2018

Local Attitudes and Prevention around the Nicaraguan Sugarcane Worker with Chronic Renal Disease

Matt Cyr
Augsburg University

Local Attitudes and Prevention around the Nicaraguan Sugarcane Worker with Chronic Renal Disease

by

Matt Cyr

Alicia Quella

Paper Submitted in Partial Fulfillment

Of the Requirements for the Degree

Of Master of Science

Physician Assistant Studies

Augsburg College

7/25/17

TABLE OF CONTENTS

INTRODUCTION

An epidemic of chronic kidney disease (CKD) in Central America and Nicaragua is referred to as Mesoamerican nephropathy (MeN).[1] It's estimated that the death toll for MeN over the past two decades has reached at least 20,000.[2] Nicaragua is included in the 10 highest overall mortality rate from kidney disease in the world.[3] MeN disproportionately affects young, male agricultural workers who do not exhibit traditional risk factors for CKD such as hypertension and diabetes.[1] A consistent risk factor for MeN is heavy manual labor in the heat, often temperatures over 35 °C with high humidity.[4] Workers generally wear long pants and long sleeves with other heavy protective gear and have an average work time of 4 hours but may vary substantially.[10] The epidemic is observed largely in sugarcane farmers in the hotter, lower altitudes on the Pacific coast.[3] Although the exact cause is unknown, many mechanisms of pathophysiology have been proposed and studied. It is important to note traditional nephrotoxic exposures may play a role and contribute to disease. These include consumption of nephrotoxins: non-steroidal anti-inflammatory drugs (NSAIDS), certain antibiotics, or exposures to heavy metals, pesticides, and fertilizers. The following is a review of the literature, an exploration of the providers' and citizens' knowledge around this disease, what is currently being done in treatment and prevention, and suggestions for improvements. This is accomplished through an analysis of published literature and personal interviews on a class visit to Nicaragua. The current hypothesis is there is inconsistent agreement upon the causes, diagnosis, treatment, and prevention of MeN. This may be due to improper education of providers, misunderstandings in the community, or simply inconsistent or understudied evidence. In this low resource and low income country, prevention is key in preventing CKD; the most emphasis must be placed on

electrolyte hydration and suitable working conditions for the workers such as shorter shifts, lighter clothing, more frequent breaks, and shade.

BACKGROUND

Prerenal kidney disease

The literature agrees that Mesoamerican nephropathy is prerenal in origin. Prerenal kidney disease, also known as acute kidney injury or acute renal failure, is defined as one or more of three criteria: the first two are a rise in serum creatinine of at least 0.3 mg/dL over a 48-hour period and/or ≥1.5 times the baseline value within the seven previous days. The third criterion is a urine volume of ≤0.5 mL/kg per hour for six hours.[5] Ultimately, prerenal disease is renal ischemia due to a decrease in tissue perfusion, which results in acute tubular necrosis, a type of intrarenal disease. Common causes of prerenal disease include volume depletion, hypotension, edematous states, renal artery stenosis, or certain drugs or chemicals referred to as nephrotoxins. Many proposed mechanisms are detailed in how renal ischemia develops in regards to the Nicaraguan sugarcane farmer population.

Proposed pathophysiology

Researchers are typically interested in the sugarcane farmer population since renal disease occurs in those who lack traditional risk factors such as older age, diabetes, and hypertension. Heat stress and dehydration are hypothesized to be the main players in kidney injury across the literature and is supported by the most recent data.[1-5, 8-10] Suggested pathophysiology explained by heat stress and excessive work includes rhabdomyolysis, hyperuricemia, hyperuricosuria, hyperosmolality-induced activation of aldose reductase-fructokinase pathway, and vasopressin effects.[3-4,9,11,12] Since the main cause of prerenal disease

