TLALELETSO

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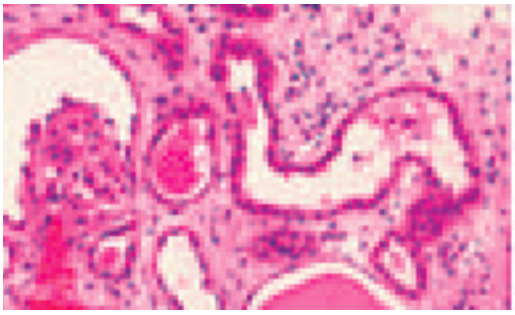

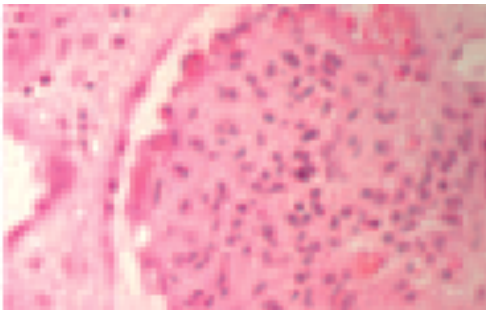

GUIDELINES UPDATE: ACUTE KIDNEY INJURY

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GUIDELINES UPDATE:

ACUTE KIDNEY INJURY

Tlaleletso is a monthly publication produced by the Botswana UPenn Partnership, in response to your expressed need to have accessible, digestible clinical information. Key clinical issues and challenges identified by doctors across Southern Botswana are explored in Tlaleletso. Each issue will summarize new scientific evidence and highlight recommendations in a user-friendly format.

This month's issue is focused on identifying and managing patients that have acute kidney injury. We review the common presentations and causes, especially in patients living with HIV. Next month Tlaleletso will address HIV and aging. If there are other topics you would like it to cover, please send us your feedback– either on content or format.

Respectfully, Mike Reid

BOTSWANA-UPENN PARTNERSHIP

Acute kidney injury (AKI) is characterized by a rapid decline in kidney function over hours to days. It is common and carries a high morbidity and mortality. However, AKI is also often preventable; therefore identification of appropriate preventive measures are crucial. In this edition of Tlaleletso we review the diagnosis and management of AKI in Botswana.

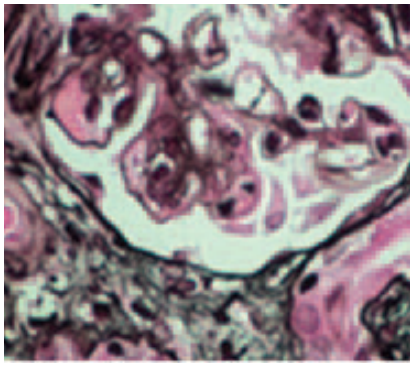
Is it common in Botswana?

While the exact incidence of AKI in Botswana is not known, it is probably far more common than many doctors and nurses realize. Data from the US suggests that AKI complicates approximately 5% of all hospital admissions and up to 30% of all ICU admissions.

In southern Africa the majority of AKI is caused by infectious processes[1]. These include diarrheal diseases, malaria and sepsis. Traditional medicines are also responsible for a significant amount of morbidity related to AKI in Southern Africa.

One small study from South Africa showed that the overall mortality from folk-remedy related kidney injury was as high as 41%. Another common cause of AKI in Africa is related to obstetric complications such as preeclampsia/eclampsia.

HIV is a very important cause of kidney disease. In South Africa there has been a 67% rise in deaths related to nephritis/nephrosis from 1999 to 2006[1,2]. This rising prevalence is likely to be causally linked to the rising burden of HIV infection and HIV-related kidney disease. Patients with HIV are also at risk of AKI because of the drugs that they may have to take – many cases of AKI in people with HIV are related to antibiotic and antifungal toxicities. Tenofovir, one of the first line drugs used to treat HIV, is an important culprit for AKI.



