other than dialysis in severe cases or general supportive care to maintain fluid and electrolyte balance and tissue perfusion.

❖ Tumour Lysis Syndrome

Prevention

The main prophylactic strategies are intravenous (IV) hydration (often by saline) and the use of hypouricemic agents, such as allopurinol and rasburicase.

- **Allopurinol (Zyloric)**

  Dose and administration — the usual allopurinol dose in adults is 100 mg/m2 every eight hours (maximum 800 mg per day).

  Because Allopurinol acts by decreasing uric acid formation, allopurinol does not reduce the preexisting serum uric acid. Thus, for patients with preexisting hyperuricemia (serum uric acid ≥7.5 mg/dL, rasburicase is the preferred hypouricemic agent.

- **Rasburicase (Fasturtec)**

  Dosing and administration — The EMA and FDA dosing guidelines both recommend a rasburicase dose of 0.2 mg/kg once daily for up to five (FDA) or seven (EMA) days

❖ Obstructive Uropathy (Postrenal AKI)

غالبا بيتعرف بالسونار وبعدين يتعمل عرض عاجل لدكتور المسالك البوليه مع

Supportive measures

فى نفس الوقت

- Prompt recognition and relief of urinary tract obstruction can successfully treat the AKI in such type
- The site of obstruction defines the treatment approach.
  - ☞ Transurethral or suprapubic bladder catheterization may be all that is needed initially for urethral strictures or functional bladder impairment.
  - ☞ Ureteric obstruction may be treated by percutaneous nephrostomy tube placement or ureteral stent placement.
  - ☞ Relief of obstruction is usually followed by an appropriate diuresis for several days.
  - ☞ In rare cases, severe polyuria persists due to tubular dysfunction and may require continued administration of intravenous fluids and electrolytes for a period

oooooooooooooooooooooooooooooooooooooooooooooooooo

III. OTHER IMPORTANT ISSUES

✪ Malnutrition

- Increased catabolism with protein energy wasting is common in severe AKI, particularly in the setting of multisystem organ failure.
- Inadequate nutrition may lead to starvation, ketoacidosis and protein catabolism.
- On the other hand, Excessive nutrition may increase the generation of nitrogenous waste and lead to worsening azotemia.

♦ According to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines, patients with AKI should achieve a total energy intake of 20–30 kcal/kg per day.

♦ Protein intake should vary depending on the severity of AKI:

- 0.8–1.0 g/kg per day in No catabolic AKI without the need for dialysis;
- 1.0–1.5 g/kg per day in patients on dialysis; and up to a maximum of 1.7 g/kg per day if hypercatabolic and receiving continuous renal replacement therapy.

♦ Trace elements and water-soluble vitamins should also be supplemented in AKI patients treated with dialysis and continuous renal replacement therapy

****

✪ Dialysis

Dialysis is indicated when medical management fails to control volume overload, hyperkalemia, or acidosis and when there are severe complications of uremia (asterixis, pericardial rub or effusion, encephalopathy, uremic bleeding)

خلى بالك جدااا

اوعى تبدأ الغسيل بدرى بدون داعى أو تتأخر لو العيان محتاج

Urgent dialysis

واحنا شرحنا الموضوع ده سابقا

- Late initiation of dialysis carries the risk of avoidable volume, electrolyte, and metabolic complications of AKI.
- On the other hand, initiating dialysis too early may unnecessarily expose individuals to intravenous lines and invasive procedures, with the attendant risks of infection, bleeding, procedural complications, and hypotension.

ملحوظه هاااامة :

Many nephrologists initiate dialysis for AKI empirically when the BUN exceeds a certain value (e.g., 100 mg/dL) or Urea > 200 mg/dl in patients without clinical signs of recovery of kidney function

وهذا الموضوع غير مثبت طبقا لل studies ولا توصى به الجايدلاينز العالميه ،، ولكنه trend موجود فى معظم دول العالم

