

eGFR decline and prior dysuria among Nicaraguan sugarcane workers

Zsuzsanna Jeney,¹ Daniel E. Weiner,² James S. Kaufman,³ Tiffany L. Stallings,¹ Nathan McCray,¹ Yan Ma,⁴ Michael Winter,⁶ Alejandro Riefkohl Lisci,⁵ Oriana Ramírez-Rubio, MD,⁵ Juan Jose Amador,⁵ Damaris López-Pilarte,⁵ Ann Aschengrau,⁵ Daniel R. Brooks,⁵ Katie M. Applebaum¹

¹Department of Environmental and Occupational Health, Milken Institute School of Public Health, The George Washington University, Washington, DC, USA, ²Division of Nephrology, Tufts Medical Center, Boston, MA, USA, ³Division of Nephrology, VA New York Harbor Healthcare System and New York University School of Medicine, New York, NY, USA, ⁴Department of Biostatistics and Bioinformatics, Milken Institute School of Public Health George Washington University, Washington, DC, USA, ⁵Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA ⁶Biostatistics and Epidemiology Data Analytics Center, Boston University School of Public Health

Background

- Nicaraguan sugarcane workers have elevated prevalence of chronic kidney disease of unknown origin, referred to as Mesoamerican Nephropathy (MeN)
- MeN lacks traditional risk factors (diabetes, obesity, hypertension); it mainly affects young male agricultural workers <50 years of age
- Dysuria (painful urination) is also common among male sugarcane workers
- Suspected risk factors of MeN and dysuria are climatic heat and strenuous physical labor
- It is unknown if dysuria may itself increase the risk of kidney dysfunction among those with high risk of MeN

Objective: To examine whether experiencing dysuria was associated with subsequent reduced kidney function among sugarcane workers

Methods

- At a sugarcane planation in northwest Nicaragua, 190
 workers were sampled within job type and year, and their
 employment and medical records were abstracted (Table
 1). Medical data included symptoms, physician diagnosis,
 laboratory results, including serum creatinine
- Reduced estimated glomerular filtration rate (eGFR) was analyzed as a binary outcome, first as eGFR < 90 and then as < 60 mL/min/1.73m2, for analysis of mild or moderate eGFR reduction, respectively
- To examine the association between prior dysuria diagnosis (ever/never) and reduced eGFR, logistic regression based on generalized estimating equations for repeated events was used to estimate the odds ratio (OR) and the 95% confidence interval (CI), adjusting for age, cumulative harvest seasons worked, proportion seasons worked as cane cutter, and period of harvest

Table 1. Characteristics of male Nicaraguan sugarcane workers (July 1, 1997 – Jun 30, 2010)

| | n (%) | Median (IQR) |
|--|------------|--------------|
| Total workers | n=190 | |
| | | |
| Age at first encounter, years | | |
| <21 | 35 (18.6) | |
| 21-30 | 79 (42.0) | |
| 31-40 | 57 (30.3) | |
| 41-50 | 9 (4.8) | |
| >50 | 8 (4.3) | |
| | | |
| Employment characteristics | | |
| Ever a cane cutter, n(%) | 78 (41.1) | |
| Work months as a cane cutter | | 25.5 (40) |
| | | |
| Medical events | | |
| Ever dysuria ^b (625 total events) | 134 (70.5) | |
| Events per worker ^b | | 3(4) |
| | | |
| eGFR characteristics (1676 total eGFR) | | |
| Ever eGFR < 90° (708 total eGFR<90) | 127 (66.8) | |
| eGFR < 90 per worker | | 3 (4) |
| | | |
| eGFR < 60° (190 total eGFR < 60) | 60 (31.9) | |
| eGFR < 60 per worker | | 2 (3) |

Results

- 70.5% of workers had at least one dysuria diagnosis, 42.3% and 11.4% of total eGFR measurements were < 90, and < 60, respectively
- 72.8% eGFR measurements were preceded by at least one dysuria diagnosis
- After adjusting for confounders, experiencing prior dysuria was significantly associated with eGFR < 90 (OR=2.27 (95% CI 1.4, 3.7)) and eGFR < 60 (OR=3.87 (95% CI 1.8, 8.3)) (Table 2)

Discussion

- Dysuria diagnosis was associated with increased risk of reduced eGFR
- Dysuria may reflect mechanical trauma from crystalluria, which may contribute to transient changes in kidney function
- The findings suggest that prevention of crystalluria and/or dysuria may reduce the risk of kidney function loss, though the results need to be replicated

Strengths & Limitations:

- Longitudinal retrospective cohort design with 13-year followup period
- Reliance on combined data from employment history and medical records
- Association between dysuria and reduced eGFR might be underestimated due to healthy worker effect
- We lacked information on use of OTC NSAIDs which may be taken to alleviate pain while experiencing dysuria, as well as behavioral factors such as alcohol consumption and smoking

Table 2. Association between eGFR < 90 and <60 and prior dysuria diagnosis among Nicaraguan sugarcane workers

| | Total number of eGFR | Number of eGFR < 90 | Number of eGFR ≥ 90 | Crude OR (95% CI) | Adjusted ^a OR (95% CI) |
|------------------|----------------------|---------------------|---------------------|----------------------|--------------------------------------|
| | n (%) | n (%) | n (%) | | |
| All encounters | | | | | |
| No prior dysuria | 456 (27.2) | 96 (13.6) | 360 (37.3) | reference | reference |
| Prior dysuria | 1218 (72.8) | 612 (86.4) | 606 (62.7) | 3.01 (2.0, 4.6) | 2.27 (1.4, 3.7) |
| Total | 1674 (100) | 708 (100) | 966 (100) | | |

| | Total number of eGFR | Number of eGFR < 60 | Number of eGFR ≥ 60 | Crude OR (95% CI) | Adjusted ^a OR (95% CI) |
|------------------|----------------------|---------------------|---------------------|----------------------|-----------------------------------|
| | n (%) | n (%) | n (%) | | |
| All encounters | | | | | |
| No prior dysuria | 456 (27.2) | 12 (6.3) | 444 (29.9) | reference | reference |
| Prior dysuria | 1218 (72.8) | 178 (93.7) | 1040 (70.1) | 5.00 (2.6, 9.5) | 3.87 (1.8, 8.2) |
| Total | 1674 (100) | 190 (100) | 1484 (100) | | |

^aAdjusted for age, cumulative harvest seasons worked as cane cutter, and period of harvest