WHAT CAUSES ACUTE KIDNEY INJURY?

PRE-RENAL CAUSES: 55% of all causes
Pre-renal AKI is the most common form of AKI and represents a physiologic response to reduced renal blood flow. The two main causes of reduced renal perfusion are volume depletion and hypotension.
Hypovolemia – from volume depletion (for example from vomiting, diarrhea, burns) or from bleeding
Renal hypoperfusion – often caused by drugs such as NSAIDS and ACE inhibitors. Also caused by renal artery stenosis
Hypotension- secondary to cardiogenic shock, sepsis or anaphylaxis
Oedematous States – from cardiac cirrhosis, hepatic cirrhosis or nephrotic syndrome.

INTRINSIC RENAL CAUSES: 40% of all causes
Intrinsic causes are diseases that directly damage the kidney
Glomerular Disease - can be caused by diseases like SLE
Interstitial Nephritis – often drug-induced (examples, NSAIDS and penicillins) or post-infective
Tubular Injury – can result from ischemia or exposure to drugs such as aminoglycosides
Vascular Diseases – rarer diseases can lead to intrinsic renal diseases, such as vasculitides and polyarteritis nodosa

POST-RENAL CAUSES: 5% of all causes
Post-renal causes are those associated with urinary tract obstruction
Inside the GU tract – stones, blood clots, bladder tumors, prostatic hypertrophy
Outside the GU tract – pelvic cancer, retroperitoneal fibrosis

UPCOMING LECTURES

September

Topics in HIV:

HIV and Aging

October

Guidelines Update:

Acute Respiratory Distress

November

Topics in HIV

HIV and Cancer

December

Holiday Quiz 2012!

INITIAL ASSESSMENT

The clinical symptoms associated with kidney disease are generally vague and nonspecific. Some have symptoms that are directly referable to the kidney (hematuria, flank pain) or associated extrarenal symptoms (oedema, hypertension). Others have vague symptoms such as "not feeling quite right", fatigue, and trouble concentrating or sleeping. These symptoms are neither sensitive nor specific for kidney disease and can easily be mistaken for other diseases such as depression. Patients may develop renal failure in the context of other diseases. Therefore it is always important to ask about vomiting, diarrhea and dehydration. It is vital to determine if the patient has taken any new drugs – including traditional medications.

Many patients are asymptomatic and renal disease is noted on routine examination to have an elevated plasma creatinine concentration.

New onset hypertension, rash, joint pains, and swelling are common signs associated with the onset of kidney disease; however, their absence does not indicate normal kidney function. Given the lack of reliable signs or symptoms of kidney disease, screening for early alterations in kidney function is essential, particularly in high-risk populations (see box).

DIAGNOSIS: FINDING THE CAUSE FOR AKI

The diagnostic approach to a patient with AKI requires a careful history, a thorough drug history and detailed physical examination. It is also important to perform certain laboratory tests including those listed below. In particular it is essential to distinguish between acute and chronic renal failure, since the approach to these two conditions is very different.

In addition, identifying chronic kidney disease may save a great deal of unnecessary investigations. Factors that suggest chronicity include long duration of symptoms, nocturia absence of acute illness and anemia. The most useful clue comes from previous creatinine measurements if these can be found. Reduced renal size and cortical thickness on ultrasound is also characteristic of chronic kidney disease.

RIFLE CLASSIFICATION

Rifle classification is a tool for correlating kidney injury with mortality. It is has been applied in HIV patients and scoring correlates well as a tool for predicting mortality[3].

