AKI management in Developing Countries

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Taipei, Taiwan, On behalf of NSARF
No conflicts of interests to be disclosed
Why do We Talk about AKI in developing country?
Patients undergoing RRT from 2010 to 2030

Worldwide

By region

Incidence of dialysis –requiring AKI in Taiwan

1998~2015

Number of Patients (y)

Taiwan National Health Insurance data

KDIGO
Developing world
12 to 40 PMP/YR

Developed world
100 to 200 PMP/YR

Community acquired AKI

KDIGO
Global variation in the incidence of AKI
What’s the difference of AKI, developing countries (DC) perspective
Specific diseases and RRT

Data from Dr Burdmann, Brazil

Lombardi, Rosa-Diez, Ferreiro, Greloni, Yu, Younes-Ibrahim, Burdmann, NDT 2014
AKI Snakebite LA

Crotalus snakebite-induced AKI

- Prospective
- 100 consecutive patients
- AKI: GFR<60 ml/min/1.73m² (first 3 days)

Comparing with polymyxin B

"AKI developed in 22% of the patients."

Mendes, Cordeiro, Burdmann, Ann Pharmacother 2009

Data from Dr Burdmann, Brazil
Comorbidity of AKI

- Vasopressor: 16% Emerging, 33% Developed
- Ventilator: 29% Emerging, 47% Developed
- Diabetes: 33% Emerging, 36% Developed
- CKD: 38% Emerging, 54% Developed

Less sepsis
Less severity of illness scores
But high mortality

Kidney recovery after AKI - 0 by 25

KIDIGO

Lancet 2016; 387: 2017-25
Water borne illness /dehydration

Venomous animals /insects/
Vector transmitted infections (endemic conditions)

Consumption of toxic plants/herbs

Obstetric disease
1. no Access to basic sanitation
2. No safe drinking-water

2.4 billion people globally
Acute kidney injury (AKI) in Chinese children

Methods and Cohort
1 month to 18 years

25 Chinese hospitals

101,836 inpatients

No AKI in 81,928 (80%)

AKI in 19,908 (20%)

† in Cr of ≥ 0.3 mg/dL in 48 hrs or ≥50% in 7 days

96% with AKI had no discharge diagnosis of AKI

Community acquired AKI
N = 7220

Diarrhea
Sepsis

0.5% mortality

Hospital acquired AKI
N = 12,688

Congenital heart
Cardiac surgery
NSAIDs
PPIs

4%
Tropical infections causing AKI

- Leptospirosis
- Dengue
- Malaria

- Leptospirosis: 1 million cases/year, 60,000 deaths/year
- Dengue: 390 million cases/year, 60,000 deaths/year
- Malaria: 214 million cases/year, 400,000 deaths/year

Srisawat et al, Textbook of Critical Care Nephrology 3rd, 2017
HIV associated Nephropathy

Major etiology of AKI in tropical area

EMJ Nephrol. 2017;5[1]:66-74.
Upsurge in AKI due to Malaria Incidence is 13-17.8%
Increasing multidrug resistance
Habitual difference, AKI in China

2,223,230 patients admitted to the 44 hospitals screened in 2013,
Traditional medicine in LMIC area

- Latin America: 40-70% of people regularly use TMs. 60-100 million people living with CKD.
- Sub-Saharan Africa: 80-90% of all people use TM for primary healthcare. Upto 100 million people living with CKD.
- India: Ayurveda and other TMs used by >1 billion people. 100-200 million people living with CKD.
- China: TCM is 20% of all healthcare services and treats 200 million people annually. 120 million people living with CKD.
Population Pyramid

Developed

Developing

Etiology of AKI during pregnancy

It occurs with bimodal distribution

1st peak
7th - 8th week

2nd peak
32th - 36th week

Based on trimester of pregnancy AKI can be classified into three groups:

First half
- Hyperemesis gravidurum
- Septic abortion

Second half
- Preeclampsia
- HELLP
- AFLP

Postpartum
- TTP
- HUS
Pediatric AKI, less than 3 years

2899,932 newborns between January 1, 2000 and December 31, 2012

Excluded:
1. Gender missing (n=2,079)
2. Death on birthday (n=11)

2897,842 newborns

1916 AKI/AKI-D < 3 y/o
- Any AKI event: Diagnosis of AKI (ICD-9-CM code: 584) or first dialysis

Severe CHD 543
Premature 351
Sepsis 240
Cancer 16
CAKUT 76
Simple CHD 204
Respiratory 181
Accident 23
Others 282