is dehydration and/or hypovolemia, an elucidation is warranted. Sugarcane farmers are exposed to intense heat that exceeds recommended work practices made by the US Occupational Safety and Health Administration.[3] Most sugarcane workers drink 1-2 liters of water per hour while working. However, this excess hyponatremic intake and excess perspiration (sweat being hypotonic) results in increased serum osmolality during the day, reduced urine volumes with elevated urinary osmolality, and high urine specific gravity.[3] This is reflective of a hypovolemic state. Therefore, those working in sugarcane fields are repeatedly dehydrated. One must supplement the fluid with electrolytes to maintain an effective balance in tonicity and volume. Repeated entry into hypovolemic states ultimately results in ischemia, renal disease, and renal failure. Specifically, kidney morphology of developing CKD after AKI is described in a sample of rats as glomerular hypertrophy, glomerulosclerosis, podocyte foot-process effacement and tubulointerstitial damage.[8] This can be compared to human biopsies which show tubular atrophy, interstitial fibrosis, and global glomerulosclerosis, often with an ischemic component.[10] One group also offers an explanation of heat stress driven by global warming.[9] Moreover, as mentioned earlier, the disease is multifactorial and could include concurrent use of NSAIDs and exposure to different nephrotoxins.[4,9-11,12] A useful depiction of proposed mechanisms for sugarcane farmers is seen in Figure 1.

The studies reviewed include many different diagnostic laboratory tests to determine the extent of disease and renal function. Some of these include a urinalysis, blood urea nitrogen, serum creatinine, serum uric acid, urine specific gravity, urine pH, urine osmolality and volume, glomerular filtration rate, and other investigational biomarkers of urine and serum. More specifically, one can biopsy the renal tissue and determine the extent of disease by histology.

Current Prevention

Electrolyte supplementation to fluids offered protection for CKD of MeN in two of the studies reviewed.[4,11] Additionally, adequate hydration with water and/or water with electrolytes has been reported to prevent an increase in serum uric acid levels that occur with heat and exercise.[3] Although hydration is an obvious preventative measure to be taken, barriers exist for Nicaraguan sugarcane farmers in obtaining necessary adequate fluid and electrolyte solutions. Many of the farmers live on the Pacific coast without means to access the healthcare in one of the larger cities in Nicaragua. Additionally, the cost of healthcare poses an obstacle as the GDP per capita was $5,300 in 2016.[6] All of the articles reviewed suggest offering preventative measures, however fail to detail specifically how one would implement prevention.

An impressive project by Edefinti et al. was done in 2010 to target the pediatric population in Nicaragua.[7] A collaborative project between nephrology units of Milan, Italy, and Managua, Nicaragua was aimed to improve the diagnosis and treatment of renal disease and CKD in Nicaraguan children. The team trained and developed a specialized unit to cover 61% of the Nicaraguan pediatric population for renal disease. They successfully implemented the project through private and public Italian funds and a Nicaraguan charity foundation. Although this is one extreme in prevention towards kidney disease, it is an example how simple training and education through worldwide collaboration can leave a healthcare system with clinical autonomy.

Somewhat easier to apply, the Latin American Society of Nephrology and Hypertension (SLANH) recognizes MeN in agricultural workers across Latin America and proposes a Hydration for Health initiative in prevention. Their website, symposiums, and outreach aim to spread awareness of the at-risk population and to ultimately prevent the disease. Education and

outreach to at-risk populations through initiatives proposed by SLANH will ultimately cure this easily preventable condition.

Possibly the organization that understands the epidemic in this population the best is the La Isla Network. They are an organization of professionals around the world who are dedicated in ending the epidemic of CKD through improving working conditions, standardizing research protocols, supporting responsible transitions to modernizing industrial practices, and providing data-driven policy recommendations. Directly, their intervention approach through a program called the WE Program is the first intervention protocol to evaluate ways to reduce the harmful effects of heat stress and CKD in sugarcane workers. It improves working conditions for cane cutters by providing them with water, rest, shade, apparel, and training. Researchers track improvements in worker health and productivity. They work with institutions around the world such as the U.S. Occupational Safety and Health Administration and the National Institute for Occupational Safety and Health at the Centers for Disease Control.

