





Decreasing The Burden Of Acute Kidney Injury In Nigeria.

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introduction

- ▣ Acute kidney injury (previously known as acute renal failure) covers a wide spectrum of injury to the kidneys, not just kidney failure
- ▣ Acute kidney injury (AKI) is a global problem, occurs in the community and is increasingly recognized in all fields of medical practice.
- ▣ It is increasingly prevalent in developing and developed countries and is associated with severe morbidity and mortality.



introduction

- ▣ AKI is a predictor of immediate and long-term adverse outcomes.
- ▣ AKI is more prevalent in (and a significant risk factor for) patients with chronic kidney disease (CKD).
- ▣ Individuals with CKD are especially susceptible to AKI which, in turn, may act as a promoter of progression of the underlying CKD.



DEFINITION

- ❑ this syndrome has been plagued by inconsistent definitions
- ❑ AKI is intended to emphasize the reversible nature of most renal insults.
- ❑ ARF is now generally reserved to describe the condition of patients who sustain kidney injury that necessitates renal replacement therapy (RRT)



DEFINITION

- ▣ The term AKI was introduced by the International Consensus Conference on Acute Dialysis Quality Initiative (ADQI) workgroup [Critical Care 2004] in place of the highly restrictive and commonly used term, acute renal failure (ARF).



definition

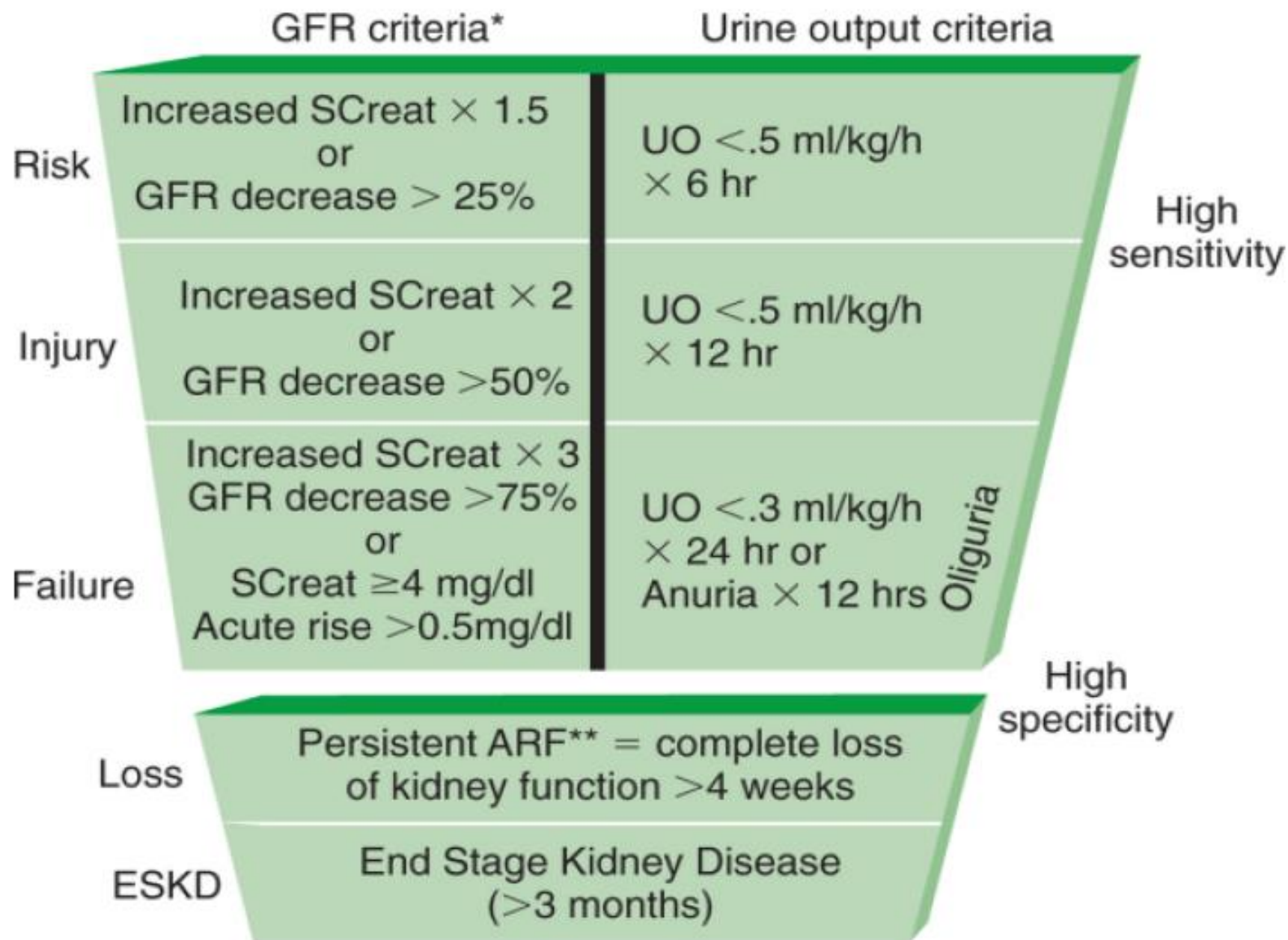
- ▣ AKI is defined as any of the following :
 - Increase in SCr by ≥ 0.3 mg/dl (≥ 26.5 $\mu\text{mol/l}$) **within 48 hours;**
OR
 - Increase in SCr to ≥ 1.5 times baseline, which is known or presumed to **have occurred within the prior 7 days;**
OR
 - Urine volume < 0.5 ml/kg/hr for **6 hours.**



STAGING

The RIFLE (Risk, Injury, Failure, Loss, End-stage) criteria for acute kidney injury

Class	Increase in Glomerular Filtration Rate	Reduced Urine Output by Symptom Duration
■ Severity		
<input type="checkbox"/> <u>R</u> isk	1.5-fold	<0.5 mL/kg/h for 6 h
<input type="checkbox"/> <u>I</u> njury	twofold	<0.5 mL/kg/h for 12 h
<input type="checkbox"/> <u>F</u> ailure	threefold*	<0.3 mL/kg/h for 24 h†
■ Outcome		
<input type="checkbox"/> <u>L</u> oss—Persistent acute kidney injury with complete loss of function for more than 4 wk		
<input type="checkbox"/> <u>E</u> nd-stage—End-stage kidney disease for more than 3 mo		





STAGING

KDIGO Staging for AKI Severity

- | AKI stage criteria | Creatinine criteria | Urine output |
|--------------------|--|--|
| AKI stage I | Increase of serum creatinine by ≥ 0.3 mg/dl (≥ 26.4 $\mu\text{mol/L}$)
or
increase to $\geq 150\%$ – 200% from baseline | < 0.5 ml/kg/hour for > 6 hours |
| AKI stage II | Increase of serum creatinine to $> 200\%$ – 300% from baseline | < 0.5 ml/kg/hour for > 12 hours |
| AKI stage III | increase of serum creatinine to $> 300\%$ from baseline
or
serum creatinine ≥ 4.0 mg/dl
≥ 354 $\mu\text{mol/L}$) after a rise of at least 44 $\mu\text{mol/L}$
or
treatment with renal replacement therapy | < 0.3 ml/kg/hour for > 24 hours
or
anuria for 12 hours |
- *The KDIGO consensus classification has yet to be validated.*



- ❑ The AKIN criteria differ from the RIFLE criteria in several ways.
- ❑ The RIFLE criteria are defined as changes within 7 days, while the AKIN criteria suggest using 48 hours.
- ❑ The AKIN classification includes less severe injury in the criteria and AKIN also avoids using the glomerular filtration rate as a marker in AKI, as there is no dependable way to measure glomerular filtration rate and estimated glomerular filtration rate are unreliable in AKI.
- ❑ AKIN notes that the diagnostic criteria proposed only after volume status has been optimized and urinary tract obstructions must be excluded when using oliguria as diagnostic criteria.