Risk factors: Medication, intervention or surgery before AKI
Outcome: death, chronic kidney disease (CKD), congestive heart failure (CHF), and
AKI in Children form 0-25 snapshot, child

- Dehydration
- Hypotension, shock
- Infection
- Nephrotoxic agents
- Primary Kidney diseases
- Post-surgical
- Systemic diseases
- Cardiac diseases
- Urinary obstruction

HIC n=147  UMIC n=72

[Link to PLOS ONE](https://doi.org/10.1371/journal.pone.0196586) May 1, 2018
Challenging problems in AKI in DC

1. Changing disease etiology
2. Climate problem
3. Health resources
In South Asia... difficulty

Original Article

Outcome in severe acute renal failure associated with malaria

Rubina Naqvi, Ejaz Ahmad, Fazal Akhtar, Anwar Naqvi and Adib Rizvi

Sindh Institute of Urology and Transplantation, Dow Medical College and Civil Hospital, Karachi, Pakistan
Etiological pattern of AKI, India

Malaria
- 1983-1995 (n=638)
  - 4.70%
- 1996-2008 (n=1767)
  - 17.09%

Diarrheal Diseases
- 1983-1995 (n=638)
  - 0.94%
- 1996-2008 (n=1767)
  - 1.93%

- 1983-1995 (n=638)
  - 36.83%
- 1996-2008 (n=1767)
  - 19.13%

Hemolytic Uremic Syndrome
- 1983-1995 (n=638)
  - 0.94%
- 1996-2008 (n=1767)
  - 1.93%


KDIGO
Climate Change Effects on Human Health
The etiology of AKI – Iran

Hooman N. J Ped Nephrology. 2014;2(3);98-103
Heat waves on AKI

International Journal of Epidemiology 37(6):1359-65
Global distribution of nephrologists per 1 million population (ISN)
Patients received RRT

Ethnic, socioeconomic, and developmental heterogeneity

Not getting dialysis

Ethnic, socioeconomic, and developmental heterogeneity

Lancet 2016; 387: 2017-25
Poverty headcount % ratio, 2015

Conflicts in Syria and Yemen have caused the poverty rate to rise in the Middle East and North Africa region.

Roughly half of the world’s countries now have poverty rates below 3 percent.

Extreme Poverty Rate

World Bank 2017
Expenditures burden in South Asia: the challenges are facing.

Limited resources and low awareness
The ISN ‘0 by 25’ Project

Risk assessment
- Tool kits
- Active surveillance

Recognition
- Clinical
- Point of care testing

Response
- Interventions: fluids, medications
- Regional stations
- Implementation of peritoneal dialysis
- Telemedicine for coordination
- Transfer to regional centers for critical cases

Renal support
- Follow-up post-AKI a local level
- Point of care testing
- Guidance via telemedicine

Urinalysis
Proteinuria
Biopsy
Imagine

AKI prediction score

Limitations of disease score

1. Disease-specific
2. Mostly from developed countries
3. Mostly for hospital-acquired acute kidney injury
4. Mostly focused on inherent risk factors
5. Limited evaluation of providers, healthcare systems, and population-level factors
6. Limited use of the process of care quality indexes
AKI recognition - The ISN ‘0 by 25’ Project

MODIFIERS
AWARENESS - CONTEXT - RESOURCES

CLINICAL SUSPICION
- History and Physical
- Preliminary diagnosis

CONFIRMATION
- Urine output
- Urinalysis
- POC testing
- Additional testing
  - Novel Biomarkers
  - Renal imaging
  - Renal Biopsy

DIAGNOSIS
- KDIGO Classification and Staging
- Establishment of etiology
- CKD determination
Salivary urea nitrogen dipstick- Angola

Eight–six patients  malaria

KDIGO
Biopsy could be necessary in LMIC

<table>
<thead>
<tr>
<th></th>
<th>Children (n=1643)*</th>
<th>Adults (n=993)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septicaemia</td>
<td>370 (23%)</td>
<td>232</td>
</tr>
<tr>
<td>HIV</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Tetanus</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Typhoid</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Cholera</td>
<td>0</td>
<td>22</td>
</tr>
<tr>
<td>Glomerular disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute glomerulonephritis</td>
<td>183</td>
<td>57</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>115</td>
<td>10</td>
</tr>
<tr>
<td>Rapidly progressive acute glomerulonephritis</td>
<td>46</td>
<td>4</td>
</tr>
<tr>
<td>Lupus nephritis</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Membranoproliferative acute glomerulonephritis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Nephrotoxin</td>
<td>270 (16%)</td>
<td>182 (18%)</td>
</tr>
<tr>
<td>Haemoglobinuria from:</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Plasmodium falciparum</em> malaria haemolysis</td>
<td>198</td>
<td>34</td>
</tr>
</tbody>
</table>
Barriers to care in AKI-sub-Saharan Africa