Patient Encounter and Sugarcane History

Carmen Rios, a 63-year-old former Nicaraguan sugarcane worker was interviewed during a class visit to Nicaragua. Carmen invited the class to her home to tell her story. Sugar production began in 1890 with Italian immigrants. The wealthy Pellas family owns many companies in Nicaragua, and today owns the sugarcane farms. In 1965, the company started using pesticides such as DDT. Shortly after, the workers became ill. Since there were not traditional risk factors present in the young, male population, it was often too late when renal disease was diagnosed. Continuing into the 1990s, an epidemic was ensuing and workers knew they were going to the fields to die. Due to the poor economy, many citizens have no other means for income. Carmen attributes the disease to the pesticides, where the current literature

suggests repeated dehydration is the cause of renal failure. When the epidemic was brought to the government's attention, they ignored the problem to avoid conflict with the corrupt Pellas family. The Central University of Nicaragua and other universities around the world began conducting studies on the sugarcane worker population. Carmen states some of the studies were funded by the Pellas, which tried to suppress or falsify any significant findings by other studies, further contributing to their corruptive reputation. After so many significant findings, as outlined previously, the Pellas and the government were forced to change.

METHODS

Articles were identified through a literature search of the online database PubMed.gov using the keywords "Mesoamerican nephropathy," "chronic renal failure," "acute renal failure," "Nicaragua," "sugarcane farmer," and "prevention." The search was limited to the English language. Supporting statistics and background information was through a Google search using the same key words as above.

Anecdotal evidence included a class visit to Nicaragua where we conversed with individuals around the issue including Carmen Rios, a former sugarcane worker and current lobbyist for sugarcane worker rights. Language interpretation was provided by Juan Carlos Lopez.

DISCUSSION

Patient and Professional Interviews

After having her brother, father, grandfather, and her husband die, Carmen Rios has dedicated her life's work to advocating for this disease in this specific population. Lobbying for

treatment and preventative measures have influenced large changes in the Nicaraguan government surrounding this condition. Chronic disease treatment such as chronic renal disease has always been covered in the social healthcare system in Nicaragua. However, efforts by activists like Carmen have influenced the government and the Pellas family to make changes. The government now provides calcium and vitamin supplementation, hypertension medication, and medication and nutritional education to those who are working in the sugarcane fields. Also, for those who worked the fields during the Sandinista Revolution, compensation is offered for the potentially harmful pesticides used. $150 USD is given to each affected worker every month. Furthermore, the Pellas no longer use harmful, nephrotoxic pesticides. A type of fungus is now used as a safe alternative. Additionally, all workers are provided with purified water and new employees are screened as part of a health surveillance program that is designed to identify workers with elevated serum creatinine.[11] Those with elevated serum creatinine are not hired. Despite these improvements, there are still challenges. Carmen states the company targets children as employees, of which many are orphans. The workers are subject to 18-hour workdays. One current policy change for Carmen and her colleagues is changing the 18-hour work day into an 8-hour workday. If dehydration, heat stress, and nephrotoxins are targeted in prevention by the government, SLANH, and many nonprofit organizations such as La Isla Network, one should see a change in the incidence of Mesoamerican nephropathy.

While Carmen lived most of her life in a rural community, it is important to address the opinions of those in the inner city of Managua, Nicaragua. The topic was tackled by Juan Pablo, a health promoter in the community. He stated the disease in the city is more focused on the traditional risk factors of kidney disease such as hypertension and diabetes. He focuses on

educating the community about the importance of a balanced diet. Juan doesn't specifically interact with the sugarcane farmer population, however he attests the disease to pesticide use.