RIFLE refers to an acronym indicating Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function, and End-stage kidney disease[4]. It is ideal in an African setting as it requires no more than monitoring urine output to be useful. Furthermore, a systematic review of 13 studies demonstrated a stepwise increase in the

RISK FACTORS FOR AKI

- Diabetes
- Older age
- Hypertension
- HIV
- Systemic infections
- Low income/education
- Urinary tract infections
- Urinary stones
- Lower urinary tract obstruction
- Cancer
- Recovery from acute kidney failure
- Exposure to certain drugs

Test	Comment
Urine Studies	
Dipstick for blood, protein	Suggests an inflammatory process
Microscopy for cells, casts, crystals	Red cell casts diagnostic in glomerulonephritis
Blood tests	
Serial urea, creatinine, electrolytes	Important metabolic consequences for AKI include high K+, and metabolic acidosis
Full blood count	Eosinophilia may present in interstitial nephritis; thrombocytopenia suggests thrombotic angiopathy
HIV test	Always confirm HIV status
Radiology	
Renal USS	Renal size, symmetry, evidence of obstruction
Other tests (where available)	
ANA, anti dsDNA	Associated with SLE and other autoimmune disorders
Hepatitis B sAg	Associated with glomerulonephritis
Creatinine Kinase	Markedly elevated in rhabdomyolysis
Serum and urine protein electrophoresis	Presence of monoclonal bands on serum electrophoresis suggests myeloma

Rifle (cont.d)

relative risk of death in patients who met the RIFLE criteria for various stages of AKI[5]. However, its drawback is the requirement for a baseline serum creatinine, which is often not available.

Risk

- 1.5 fold increase in serum creatinine
- Urine output <0.5mg/kg for 6 hours

Injury

- Twofold increase in serum creatinine
- Urine output <0.5mg/kg for 12 hours

Failure

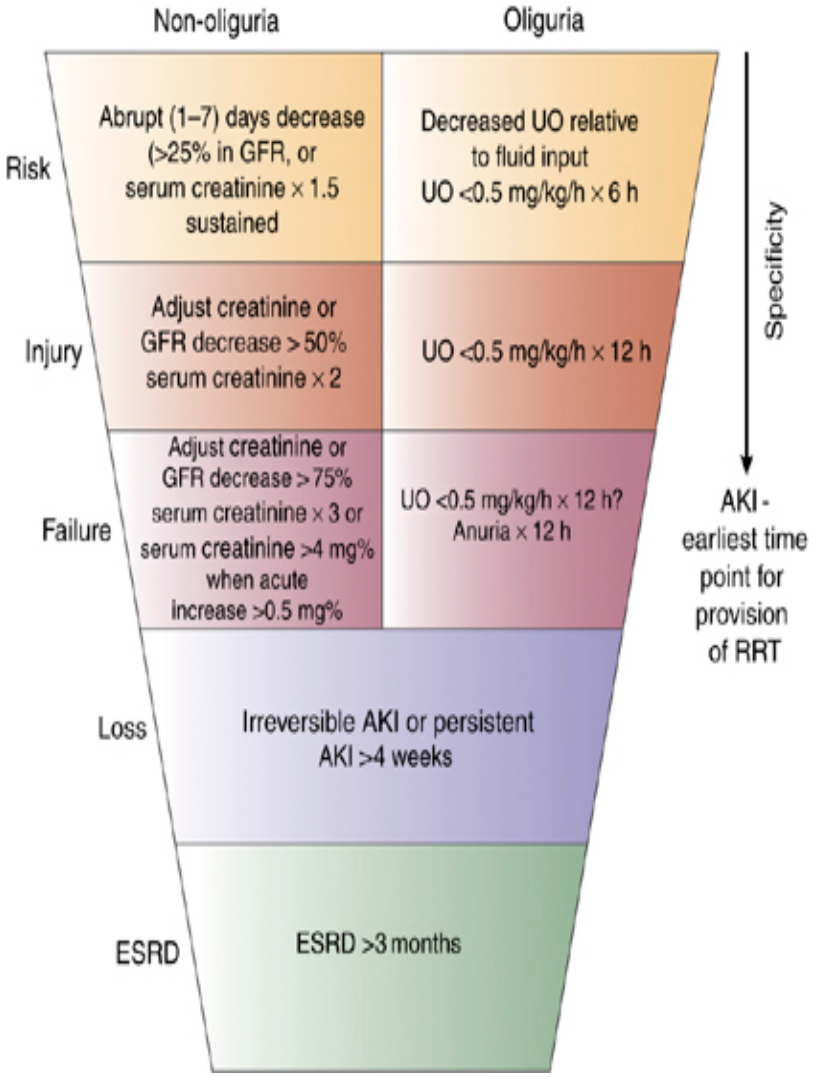
- Threefold increase in serum creatinine
- Urine output <0.5mg/kg for 24 hours or anuria for 12 hours