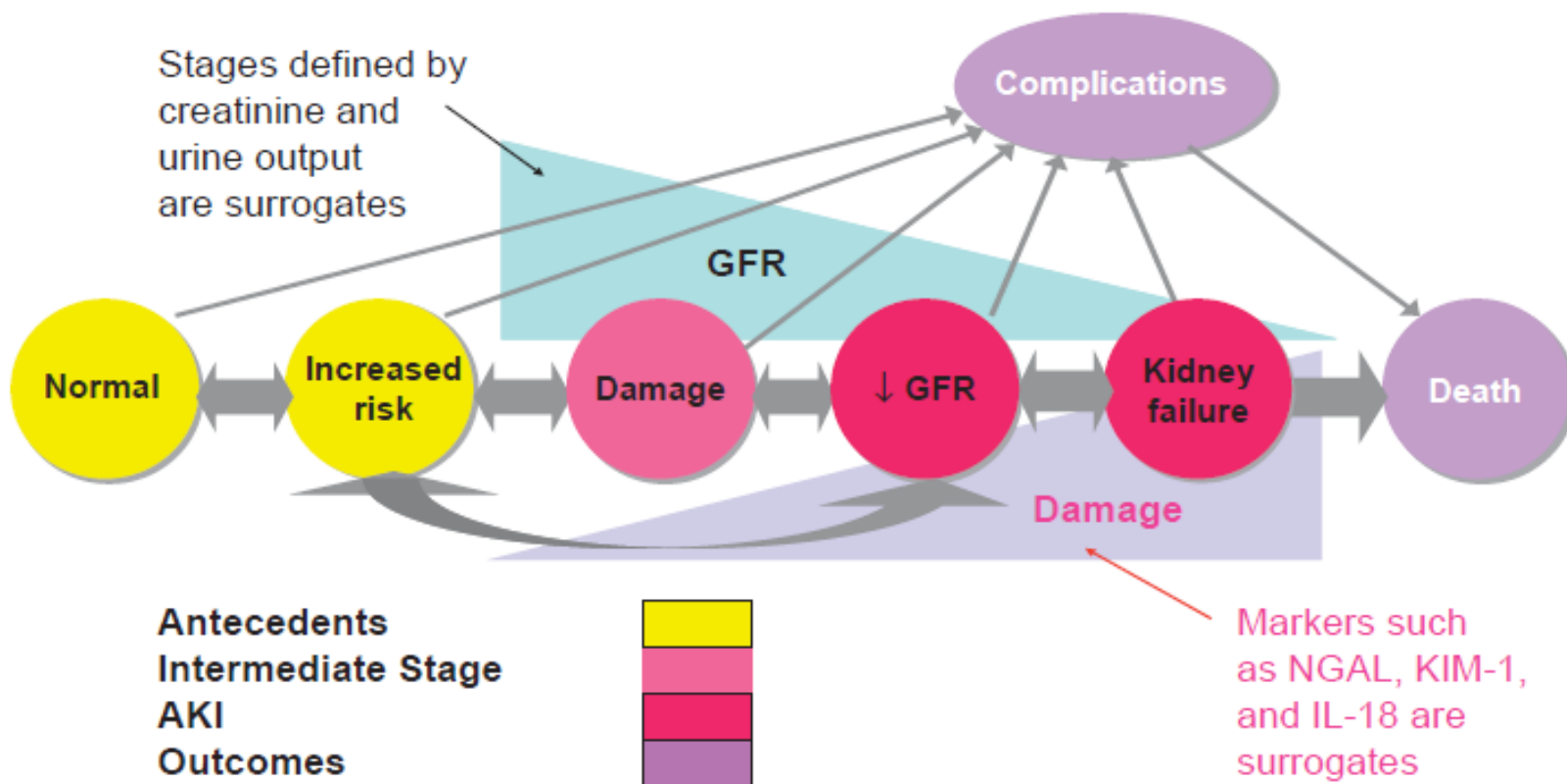


AKI staging	Urine output	RIFLE	
Serum creatinine	(common to both)	Class	Serum creatinine or GFR
Stage 1 Increase of more than or equal to 0.3mg/dl ($\geq 26.5 \mu\text{mol/l}$) or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg/h for more than 6 hours	Risk	Increase in serum creatinine $\times 1.5$ or GFR decrease $> 25\%$
Stage 2 Increased to more than 200% to 300% (> 2 - to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours	Injury	Serum creatinine $\times 2$ or GFR decreased $> 50\%$
Stage 3 Increased to more than 300% (> 3 -fold) from baseline, or more than or equal to 4.0mg/dl ($\geq 354 \mu\text{mol/l}$) with an acute increase of at least 0.5mg/dl ($44 \mu\text{mol/l}$) or on RRT	Less than 0.3 ml/kg/h for 24 hours or anuria for 12 hours	Failure	Serum creatinine $\times 3$, or serum creatinine $> 4 \text{ mg/dl}$ ($> 354 \mu\text{mol/l}$) with an acute rise $> 0.5 \text{ mg/dl}$ ($> 44 \mu\text{mol/l}$) or GFR decreased $> 75\%$
		Loss	Persistent acute renal failure=complete loss of kidney function > 4 weeks
		End-stage kidney disease	ESRD > 3 months

Comparison of RIFLE and AKIN criteria for diagnosis and classification of AKI



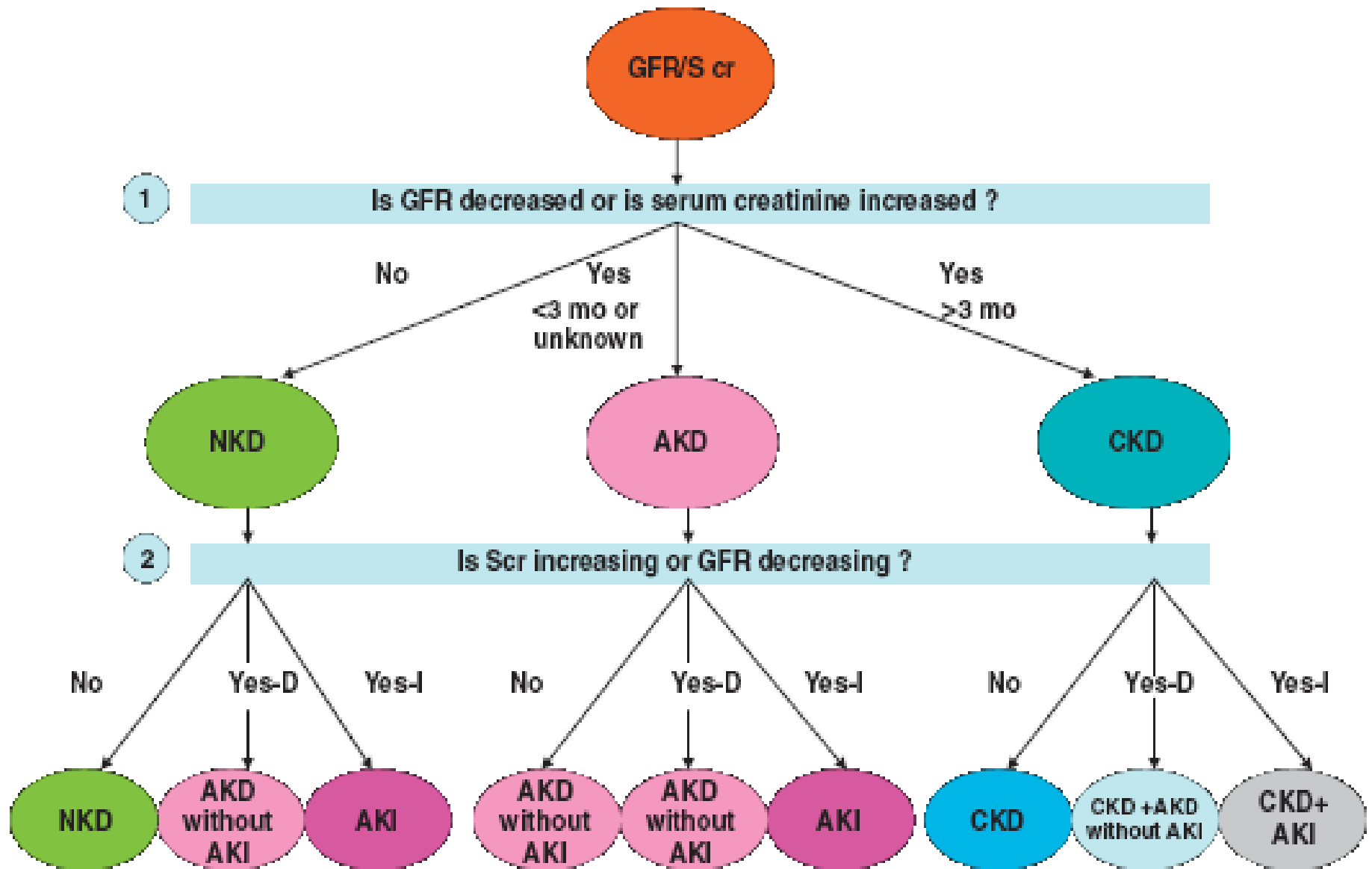
conceptual model for aki





KDIGO DEFINITIONS - GUIDELINES 2012

(KI Supplement March 2012)





EPIDEMIOLOGY

- ▣ The worldwide incidence of acute kidney injury is poorly known because of underreporting, regional disparities, and differences in definition and case mix.
- ▣ New definitions call for revision of the problem with unified criteria.⁵



EPIDEMIOLOGY

- Uncertainty regarding the true incidence of AKI limits awareness of the problem thereby reducing political visibility of the disorder and hampering efforts to prevent its occurrence.
- developed countries
 - occurs predominantly in urban intensive care units
 - associated with multiorgan failure and sepsis, high mortality, and occurrence in older populations.
- cases in urban areas of the developing world have similar characteristics to those in the developed world



EPIDEMIOLOGY

- ▣ notable differences exist between developing and developed countries: Incidence seems higher in the former, but underreporting compounded by age and gender disparities makes available data unreliable.
- ▣ in developing countries, incidence varies seasonally; incidence peaks cause critical shortages in medical and nursing personnel. 5



EPIDEMIOLOGY: international

- Prevalence
 - 1% all patients admitted to hospital
 - 10-30% patients admitted to ICU
- Etiology
 - Hemodynamic 30%
 - Parenchymal 65%
 - Acute tubular necrosis 55%
 - Acute glomerulonephritis 5%
 - Vasculopathy 3%
 - Acute interstitial nephritis 2%
 - Obstruction 5%



