MANAGEMENT OF ACUTE KIDNEY INJURY

Recognition and Assessment

Acute Kidney Injury (AKI) is a rapid decline in kidney function, occurring over hours to days, resulting in a failure to maintain fluid, electrolyte and acid-base homoeostasis.

- An abrupt (within 48hrs) absolute increase in the serum creatinine (s[Cr]) of $\geq 0.3\text{mg/dL}$ ($26\mu\text{mol/L}$) from baseline; or a percentage increase in the s[Cr] of $\geq 50\%$ within seven days
- Or oliguria of < $0.5\text{mL/kg/h}$ for $>6\text{hrs}$

Staging of AKI:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum Creatinine (SCr) (mmol/l)</th>
<th>Urine O (UOP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5–1.9 times baseline OR $\geq 0.3\text{mg/dL} (\geq 26.5\text{mmol/L})$ increase</td>
<td>&lt; $0.5\text{mL/kg/hr}$ for 6–12 hours</td>
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<tr>
<td>2</td>
<td>2.0–2.9 times baseline</td>
<td>&lt; $0.5\text{mL/kg/hr}$ for X12 hours</td>
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<tr>
<td>3</td>
<td>3.0 times baseline OR Increase in SCr to $\geq 4.0\text{mg/dL} (\geq 353.6\text{mmol/L})$ OR Initiation of RRT OR, In patients &lt;18 years, decrease in eGFR to &lt;35ml/min per 1.73m2</td>
<td>&lt; $0.3\text{mL/kg/hr}$ for X24 hours OR Anuria for X12 hours</td>
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</table>

Adapted from [1]
Risk Factors:

All emergency admissions should have blood for Urea and Electrolytes (UEs) on admission compared with base line, and subsequently as appropriate and electronic alerts should be in place[2,3]. More attention to at risk patients for applying primary prevention measures[1,3]:

- Age ≥65, Sepsis, deteriorating National Early Warning Score (NEWS), Chronic Kidney Disease (CKD), heart failure, liver disease, diabetes mellitus, previous AKI, oliguria (UOP < 0.5ml/kg/hour), hypovolaemia, neurological or cognitive impairment, use of potentially nephrotoxic drugs (NSAIDS, aminoglycosides, ACEi, ARB, diuretics), use of iodinated intravenous contrast and patients with possible obstruction[3].

Causes:

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Incidence</th>
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<tr>
<td>Pre-renal: acute renal hypoperfusion</td>
<td>28%</td>
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<td>Intrinsic renal: acute diseases of renal parenchyma (predominantly ATN, accounts for ~ 85%* cases)</td>
<td>58%</td>
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<td>- Large renal vessels disease 1% (TED, HT emergency, scleroderma)</td>
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<td>- Small renal vessels and glomerular disease 4% (including AVR)</td>
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<td>- ATN* 45% (ischemic – 50%): unresolved pre-renal; toxic (35%): drugs, contrast; sepsis</td>
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<tr>
<td>- Tubulointerstitial disease 2% (AIN, ACR, viral, drugs, infiltrative)</td>
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<tr>
<td>- Intra-tubular obstruction (MG, Hb, MM, drugs)</td>
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<tr>
<td>Post-renal: obstruction of the urinary tract – (prostate, stones, extrinsic compression, clots)</td>
<td>10%</td>
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</table>

* Abbreviations: TED=Thrombo-Embolic Disease, HT=Hypertension, AVR=Acute Vascular Rejection, ATN=Acute Tubular Necrosis, AIN=Acute Interstitial Nephritis, ACR=Acute Cellular Rejection, MG=Myoglobin, MM=Multiple Myeloma

Acute on CKD in 13% of AKI cases: mostly due to ATN and pre-renal disease.

Adapted from:[4]

Hospital-acquired AKI is often multifactorial, with contributions from hypotension, sepsis and drugs.
Management of Acute Kidney Injury

Assessment

1. Detailed history: with particular reference to features associated with volume depletion, sepsis, cardiogenic or multi-system disorder
   - Past medical history (risk factors). Obtain previous UEs for evidence of pre-existing CKD
   - Careful drug history: antibiotics, NSAIDs, diuretics, ACEi, ARB, non-prescribed drugs

2. Purposeful physical examination: assessment of hydration status – skin turgor, pulse, JVP, lying/standing BP, meticulous documentation and vigil review of input output fluid balance charts and signs of fluid overload
   - Look for: signs of urinary tract obstruction – palpable bladder; fundi – papilloedema; skin rash; arthritis