Increased susceptibility to acute kidney injury
- Infections
- Lack of vaccinations (e.g., for diarrhoea, pneumonia)
- Poor water supply
- Nephrotoxin exposure

Symptomatic acute renal failure

Delay
Poor access to primary health care
- Lack of awareness
- Lack of early detection
- Lack of treatment

Delay
Search for resources
Female sex?

Delay
Traditional remedies

Renal failure not diagnosed

Health-care clinic or hospital

Delay
Search for resources
- Patient – funds, consent
- Hospital – supplies, staff, electricity, water
- Female sex?

Renal failure diagnosed

Delay
Referral where dialysis is available

Lancet Glob Health 2016;
4: e242-50
### Minimum treatment parameter requirements in the community setting

<table>
<thead>
<tr>
<th>Minimum treatment/parameters requirements</th>
<th>Suspected AKI</th>
<th>Confirmed AKI</th>
<th>Complete response</th>
<th>Persistent AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid resuscitation</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Fluid challenge</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Furosemide stress test</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemodynamic parameters: BP, HR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capillary refill</td>
<td></td>
<td></td>
<td></td>
<td>Nephrology referral书 for ongoing volume needs risk of volume overload avoidance of nephrotoxic drugs</td>
</tr>
<tr>
<td>Urinalysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UOP, fluid balance</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
A Nurse Led Intervention

Stop AKI in Malawi

'STOP' AKI!
Sepsis and hypoperfusion
(Dehydration, haemorrhage, cardiac failure, liver failure, renovascular insult)

Toxicity
(Drugs, contrast)

Obstruction
(Tumour, stones, extrinsic compression)

Parenchymal kidney disease
(Glomerunephritis, rhabdomyolysis)

Remember.... Prevent AKI!
The 4 'M's
Monitor Patient
(vital signs, regular blood tests, fluid charts, urine volumes)

Maintain Circulation
(hydration, resuscitation, oxygenation)

Minimise Kidney Insults
(e.g. nephrotoxic medications, surgery or high risk interventions, hospital acquired infection)

Manage The Acute Illness
(e.g. sepsis, heart failure, liver failure)

You can make a difference!

J Ren Care. 2016 Dec;42(4):196-204
• Regional differences in choice of RRT modality
# Treatment of AKI in DC

<table>
<thead>
<tr>
<th></th>
<th>DEVELOPED WORLD</th>
<th>DEVELOPING WORLD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TREATMENT</strong></td>
<td>RRT widely immediately available</td>
<td>Poorly available</td>
</tr>
<tr>
<td></td>
<td>IHD&gt;CRRT&gt;SLED&gt;PD</td>
<td>PD&gt;&gt;IHD</td>
</tr>
<tr>
<td><strong>TRANSPORTATION</strong></td>
<td>Immediate</td>
<td>Severe delays→ increased mortality</td>
</tr>
<tr>
<td><strong>COSTS</strong></td>
<td>High, affordable</td>
<td>Low, unaffordable, increases mortality</td>
</tr>
</tbody>
</table>
Costs of dialysis therapy in AKI

US$/dia

- iHD
- CRRT

Manns* (Crit Care, 2003)

- CRRT
- SLED

Berbece* (Kid Int, 2006)

- iHD
- PD

Ponce (Botucatu, 2010)

- CRRT

Chitalia (India) (Kid Int, 2002)

Automatic

Manual

KDIGO
All-cause mortality in hospital

2,223,230 patients admitted to the 44 hospitals screened in 2013, 154,950 (7.0%) AKI