EPIDEMIOLOGY: international

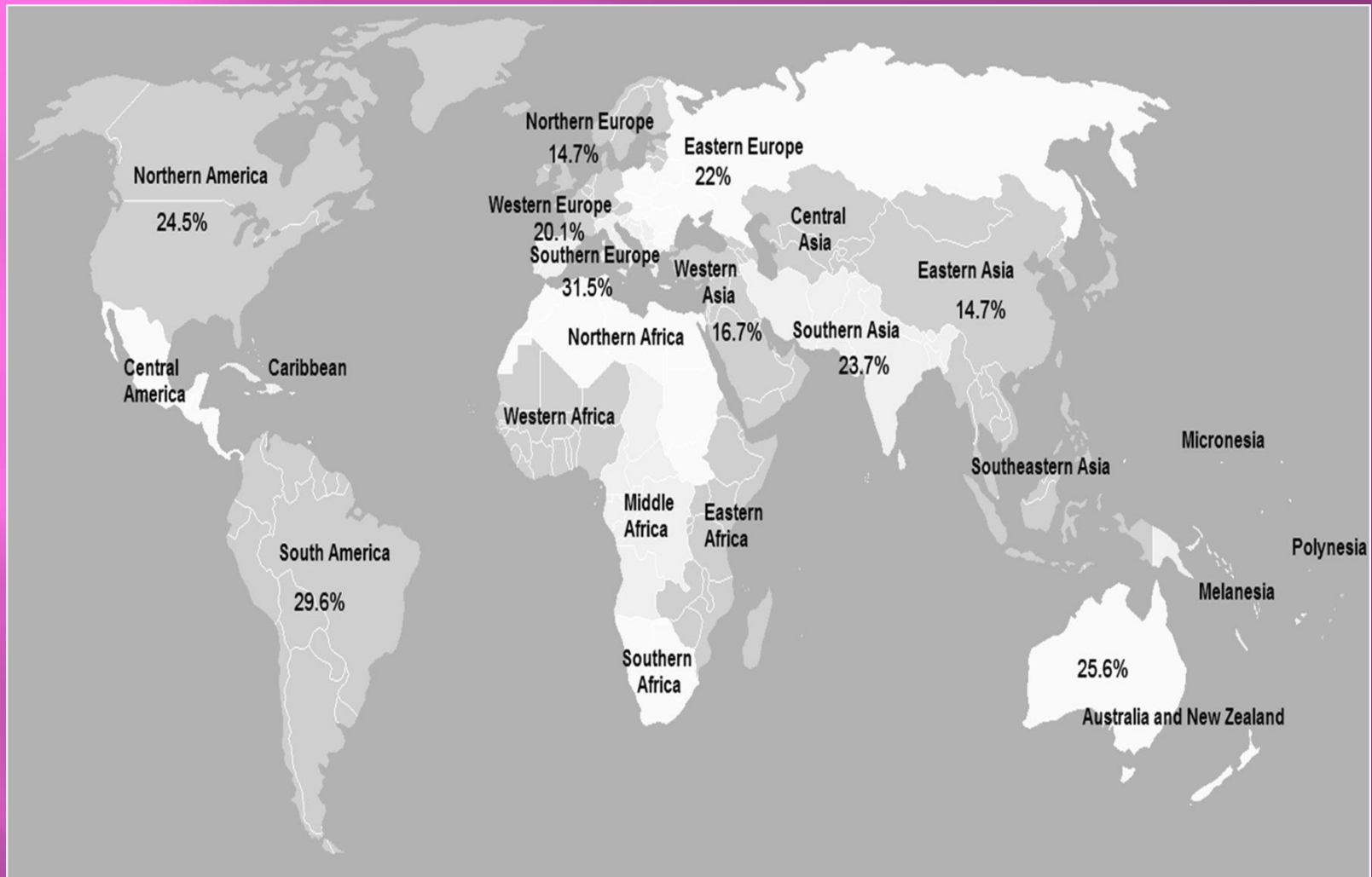
▣ **United States**

- approximately 1% of patients at the time of admission.
- estimated incidence rate of AKI during hospitalization is 2-5%.
- within 30 days postoperatively in approximately 1% general surgery
- up to 67% of intensive care unit (ICU) patients.
- Approximately 95% of consultations with nephrologists are related to AKI.
- appropriate nephrologist referral rate is approximately 70 cases per million population.

▣ **Canada**

- much higher incidence of AKI than previous reports, with a rate of 18.3%

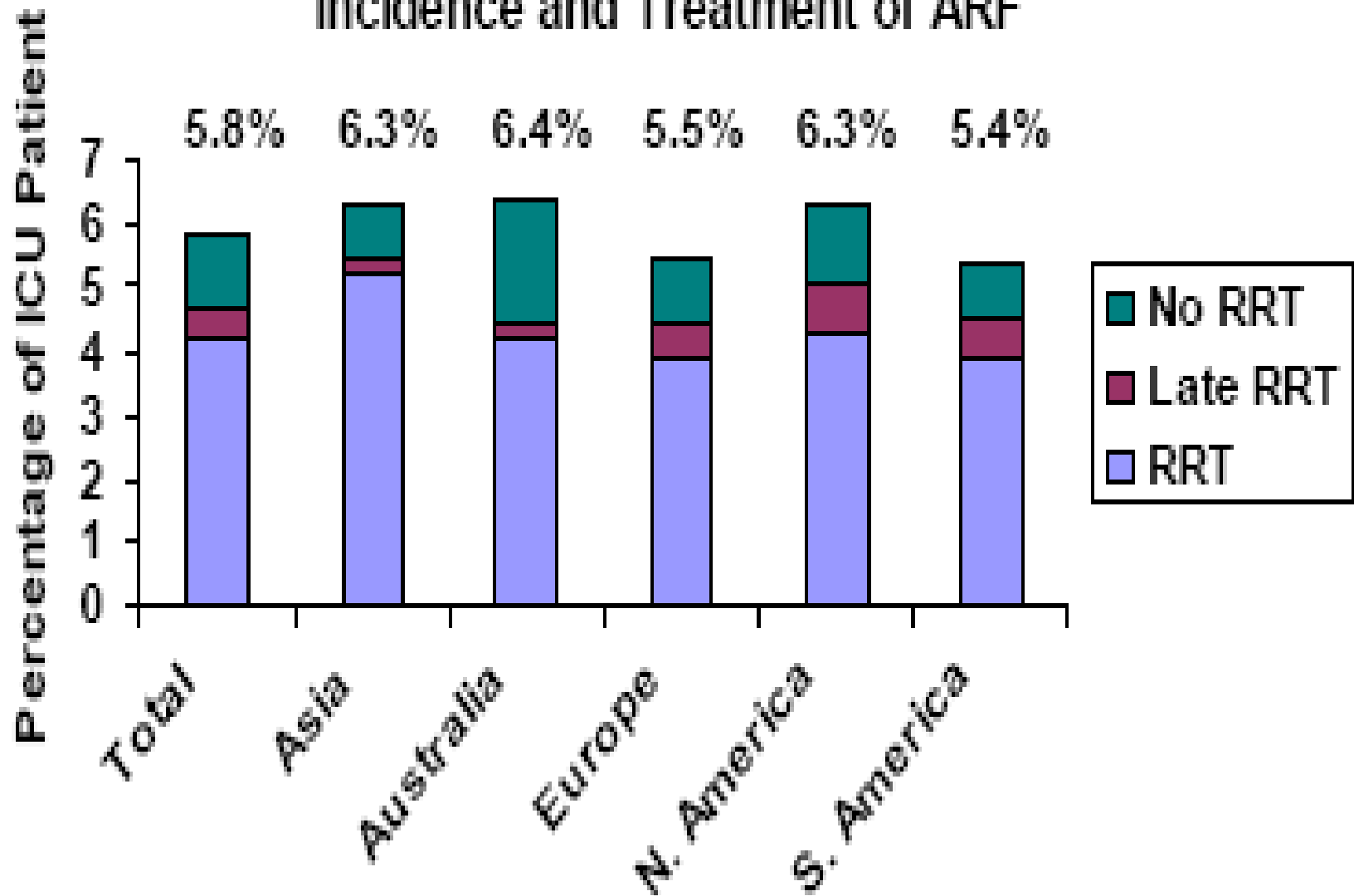
Pooled incidence rate of AKI by world zones in studies that used a KDIGO-equivalent serum creatinine-based AKI definition.