3. Look for evidence of Multiple Organ Failure (MOF)
   - Patient looks severely ill/exhausted/obtund
   - Hypotension (MAP <80mmHg) despite initial fluid administration.
   - Presser agents/inotrope dependency
   - Impaired gas transfer: hypoxaemia (PaO₂ <10kPa) despite 40% O₂
   - Metabolic acidosis – compensated or non-compensated
   - CXR: pulmonary venous congestion

   It is crucial to early identify the developing or established MOF and refer to ICU for further assessment and management

Investigations

Urgent for all patients:
   - Urine dipstick (preferably non-catheter): blood, leucocytes, protein, nitrites and glucose
   - FBC; clotting, UEs, Ca, Pi, LFTs, glucose, CK, CRP
   - ABG to assess acidosis, hypoxia
   - ECG – manifestations of hyperkalaemia or arrhythmias
   - US KUB within 24hrs if no cause identified; 6hrs in trauma or if obstruction is suspected
   - CXR – signs of: fluid overload, infection, Wegner Granulomatosis or Goodpasture’s syndrome
   - Blood and urine cultures – if sepsis is suspected
   - HB, HC and HIV if clinically indicated or dialysis is anticipated
Selected patients with active urinary sediment (Blood, Protein, Casts):

- Immunology screen (ANA/C3/C4/ANCA/Anti-GBM) – acute Gln/vasculitis
- Serum Igs, electrophoresis and urine electrophoresis
- Urine myoglobin to confirm rhabdomyolysis
- LDH, blood film to aid diagnosing thrombotic micro-angiopathies

Differential Diagnosis: Pre-renal vs ATN – avoid over intravenous fluid resuscitation, especially in ATN patients for fear of fluid overload

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<tr>
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<th>Pre-renal</th>
<th>ATN</th>
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<tbody>
<tr>
<td>S Ur/Cr ratio</td>
<td>&gt;20:1</td>
<td>10:1</td>
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<tr>
<td>U SG/ Osmolality</td>
<td>1.015/&gt;500</td>
<td>1.010/300mOsm/kg</td>
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<tr>
<td>U Na/FENa⁺</td>
<td>&lt;20/&lt;1%</td>
<td>&gt;40mmol/l /&gt;2%</td>
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FENa⁺ = the percentage of the sodium filtered at the glomerulus that is secreted in the urine.

Markers of CKD: elevated iPTH, small kidneys < 9cm, anaemia, high phosphate, low bicarbonate

**RESPONSE**

**Referral to Renal Team**

Discuss with the renal team any patient with¹:

- AKI of unclear cause (e.g. no evidence of volume depletion, sepsis, etc.)
- Inadequate response to treatment
- Active urinary sediment (proteinuria or haematuria without evidence of UTI or trauma due to catheterisation)
- Multi-system disorder
- Stage 3 AKI; Residual eGFR ≤ 30; CKD 4 and 5
- Kidney transplant

(Refer patients with obstructive uropathy to the urology team)

**IMMEDIATE TREATMENT**: Treatment is largely supportive

<table>
<thead>
<tr>
<th>AKI: Volume depletion</th>
<th>AKI: Sepsis</th>
<th>AKI: Euvolaemic patients</th>
<th>AKI: Cardiogenic shock</th>
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</table>
| Volume resuscitation  | • Volume resuscitation*  
|                        | • Take cultures  
|                        | • Prompt antibiotic administration as per local protocols | • Supportive treatment  
|                        | • Refer to renal team | • Supportive treatment  
|                        |                        | • Refer to cardiology |
*Volume resuscitation (see chapter on intravenous fluids):
  o Correct with IV isotonic crystalloid (0.9% NS/or Hartmann’s solution)
  o Once rehydrated, continue IV crystalloid to match urine output + 30ml/hr under monitoring of electrolyte levels
  o Consider CV line: keep CVP 10–14cm H₂O
  o If BP low despite the above consider pressor agents/inotropes

- Discontinue/avoid nephrotoxins e.g. NSAIDs/(ACEi, ARB – temporarily until improvement and stabilisation[3])
- Drugs in adjusted renal dose
- Do not offer low dose dopamine to treat AKI[1,3]
- Do not offer diuretics unless in volume overload[1,3]

Renal Support

Urgent referral to the nephrologist/intensivist for those who need emergency RRT (continuous HF, HDF, HD – according to local resources and expertise) for life threatening complications if medical treatment fails[1,3]:

<table>
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<tr>
<th>Pulmonary oedema†</th>
<th>Severe hyperkalaemia‡</th>
<th>Severe acidosis§</th>
<th>Uraemic complications: e.g. pericarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Urgent oximetry/ABG/ECG/CXR</td>
<td>● Do not wait for a repeat K level before starting treatment</td>
<td>● IV Normal Saline 1000ml followed by 1.26% sodium bicarbonate 500ml over 4hrs</td>
<td>● Analgesia (avoid NSAIDs)</td>
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<tr>
<td>● O2 therapy</td>
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<td>● Oral sodium bicarbonate</td>
<td>● Heparin-free dialysis</td>
</tr>
<tr>
<td>● Stop IV fluids</td>
<td></td>
<td>● Avoid volume overload</td>
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<tr>
<td>● IV furosemide 40mg/repeat if patient is improving or awaiting RRT</td>
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<tr>
<td>● IV morphine 2.5mg +10mg metoclopramide</td>
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<tr>
<td>● Consider GTN infusion</td>
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† Fluid overload in critically ill patients, including those with AKI, is associated with worse outcome[6]. ‡ Treatment of Hyperkalaemia, see chapter on hyperkalaemia.
§ AKI-related metabolic acidosis: can usually be corrected with bicarbonate and should rarely require urgent dialysis if not accompanied by volume overload or uremic symptoms[6]. No standard criteria (PH or HCO₃ level) for initiating dialysis for acidosis exist as there is no available data[6]. Involve the dietician to ensure adequate nutrition[5,7].
Starting RRT should be based on the condition of the patient as a whole and trends in laboratory tests, not on an isolated urea, creatinine or potassium value[1,3]. The optimal time for starting RRT is unclear[1,3]. Early as opposed to late starting of RRT in AKI was not associated with differences in mortality (ICU/hospital), or in renal recovery among survivors in a small RCT[8]; another smaller RCT[9] and a heterogeneous systematic review[10] and observational studies suggested benefit from starting early[1].

Monitoring Treatment
- Physiological surveillance (NEWS) should be performed for all patients with AKI to identify early signs of deterioration that may require escalation in the level of care[6]
- Daily biochemical screen
- Monitoring of underlying cause
- Avoid urinary catheter unless very essential

Subsequent Management/Rehabilitation
Depends on the precipitating cause, treatment administered and the outcome
- Resolved pre-renal AKI: can be managed and followed up by general physicians
- Intrinsic renal disease (ATN in ~ 85% cases): general physicians can follow up uncomplicated, completely resolved ATN. Renal physicians will follow those with non- or partially resolved AKI and patients needing immunosuppression or RRT.

Discharge Policy
Arrange Outpatient Department (OPD) follow up if renal function remains abnormal.

Prevention of AKI:
The mainstay of AKI prevention is good medical care
- Ensure adequate hydration status
- Prevention of hypotension
- Prompt treatment of sepsis
- Avoid nephrotoxic agents
CONCLUSION

The ISN has put the human rights case for the initiative:
A goal of “zero preventable deaths from AKI by 2025”... No one should be dying of untreated AKI in low-resource regions by 2025\[11\]

PRACTICAL EXERCISE

A 27-year-old footballer was involved in a road traffic accident. He sustained blunt chest and abdominal trauma and multiple bone fractures. He was tachycardic and hypotensive on arrival to emergency department. Fluid resuscitation included 4L normal saline and three units of blood – haemodynamically stabilised. Non-contrast CT showed massive haematoma related to right mid-shaft femur fracture.

Disease Progression:

Day 2: He became unwell, complaining of abdominal pain. BP 90/50 mmHg, moderate ankle swelling. UOP dropped to 15ml/hr, had total fluids of 11L IV since admission. Abdomen was severely distended. Serum creatinine 92μmol/L, and serum lipase was high. CXR: revealed elevated diaphragms, and US showed massive ascites.

Day 3: remained hypotensive, tachycardic, oligo-anuric despite adequate fluid therapy, moderate ankle swelling and CVP was 17cmH₂O. Serum creatinine was 185μmol/l, s[K] and bicarbonate were normal. u[Na] 11mmol/L, with bland urine sediment.

Questions:

Q1. What is the cause of the AKI?
A1. Abdominal Compartment Syndrome (ACS) causing increased renal vein pressure and decreased renal perfusion

Q2. Name a bedside, definitive diagnostic test?
A2. Measurement of Intra-Abdominal Pressure (IAP): bladder (intra-vesical) pressure was 30mmHg (IAP: normal range 5–7mmHg).

Q3. What is the immediate therapeutic intervention?
Q4. Additional therapy includes:
   a. Administering IV colloids aiming for a higher CVP
   b. Avoiding analgesics and sedation
   c. Immediate pharmacological paralysis and ventilation
   d. Starting renal replacement therapy
   e. Involving the surgical team

A4. Additional therapy includes statement, (e), open abdominal decompression may be required if the condition deteriorates. Ensure sufficient pain control and sedation to improve abdominal wall compliance and relaxation.

REFERENCES