<table>
<thead>
<tr>
<th>KDIGO AKI criteria†</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 years increase)</td>
<td>1.33 (1.25–1.42)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sex (male vs female‡)</td>
<td>1.21 (0.99–1.49)</td>
<td>0.06</td>
</tr>
<tr>
<td>History of cardiovascular disease (yes vs no‡)</td>
<td>1.25 (1.03–1.53)</td>
<td>0.0263</td>
</tr>
<tr>
<td>Diabetes (yes vs no‡)</td>
<td>1.11 (0.88–1.39)</td>
<td>0.39</td>
</tr>
<tr>
<td>Chronic kidney disease (yes vs no‡)</td>
<td>0.81 (0.63–1.03)</td>
<td>0.09</td>
</tr>
<tr>
<td>Delayed vs timely‡ recognition of AKI</td>
<td>1.29 (0.89–1.89)</td>
<td>0.18</td>
</tr>
<tr>
<td>Severe comorbidity (yes vs no‡)</td>
<td>4.84 (3.86–6.06)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AKI stage at peak</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1‡</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.89 (1.46–2.44)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3</td>
<td>1.95 (1.38–2.75)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Peak serum creatinine (natural logarithm transformed)</td>
<td>1.87 (1.42–2.47)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RRT indication (yes vs no‡)</td>
<td>1.46 (1.13–1.90)</td>
<td>0.0042</td>
</tr>
<tr>
<td>Renal referral (yes vs no‡)</td>
<td>0.61 (0.47–0.80)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Academic vs local‡ hospital</td>
<td>1.14 (0.91–1.43)</td>
<td>0.26</td>
</tr>
</tbody>
</table>
AKI Snapshot, Taiwan

Follow up since AKI

Who follows the patient?

- Nephrologist: 27%
- Internist: 50%
- General Practitioner: 1%
- Intensivist: 2%
- Others: 20%
- Unknown: 1%

Yes: 91 (58%)
No: 64 (41%)
Unknown: 1 (1%)
# Nephrology referral and outcome

## Long term dialysis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Early Nephrology Referral</th>
<th>Control</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harel 2013</td>
<td>83 1184</td>
<td>32 1184</td>
<td>2.71 [1.79, 4.11]</td>
</tr>
<tr>
<td>Karsarji 2017</td>
<td>76 500</td>
<td>353 1576</td>
<td>0.62 [0.47, 0.81]</td>
</tr>
<tr>
<td>Meier 2011</td>
<td>22 634</td>
<td>249 3462</td>
<td>0.35 [0.22, 0.54]</td>
</tr>
<tr>
<td>Silva 2013</td>
<td>81 128</td>
<td>57 68</td>
<td>0.33 [0.16, 0.70]</td>
</tr>
<tr>
<td>Vincent 2019</td>
<td>1954 7550</td>
<td>737 12710</td>
<td>5.67 [5.18, 6.21]</td>
</tr>
<tr>
<td>Xie 2014</td>
<td>3 38</td>
<td>2 131</td>
<td>5.53 [0.89, 34.38]</td>
</tr>
</tbody>
</table>

Total (95% CI): 10234 19131 100.0% 0.69 [0.33, 3.87]

## Long term mortality

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Nephrology referral</th>
<th>Not referral</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harel 2013</td>
<td>100 1184</td>
<td>126 1184</td>
<td>0.77 [0.59, 1.02]</td>
</tr>
<tr>
<td>Meier 2011</td>
<td>100 634</td>
<td>710 3462</td>
<td>0.53 [0.42, 0.66]</td>
</tr>
<tr>
<td>Silva 2013</td>
<td>154 196</td>
<td>90 170</td>
<td>3.26 [2.07, 5.14]</td>
</tr>
<tr>
<td>Vincent 2019</td>
<td>3096 7550</td>
<td>5604 12710</td>
<td>0.88 [0.83, 0.93]</td>
</tr>
</tbody>
</table>

Total (95% CI): 9764 17525 100.0% 0.86 [0.82, 0.91]
Acute kidney injury risk levels and dimensions

Population

Healthcare System

Provider

Patient

Environment

Water quality
Sanitation
Natural disasters
Earthquake
Famine
Geography
Tropical
High Altitude
Politics
War zone

Socioeconomic/Cultural

Housing
Nutrition
Public Health
Healthcare Access
Health insurance
Health Center
Transportation
Health Beliefs
Literacy
Access to internet
Multidisciplinary care Team for kidney disease

Multidisciplinary Care Team for CKD Patients in Hospitals/Clinics—Preparatory works in a pilot study

DM
HTN
Diet
Public approach

1. Awareness of nephrotoxin, chemicals
2. Control of infection and vector
3. Surveillance of pharmacy
4. Safe water and food
5. Referral to nephrologist
AKI in increasing rapidly in DC, limited awareness.

AKI specific risk in DC deserve long-term follow up.

Water and health care system, resources.

Tropical AKI irrevocably linked to tropical co-system and culture.
Thank you