✪ Modes of dialysis

==========

- When dialysis is needed, most patients will be put on hemodialysis machine
- Hemodialysis can be used intermittently or continuously and can be done through convective clearance, diffusive clearance, or a combination of the two.
- Vascular access is through the femoral, internal jugular, or subclavian veins.
- Hemodialysis is an intermittent procedure that removes solutes through diffusive and convective clearance.
- Hemodialysis is typically performed 3–4 h per day, three to four times per week, and is the most common form of renal replacement therapy for AKI.
- Continuous renal replacement therapy (CRRT) can be performed by (continuous venovenous hemofiltration [CVVH])
- continuous venovenous hemodialysis [CVVHD]), a technology similar to hemodialysis except at lower blood flow and dialysate flow rates so it is suitable for patients with AKI with unstable BP and hemodynamics

المكنه بتاعة ال CVVHD أو ال modality دى بتستخدم فى مرضى ال AKI اللى ضغهم واطى و shocked وحالتهم العامه سيئه ومحجوزين فى العنايه

Quiz:

28 years old woman came to you at Casuality with repeated vomiting and fatigue, She has recent labs that were done 1 day ago showing Creatinine : 5.1 & BUN : 88

She reported that she was healthy and good before until she has developed Gastroenteritis 5 days ago and she was seen by a doctor who diagnosed her as Gastroenteritis and gave her fluids, ciproflixaxin , flagyl and anti-diarrheal

CBC:

- ***Hgb: 8.6***
- ***MCV: 83***
- ***WBC's: 4500***
- ***Platelets: 62000***

U/S normal kidneys

What's your opinion?!!

****

DD of such case

- If the patient has recent onset of AKI + low platelets + anemia at the same time that is preceded by diarrhoea --> **suggestive of HUS**

لكن لازم ازود الكلمتين دول عشان اقدر احلف على التشخيص

- To be confirmed by the following labs

✪ **Evidence of MAHA**

- High retics
- High LDH
- Low haptoglobin

± High indirect bilirubin (the latter is not essential)

✚ Negative Coomb's test مهم

- Low platelets (recent)

- Established AKI

كمان هتشوف ال baseline creat كان كام ؟ وتتاكد بالمعايير اللى قولنا عليها

✪ **Evidence of fragmented RBC's (schistocytes) on blood film**

✪ طبعا هنا اول احتمال يطلق عليه

Thrombotic microangiopathy (HUS vs TTP)

HUS is more likely as there are no neurological features or fever;

Also there is a preceding Diarrhea (D+ HUS)

كمان الصح أن حضرتك تتأكد أن الاسهال ده كان

Bloody or dysentery

لانه ماشى مع ال

E.Coli 0157: H7 (shigatoxin)

Or

Shigella (shiga toxin)

ᗧ لو ال workup اتعمل وأثبت الحاجات اللى ذكرتها دى تبقى

Established HUS

إنما من غير اللى ذكرته ده ما ينفعش اقول HUS وابقى متأكد

Other DD

1) New onset of AKI due to dehydration (preceding GE & repeated vomiting) on top of old undiagnosed Bicytopenia!! (Past history is not clear خلى بالك)

   BUN/Creat ratio in such case against Pre-renal AKI & GE induced AKI

2) AKI due to sepsis complicated by DIC

   DIC = (MAHA + low platelets)

But what is against?!

If sepsis, you would find other MODS (Multi-organ dysnfunction syndrome)

- Liver affection ↑ ALT
- CNS affection (confusion)
- CVS (shock)
- QSOFA often ≥ 2

3) AKI as acute interstitial nephritis (ciprofloxaxin induced) on base of undiagnosed Bicytopenia!! (Past history is unclear)

حتى لو قالتلك أنها عمرها ما اشتكت من حاجه ،،

لان الBicytopenia

ربما تكون

Asymptomatic

4) SLE can cause Bicytopenia & AKI

But the context of scenario is not straightforward for SLE also you must ask about criteria

ولو كانت كبيره فى السن كنا هتحط احتمال ال

Multiple myeloma

معانا كمان لانه بيعمل كل ده ،،بس طبعا مالوش علاقه بالاسهال خالص

KEY MESSAGE

You should take thorough history

If you suspect a certain disease, You must confirm the diagnosis according to its criteria

In Order to clinch your final diagnosis; otherwise, you will often have DD