Acute kidney injury in the tropics: What are the challenges?

Vivekanand Jha
Tropical zones where all twelve months have mean temperatures > 18 °C (64.4 °F).
<table>
<thead>
<tr>
<th>Temperate</th>
<th>Tropical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spring</td>
<td>Dry season</td>
</tr>
<tr>
<td>Summer</td>
<td>Cool</td>
</tr>
<tr>
<td>Autumn</td>
<td>Hot</td>
</tr>
<tr>
<td>Winter</td>
<td>Wet Season</td>
</tr>
</tbody>
</table>
Waterborne diseases account for > 2.2 m deaths and >82 m DALYs

Waterborne infections cause kidney injury:
- Direct: diarrheal diseases, salmonellosis, shigellosis, cholera,
- Vector borne: malaria, dengue,
- Leptospirosis, schistosomiasis

Indirect effect of diarrheal diseases on other causes of kidney injury

The United Nations World Water Development Report
Global GDP per capita by latitude

“Tropical Underdevelopment” © 2001 by Jeffrey D. Sachs, used by permission of The Wiley Agency LLC

Relevance to (kidney) health

• High prevalence of
  – Vector-transmitted infections
  – Water-borne illnesses
  – Recurrent dehydration

• Encounter with venomous animals/insects

• Consumption of potentially toxic plants/herbs
Geographic, biodiversity climate & socio-economic variables are linked with richness of infectious diseases

Morand et al. PLoS ONE 9(2): e90032
AKI in Tropical Countries

- Grossly under-reported.
- Pattern and prevalence of community acquired ARF significantly different from the developed world.
- The pattern may differ between various tropical countries and even in different regions of the same country.
- The average age lower compared to advanced countries (mean age 34 yrs in India).
AKI in the Tropics

• High incidence of AKI requiring RRT in rural areas with scarce healthcare resources*
• Patient population much younger
• Most have isolated renal involvement at onset
• Little/no background CKD
• Renal support would lead to (?) substantial recovery

*Jha V, Semin Nephrol 2008
Distribution of CA-AKI in the tropics
Most Common Causes of AKI

Katz et al., 2000
<table>
<thead>
<tr>
<th>Plant</th>
<th>Areas from where reported</th>
<th>Active molecule</th>
<th>Renal manifestation</th>
<th>Other manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloe capensis (cape aloe)</td>
<td>Zimbabwe, S Africa</td>
<td>Aloins, aloinosides</td>
<td>Acute renal failure</td>
<td>Gastrointestinal fluid loss, dehydration</td>
</tr>
<tr>
<td>Catha edulis (khat leaf)</td>
<td>East Africa, Arab peninsula</td>
<td>S-cathione, Ephedrine</td>
<td>Acute tubular necrosis</td>
<td>Hepatotoxicity</td>
</tr>
<tr>
<td>Colchicum autumnale (meadow saffron)</td>
<td>Turkey</td>
<td>Colchicine</td>
<td>Acute tubular necrosis</td>
<td>Hemorrhagic gastroenteritis, muscle paralysis, respiratory failure</td>
</tr>
<tr>
<td>Dioscorea quartiniana (yam)</td>
<td>Africa, Asia</td>
<td>Discorine, dioscine</td>
<td>Acute tubular necrosis</td>
<td>Convulsions, symptoms related to inadequate processing</td>
</tr>
<tr>
<td>Glycerrhiza glabrata (Liquorice)</td>
<td>Japan</td>
<td>Glycerrrhizic acid</td>
<td>Acute tubular necrosis</td>
<td>Rhabdomyolysis, hypokalemia</td>
</tr>
<tr>
<td>Larrea tridentate (chapparal)</td>
<td>Chile, South Africa</td>
<td>Nordihydroguaiaretic acid, s-quinone</td>
<td>Renal cysts</td>
<td>Hepatic failure</td>
</tr>
<tr>
<td>Securidacea longipedunculata (violet tree, wild wisteria)</td>
<td>Congo</td>
<td>Methysalicylate, securinine, saponins</td>
<td>Acute tubular necrosis</td>
<td>Vomiting, diarrhoea Root, bark used as intravaginal poison</td>
</tr>
<tr>
<td>Semacarpum anacardium (marking nut)</td>
<td>India</td>
<td>Phenols</td>
<td>Acute tubular necrosis</td>
<td>Fever, dysuria, hematuria</td>
</tr>
<tr>
<td>Uncaria tomentosa (cat’s claw, una de gato)</td>
<td>Peru</td>
<td>Oxindole alkaloids, pentacyclic triterpenes</td>
<td>Acute interstitial nephritis</td>
<td></td>
</tr>
</tbody>
</table>