Loss

- Complete loss of renal function for more than 4 weeks

ESRD

- Complete loss of renal function for >3 months[1]



J Himmelfarb, Nature (2006)

MANAGEMENT

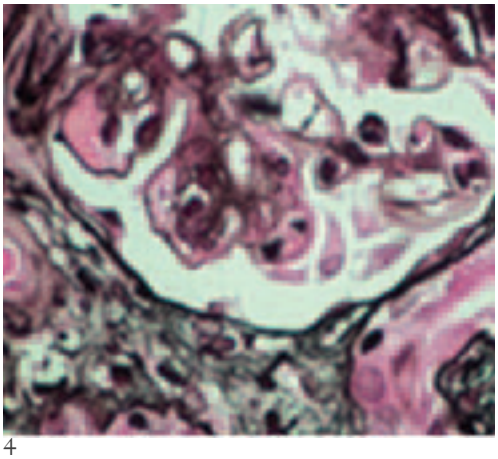
Even though the precise management of AKI is largely dependent on the cause of the renal failure, there are specific measures that should be adopted regardless of the underlying causes.

It is essential that any nephrotoxic medications are stopped and all medications are dosed for decreased creatinine clearance. If the patient is HIV positive and already on HAART, HAART should NOT be stopped but Tenofovir should be exchanged for zidovudine or abacavir if the patient has a Hgb<7g/dl.

Prompt intravenous fluids and urinary catheterization should be considered in all but the most stable patients. Monitor the in- and output of the patient, in an awake patient this does NOT make a urinary catheter necessary; a bucket for urine collection at the bedside is usually sufficient. Other initial interventions should be determined by the cause:

Pre-renal: in patients with pre-renal failure, aggressive IV fluid resuscitation is essential.

Intra-renal: The most common causes of acute renal failure is acute tubular necrosis, for which the treatment is largely supportive: the goals are to maintain fluid and electrolyte balance, provide nutritional support and prevent or treat complications. If it is drug-



Post-renal: In patients with post-renal obstruction, it may be appropriate to place a urinary catheter to relieve obstruction. Referral to a urologist at PMH may also be indicated.

Note: In spite of much research, no drug treatment has as yet been shown to limit the progression of, or speed up recovery from AKI and some drugs may be harmful[6] The use of furosemide warrants particular mention, as this is a commonly used drug. A meta-analysis of other trials showed that furosemide is ineffective in preventing and treating AKI and that high doses may be associated with ototoxicity[7].

Dialysis

There is a limited role for dialysis for treatment of AKI. Research does suggest that some patients may benefit from peritoneal dialysis for management of AKI – but in all cases it is necessary to determine the underlying cause of renal impairment before referring for dialysis. Select cases of acute renal failure may be referred to PMH for hemodialysis after consultation with the on-call specialist.

Specific Indications for acute dialysis include the following:

1. Acidosis
2. Electrolytes (hyperkalemia, hypercalcemia)
3. Intoxications (methanol, polyethylene glycol, aspirin, etc)
4. Intractable Volume Overload
5. Uremia (as manifested by uremic frost, encephalopathy, pericarditis)

Biopsy

On rare occasion, there is a role for renal biopsy. These are done at PMH by nephrology specialist and should be reserved for suspected kidney disease without defined etiology by non-invasive studies. Before considering a biopsy, it is essential that patients are discussed with a nephrology specialist.