Susantitaphong P et al. CJASN doi:10.2215/CJN.00710113

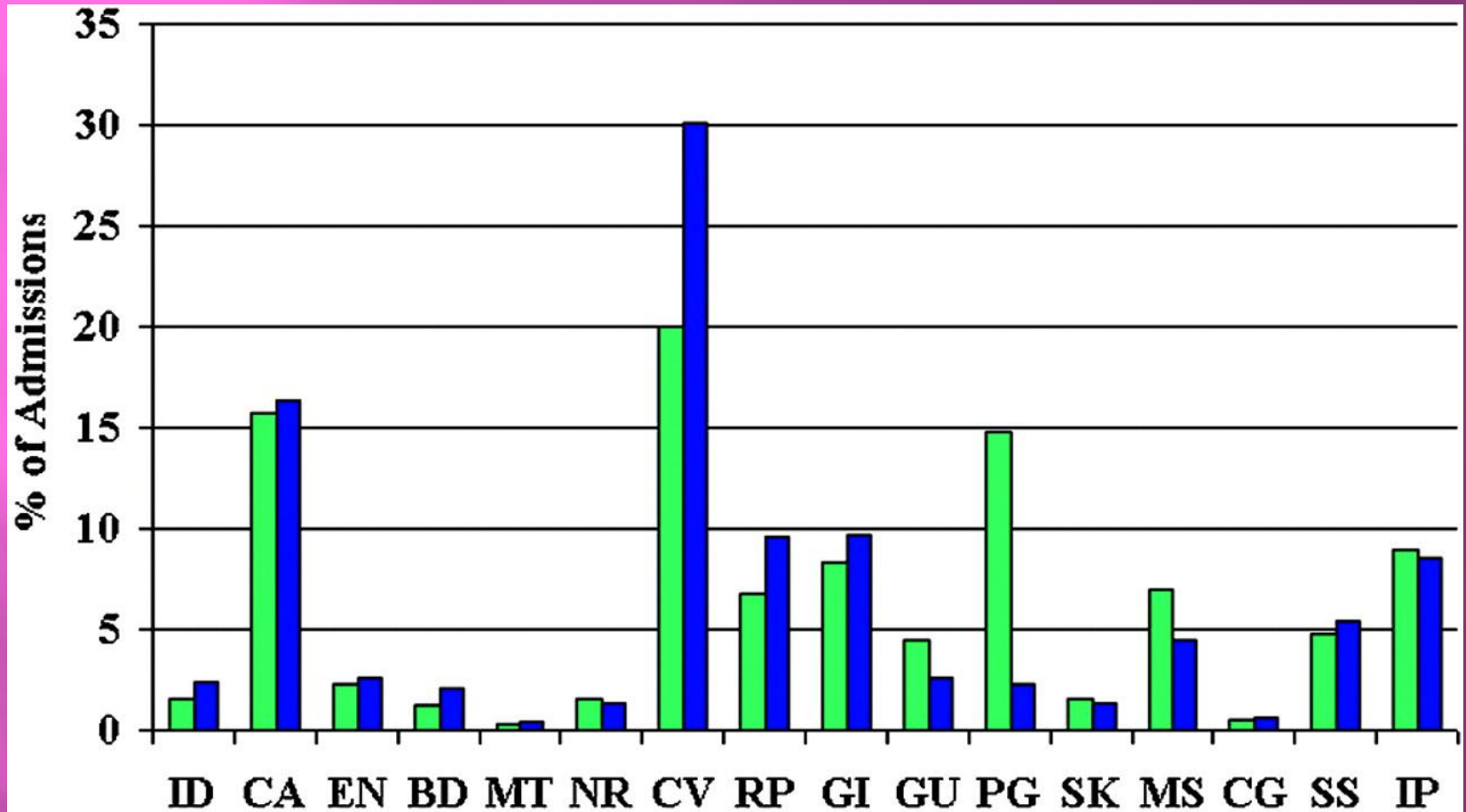
CJASN

Incidence and Treatment of ARF



n ≈ 30,000 ICU pts, 53 centres, 23 Countries AKI ≈ 2000₁

Distribution of admissions by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) category.



Chertow G M et al. JASN 2005;16:3365-3370





EPIDEMIOLOGY

- ▣ ARF is an independent risk factor for mortality Medical wards about 5% of medical admissions
- ▣ It is associated with a significant prolongation in length of hospital stay in survivors.
- ▣ 6.7% Paediatric admissions (Calabar)
- ▣ Hospital prevalence (Paediatric population) -11.7 cases/year (Port Harcourt)
- ▣ ICU: 5-30% of ICU admissions



EPIDERMIOLOGY MORTALITY

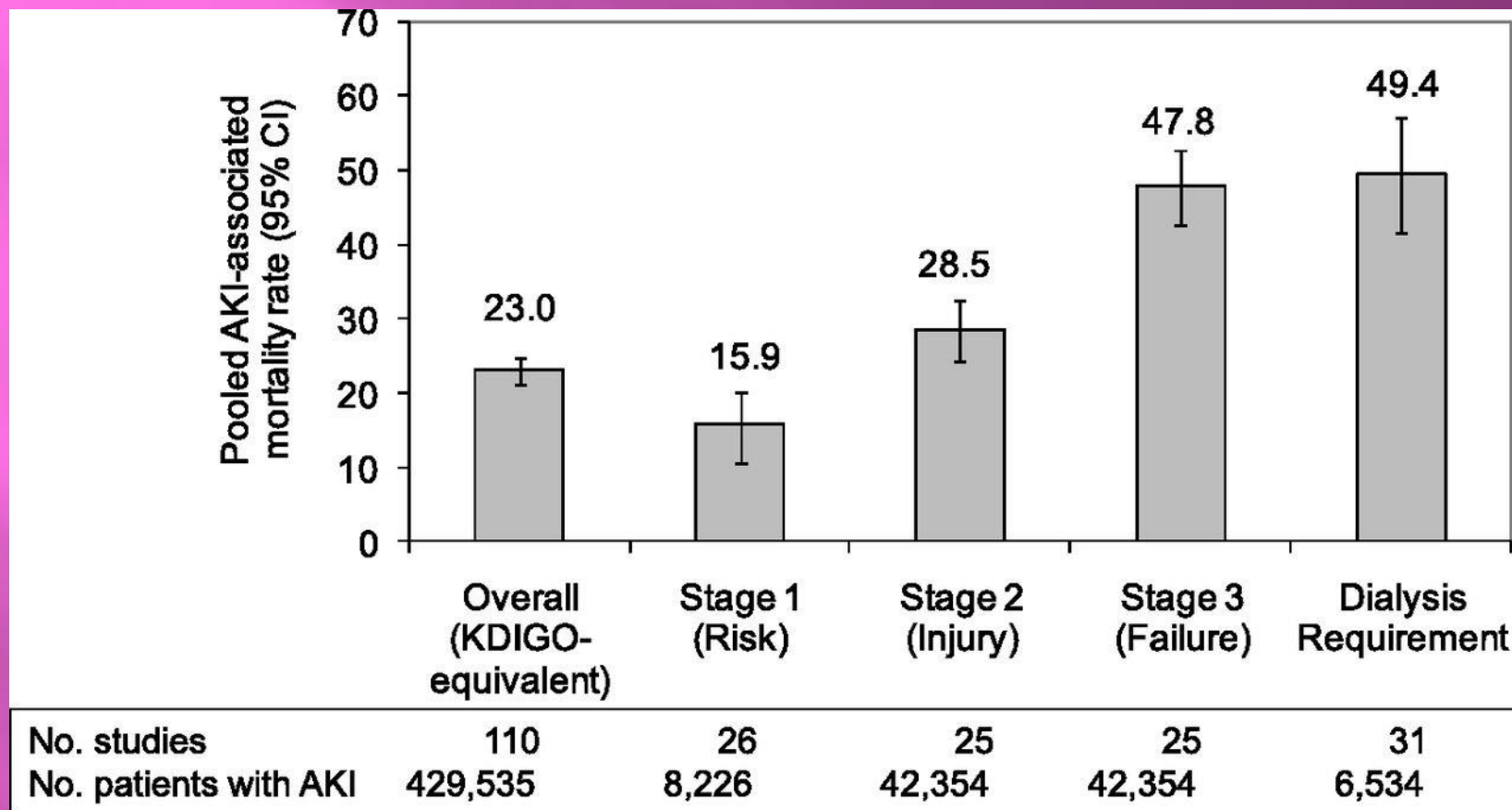
- ▣ Dialysis requiring patients: 40-90%
- ▣ Increased mortality even in patients not requiring dialysis
 - ▣ 25% increase in creatinine associated with a mortality rate of 31% compared with 8% for matched patients without renal failure



EPIDERMIOLOGY MORTALITY

- ▣ About 80.5% were < 40yrs
- ▣ Overall mortality was 47.6%
- ▣ Mortality rates of patients on HD %PD were 15% and 67% respectively (chijoke ilorin 2011)

Pooled AKI-associated mortality rate in studies that used a KDIGO-equivalent serum creatinine-based AKI definition and staging system, or dialysis requirement.