Published Division

Another challenge within the community is the extensive belief that nephrotoxic chemicals are the main cause of the epidemic. Several studies have found an association between self-reported chemical use and CKD.[11] In order to target the root of the problem, education across the community must involve proper hydration, rest, and shade. There is also a strong belief among local physicians and pharmacists that inadequate hydration and strenuous labor are the main occupational factors responsible for CKD.[12] And there may be a fear of the workers to hydrate during the day due to the worker's belief of ingesting contaminated water.[12]

A study that interviewed 10 physicians and 9 pharmacists focused on the attitudes of many issues surrounding CKD in those working hard labor jobs.[12] Some main findings of the study that are pertinent to the issue being discussed is first, there was an agreement of the increasing number of CKD cases each year in this population. One physician suggested this could be due to the increased awareness of the disease in the population or there is truly an increasing epidemic. The repeated theme again supported, is that there is a disagreement about the true cause. Nine physicians referred to an exposure at work, but seven stated the major player was exposure to the sun and heat, and all agreed that the disease was multifactorial. However, eight of nine pharmacists blame contaminated water or dehydration. It's important to highlight the discrepancy due to it affecting how renal disease is treated, prevented, and how policy will be developed. Figure 2 illustrates the strength in relationships between renal disease and its causes based on the perceived opinions of the interviewed physicians and pharmacists.

Suggestions

Areas for improvement include expanded government policy. Due to perceived nephrotoxic chemicals still being used, the Nicaraguan government could follow El Salvador's vote to ban 53 agrichemicals including 2,4-D, paraquat, DDT, and glyphosate, among others.[11] Additionally, regional preventative health programs should be developed in the workplace, community level, and in the healthcare setting.[12] Surveillance programs should be implemented in any setting where hard, manual labor is being done. Some examples of labor in Nicaragua that put workers at risk include agriculture workers, miners, construction workers, and bricklayers. Country wide policy should be developed to focus on heat exposure, time working, hydration, and overall health. Furthermore, assessments of water quality in communities should be tested to rule in or out the potential cause for nephrotoxic chemicals in water consumption. Lastly, education for providers in Nicaragua should be standard and consistent when diagnosing and treating Mesoamerican nephropathy. More agreement between healthcare practitioners, researchers, and the government will hopefully trickle down to a consensus between communities. This would result in proper directed treatments and prevention measures across the region.

Ultimately, these suggestions should all attempt to target CKD with prevention in mind. The most important goal is to prevent the prerenal disease by increasing blood flow, electrolytes, and nutrients to the kidneys, thus averting ischemia and intestinal disease. This is accomplished through simple and affordable methods including fluid and electrolyte hydration, further supplemented by rest, shade, frequent breaks, and cool clothing. Efforts toward these direct causes will have the most impact and most favorable outcomes without having to acquire additional resources.

Personal Reflection and Public Health

The public health issue for the sugarcane workers in Nicaragua cannot be fully understood until one dives into the culture of the affected population. This one disease brings light to all other issues surrounding Nicaraguan healthcare and government. Large barriers exist when accessing healthcare, despite the socialized system. Dr. Leonel Arguello, an epidemiologist and president of the Nicaraguan Association for general practitioners, stated during a visit that, "70% of Nicaraguans make less than $2 per day." If an aspect of one's health is not provided for, most will not be able to cover the bill. Furthermore, with limited income, families are not able to physically transport themselves or their family to the healthcare centers in the city, away from the Pacific coast. There are few rural healthcare centers to provide care to those in rural areas. Citizens may have to take an entire day off work to see a provider. A mother caring for her children may not have the ability for someone else to watch her children when she needs to see a provider, thus she ends up staying home. Finally, if one cannot access the healthcare center, they are not able to aid themselves and their family with preventative knowledge of many diseases. Patients also may not be able to access the internet or other educational options to learn how to supplement their health. They rely on those in their community for information instead of those at the healthcare centers. However, those that do make it to the healthcare center for Mesoamerican nephropathy, the difference in attitudes differ when approaching the disease. Thus, when they return home, they are provided with education that may or may not be correct and standard, and further put the community at risk in terms of prevention.

