A longitudinal evaluation of kidney function among sugarcane workers in Guatemala

Jaime Butler-Dawson¹, Lyndsay Krisher¹, Claudia Asensio², Alex Cruz², Liliana Tenney¹, David Weitzenkamp¹, Miranda Dally¹, Edwin J. Asturias³, and Lee S. Newman¹

¹Center for Health, Work & Environment, Colorado SPH
²Pantaleon, Guatemala
³Division of Pediatric Infectious Diseases, University of Colorado
Disclosures

• CU MOU and contract with Pantaleon Group to apply Total Worker Health® principles to worker health, safety & well-being
• CU investigators received partial salary from contract
• Speakers have no financial or other relationship to any devices, products, laboratories or services
Overview

1. Chronic kidney disease of unknown origin (CKDu)
2. CKDu epidemiology in Central America
3. Evaluation of sugarcane workers in Guatemala
   • Methods
   • Results
   • Summary
4. Future research
Worldwide distribution of CKDu

- Progressive loss of kidney function
- Unknown etiology, not linked to diabetes, hypertension, or other common causes
- Clusters of CKDu
  - Past 2 decades
  - Hot / humid regions
  - Poor agricultural communities
  - Males
  - Aged 30 to 60 years
- Likely multifactorial

Center for Health, Work & Environment
Colorado School of Public Health

University of Colorado
Colorado State University
University of Northern Colorado
Leading hypotheses for CDKu epidemic

1. Occupational exposures
   • Repetitive dehydration
   • Heat stress
   • Acute kidney injury leading to CKDu

2. Environmental exposures
   • Nephrotoxic heavy metals in drinking water
   • Agrochemicals in work or home environment (dermal, inhalation, ingestion)
   • Bioaccumulation of chronic low exposures
Other hypothesized risk factors

• Nephrotoxic agents
  • NSAIDs
  • Nutrition (highly sweetened beverage consumption)
  • Tobacco
  • Infectious diseases, e.g. Leptospirosis

• Personal risk factors
  • Acclimatization differences
  • Genetics

• Additive effects
  • Dehydration + nephrotoxins
  • Failure to excrete toxicants -> increased bioaccumulation
Epidemiology of CKDu in Central America

- >20,000 deaths, 2005-09
- Leading cause of mortality in Nicaragua & El Salvador
- Main risk factors:
  - Lower altitude communities
  - Males
  - Occupation
    - Sugarcane: greatest prevalence
    - Cotton & mine: less frequent
    - Coffee: no excess disease
Evaluation of sugarcane workers in Guatemala

Objectives:

1. Describe disease epidemiology

2. Examine risk factors associated with kidney function across harvest
Sugarcane plantation practices

- 4,000 field workers hired annually
  - Local and migrant workers
  - Cane cutters and production workers

- Pre-employment health screening
  - Past medical history survey
  - Medical examination
  - Serum creatinine < 1.45 mg/dL
Sugarcane work

- Heavy exertion
- Long work hours (>8 hours)
- Intense heat & sun exposure
  - Heat conditions exceed OSHA recommendations
- Machetes to cut cane
- Paid by amount of cane cut (average 6 tons/day)
Health promotion practices

• Water, rest and shade guidelines
  • ≥ 2.5 L electrolyte solution
  • ≥ 16 L water
  • Breaks: 3 x 30 min and 1 x 60 min

• Field nurse aides and physicians
  • Educate: hygiene, nutrition and risks of using drugs and non-prescription medicines
  • Address health issues in field

• PPE
  • Goggles, hat, gloves, wrist / shin guards, boots
Methods

Pre-employment screening
- N=4000
- Survey
- Medical exam
- Serum creatinine to calculate eGFR

End of harvest rescreening
- N=407
- Survey
- Medical exam
- Serum creatinine to calculate eGFR

November 2015

May 2016

6-month harvest season

Photo courtesy of Amanda Walker
Results: Kidney function outcomes

Outcome 1: eGFR<60, end of harvest
- Incidence: 3% (21/407)
- 22% of 4000 workers left early
  - Worse kidney function at pre-employment
  - More likely to be from highlands

Outcome 2: ∆ eGFR
- Stable/improved: 64% (260/407)
- Decline: 36% (147/407)
  - 6% (24/407) decline eGFR>20%
### Results: Univariate risk factors of eGFR < 60