Susantitaphong P et al. CJASN doi:10.2215/CJN.00710113



AETIOPATHOGENESIS

- The mechanisms involved in the etiology of AKI are as follows:
 - endothelial injury from vascular perturbations
 - direct effect of nephrotoxins
 - abolishment of renal autoregulation
 - formation of inflammatory mediators



AETIOPATHOGENESIS

- ▣ Necrosis and apoptosis of tubular cells
 - lead to tubular obstruction and subsequent reduction of GFR
 - elevated intracellular calcium levels from tubular damage cause a series of cellular-level alterations that culminate in increased tubuloglomerular feedback, and thus, diminished GFR

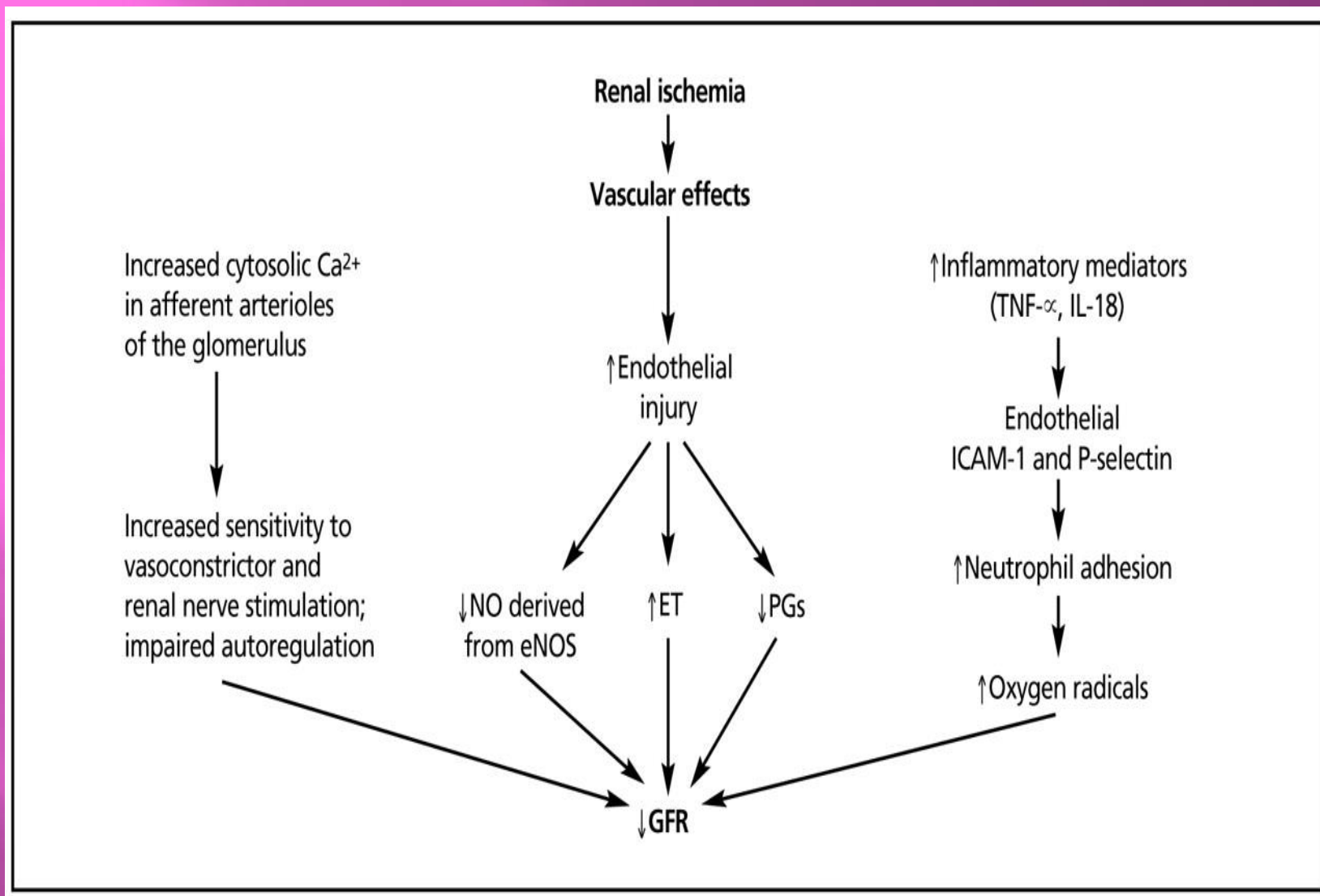
- ▣ Vascular compromise causes
 - increased cytosolic calcium
 - elevated endothelial injury markers
 - production of inflammatory mediators which result in reduced GFR.



AETIOPATHOGENESIS

- ▣ persistent imbalance between the mediators of vasoconstriction and -dilatation that
 - result in intrarenal vasoconstriction eventually, ischemia.
 - vasoconstrictors include angiotensin II, endothelin, thromboxane, and adenosine.
 - The vasodilators include prostaglandin and endothelial-derived nitric oxide.
- ▣ High levels of vasoconstrictors and low levels of vasodilators cause continued hypoxia and cell damage or cell death.
- ▣ Endothelial-derived nitric oxide is under investigation as a potential therapeutic option to help break this cycle of ischemia.

Mechanisms of acute kidney injury: a molecular viewpoint.





risk factors

- Chronic kidney disease (or history of)
- Diabetes mellitus
- Heart failure
- Sepsis
- Hypovolaemia
- Age 65 years or over
- nephrotoxic drugs
- Use of contrast agents within past week
- Oliguria
- Hepatic disease
- Dehydration:- Limited access to fluids, such as via neurological impairment
- Deteriorating early warning scores
- Symptoms or history of urological obstruction



Classification

- ▣ **Urine Volume**
 - Oliguric
 - Non oliguric
- ▣ **Medical Specialty**
 - Medical
 - Surgical
 - Obstetrics/ gynaecological
 - Intensive care (ICU)
- ▣ **Aetiological classification**
 - Prerenal
 - Renal/ intrinsic
 - Post renal/ obstructive



Classification by etiology

▣ Prerenal AKI

- secondary to underperfusion of otherwise normal, functioning kidneys (structurally intact nephrons)
- hallmark of prerenal AKI is rapid reversibility.
- Prerenal kidney injury can result from volume depletion that is the result of renal or extrarenal losses, fluid sequestration, or inadequate perfusion pressures secondary to heart failure, cirrhosis, or sepsis.
- Brisk correction of kidney injury with volume repletion supports a prerenal etiology.
- Conversely, kidney injury refractory to fluid administration suggests an intrinsic renal process.



Classification by etiology

▣ Prerenal AKI

- Hypotension
- Hypovolaemia
 - Fluid Loss
 - Blood Loss
- Poor Pump Function
 - Cardiogenic Shock
 - Congestive Cardiac Failure
 - Pericardial effusion
- Haemodynamic
 - Contrast Neph
 - Prostaglandin Inhibition
 - CyA, Tacrolimus, ACE Inhibitors
- Hepatorenal syndrome
- sepsis



Classification by etiology

- **Renal (35-40% of AKI)**
- In response to cytotoxic, ischemic, or inflammatory insults to the kidney, with structural and functional damage
 - **Vascular**
 - Renal infarction, RAS, RVT
 - Malignant HT
 - **Tubular**
 - **Ischaemic**
 - **Nephrotoxic**
 - Intratubular Obstruction - myoglobin, hb, myeloma chains, uric acid, tumor lysis,
 - drugs (indinavir, acyclovir, oxalate in ethylene glycol toxicity)
- **Glomerular**
 - AGN
 - Vasculitis
 - Thrombotic microangiopathy TTP, HUS
 - Pre Eclamptic Toxaemia
- **Interstitial**
 - Drug induced TIN
 - Tumour infiltration



Classification by etiology

- **Postrenal AKI**
- Approximately 10% of AKI
- Urinary tract obstructions
 - within the urinary system
 - stones
 - Tumors
 - outside the urinary system
 - Tumors
 - retroperitoneal fibrosis



Classification by Volume

oliguric vs nonoliguric AKI

- oliguric or nonoliguric patients can have a rapid or slow rise in creatinine levels, and may have qualitative differences in urine solute concentrations and cellular content.
- **Abt 50-60% of all causes of AKI are nonoliguric**
- This lack of a uniform clinical presentation reflects the variable nature of the injury.
- **Classifying AKI as oliguric or nonoliguric on the basis of daily urine excretion has prognostic value.**
- Oliguria is defined as a daily urine volume of less than 400 mL and has a worse prognosis, except in prerenal injury.
- **Anuria is defined as a urine output of less than 100 mL/day and, if abrupt in onset, suggests bilateral obstruction or catastrophic injury to both kidneys.**



AKI in the tropics

- ❑ Severe acute kidney injury (AKI) occurs in 2-7% of all hospital admissions and is an independent poor prognostic marker.
- ❑ information on the long-term outcome of AKI and the factors influencing this is limited.
- ❑ Single centre retrospective analysis of 481 consecutive patients over a period of 39 months. Follow-up: 12 months. Primary and secondary outcomes: overall mortality and RRT dependency at 30 days, 90 days and 1 year.
- ❑ Survival at 30 days, 90 days and 1 year was 54.4, 47.2 and 37.6%, respectively. The short- and long-term survival outcome of severe AKI requiring RRT remains poor.
- ❑ Among those who survive, a significant number either continue to require RRT or have residual renal impairment necessitating ongoing follow-up.⁸



AKI in the tropics

- ▣ Acute kidney injury (AKI) is one of the most challenging problems faced by clinicians in the tropics owing to its fast-changing burden.
- ▣ AKI in the tropics is strikingly different from that in the developed world in terms of etiology and presentation.
- ▣ there is a stark contrast between well-developed and poor areas in the tropics. The true epidemiological picture of AKI in the tropics is not well understood due to the late presentation of patients to tertiary centers.