Other plants: Euphorbia metabolensis, Crotalaria labminifolia, Artemisia absinthium and Mentha pulegium

Jha V, Oxford Textbook of Medicine 6th Ed
Management

• Presentation often delayed
• Uncertain etiology
• Multisystem involvement
• Limited availability of dialysis
• Acute peritoneal dialysis mainstay of treatment in remote areas
Challenges
Economic impact of ESRD treatment

Ramachandran and Jha, PLOS One 2013
Changing disease epidemiology

Scrub Typhus Is an Under-recognized Cause of Acute Nephritis

Ferraria, Leila, et al.

DOI: 10.1093/ndt/gfg260

Plasmodium vivax malaria complicated by acute kidney injury: experience at a referral hospital in Uttarakhand, India

Reshma Kaushik, Rajeev M. Kaushik, Rajesh Kakkar, Anita Sharma and Harish Chandra

Department of Medicine; Department of Pathology, Himalayan Institute of Medical Sciences, HIHT University, Swami Ram Nagar, PO Doiwala, Dehradun 248140, Uttarakhand, India

*Corresponding author: Tel: +91 135 2471 283/376, +91 94 1019 0244; E-mail: rmkaushik1@gmail.com; rmkaushik1@rediffmail.com
ID outbreaks and loss of biodiversity

Morand et al.  
*PLoS ONE*  
9(2): e90032
Climate Change and the Emergent Epidemic of CKD from Heat Stress in Rural Communities: The Case for Heat Stress Nephropathy

Worldwide annual maximum temperature changes

Tmax Change 1945–2014

Average Tmax 1951–2010

Degrees Celsius
Heat Stress
Water Shortage
Overexertion

Sweat

Low Grade Rhabdomyolysis
Nucleotide Release
Uric acid Generation
Lactic Acid Production

Hyperosmolarity
Vasopressin Release
Aldose Reductase Activation
Endogenous Fructose Release
Fructokinase Stimulation

Hyperthermia
Vasopressin Release
Rhabdomyolysis
Reduced Renal Blood Flow

Extracellular Volume Depletion
Low Blood Pressure
Reduced Renal Blood Flow
Renin Angiotensin Activation
Urinary Acidification

Vasopressin Effects on the Kidney Tubule
Fructose Metabolism in Proximal Tubule with Oxidants and Chemokine Release
Uricosuria and Urate Crystal formation in Urine
Hypokalemia mediated Ischemic Injury to the Kidney
Renal Ischemia

Repeated Acute Kidney Injury
Chronic Interstitial Fibrosis
Tropical infections, AKI and CKD

- Diabetes
- Hypertension
- Infection
- Chronic kidney disease
- Acute kidney disease
- Acute kidney injury
- Resolved
icddr,b

Dhaka, Bangladesh

SAVING LIVES

For more than 50 years, icddr,b has provided practical, low-cost, lifesaving solutions to health problems that affect billions of people living in poverty across the globe and in its host country of Bangladesh.

Dedicated to saving lives, icddr,b is an international health research organisation located in Bangladesh. Through translation of research into treatment, training and policy advocacy icddr,b addresses some of the most critical health concerns facing the world today.
Research agenda

• Tropical AKI registry to document disease pattern and variations
• Long-term impact of tropical AKI
• Financial impact of AKI on patient families and society
• Development and testing of models of service delivery, aimed at
  – early identification,
  – prevention and
  – early intervention in the community
Conclusions

• Tropical AKI irrevocably linked to tropical ecosystem and culture
• AKI incidence and pattern reflects unfinished public health agenda
• Presentation and outcome depend on treatment availability
• More information and awareness needed in the community
• Climate change to have a major impact, danger of slipping on gains
• Research needs to focus on this “neglected disease”
Greetings colleagues,

This week *ISN Education* brings a collection of presentations from ISN leaders on the topic of Acute Kidney Injury that were presented within the context of several recent Continuing Medical Education (CME) programs. The presentations cover recent advances in nephrology and treatment strategies.

I hope you will enjoy the presentations,

Fredric Finkelstein  
*ISN CME programs Chair*

**Kidney International Highlights**

*Intermittent Hemodialysis and Isolated Ultrafiltration: Renal Replacement Therapy for Acute Kidney Injury* - by Peter Mount

*AKI: Detection and Early Intervention* - by Peter Mount

*Non-dialytic treatment for AKI* - by Neesh Pannu