CONCLUSION

Renal disease in sugarcane workers in Nicaragua and Central America is a unique population that is experiencing high mortality. Many reasons have been proposed when trying to explain the cause of the disease. Multifactorial features of dehydration, heat stress, and nephrotoxins may all contribute in some way, however most literature agrees dehydration and heat stress are the main players. There is already a great awareness about this disease due to advocacy work from nonprofits, published literature, and lobbying citizens such as Carmen Rios. However, there is a significant disagreement between Nicaraguan providers about the cause of the disease and the way to approach it through prevention. This disagreement leads to misconceptions in the community. For example, the consensus of literature suggests focusing on hydration as preventative measures, while Carmen and Juan believe contaminated water is the issue. Also, pharmacists and physicians interviewed do not entirely agree with each other. The opinions include different avenues toward solving the problem. The analysis of the literature, Nicaraguan citizens, and local providers demonstrate how a public health issue can uncover larger problems in healthcare and government, including the access and delivery of healthcare. Directly, one can target the public health issue through better workers' rights, additional research, and supplemental and specific prevention. Indirectly, the healthcare provider education must be improved through standard protocols and consistent education across all providers. Again, this disease proves to be one exposing larger difficulties and complexities across nations in the way healthcare is approached.

REFERENCES

1. Laws RL, Brooks DR, Amador JJ, et al. Biomarkers of kidney injury among Nicaraguan Sugarcane Workers. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. 2016;67(2):209-217. http://www.ncbi.nlm.nih.gov/pubmed/26454687. doi: 10.1053/j.ajkd.2015.08.022.

2. Oriana Ramirez-Rubio, Michael D McClean, Juan José Amador, Daniel R Brooks. An epidemic of chronic kidney disease in Central America: An overview. *Journal of Epidemiology and Community Health (1979-)*. 2013;67(1):1-3. http://www.jstor.org/stable/43281463. doi: 10.1136/jech-2012-201141.

3. Roncal-Jimenez C, García-Trabanino R, Barregard L, et al. Heat stress nephropathy from exercise-induced uric acid crystalluria: A perspective on mesoamerican nephropathy. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. 2016;67(1):20. http://www.ncbi.nlm.nih.gov/pubmed/26455995.

4. Wesseling C, Aragón A, González M, et al. Heat stress, hydration and uric acid: A cross-sectional study in workers of three occupations in a hotspot of mesoamerican nephropathy in nicaragua. *BMJ Open*. 2016;6(12):e011034. http://search.proquest.com/docview/1847397235. doi: 10.1136/bmjopen-2016-011034.

5. Erdbruegger U. Etiology and diagnosis of prerenal disease and acute tubular necrosis in acute kidney injury. In: Post T, ed. *UpToDate*. Waltham, Mass.: UpToDate; 2017. www.uptodate.com. Accessed May 7, 2017.

6. Central Intelligence Agency. The world factbook: Nicaragua. https://www.cia.gov/library/publications/the-world-factbook/geos/nu.html.

7. Edefonti A, Marra G, Castellón Perez M, Sandoval Díaz M, Sereni F. A comprehensive cooperative project for children with renal diseases in nicaragua. *Clinical nephrology*. 2010;74 Suppl 1:S119. http://www.ncbi.nlm.nih.gov/pubmed/20979976.

8. Wijkström J, González-Quiroz M, Hernandez M, et al. Renal morphology, clinical findings, and progression rate in mesoamerican nephropathy. *American Journal of Kidney Diseases*. 2017. doi: 10.1053/j.ajkd.2016.10.036.

9. Roncal-Jimenez CA, García-Trabanino R, Wesseling C, Johnson RJ. Mesoamerican nephropathy or global warming nephropathy? *Blood purification*. 2016;41(1-3):135-138. http://www.ncbi.nlm.nih.gov/pubmed/26766409. doi: 10.1159/000441265.

10. García-Trabanino R, Jarquín E, Wesseling C, et al. Heat stress, dehydration, and kidney function in sugarcane cutters in el salvador – A cross-shift study of workers at risk of mesoamerican nephropathy. *Environmental Research*. 2015;142:746-755. http://www.sciencedirect.com/science/article/pii/S0013935115300281. doi: 10.1016/j.envres.2015.07.007.

11. Laws RL, Brooks DR, Amador JJ, et al. Changes in kidney function among nicaraguan sugarcane workers. *International journal of occupational and environmental health*. 2015;21(3):241-250. http://www.ncbi.nlm.nih.gov/pubmed/25631575. doi: 10.1179/2049396714Y.0000000102.

12. Ramirez-Rubio O, Brooks DR, Amador JJ, Kaufman JS, Weiner DE, Scammell MK. Chronic kidney disease in nicaragua: A qualitative analysis of semi-structured interviews with physicians and pharmacists. *BMC public health*. 2013;13(1):350. http://www.ncbi.nlm.nih.gov/pubmed/23590528. doi: 10.1186/1471-2458-13-350.

APPENDIX

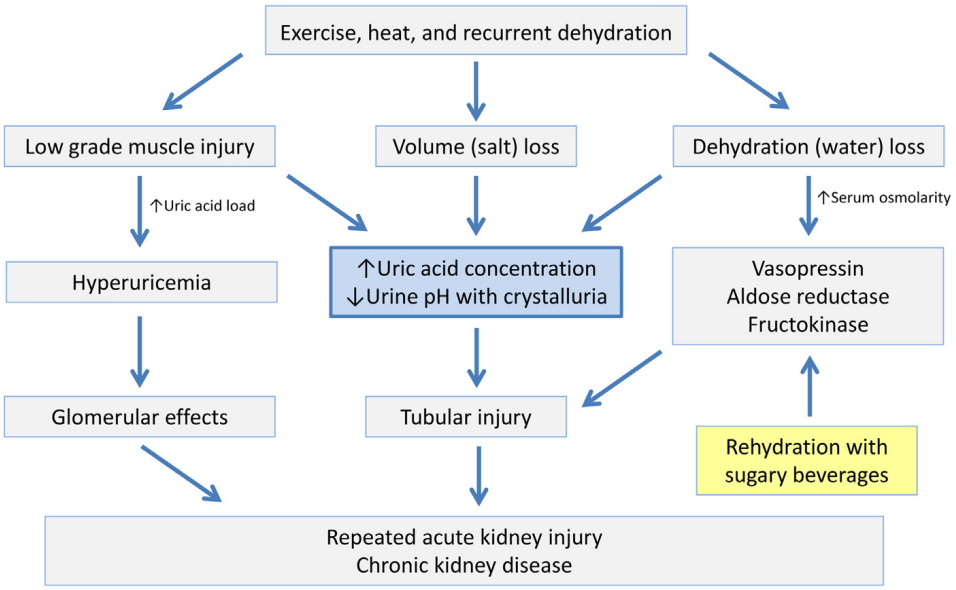

Figure 1: Proposed mechanisms for Mesoamerican nephropathy.[3]