AKI in the tropics

- ❑ Infections remain the major culprit in most cases of AKI, with high mortality rates in the tropics.
- ❑ Human immunodeficiency virus–related AKI, related to nephrotoxicity due to antiretroviral therapy, is on the rise.
- ❑ Acute tubular necrosis and thrombotic microangiopathy are the most common mechanisms of AKI.
- ❑ **A notable problem in the tropics is the scarcity of resources in health centers to support patients who require critical care due to AKI.**



ETIOLOGY IN THE TROPICS

- ▣ Sepsis
- ▣ acute diarrheal diseases still top the list in the etiology of AKI in the tropics.
- ▣ ingestion of toxic herbs or chemicals
- ▣ Poisoning
- ▣ obstetric complications
- ▣ envenomation



ETIOLOGY IN THE TROPICS

- ▣ These factors are associated with
 - low levels of income
 - poor access to treatment
 - social or cultural practices (such as the use of traditional herbal medicines and treatments) that contribute to poor outcomes of patients with AKI.



peculiarities of AKI in the tropics

- ▣ Natural medicines, used by traditional healers, add to the burden of AKI in some tropical areas
- ▣ relatively younger age of patients in the tropics.
- ▣ gross inadequacy of treatment facilities in the tropics, which accounts for the increasing mortality.
- ▣ endemic malnutrition, a relative state of hypovolemia due to increased sweating and peripheral vasodilatation due to the hot climate



factors affecting outcome

- ❑ Elderly
- ❑ Majority of these patients are prone to multiple renal insults.
- ❑ Underlying chronic illness
- ❑ Presence of cardiac failure
- ❑ Sepsis,
- ❑ Oliguria, need for RRT
- ❑ Increasing number of organ failure is associated with poor outcome.⁷



EPIDEMIOLOGY

- ▣ The pattern of AKI is vastly different from that in more developed countries. There are no reliable statistics about the incidence of AKI in Africa. Infections (malaria, HIV, diarrheal diseases, and others), nephrotoxins, and obstetric and surgical complications are the major etiologies in Africa.



EPIDEMIOLOGY

- ▣ Most causes of AKI in developing tropical countries are preventable
- ▣ strategies to improve the outcomes and reduce the burden of tropical AKI require
 - ▣ improvements in basic public health
 - achieved through effective interventions
 - ▣ increased access to effective medical care (especially for patients with established AKI).

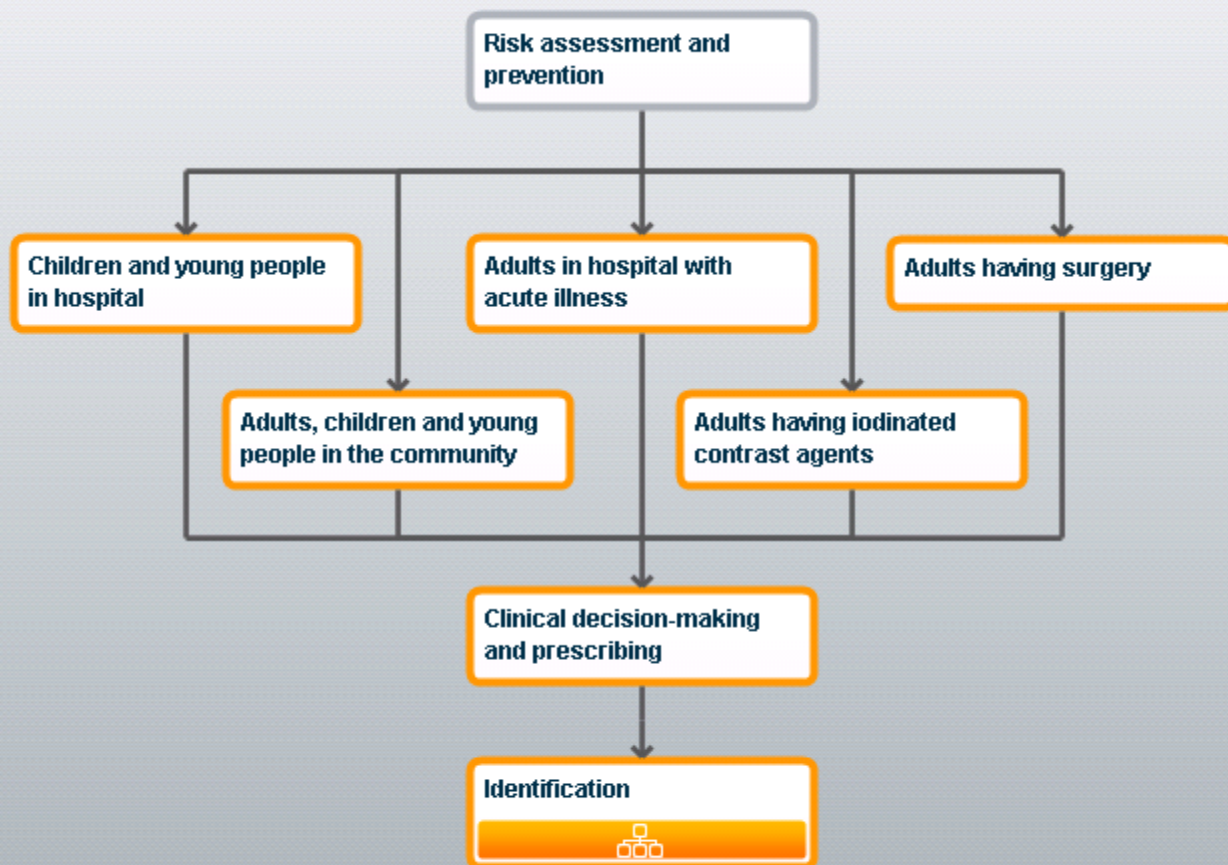


▣ **Reasons for poor survival**

- Inadequate dialysis prescription
- Inability of dialysis to replace endocrine, cytokine, metabolic and immunologic functions of the kidneys
- Delay in initiating dialysis
- Lack of facilities for biochemical indices like carbamylated hemoglobin, parathyroid hormone, cystatin C
- Ultrasonographic findings are not discriminatory enough
- Management is capital intensive

Risk assessment and prevention of acute kidney injury

Acute kidney injury ▾



NICE Pathways

An online tool providing quick and easy access, topic by topic, to the full range of guidance from NICE

[Click here to go the pathway](#)



DIAGNOSIS

- ▣ AKI can be readily identified by close monitoring of routine serum creatinine and urine output results

General guidelines for differentiating the etiology of acute kidney injury (ie, prerenal vs renal) using laboratory studies.

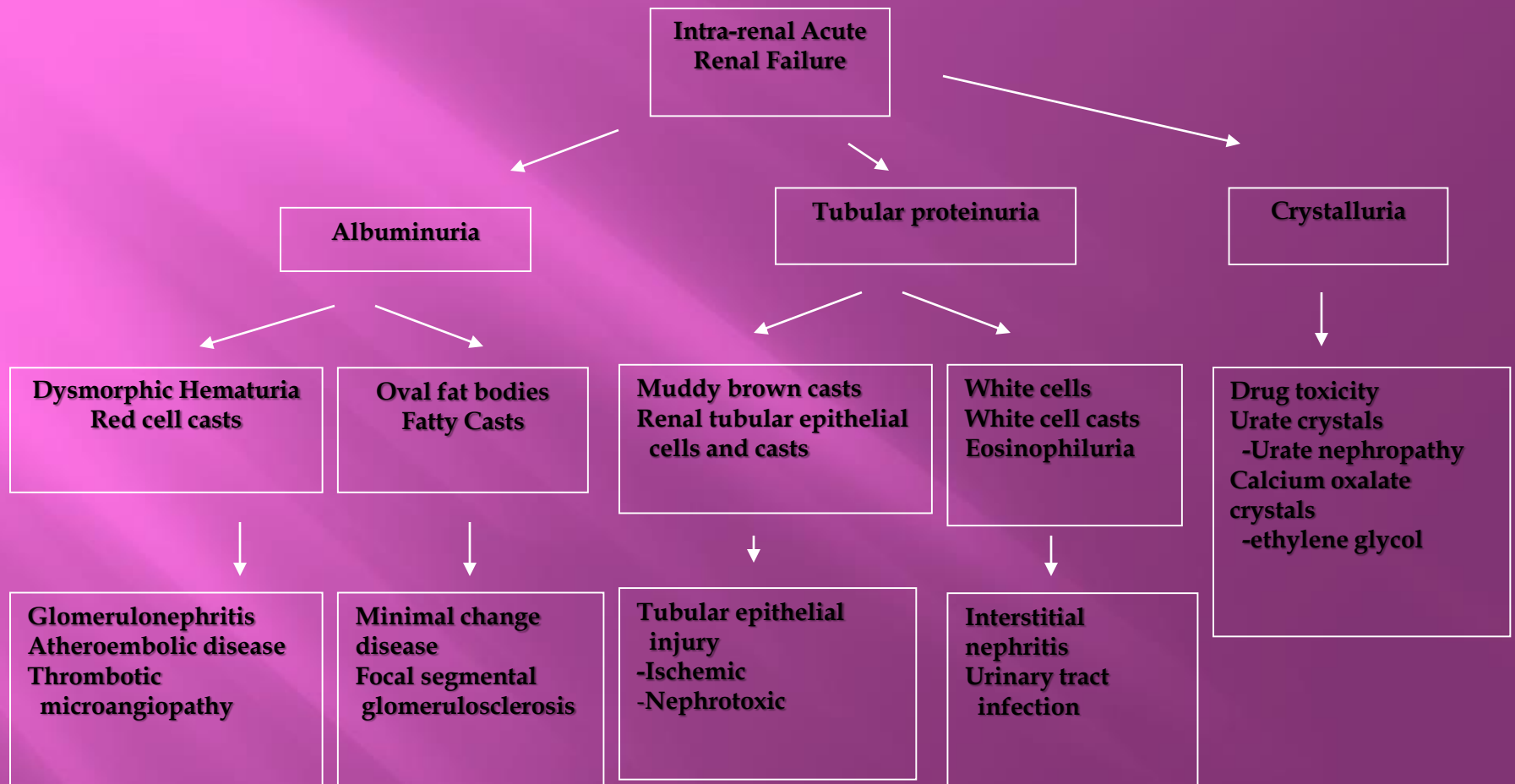
Indices	Prerenal	Renal
Blood urea nitrogen to creatinine ratio	>20	<20
Fraction of filtered sodium, %	<1	>2
Fractional excretion of urea, %	<35	>35
Urine osmolality, mOsm/L	>500	<400
Urine sediment, cast type	bland, hyaline	granular
Urine sodium, mEq/L	<20	>40



