Acute kidney injury in children

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AKI is defined as

- Abrupt loss of kidney function that results in a decline in glomerular filtration rate (GFR).
- Retention of urea and other nitrogenous waste products.
- Dysregulation of extracellular volume and electrolytes.

- Acute kidney failure (AKF) …
- Acute kidney injury (AKI)… The term AKI has largely replaced acute renal failure (ARF), as it more clearly defines renal dysfunction as a continuum rather than a discrete finding of failed kidney function, because even modest reduction in kidney function are associated with worse outcome.

- AKI = Decrease in glomerular filtration rate (GFR)= rise in serum creatinine from baseline = -+ Reduction in urine output.

_ nonrenal factors affecting S.Cr

Age

Gender

Muscle mass

Presence of sepsis

The nutritional and hydration status of the child

- Creatinine used as a major predictor of kidney injury despite its limitation
- Urine output is so important but has limitations

_ Difficult to measure

_ Affected by hydration status, fluid use and diuretics .

* Degree of oliguria is strongly associated with poor outcome.*

Definitions

- PRIFLE

— pRIFLE is a pediatric modification of the adult RIFLE classification and consists of three graded levels of injury (Risk, Injury, and Failure) based upon the magnitude of change in estimated GFR (eg, changes in serum creatinine) or urine output, and two outcome measures (Loss of kidney function and End-stage kidney disease)

Pediatric RIFLE Classification of acute kidney injury

pRIFLE stage	Estimated creatinine clearance (eCCl)	Urine output
R = Risk for renal dysfunction	eCCl decreased by 25 percent	<0.5 mL/kg per hour for 8 hours
I = Injury to the kidney	eCCl decreased by 50 percent	<0.5 mL/kg per hour for 16 hours
F = Failure of kidney function	eCCl decreased by 75 percent or eCCl <35 mL/min per 1.73 m^2	<0.3 mL/kg per hour for 24 hours or anuria for 12 hours
L = Loss of kidney function	Persistent failure >4 weeks	
E = End-stage renal disease	Persistent failure >3 months	

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GFR calculator

original Schwartz formula

Serum creatinine		mg/dL
Height		cm
Premature infant	○ Yes	
	○ No	
Age		yr
Sex	○ Female	
	○ Male	
Creatinine assay	○ Jaffe	
	○ Enzymatic	

Definition

- KDIGO

_●Increase in serum creatinine by ≥0.3 mg/dL from baseline (≥26.5 mcmol/L) within 48 hours; OR

●Increase in serum creatinine to ≥1.5 times baseline within the prior seven days; OR

●Urine volume ≤0.5 mL/kg/hour for six hours

Criteria for the Kidney Disease Improving Global Outcomes (KDIGO) acute kidney injury for children

Stage	Serum creatinine (SCr)	Urine output
1	Increase to 1.5 to 1.9 times baseline, OR increase of ≥0.3 mg/dL (≥26.5 mcmol/L)	<0.5 mL/kg per hour for 6 to 12 hours
2	Increase to 2 to 2.9 times baseline	<0.5 mL/kg per hour for ≥12 hours
3	Increase greater than 3 times baseline, OR SCr ≥4 mg/dL (≥353.6 mcmol/L), OR Initiation of renal replacement therapy, OR eGFR <35 mL/min per 1.73 m^2 (<18 years)	<0.3 mL/kg per hour for ≥24 hours, OR Anuria for ≥12 hours

The time frames for the increases in serum creatinine are:

- Increase of SCr ≥0.3 mg/dL (≥26.5 mcmol/L) within 48 hours
- Increase in SCr >1.5 times the baseline within the prior seven days

eGFR: estimated glomerular filtration rate.

RISK FACTORS

- Critically ill patients.
- Neonates .
- Nephrotoxin use.
- Comorbid conditions.
- Others.

CLASSIFICATIONS

- Prerenal disease
- Intrinsic kidney disease
- Postrenal disease

Prerenal disease

- Volume-responsive or functional AKI.
- Caused by reduced renal perfusion.