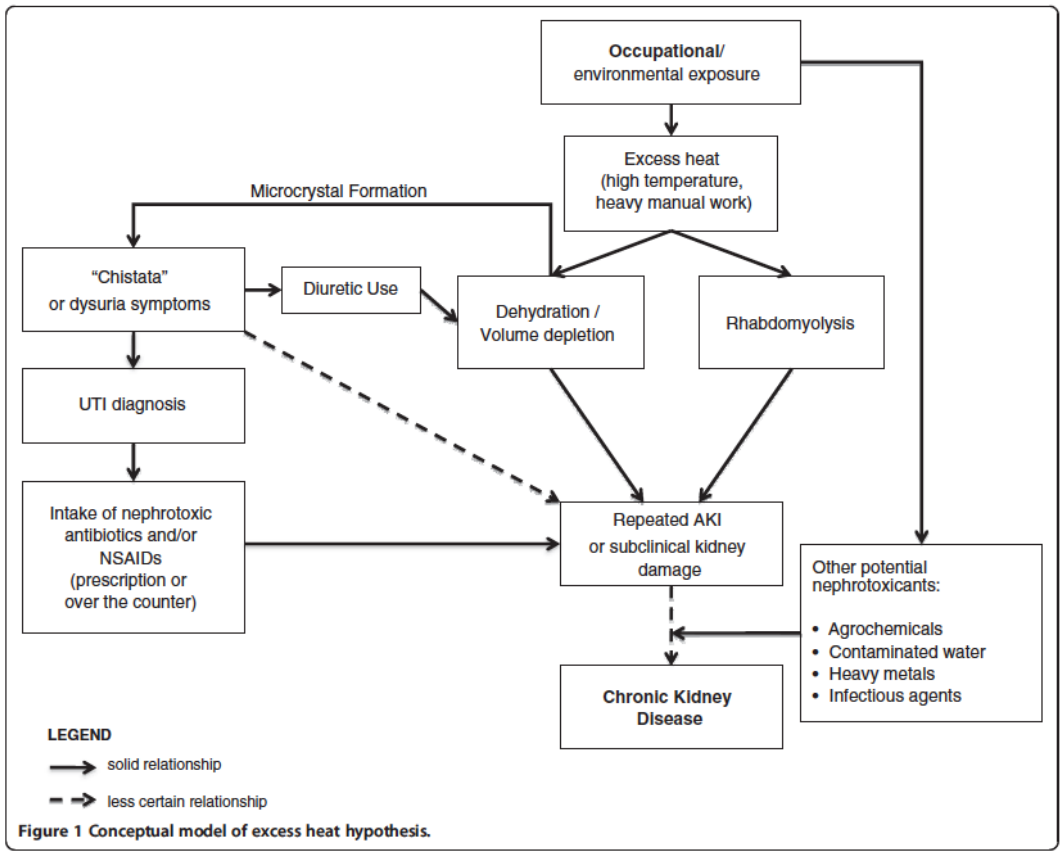

Figure 2: Nicaraguan physicians' and pharmacists' certainty of related causes to renal disease.

AUGSBURG UNIVERSITY

Augsburg University Institutional Repository Deposit Agreement

By depositing this Content ("Content") in the Augsburg University Institutional Repository known as Idun, I agree that I am solely responsible for any consequences of uploading this Content to Idun and making it publicly available, and I represent and warrant that:

- I am *either* the sole creator or the owner of the copyrights in the Content; or, without obtaining another's permission, I have the right to deposit the Content in an archive such as Idun.
- To the extent that any portions of the Content are not my own creation, they are used with the copyright holder's expressed permission or as permitted by law. Additionally, the Content does not infringe the copyrights or other intellectual property rights of another, nor does the Content violate any laws or another's right of privacy or publicity.
- The Content contains no restricted, private, confidential, or otherwise protected data or information that should not be publicly shared.

I understand that Augsburg University will do its best to provide perpetual access to my Content. To support these efforts, I grant the Board of Regents of Augsburg University, through its library, the following non-exclusive, perpetual, royalty free, worldwide rights and licenses:

- To access, reproduce, distribute and publicly display the Content, in whole or in part, to secure, preserve and make it publicly available
- To make derivative works based upon the Content in order to migrate to other media or formats, or to preserve its public access.

These terms do not transfer ownership of the copyright(s) in the Content. These terms only grant to Augsburg University the limited license outlined above.

Initial one:

MC I agree and I wish this Content to be Open Access.

___ I agree, but I wish to restrict access of this Content to the Augsburg University network.

Work (s) to be deposited

Title: Local Attitudes and Prevention around the Nicaraguan Sugarcane Worker with Chronic Renal Disease

Author(s) of Work(s): Matthew Cyr, Alicia Quella PhD

Depositor's Name (Please Print): _____

Author's Signature: _____ Date: 8/21/18

If the Deposit Agreement is executed by the Author's Representative, the Representative shall separately execute the Following representation.

I represent that I am authorized by the Author to execute this Deposit Agreement on the behalf of the Author.

Author's Representative Signature: _____ Date: _____