DIAGNOSIS

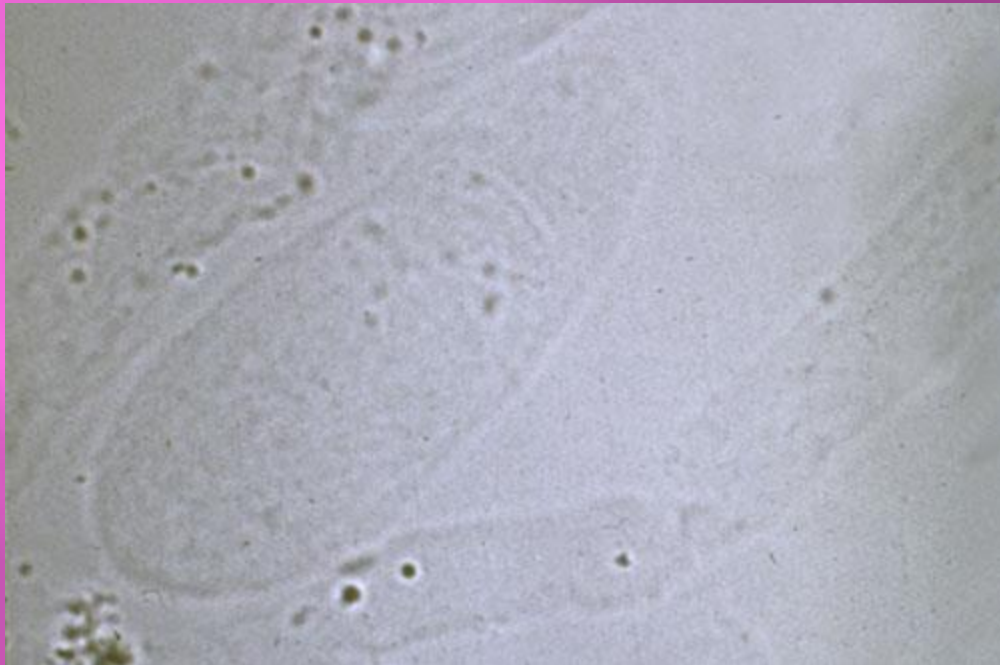
- For patients with prerenal AKI, urinalysis is typically bland or with hyaline casts, urine sodium is low (ie, $<1\%$), and urine osmolality is high.

DIAGNOSIS: Urinary Sediment Findings in Intra-Renal Acute Renal Failure





URINE MICROSCOPY



Hyaline Casts:

Better seen with low light.

Non-specific.

Composed of Tamm-Horsfall mucoprotein.



URINE MICROSCOPY



Granular Casts:

Represent degenerating cellular casts or aggregated protein.

Nonspecific.

Waxy Casts:

Smooth appearance.

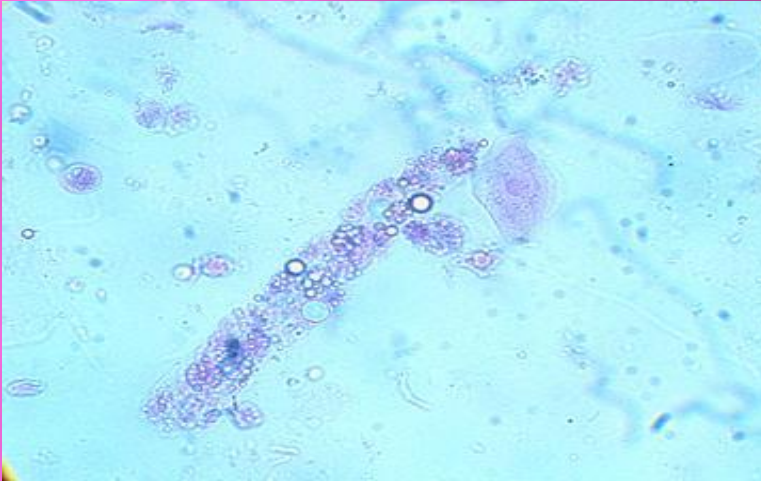
Blunt ends.

May have a “crack”.

Felt to be last stage of degenerating cast – representative of chronic disease.



URINE MICROSCOPY



Fatty Casts:

Seen in patients with significant proteinuria.

Refractile in appearance.

May be associated with free lipid in the urine.

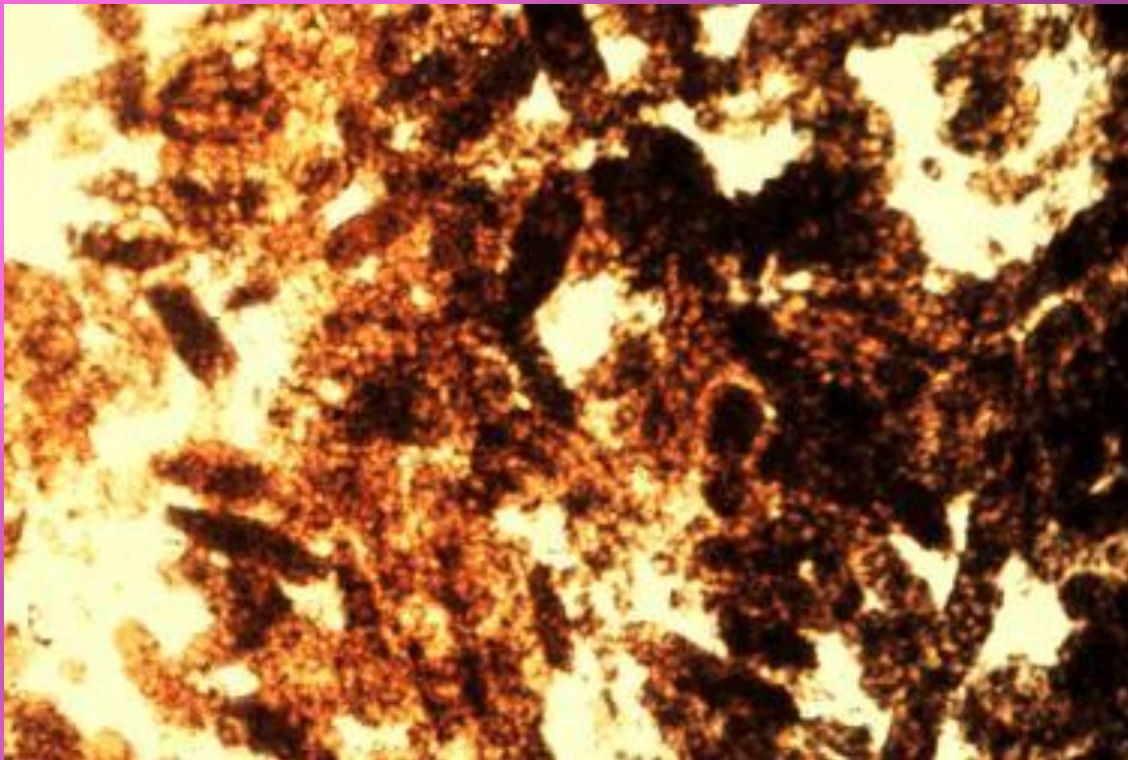
Can see also “oval fat bodies” – RTE’s that have ingested lipid.

Polarize – demonstrate “Maltese cross”.

UpToDate Images.



URINE MICROSCOPY



Muddy Brown Casts:

Highly suggestive of ATN.

Pigmented granular casts as seen in hyperbilirubinemia can be confused for these.