- Hypovolemia (bleeding or gastrointestinal, urinary or cutaneous losses).

- Reduction of effective circulation (eg, heart failure, septic shock, and cirrhosis).

Decrease GFR → preserved tubular function → water and sodium reapsorption → oligurea .

Intrinsic kidney disease

- intrarenal AKI is characterized by structural damage to the renal parenchyma.
- The most common causes of intrinsic disease are :

-Prolonged hypo perfusion.
-Sepsis.
- Nephrotoxins
- Severe glomerular diseases.

Causes of prerenal and intrinsic pediatric acute kidney injury

Mechanism	Etiology
Prerenal causes	
Decreased intravascular volume	Dehydration, hemorrhage, diuretics, burns, shock, nephrotic syndrome
Decreased cardiac function	Heart failure, arrhythmias
Peripheral vasodilatation	Sepsis, anaphylaxis, antihypertensive medication
Renal vasoconstriction	Sepsis, nonsteroidal antiinflammatory drugs, ACE inhibitor
Intrinsic causes	
Tubular injury (acute tubular necrosis)	Prolonged ischemia, nephrotoxins, hypotension, sepsis
Renal vascular diseases	Hemolytic uremic syndrome, vasculitides, thrombosis
Interstitial diseases	Interstitial nephritis, infections, malignant infiltrations
Glomerulonephritides	Post-infectious glomerulonephritis, rapidly progressive glomerulonephritis, Henoch-Schönlein purpura

ACE: angiotensin converting enzyme.

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Postrenal disease

- obstructive AKI is typically the result of congenital or acquired anatomic obstructions to the lower urinary tract.

Examples :

- Posterior urethral valve .
- Stones.
- clots.
- neurogenic bladder
- medications that cause urinary retention

Urine output

- The degree of oliguria affects fluid and electrolyte management and is strongly associated with poor outcomes.

- Anuria – No urine output.

- Oliguria – Urine output <1 mL/kg/h in infants and <0.5 mL/kg/h in children and adults for > six hours.

-Nonoliguria – Urine output for greater than six hours of >1 mL/kg/h for infants and >0.5 mL/kg/hfor children and adults.

- Polyuria – Urine output of greater than 3 mL/kg/h.

- patients with a urinary concentrating defect will present with polyuric AKI, particularly those with acute tubular necrosis and those with nephrotoxic AKI.

ETIOLOGY AND PATHOGENESIS

- The causes and mechanisms of pediatric AKI can be classified based on the anatomic location of the initial injury.

-Vascular – Blood from the renal arteries is delivered to the glomeruli. Interruption of perfusion to the kidneys results in prerenal AKI.

-Glomeruli – Ultrafiltration occurs at the glomeruli forming an ultrafiltrate, which subsequently flows into the renal tubules. Glomerular injury resulting in disruption of glomerular filtration rate (GFR) is one of the major causes of intrinsic AKI.

ETIOLOGY AND PATHOGENESIS

-Renal tubule – Reabsorption and secretion of solute and/or water from the ultrafiltrate occurs within the tubules. Acute tubular necrosis due to nephrotoxins or hypoperfusion is one of the major causes of intrinsic AKI.

- Urinary tract – The final tubular fluid, the urine, leaves the kidney, draining sequentially into the renal pelvis, ureter, and bladder, from which it is excreted through the urethra. Postrenal AKI is due to obstruction of urine anywhere along the urinary tract in a single kidney, and in patients with two kidneys, bilateral obstruction usually at the bladder or urethral level.

CLINICAL FINDINGS

- Clinical presentation.

-Edema (due to progressive fluid accumulation).

-Decreased or no urine output.

-Gross and microscopic hematuria,

-Hypertension.

-Rash, arthritis, and abdominal pain

- Malaise and vomiting

laboratory findings

- Elevations of serum creatinine.
- Elevation of blood urea nitrogen (BUN).
- Abnormal urinalysis.
- Hyperkalemia.
- Abnormal serum sodium .

-Hyponatremia due to dilution from fluid retention

-Hypernatremia is less common in children with AKI.

laboratory findings

- High anion gap metabolic acidosis is common and is secondary to the impaired kidney excretion of acid, and reabsorption and regeneration of bicarbonate.
- Hypocalcemia is common in AKI, and is due to increased serum phosphate and impaired kidney conversion of vitamin D to the active form
- Hyperphosphatemia in AKI is primarily due to impaired kidney excretion and can contribute to hypocalcemia

Creatinine

- Used to identify reduced glomerular filtration rate (GFR) as an indication of AKI.
- Normal levels vary depending on the age, gender, muscle mass, and the nutritional and hydration status of the child.

- The following are the ranges of normal serum creatinine values by age.

Newborn – 0.3 to 1 mg/dL (27 to 88 micromol/L)
Infant – 0.2 to 0.4 mg/dL (18 to 35 micromol/L)
Child – 0.3 to 0.7 mg/dL (27 to 62 micromol/L)
Adolescent – 0.5 to 1 mg/dL (44 to 88 micromol/L)

Creatinie has limitations

Limitations of S.creatinine

- - It is insensitive to small changes in GFR, and is not a real-time indicator.
- - It may not change until up to 50% of kidney function is lost and rise up to 48- 72 h! after an insult.
- - It's concentration affected by age, sex, muscle mass, and volume status

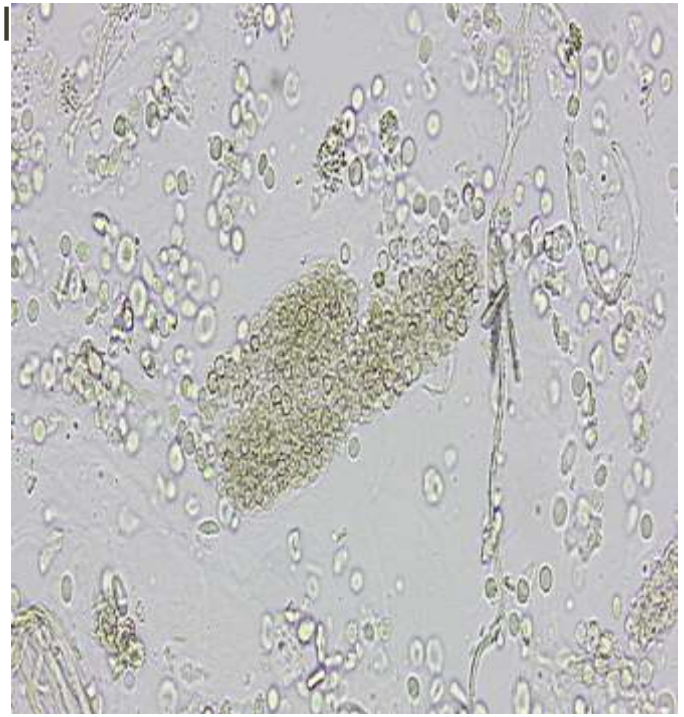
Cystatin C

- Is a protein produced by all nucleated cells at a steady rate.
- It is freely filtered by the kidney with complete reabsorption and catabolism in the proximal tubule and no significant urinary excretion .
- Much less affected by non renal factors that complicate creatinine measurements.

  *Cystatin C can replace creatinine *

Urinalysis

- Normal
- Hematuria and/or protei
- Granular cast
- Dysmorphic RBCS.



Biomarkers of AKI

- Novel biomarkers:

- Neutrophil gelatinase-associated lipocalin (NGAL)
- kidney injury molecule-1 (KIM-1)
- Interleukin-18 (IL-18)
- Fibroblast growth factor 23 (FGF23)
- Insulin growth factor binding protein 7 (IGFBP-7)
-Tissue inhibitor of metalloproteinases 2 (TIMP-2)

(**show promise in both their diagnostic and prognostic utility in the setting of AKI, and may allow for early intervention prior to the onset of serum creatinine rise, severe metabolic derangements, and fluid overload**)

APPROACHE

- Given the multiplicity of causes of ARF, a structural approach to the clinical history and examination is important 1. History:
- History of any prodromal illness:

- Diarrhea +_ blood with associated dehydration

- Other events may result in volume depletion

- Acute pharyngitis/skin infection

- Fever

- Rash, arthropathy

Presence or absence of urinary symptoms:

- Hematuria, dysuria, frequency, loin or abdominal pain

- Poor urinary stream

- Oliguria, anuria

APPROACHE

-Antenatal history

- Drug history

- History of toxins

- History of foreign travel

- Urine output, fluid intake, fluid losses

- Recent wt measurements

- Previous significant illness (liver, cardiac) or surgery

- Family history of renal diseases

APPROACHE EX

Wt + Ht

Temperature

State of hydration

- dehydration
- generalized edema

Hemodynamic status

- Intravascular volume depletion (signs)
- Intravascular volume overload (signs)

Respiratory status (tachypnea, fluid overload)

PH.EXAM

Abdominal examination

- renal masses
- palpable bladder
- costo-vertebral tenderness

Neurological examination

- confusion, drowsiness
- manifestations of hypocalcaemia
- focal neurological abnormality

Full systems examination for causes or sequelae of renal failure

Rash, arthropathy

IDENTIFYING THE UNDERLYING

History of fluid loss

- Diarrhea, vomiting
- Burns
- Surgery
- Shock

Exposure to nephrotoxic agents

- Nonsteroidal antiinflammatory drugs
- Aminoglycosides
- Contrast agents

Factors associated with glomerular diseases

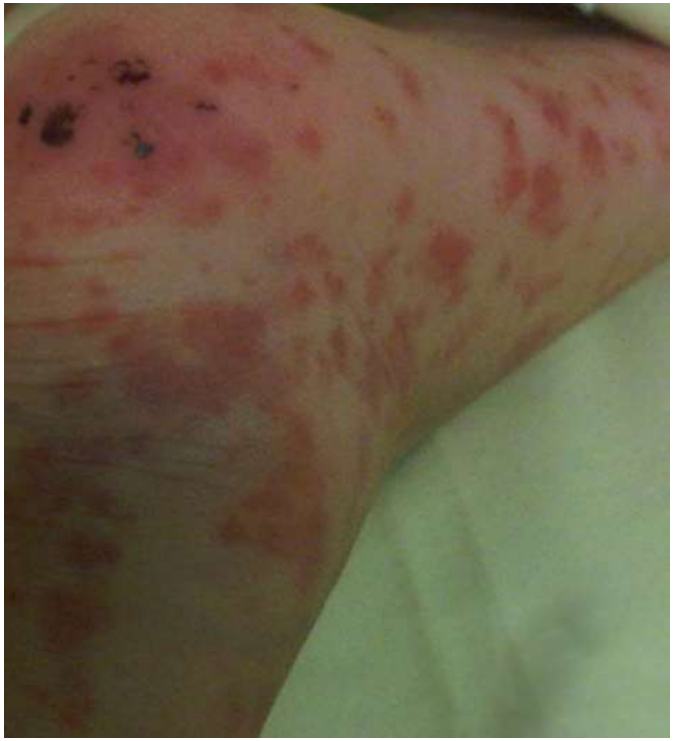
- Streptococcal infection: Poststreptococcal glomerulonephritis
- Bloody diarrhea: Hemolytic uremic syndrome
- Joint symptoms, rash, or purpura: Henoch-Schönlein purpura

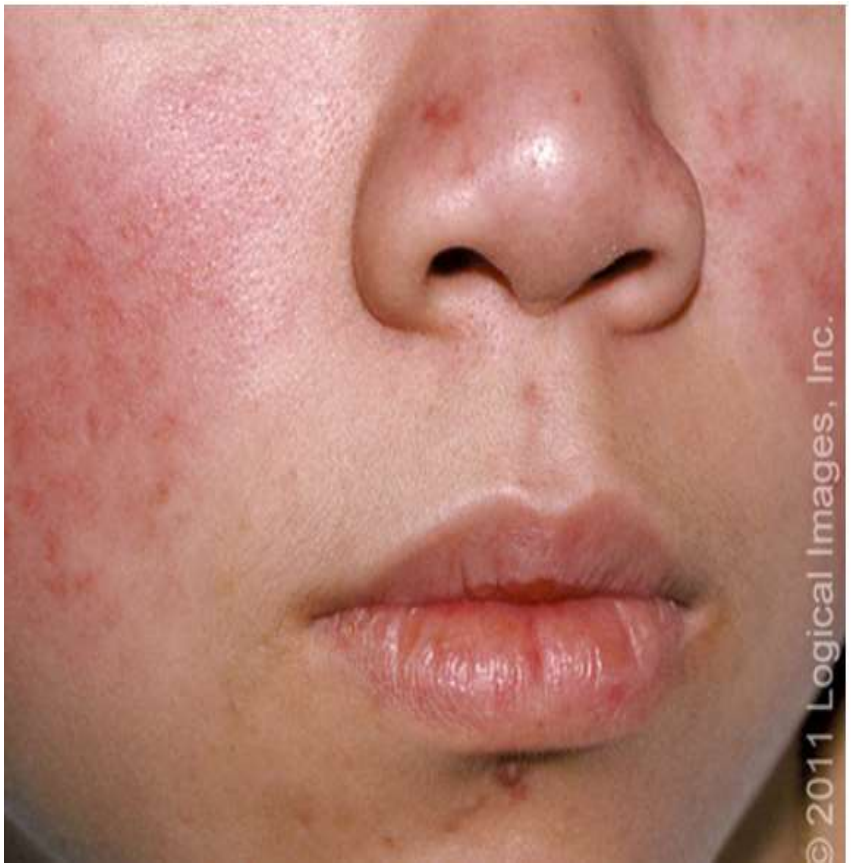
Signs of obstruction

- Complete anuria
- Poor urinary stream

History

- A short duration of vomiting, diarrhea, or decreased oral intake associated with decreased urine output suggests prerenal AKI.
- A history of bloody diarrhea three to seven days prior to the onset of oliguria suggests hemolytic uremic syndrome.(HUS).
- A history of pharyngitis or impetigo a few weeks prior to the onset of gross hematuria or edema suggests poststreptococcal glomerulonephritis. (See "Poststreptococcal glomerulonephritis".)
- In hospitalized patients, nephrotoxic medications or periods of hypotension are associated with intrinsic AKI.
- Systemic complaints (eg, fever, joint complaints, and rash) may be seen in patients with autoimmune diseases or vasculitides, such as immunoglobulin A vasculitis (Henoch-Schönlein purpura) or systemic lupus erythematous (SLE)

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Physical examination

- Signs of volume depletion (eg, dry mucous membranes, tachycardia, decreased skin turgor, orthostatic falls in blood pressure, and decreased peripheral perfusion) are indicative of prerenal AKI.

- Edema may be present in children with nephrotic syndrome or glomerulonephritis.
- Hypertension is a common finding in children with glomerulonephritis
- Rash is commonly seen in children with AKI due to IgAV (HSP), interstitial nephritis, and the acute onset of SLE
- Enlarged palpable kidneys may be an indication of renal vein thrombosis.
- An enlarged bladder may suggest urethral obstruction.

Physical signs

Signs of intravascular volume depletion

- Tachycardia
- Delayed capillary refill
- Low blood pressure
- Weak peripheral pulses
- Dry mucous membranes

Signs of fluid overload

- Edema
- Hypertension
- Heart failure
- Pulmonary edema

Palpably enlarged kidneys

- Polycystic/multicystic kidney disease
- Renal vein thrombosis

Signs of obstruction

- Poor urinary stream
- Palpably enlarged bladder
- Therapeutic catheterization

Renal disease due to systemic causes

- Rash: Henoch-Schönlein purpura, acute presentation of systemic lupus erythematous, interstitial nephritis due to drug reaction
- Joint findings (tenderness or swelling): Henoch-Schönlein purpura, acute presentation of systemic lupus erythematous

FLUID OVERLOAD

- Fluid overload = current weight >10 percent above their admission weight.
- It is independently associated with increased morbidity and mortality.

Tests to distinguish between prerenal and intrinsic ATN

- Fractional excretion of sodium.

FENa is calculated from measured concentrations of urinary sodium (UNa) and creatinine (UCr), and plasma sodium (PNa) and creatinine (PCr):

$$\text{FENa, percent} = \frac{\text{UNa} \times \text{SCr}}{\text{SNa} \times \text{Ucr}} \times 100$$

- Fractional excretion of urea (FEUrea).

Measurement	Prerenal AKI	Intrinsic AKI
Urine specific gravity	>1.020	<1.010
Urine/plasma creatinine	>40	<20
Urine Na (mEq/L)	<20	>40
FENa	<1 percent	>2 percent
FEUrea	<35 percent	>50 percent

Additional laboratory measurements

- Complete blood count –

- Microangiopathic hemolytic anemia /thrombocytopenia is diagnostic for hemolytic uremic syndrome.

-Eosinophilia and/or urine eosinophiluria may be present in some cases of interstitial nephritis

- Complement studies including C3, C4, CH50, and AH50
- Serologic testing for streptococcal infection
- Elevated serum levels of aminoglycosides are associated with ATN
- Uric acid increse in tumor lysis syndrome .

Life threatening emergencies in AKI

- Hyperkalemia
- Metabolic acidosis
- Shock
- Pulmonary edema
- Hypertension
- Hyponatremia, Hypernatremia
- Hypocalcemia

Hyperkalemia:

- K > 6.5 mmol/l … emergency treatment.
- - 10% calcium gluconate IV (0.5-1 ml/kg over 10 min. (reduces toxicity)
- - Salbutamol nebulizer (2.5-5mg), max 2 hourly
- - Salbutamol IV (4mic/kg over 10 min)
- - Sodium bicarbonate 8.4% IV (1-2 mmol/kg), over 30 min
- - Glucose and insulin IV, bolus or continuous infusion
- - Calcium resonium, sodium resonium orally or per rectum , 1gr/kg every 4 hours intialy,(removes K).

Blood pressure

- Hypertension in patients with AKI is mostly due to volume overload.

Diuretics should be considered first

Consider other agents:

- Calcium channel blockers

- Labetalol if severe hypertension + signs of encephalopathy

Dialysis if no response

Kidney imaging

- kidney ultrasound should be considered in all children with AKI of unclear etiology.

-Document the presence of one or two kidneys

-Delineate kidney size

- Renal parenchyma.

-Urinary tract obstruction

-Occlusion of the major renal vessels.

Kidney biopsy

- A kidney biopsy is rarely indicated in AKI

MANAGEMENT

- RRT modalities for AKI :

(Peritoneal dialysis, Hemodialysis or hemofiltration)

- Peritoneal dialysis. Can be started immediately in the child with AKI
- Hemodialysis removes toxins rapidly, requires experience for small children and hemodynamically unstable patients.
- CRRT facilitates hemodynamic stability. Can be used in small children and neonates requiring intensive care.

RRT (Renal Replacement Therapy) INDICATIONS

- RRT is required when conservative care fails.

Indications for dialysis:

-BUN exceeding 100mg/dl + increasing rate
-CHF with oligo-anuria unresponsive to diuretics
-Hypertensive encephalopathy
-Hyperkalemia with ECG abnormalities
-Refractory hypernatremia / hyponatremia
-Persistent severe acidosis

OUTCOME

- Although previously it was believed that most patients who developed AKI fully recovered, it is now recognized that those who experience AKI have increased risk for :

subsequent AKI,

progressive CKD, and
increased mortality.

In the pediatric literature, AKI is consistently associated with poor outcomes, similar to adults.

AKI is an independent risk factor for prolonged stay in the PICU, longer duration of mechanical ventilation, and increased mortality among critically ill children.

THE END.