<table>
<thead>
<tr>
<th></th>
<th>Abnormal, eGFR &lt; 60</th>
<th>Normal, eGFR ≥ 60</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Residence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local</td>
<td>8%</td>
<td>92%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Migrant</td>
<td>2%</td>
<td>98%</td>
<td></td>
</tr>
<tr>
<td><strong>Pre-employment eGFR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>73%</td>
<td>37%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Normal</td>
<td>3%</td>
<td>97%</td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10%</td>
<td>90%</td>
<td>0.49</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10%</td>
<td>90%</td>
<td>0.49</td>
</tr>
<tr>
<td><strong>Days worked</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>141 (9)</td>
<td>146 (9)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Ave tons cut/day</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.3 (0.6)</td>
<td>5.8 (0.8)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Water intake/day (L)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-4</td>
<td>15%</td>
<td>85%</td>
<td>0.04</td>
</tr>
<tr>
<td>5-10</td>
<td>4%</td>
<td>96%</td>
<td></td>
</tr>
<tr>
<td>&gt; 10</td>
<td>4%</td>
<td>96%</td>
<td></td>
</tr>
<tr>
<td><strong>Soda or juice glasses/day</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 1</td>
<td>4%</td>
<td>96%</td>
<td>0.17</td>
</tr>
<tr>
<td>2</td>
<td>6%</td>
<td>94%</td>
<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>10%</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td><strong>Tobacco smoker</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>12%</td>
<td>88%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Never/Former</td>
<td>4%</td>
<td>96%</td>
<td></td>
</tr>
<tr>
<td><strong>NSAIDs, ≤3 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2%</td>
<td>98%</td>
<td>0.04</td>
</tr>
<tr>
<td>Yes</td>
<td>7%</td>
<td>93%</td>
<td></td>
</tr>
</tbody>
</table>
### Results: Multivariate risk factors of eGFR < 60

<table>
<thead>
<tr>
<th>Abnormal eGFR (&lt;60) at end of harvest*</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High pre-employment creatinine, &gt;1.25 mg/dL (ref: ≤ 1.25)</td>
<td>28.54 (9.68-84.18)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Current smoker (ref: Never/former)</td>
<td>2.90 (0.87-9.67)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*Controlled for age
## Results: Multivariate risk factors of $\Delta$ eGFR

<table>
<thead>
<tr>
<th>Change in eGFR during harvest*</th>
<th>Mean Difference ($\beta$)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worksite</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>-11.93</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>B ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local</td>
<td>-3.67</td>
<td>0.02</td>
</tr>
<tr>
<td>Migrant ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobacco Smoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>-4.90</td>
<td>0.03</td>
</tr>
<tr>
<td>Never/former ref</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Controlled for age
Summary

• Decline in kidney function related to both occupational and individual factors.

• 36% of workers had decline in kidney function, despite efforts to improve hydration, rest and shade.
  • No sig. differences between those who declined vs. improved: water intake, electrolyte solution intake, or physical exertion.
  • Drivers in addition to heat stress and dehydration may contribute.

• 22% of 4000 workers left early: healthy worker effect likely.
  • May have undiagnosed kidney injury.
  • May be acclimatization (migrant workers more likely to leave early).
Future research

• Collect quantitative measurements of environmental exposures and risk factors.
  • Nephrotoxic agrochemicals and heavy metals in water sources, NSAID use, tobacco use, hydration status and heat stress

• Collect data at earlier, multiple time points during season to evaluate disease progression and reasons workers leave early.

• Evaluate interventions that aim to increase hydration, rest and include tobacco cessation.
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• Carol Brown
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Criteria of typical CKD*

- Serum creatinine used to calculate reduced kidney function, eGFR
- One of the following criteria for > 3 months:
  1. GFR <60 mL/min per 1.73m²
     - (CKD stage 3 or worse)
  2. Marker of kidney damage found

### Table 10. Stages of Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or ↑ GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild ↓ GFR</td>
<td>60–89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30–59</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15–29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 (or dialysis)</td>
</tr>
</tbody>
</table>

*National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (KDOQI)
Agribusiness Partnership

• Pantaleon – major sugar cane producer in Central America

• Goal - to assess and improve the health, safety, and well-being of its sugarcane workers in Guatemala

• Independent analysis and authority to publish findings
Results: Demographics

Individual factors
• Age: 28 yrs (median), 18-67y
• Migrant: 50%
• Used pesticides on own land: 39%
• ≥ 1 sugary drinks: 98%
• NSAID use in past 3 months: 70%
• Current smokers: 13%

Occupational factors
• Cane cutters: 82%
• Worksite A: 76%
• Harvests worked: 8 (median)
• >10 L water at work per day: 74%
• Electrolyte solution per day: 2.5 L (median)