Acute Renal Failure



**White Blood Cell
Casts:**

**Raises concern for
interstitial nephritis.**

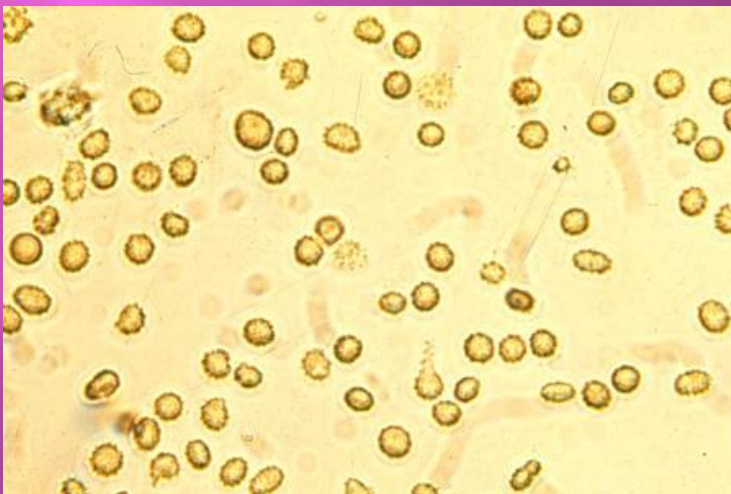
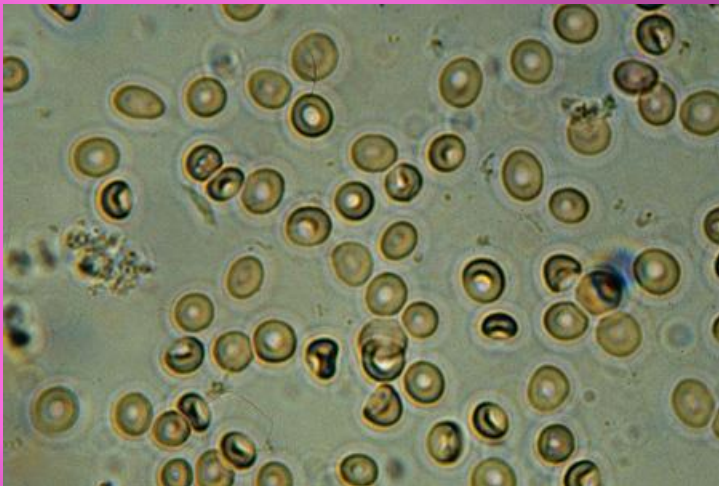
**Can be seen in other
inflammatory disorders.**

**Also seen in
pyelonephritis.**



Acute Renal Failure

▣ Hematuria



Nonglomerular hematuria:

Urologic causes.

Bladder/Foley trauma.

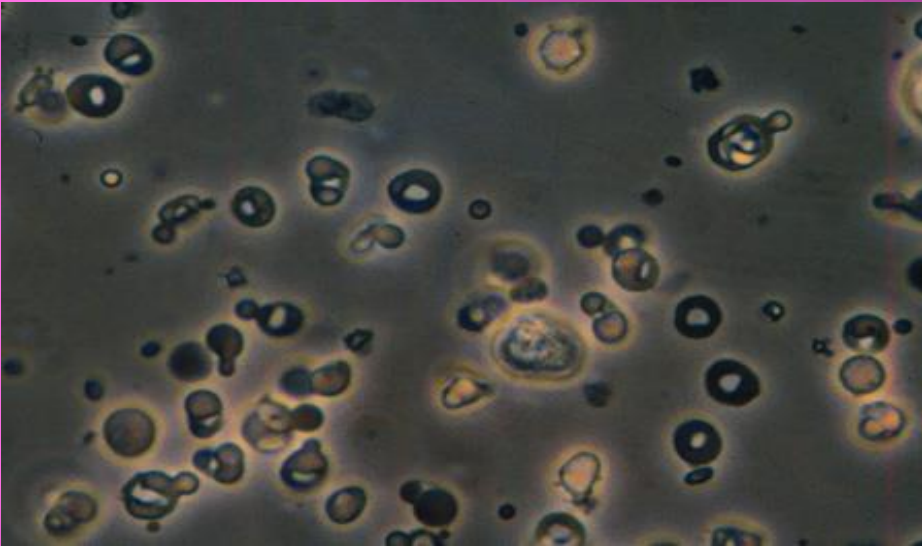
Nephrolithiasis.

Urologic malignancy.

May be “crenated” based upon age of urine, osmolality – NOT dysmorphic.



URINE MICROSCOPY



Dysmorphic Red Cells:

Suggestive of glomerular bleeding as seen with glomerulonephritis.

Blebs, buds, membrane loss.

Rarely reported in other conditions - DM, ATN.



Red Blood Cell Casts:

Essentially diagnostic of vasculitis or glomerulonephritis.



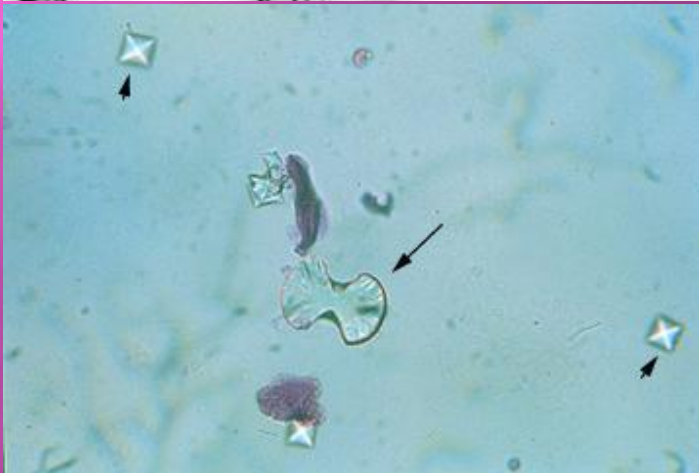
URINE MICROSCOPY



Uric acid crystals:

Seen in any setting of elevated uric acid and an acidic urine.

Seen with tumor lysis syndrome.



Calcium oxalate crystals:

Monohydrate – dumbbell shaped, may be needle-like.

Dihydrate – envelope shaped.

Form independent of urine pH.

Seen acutely in ethylene glycol ingestion.



management



AKI Stage

High Risk	1	2	3
Discontinue all nephrotoxic agents when possible			
Ensure volume status and perfusion pressure			
Consider functional hemodynamic monitoring			
Monitor Serum creatinine and urine output			
Avoid hyperglycemia			
Consider alternatives to radiocontrast procedures			
Non-invasive diagnostic workup			
Consider invasive diagnostic workup			
Check for changes in drug dosing			
Consider Renal Replacement Therapy			
Consider ICU admission			
Avoid subclavian catheters if possible			



management

- ❑ current treatment for AKI is mainly supportive in nature
- ❑ Prerenal azotemia from volume depletion is usually responsive to isotonic saline repletion.
- ❑ Treatment of ATN requires the discontinuation of nephrotoxic agents, maintenance of optimum hemodynamics, and close surveillance for complications of renal dysfunction
- ❑ Postrenal etiologies dictate obstruction removal.
- ❑ Numerous pharmacologic agents have proven effective in preventing or ameliorating experimental AKI but none of these substances has been translated successfully to clinical practice



management

- ▣ AKI can be prevented by early recognition and treatment of the underlying cause, for example:
 - Early treatment of infections/sepsis
 - Early treatment/prevention of dehydration
 - Correcting hypovolaemia

- ▣ AKI can also be prevented by:
 - Monitoring use of drugs such as NSAIDs and ACE inhibitors, especially if a patient is acutely unwell
 - Taking care with at-risk patients who need iodinated contrast agents with scans



management

- ▣ RRT is the central component of care for patients with severe AKI.
- ▣ indications for RRT include:
 - volume overload
 - Hyperkalemia
 - metabolic acidosis
 - overt uremic symptoms.
- ▣ Generally, no robust data suggest the benefit of one RRT treatment modality over another



challenges

- ❑ Late presentations of patients to the hospitals
- ❑ Lack of adequate information about the features of renal disease
- ❑ Lack of knowledge by the patient on steps to take.
- ❑ Inertia of the populace to take up routine screening and check up
- ❑ Huge dependence on the use non prescription medications including fake and substandard drugs
- ❑ Lack of
- ❑ High cost of dialysis (including consumables) and the presence of few centers with adequate manpower, technical know how to run and maintain the machines where present
- ❑ Usage of outdated machines
- ❑ Lack of political drive to subsidize treatment



Reducing the burden

- ▣ Most etiologies of AKI can be prevented by interventions at the individual, community, regional, and in-hospital levels.
- ▣ Treatment with dialysis is often unavailable or too costly so there must be community-wide efforts to eradicate causes of AKI, expedite diagnosis, and aggressively manage prerenal conditions and specific infections.



Reducing the burden

- Effective measures must include community-wide efforts to increase an awareness of the devastating effects of AKI and provide guidance on preventive strategies, as well as early recognition and management



Reducing the burden

- Efforts should be focused on minimizing causes of AKI
- increasing awareness of the importance of serial measurements of serum creatinine in high-risk patients
- and documenting urine volume in acutely ill people to achieve early diagnosis
- there is as yet no definitive role for alternative biomarkers. Protocols need to be developed to systematically manage prerenal conditions and specific infections.



Reducing the burden

- ▣ More accurate data about the true incidence and clinical impact of AKI will help to raise the importance of the disease in the community, increase awareness of AKI by governments, the public, general and family physicians, and other health-care professionals to help prevent the disease.

conclusion

- ▣ **Prevention is the key to avoid the heavy burden of mortality and morbidity associated with AKI.**

Thank you



references

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