The major indications for renal biopsy include:

1. Isolated glomerular hematuria with proteinuria
2. Nephrotic syndrome
3. Acute nephritic syndrome
4. Unexplained acute or rapidly progressive renal failure

MANAGEMENT PRINCIPLES IN AKI[8]

- Identify and correct pre-renal and post-renal factors
- Optimize cardiac output and renal blood flow
- Review drugs: stop any nephrotoxic drugs and adjust doses where appropriate
- Accurately monitor fluid balance and daily body weight
- Identify and treat acute complications (hyperkalemia, acidosis, pulmonary oedema)
- Optimize nutritional support: adequate calories and potassium restriction
- Identify and treat infection, minimize indwelling lines, remove catheter if anuric
- Transfer to PMH for initiation of dialysis before uremic complications emerge

HIV and kidney disease – Box

Renal disease is a relatively common complication in patients infected with HIV. A collapsing form of focal segmental glomerulosclerosis is considered the most common form of HIV nephropathy, with up to 60% of renal biopsies showing this in one study[1]. While there is no proven effective therapy for HIV associated nephropathy the initiation of HAART can slow or even halt the decline of renal function. Thereby all patients should receive HAART therapy (irrespective of CD4 count) if they have renal impairment and also an angiotensin converting enzyme inhibitor (ACE-inhibitor). In patients with HIV and kidney disease, regardless of the underlying cause of kidney disease, the presence of proteinuria and/or decreased renal function is associated with increased mortality.

Patients with kidney disease and HIV should be monitored closely. It is important to proceed with caution when initiating tenofovir-containing regimens in such patients – the Botswana HIV guidelines recommend *not* using tenofovir in patients with a creatinine clearance of less than 60 cc/min. Certain other HIV medications, including lamivudine (3TC) and zidovudine (AZT) also need to be dose-adjusted in patients with chronic kidney disease and reduced creatinine clearance (see over page). Patients who develop renal failure while on Tenfovir are not to be re-exposed to it. However, patients who have a history of renal failure that was not associated with TDF may be started on TDF with close monitoring of the renal function if the Creatinine Clearance is >60cc/min.

SPECIAL THANKS:

Michelle Haas
Matt Dasco
Mike Pendleton

SUMMARY

Acute kidney injury is a life threatening illness with high mortality. It is a common presenting problem in medical patients in Botswana, especially among people living with HIV. The priorities in management of AKI include early recognition, optimization of fluid balance, identification and treatment of underlying causes and timely referral for evaluation by a nephrology specialist when appropriate.

Key Points:

- Most cases of renal failure occur in the context of other conditions, such as trauma, sepsis/shock, HIV, or post-infectious states.
- The initial approach to a patient with renal failure should include:

- Classification as pre-renal, intrinsic renal, or post-renal
- A careful medication history (including traditional medicines)
- Consideration of underlying chronic kidney disease
- Urinalysis and dipstick
- Urinary catheterization
- Empiric hydration with normal saline in the absence of volume overload or pulmonary edema

Got a clinical question about a complicated medical patient
Or a patient with HIV?
Mike Reid
267 724 78 777
OR
Miriam Haverkamp
267 76516520

Want to read more? Check out the references below:

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Renal Adjustments for 3TC:

* CrCl 30-50cc/minute: 150 mg. OD
* CrCl 15-29 cc/minute: 150 mg. once then continue 100 mg. OD
* CrCl 5-14 cc/minute: 150 mg. once then continue 50 mg. OD
* CrCl ≤5 or dialysis: 50 mg. once then continue 25 mg. OD

  (Note: take dose after HD session on dialysis days)

Renal Adjustments for AZT:

* CrCl<15cc/minute or hemodialysis: 300 mg. OD: