

Third International Workshop on Chronic Kidney Diseases of Uncertain/Non-Traditional Etiology in Mesoamerica and Other Regions

March 20 – 22, 2019
San José, Costa Rica



https://tools.niehs.nih.gov/conference/ckd_2019



Table of Contents

Agenda ----- 3
Working Group Descriptions ----- 9
Poster Abstracts ----- 20
Participant List-----101



Agenda





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Workshop Agenda

Red and Aqua rooms are located on the third floor.

Tuesday, March 19, 2019

4:00 – 7:00 p.m. Registration **Red Room Foyer**
Note: All participants must sign a declaration of interests form before completing their registration.

Wednesday, March 20, 2019

7:00 – 8:00 a.m. Optional Morning Sessions

Heat Exposure Assessment for Epidemiology Studies **Aqua C Room**

- Vidhya Venugopal, Sri Ramachandra University, India; Daniel Rojas, Universidad Nacional, Costa Rica; Andrés Robles, SALTRA, TEC, Costa Rica

Epidemiology Study Design

- English Lecture: Ben Caplin, University College London **Aqua A Room**
- Spanish Lecture: Marvin González Quiroz, Center for Research in Health, Work, and Environment (CISTA)/UNAN-León, Nicaragua **Aqua D Room**

7:30 – 8:15 a.m. Registration **Red Room Foyer**
Note: All participants must sign a declaration of interests form before completing their registration.

8:30 a.m. Inauguration **Red Room**
Welcome and Opening Remarks From Funders, Organizers, and Host Institution

- Dr. Denis Angulo Alguera, Vice Minister of Health, Costa Rican Ministry of Health
- Dr. Román Macaya Hayes, Caja Costarricense de Seguro Social
- Dr. Linda Birnbaum, Director, National Institute of Environmental Health Sciences (NIEHS) and National Toxicology Program, National Institutes of Health (NIH), U.S.
- Dr. Enrique Pérez-Flores, Pan American Health Organization (PAHO)/ World Health Organization (WHO), Costa Rica
- Dr. Poonam Khetrpal Singh, Regional Director, WHO South East Asia Region
- Representative, Vice Rectory for Research, Universidad Nacional Costa Rica (UNA)
- Dr. Ricardo Correa-Rotter, Consortium for the Epidemic of Nephropathy in Central America and Mexico (CENCAM)
- Dr. Jennifer Crowe, Central American Program for Health Work and Environment Program (SALTRA), IRET-Universidad Nacional, Costa Rica





9:30 a.m.	Meeting Objectives and Instructions <ul style="list-style-type: none"> • Marvin González Quiroz, CISTA UNAN-León, Nicaragua; CENCAM Board Member; Workshop Organizing Committee 	Red Room
9:45 a.m.	Keynote Address Endemic CKDu: Is It Primarily an Occupational Disease? <ul style="list-style-type: none"> • Catharina Wesseling, Karolinska Institutet, Sweden; La Isla Network, Washington, D.C. 	Red Room
10:30 a.m.	Break and Poster Viewing	Red Room Foyer
11:00 a.m.	World Café: Meet Others, Share Experiences, and Exchange Ideas <ul style="list-style-type: none"> • Moderator: Kristina Jakobsson, University of Gothenburg, Sweden, CENCAM Co-Chair, Workshop Organizing Committee 	Aqua Rooms
12:30 p.m.	Lunch	Red Room Foyer
1:30 p.m.	Plenary Presentations by All Working Groups Brief introductions of working group themes, including an overview of the present science and questions that remain to be solved so that all delegates have a common understanding. <ul style="list-style-type: none"> • Moderators: Daniel Brooks, Boston University, CENCAM Board Member, Workshop Organizing Committee; and Jennifer Crowe, SALTRA, IRET, UNA, CENCAM, Workshop Organizing Committee 	Red Room
3:30 p.m.	Break and Poster Exhibition <i>Authors present</i>	Red Room Foyer
4:30 p.m.	Working Groups: Session One Introductory session, discussion of relevant or past work that can be shared, planning for day two of workshop <ul style="list-style-type: none"> • Analytical Epidemiology • Biomarkers of Renal Function • Clinical Presentation and Treatment • Heat Load/Dehydration and Work Load • Assessing Exposures to Pesticides, Other Agrochemicals, and Metals • Surveillance and Screening • Molecular Approaches to CKDu: Genetics, Epigenetics, and Infectious Disease • Pathology 	Red Room Second Floor, Little Room Aqua A Room Aqua D Room Aqua C Room Aqua B Room Second Floor, Black 1 Room Second Floor, Black 2 Room
5:30 p.m.	Reflections From the Day and Adjourn <ul style="list-style-type: none"> • Aurora Aragon, CISTA UNAN-León, Nicaragua • Christer Hogstedt, Karolinska Institutet, Sweden 	Red Room
5:30-6:00 p.m.	Posters Available for Further Viewing	Red Room Foyer





Thursday, March 21, 2019

7:00 – 8:15 a.m.	<p>Optional Morning Sessions</p> <p>Pesticides and Agrochemicals Exposure Assessment</p> <ul style="list-style-type: none"> • Spanish Lecture: Aurora Aragon, CISTA UNAN-León, Nicaragua; Andres Cardenas, University of California, Berkeley; Lesliam Quiros-Alcala, University of Maryland • English Lecture: Katherine James, University of Colorado-Anschutz Medical Campus; Alison Sanders, Icahn School of Medicine at Mount Sinai <p>Update on Biomarkers of Renal Function</p> <ul style="list-style-type: none"> • Carl-Gustaf Elinder, Karolinska Institutet, Sweden 	<p>Aqua A Room</p> <p>Aqua C Room</p> <p>Aqua D Room</p>
8:30 a.m.	<p>Summary of Key Points From Previous Day and Starting Points for Day Two</p> <ul style="list-style-type: none"> • Nalika Gunawardena, National Professional Officer (Non-Communicable Diseases and Health Systems), WHO Country Office, Sri Lanka; Workshop Organizing Committee • Carolina Guzmán-Quilo, SALTRA-Guatemala 	Red Room
9:00 a.m.	Working Groups: Session Two	
10:30 a.m.	Break and Poster Viewing	Red Room Foyer
11:00 a.m.	Working Groups: Session Three	
12:30 p.m.	Lunch	Red Room Foyer
1:30 p.m.	<p>Working Groups: Session Four</p> <p>Cross-Cutting Discussions Across Working Groups</p>	
3:30 p.m.	<p>Break and Poster Exhibition</p> <p><i>Authors present</i></p>	Red Room Foyer
4:30 p.m.	<p>Working Groups: Session Five</p> <p>Preparation of Working Group End-of-Conference Summaries and Planning for Post-Conference Reports</p>	
5:30 p.m.	<p>Reflections From the Day and Adjourn</p> <ul style="list-style-type: none"> • Susan Mendley, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), Workshop Organizing Committee • Joaquin Barnoya, Instituto de Investigación y Estudios Superiores en Salud, Universidad Rafael Landivar, Guatemala 	Red Room
5:30-6:00 p.m.	Posters Available for Further Viewing	Red Room Foyer





Friday, March 22, 2019

7:00 – 7:50 a.m.	Morning Session	Red Room
	<p>Ethical Considerations for CKDu Research: An Initial Conversation</p> <ul style="list-style-type: none"> • Roundtable conversation 	Red Room
8:00 a.m.	CENCAM General Assembly	Red Room
9:00 a.m.	<p>Plenary Presentations by All Working Groups</p> <p><i>(Approximately 10 minutes for each group, including discussion)</i></p> <p>Summary from each working group, including content covered, progress made during the workshop, collaborations, and future directions</p> <ul style="list-style-type: none"> • Moderators: Daniel Brooks, Boston University, CENCAM Board Member, Workshop Organizing Committee; and José Escamilla, PAHO/WHO 	Red Room
10:30 a.m.	Break	Red Room Foyer
10:45 a.m.	<p>Panel Discussion With Focus on Collaboration and Cooperation</p> <ul style="list-style-type: none"> • Panel: One representative from each working group, as well as NIH and WHO representatives • Moderator: Bonnie Joubert, NIEHS, Workshop Organizing Committee 	Red Room
11:30 a.m.	<p>Scientific Summary of the Meeting</p> <ul style="list-style-type: none"> • Ricardo Correa-Rotter, Head, Department of Nephrology and Mineral Metabolism, National Medical Science and Nutrition Institute Salvador Zubiran, Mexico, CENCAM Co-Chair, Workshop Organizing Committee 	
Noon	Lunch	Red Room Foyer
1:15 p.m.	<p>Relevance and Possible Strategies for the Application of Research Toward CKDu Policies: A Conversation</p> <ul style="list-style-type: none"> • Moderators: Olivia Brathwaite, Central America Subregion, PAHO/WHO; and Agnes Soares, PAHO/WHO 	Red Room
3:00 p.m.	<p>Closing Remarks and Adjourn</p> <ul style="list-style-type: none"> • Jennifer Crowe, SALTRA, IRET, UNA, CENCAM Board Member, Workshop Organizing Committee • Marvin González Quiroz, CISTA UNAN-León, Nicaragua; CENCAM Board Member; Workshop Organizing Committee 	





Morning Sessions*

- Heat Exposure Assessment for Epidemiological Studies (English and Spanish)
- Epidemiology Study Design and Methods (English and in Spanish)
- Exposure Assessment of Pesticides, Other Agrochemicals, and Metals (English and Spanish)
- Update on Biomarkers for Renal Function (English)
- Ethical Considerations in CKDu Research (simultaneous translation)

* *The content of the Heat, Epidemiology, and Exposure Assessment sessions is designed for an audience new to the topics.*

World Café

The previous two international workshops on Mesoamerican Nephropathy and CKDu found that rotating table discussions using a modified World Café format (www.theworldcafe.com) enabled a collaborative dialogue across workshop participants. This method will be used again to create an engaged and open atmosphere for participants to meet each other while having a dedicated and open focus on the aims of the workshop.

Posters

More than 40 abstracts have been accepted and will be presented as posters. Abstracts are available electronically in the meeting booklet.

Policy Session

The policy session will discuss the implications of workshop conclusions for communities and health professionals, as well as strategies for communicating research findings to policymakers.

CENCAM General Assembly

A CENCAM general assembly meeting is held Friday morning (open for all; however, only members may vote)

Translation

The inauguration will be held in English and Spanish depending on each speaker's country of origin. Simultaneous interpretation (with headsets) will be provided for English/Spanish on Wednesday and Friday. Working groups and World Café leaders will strive to make sure both English and Spanish speakers are able to express themselves. Most morning sessions have lectures in both English and Spanish.





Working Groups



Analytical Epidemiology

- David Wegman, University of Massachusetts, Lowell
- Shuchi Anand, Stanford University
- Christer Hogstedt, Karolinska Institutet

The Analytical Epidemiology (AE) Working Group is organizing sessions to discuss epidemiological approaches to investigating causes of and interventions for CKDu. To bring participants up to date on developments since the last SALTRA/CENCAM workshop in 2015, we plan to have, in advance, a summary of leading case-control, cohort, and intervention studies, primarily from Central America and Sri Lanka, which will be briefly reviewed in our first session. That session will also identify AE issues that participants see as priorities. Our second session will engage participants in discussing how recent epidemiology studies have addressed some challenges specific to CKDu, particularly in under-resourced settings, seeking to identify key elements relevant to field epidemiology studies in such settings. Our third session will involve learning about and exploring on-going or planned studies with discussion on issues, such as biospecimen and data collection, analysis and reporting, results feedback, and ethics. A parallel session will discuss intervention study issues, design, and experience. Our fourth session is being designed to be collaborative with several other working groups. Those sessions will run in parallel in collaboration with working group members from Pesticide/Metals, Infection/Molecular Factors, Heat Stress, and Biomarkers. Our fifth and last session will be to develop recommendations on analytical epidemiology and intervention studies moving forward.

Epidemiología Analítica

- David Wegman, Universidad de Massachusetts, Lowell
- Shuchi Anand, Universidad de Stanford
- Christer Hogstedt, Instituto Karolinska
- Marvin González, CISTA/UNAN-León

El Grupo de Trabajo de Epidemiología Analítica (EA) está organizando sesiones para discutir los enfoques epidemiológicos para investigar las causas e intervenciones en ERCnt. Para que los participantes estén al tanto de los avances científicos desde el último taller SALTRA / CENCAM en 2015, planeamos elaborar un resumen de los principales estudios de casos - controles, cohortes e intervenciones realizados principalmente en América Central y Sri Lanka, que serán brevemente discutidos en nuestra primera sesión. Esa sesión también identificará los problemas de EA que los participantes consideren prioritarios. Nuestra segunda sesión involucrará a los participantes en la discusión de cómo los estudios epidemiológicos recientes han abordado algunos desafíos específicos de ERCnt, particularmente en entornos de escasos

recursos, buscando identificar elementos clave en los estudios de epidemiología de campo en dichos entornos. Nuestra tercera sesión incluirá el aprendizaje y la exploración de estudios en curso o planificados con discusión sobre temas, como muestras biológicas y la recolección de datos, análisis e informes, retroalimentación de resultados y ética. Una sesión paralela tratará temas de diseño y experiencia en estudio de intervención. Nuestra cuarta sesión estará diseñada para colaborar con otros grupos de trabajo. Esas sesiones se ejecutarán en paralelo en colaboración con miembros del grupo de trabajo de plaguicidas/Metales, Infección/Factores Moleculares, Estrés Térmico y Biomarcadores. Nuestra quinta y última sesión consistirá en desarrollar recomendaciones sobre epidemiología analítica y estudios de intervención en el futuro.

Biomarkers of Abnormal Kidney Function

- Ben Caplin, University College London Centre for Nephrology
- Carl-Gustaf Elinder, Stockholm County Council; Karolinska Institutet

In the working group on Biomarkers of Abnormal Kidney Function, we will discuss possibilities, pros and cons for using biochemical analysis of blood and urine to diagnose, assess, evaluate, and if possible, to prognosticate CKDu. We will consider the use of biomarkers for both individuals and for epidemiological studies and surveillance programs on renal health. We will discuss and evaluate the utility of biomarkers that have been employed to date, including differentiating between acute and chronic effects. We will also explore the potential utility of other measures related to kidney injury and/or function. In addition, we will address issues of field collection; sample processing, handling, and storage; laboratory analysis; and quality assurance. We welcome all to share your expertise to help develop and sharpen our tools in diagnosing and investigating CKDu during this workshop.

Biomarcadores de la función renal anormal

- Ben Caplin, Centro Universitario de Londres para Nefrología
- Carl-Gustaf Elinder, Consejo del Condado de Estocolmo; Instituto Karolinska

En el grupo de trabajo sobre Biomarcadores de la Función Renal Anormal, analizaremos las posibilidades, las ventajas y desventajas de utilizar el análisis bioquímico en suero y orina para diagnosticar, valorar, evaluar y, si es posible, pronosticar la ERCnt. Consideraremos el uso de biomarcadores tanto a nivel individuo como para estudios epidemiológicos y programas de vigilancia en salud renal. Discutiremos y evaluaremos la utilidad de los biomarcadores que se han empleado hasta la fecha, incluyendo la diferencia entre efectos agudos y crónicos. También exploraremos la utilidad potencial de otras medidas relacionadas con la lesión y/o la función renal. Además, abordaremos temas de recolección de campo; procesamiento, manejo y

almacenamiento de muestras; análisis de laboratorio; y control de calidad. Invitamos a todos a compartir su experiencia para ayudar a desarrollar y mejorar nuestras herramientas en el diagnóstico e investigación de ERCnt durante este taller.

Clinical Presentation and Treatment

- Ricardo Correa Rotter, National Medical Science and Nutrition Institute Salvador Zubiran; International Society of Nephrology; National Researcher III Conacyt, Mexico
- Susan Mendley, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases

As a group of experienced nephrologists, our goal will be to better understand the clinical characteristics and treatment strategies of CKD of uncertain etiology in different parts of the world. The working group will assess the unique features of the disease in each participant's region and note its clinical presentation and how it comes to medical attention. We will review how different health systems and local medical providers handle this clinical burden. One of our goals will be to develop plans for early detection of kidney disease, preventive measures when possible, recommendations for slowing progression of disease, and treatment of moderately advanced and advanced CKD.

Presentación Clínica y Tratamiento

- Ricardo Correa Rotter, Instituto Nacional de Ciencia Médica y Nutrición Salvador Zubiran; Sociedad Internacional de Nefrología; Investigador Nacional III Conacyt, México
- Susan Mendley, Instituto Nacional de Salud, Instituto Nacional de Diabetes y Enfermedades Digestivas y Renales

Como grupo de nefrólogos con experiencia, nuestro objetivo será comprender mejor las características clínicas y las estrategias para tratar la ERC de etiología desconocida en diferentes partes del mundo. El grupo de trabajo evaluará las características únicas de la enfermedad en la región de cada participante y tomará nota de su presentación clínica y del manejo médico que se le brinda durante la atención médica. Revisaremos cómo los diferentes sistemas de salud y los proveedores de servicios médicos locales manejan esta carga clínica. Uno de nuestros objetivos será desarrollar planes para la detección temprana de la enfermedad renal, medidas preventivas cuando sea posible, recomendaciones para disminuir el progreso de la enfermedad y el tratamiento de la ERC en fase moderadamente avanzada y avanzada.

Heat Load/Dehydration and Workload

- Vidhya Venugopal, Sri Ramachandra University

The Heat Load/Dehydration and Workload Working Group is organizing sessions to discuss the role of heat stress and workload in CKDu development and progression on working populations. A preliminary session on heat and workload was conducted during the 2015 CENCAM workshop. More evidence has emerged since then and the recent studies on heat stress/workload and CKD will be discussed. On the WG #1 (Day 1), discussions are planned based on the literature sent to the participants in advance from select developing countries for all the working sessions in this WG (excel sheets with links) to identify key issues, gaps and prepare for focused discussions on each of the working sessions for the following day. On day 2, our WG session #2 will focus on the geographical distribution of the studies on heat load, dehydration, and CKD/CKDu to understand the spread and breadth of the problem and identify hot spots. WG Session #3 will focus on methods and discuss the types/kinds of measurements/parameters, used to assess heat load, dehydration, and CKDu/renal issues, the pros and cons, challenges, and when and where they are suitable. The discussion is expected to lead to a development of a standard protocol of measuring heat load, heat strain and workload for use in CKDu studies. Working group session #4 will focus on the available types of intervention studies to control heat stress and workload in occupational settings. There is a possibility of doing this session jointly with WG-AE (Session #4) for a better outcome of this session. WG Session #5 will focus on summarizing the discussions of the WG and plan for future collaborative projects and post-conference summary.

Carga de Calor/Deshidratación y Carga de Trabajo

- Vidhya Venugopal, Universidad Sri Ramachandra

El Grupo de Trabajo de Carga de Calor/Deshidratación y Carga de Trabajo está organizando sesiones para discutir el papel del estrés por calor y la carga de trabajo en el desarrollo de ECRnd y su progreso en poblaciones trabajadoras. Se llevó a cabo una sesión preliminar sobre el calor y la carga de trabajo durante el taller CENCAM de 2015. Desde entonces, han surgido más pruebas y se discutirán los estudios recientes sobre estrés por calor/carga de trabajo y ERC. En el GT # 1 (Día 1), las discusiones se planifican en base a la literatura que se envía a los participantes con anticipación desde países en desarrollo seleccionados para todas las sesiones de trabajo en este GT (hojas de Excel con enlaces). Esto para identificar problemas clave, vacíos y prepararse para discusiones enfocadas en cada una de las sesiones de trabajo para el día siguiente. En el día 2, nuestra sesión GT # 2 se centrará en la distribución geográfica de los estudios sobre la carga de calor, la deshidratación y la ERCnt/ problemas renales para comprender la extensión y la amplitud del problema e identificar las áreas geográficas más

afectadas. La sesión GT # 3 se centrará en los métodos y discutirá los tipos de medidas/parámetros, utilizados para evaluar la carga térmica, la deshidratación y los problemas de ERCnt/problemas renales, los pros y contras, los desafíos, y cuándo y dónde son adecuados. Se espera que la discusión conduzca al desarrollo de un protocolo estándar de medición de la carga térmica, la tensión térmica y la carga de trabajo para su uso en estudios ERCnt. La sesión # 4 del grupo de trabajo se centrará en los tipos de estudios de intervención disponibles para controlar el estrés por calor y la carga de trabajo en entornos ocupacionales. Existe la posibilidad de realizar esta sesión conjuntamente con GT-EA (sesión # 4) para un mejor resultado de esta sesión. La sesión # 5 del GT se centrará en resumir las discusiones del GT y en planear futuros proyectos de colaboración y el resumen posterior a la conferencia.

Assessing Exposures to Pesticides, Other Agrochemicals and Metals

- Catharina Wesseling, Karolinska Institutet

The Pesticide-Metal Working Group has the objective to bring scientists together to 1) review the state of the art of pesticides/agrochemicals, metals (and possibly other toxic agents such as PAH) as potential causes or progressors of the CKDu epidemics in Mesoamerica, Sri Lanka and India, and 2) discuss methodologies needed to properly assess exposures and potential associations between exposures and CKDu. We plan to distribute beforehand a summary of current knowledge on the potential causal role of these toxic agents among participants of our WG. In the first session we will present and review briefly data from Mesoamerica, Sri Lanka and India, including use of nephrotoxic pesticides and exposure data, and data on associations with CKDu. The main strengths and limitations of the studies will be discussed. In the second session, subgroups for metals and pesticides will be formed. An outline for a pesticide exposure assessment approach will be presented focusing on questionnaires, external quantitative measurements and biomonitoring. Participants will be engaged in discussion of its feasibility in specific CKDu settings. In the third session, the possibility to reach common basic protocols that assess toxic agents and interactions with heat stress will be addressed. During the fourth session subgroups of the WG will work together with the Analytical Epidemiology group to discuss suitable study designs for pesticides / metals and for interactions of toxic agents with heat stress. The fifth session will be used to summarize and discuss recommendations for future studies.

Evaluación de exposiciones a plaguicidas, otros productos agroquímicos y metales

- Catharina Wesseling, Instituto Karolinska

El Grupo de Trabajo de plaguicidas-Metales tiene el objetivo de reunir a los científicos para 1) revisar el estado del arte de los plaguicidas / agroquímicos, metales (y posiblemente otros agentes tóxicos como los hidrocarburos aromáticos policíclicos (PAH)) como posibles causas o factores progresores de las epidemias de ERCnt en Mesoamérica, Sri Lanka y la India, y 2) discutir las metodologías necesarias para evaluar adecuadamente las exposiciones y las posibles asociaciones entre las exposiciones y ERCnt. Planeamos distribuir de antemano un resumen del conocimiento actual sobre el posible papel causal de estos agentes tóxicos entre los participantes de nuestro Grupo de Trabajo. En la primera sesión presentaremos y revisaremos brevemente los datos de Mesoamérica, Sri Lanka e India, incluido el uso de plaguicidas nefrotóxicos y los datos de exposición, y datos sobre asociaciones con ERCnt. Se discutirán las principales fortalezas y limitaciones de los estudios. En la segunda sesión, se formarán subgrupos de trabajo para metales y plaguicidas. Se presentará un esbozo para un enfoque de evaluación de la exposición a plaguicidas que se centrará en cuestionarios, mediciones cuantitativas externas y biomonitoreo. Los participantes se participarán en la discusión de su viabilidad para ERCnt en específico. En la tercera sesión, se abordará la posibilidad de diseñar protocolos básicos comunes que evalúen los agentes tóxicos y las interacciones con el estrés por calor. Durante la cuarta sesión, los subgrupos del GT trabajarán junto con el grupo de Epidemiología Analítica con el fin de analizar los diseños de estudio adecuados para plaguicidas / metales y las interacciones de los agentes tóxicos con el estrés por calor. La quinta sesión se utilizará para resumir y discutir recomendaciones en miras de futuros estudios.

Surveillance and Screening

- Jennifer Crowe, IRET, National University (Costa Rica)
- Agnes Soares, Pan American Health Organization, PAHO

The Surveillance & Screening Working Group is organizing sessions to: review the current knowledge on the prevalence of the disease at global level and what has changed since last meeting; assess the status of CKDu surveillance in place in the affected countries and their results; and review and critically assess prevalence studies and screening data (strengths, weaknesses and needs) to propose recommendations for future studies. Furthermore, the group will address aspects of ethics related to surveillance & screening CKDu in populations in conditions of vulnerability. During **Session # 1** (Day 1), there will be introductory brief oral presentations and discussions based on information sent to the participants in advance to the meeting. On Day 2, **Session # 2** will focus on the situation analysis of CKDu surveillance systems

in place, including information flow and reporting, on parameters and biomarkers used and, on problems identified on session # 1. **Session # 3** will review existing protocols and address strengths and weaknesses of prevalence studies of CKDu done in Central America and in other Regions, and address research needs. **Session # 4** will discuss barriers and facilitators for implementing surveillance system for CKDu, criteria for screening in different settings (e.g. population-based/ occupational/targeted), and ethic aspects related to these activities. It will conclude on knowledge gaps and suggest types of questions for future research. Joint sessions might be held with the clinical group to discuss early biomarkers, with the analytical group to harmonize recommendations for prevalence studies, and with other groups to discuss exposure assessment for prevalence studies and for environmental and occupational surveillance (e.g. pesticides and other exposures; heat stress etc.). **Session # 5** will summarize the discussions of the WG and prepare the report that will be presented to the proceedings of the conference. A Q & A document will be prepared to facilitate the discussion with policy decision-makers.

Vigilancia y tamizaje

- Jennifer Crowe, IRET, Universidad Nacional (Costa Rica)
- Agnes Soares, Organización Panamericana de la Salud, OPS

El grupo de trabajo de vigilancia y tamizaje está organizando sesiones para: revisar el conocimiento actual sobre la prevalencia de la enfermedad a nivel mundial y lo que ha cambiado desde la última reunión; evaluar el estado de la vigilancia de CKDu en los países afectados y sus resultados; revisar y evaluar críticamente los estudios de prevalencia y de tamizaje (fortalezas, debilidades y necesidades) para brindar recomendaciones a futuros estudios. Además, el grupo abordará aspectos de ética relacionados con vigilancia y tamizaje de CKDu en poblaciones en condiciones de vulnerabilidad. Durante Sesión # 1 (Día 1), se realizarán presentaciones orales breves de carácter introductorio y discusiones basados en la información enviada a los participantes previo al taller. En el día 2, la sesión # 2 se centrará en el análisis de la situación de los sistemas de vigilancia CKDu en los países, incluyendo el flujo de información y la presentación de informes, sobre los parámetros y biomarcadores utilizados y, en los problemas identificados en la sesión # 1. La sesión # 3 revisará los protocolos existentes y se abordarán las fortalezas y debilidades de los estudios de prevalencia de CKDu realizados en Centroamérica y en otras regiones, e identificar las necesidades de investigación. La sesión # 4 discutirá acerca de los obstáculos y responsables para la implementación de sistema de vigilancia en CKDu, los criterios para tamizajes en diferentes entornos (por ejemplo, basado en la población / ocupacional / dirigido a una población específica) y los aspectos éticos relacionados con estas actividades. Se concluirá con los vacíos de conocimiento y sugerencia de las posibles preguntas de investigación para futuras investigaciones. Quizás se puedan realizar sesiones conjuntas con el grupo de investigaciones clínicas para discutir sobre los

biomarcadores de daño renal temprano, con el grupo de epidemiología analítica para armonizar recomendaciones para estudios de prevalencia y con otros grupos para discutir sobre la evaluación de las exposiciones en los estudios de prevalencia y para vigilancia ambiental y laboral (por ejemplo, pesticidas y otras exposiciones; estrés por calor, etc.). La sesión # 5 resumirá las discusiones del grupo de trabajo y preparará el informe que será presentado en la plenaria de la conferencia. Un documento con preguntas y respuesta será preparado para facilitar la discusión con tomadores de decisiones.

Molecular Approaches to CKDu: Genetics, epigenetics, and infectious disease

- David Friedman, Harvard Medical School

The goal of our working group is to find ways to bring powerful molecular technologies to the problem of CKDu. We will consider approaches including genetics, epigenetics, pathogen detection, and other methods for understanding CKDu at a molecular and translational level. Both testing of prevailing hypotheses and new hypothesis generation using technologies capable of asking huge numbers of questions in parallel are of interest to our group. We will ask how these molecular tools can help understand the biology of the disease and also make predictions about which individuals are susceptible. While technology is central to this type of investigation, a major purpose of these sessions is to introduce interested non-experts to the available tools and consider what types of study design are best suited to study particular questions at a molecular level. We plan to enrich the conversation by engaging on topics of shared interest with other groups such as epidemiology and pathology through combined sessions. We also hope to engage the wider group in thinking through the critical issues of ethics, consent, and local capacity building.

Enfoques Moleculares de la ECRd: Genética, epigenética y enfermedades infecciosas

- David Friedman, Harvard Medical School

El objetivo de nuestro grupo de trabajo es encontrar maneras de utilizar tecnologías moleculares especializadas en el problema de ECRnt. Consideraremos enfoques que incluyen la genética, la epigenética, la detección de patógenos y otros métodos para comprender la CKDnt a nivel molecular y traslacional. Además, de poner en prueba las hipótesis actuales como las nuevas hipótesis que se vayan generando mediante la utilización tecnologías que sean capaces responder un gran número de preguntas en paralelo que sean de interés para nuestro grupo. Preguntaremos cómo estas herramientas moleculares pueden ayudar a comprender la biología de la enfermedad y también hacer predicciones sobre qué individuos pueden ser susceptibles.

Si bien la tecnología es fundamental para este tipo de investigación, uno de los objetivos principales de estas sesiones es presentar a los no expertos interesados las herramientas disponibles y considerar qué tipos de diseño de estudios son los más adecuados para estudiar aspectos particulares a nivel molecular. Planeamos enriquecer la conversación involucrándonos en temas de interés compartido con otros grupos, como epidemiología y patología, a través de sesiones combinadas. También esperamos involucrar a todo el grupo para que reflexione sobre los temas críticos de ética, consentimiento y creación de capacidad local.

Pathology

- Brian Berridge, National Institute of Environmental Health Sciences, National Toxicology Program
- Julia Wijkstrom, Karolinska Institutet

There is a developing breadth of experience characterizing histopathologic changes in renal biopsies of patients in Mesoamerica and Asia suspected of having so-called 'Chronic Kidney Disease of Unknown Origin'. Consistencies in the features of these biopsies may offer clues to potential etiologies and pathogeneses that might be exploited to mitigate risk of disease or disease progression in patients, agricultural workers and their families. This workshop will bring together scientists with experience reviewing patient biopsies with scientists who experimentally investigate xenobiotic-induced renal disease. Our aims will be to build a global partnership of renal pathologists and scientists, align on key pathologic features of this unique disease, speculate on pathogeneses and develop a descriptive schema and protocol for biopsy characterization. Participants will also engage clinical scientists to discuss clinical protocols for early identification of patients with developing disease, approaches to patient monitoring to increase our understanding of disease progression as well as identify potential areas for experimental investigation.

Patología

- Brian Berridge, Instituto Nacional de Ciencias de la Salud Ambiental, Programa Nacional de Toxicología
- Julia Wijkstrom, Instituto Karolinska

Se está desarrollando una amplia experiencia que caracteriza los cambios histopatológicos en las biopsias renales de pacientes en Mesoamérica y en Asia, sospechosos de tener la denominada "Enfermedad renal crónica de origen desconocido". Las similitudes en las características de estas biopsias pueden ofrecer pistas sobre posibles etiologías y patogénesis que podrían explotarse para mitigar el riesgo de enfermedad o progresión de la enfermedad en pacientes, trabajadores agrícolas y sus familias. Este taller reunirá a científicos con experiencia

en la revisión de biopsias de pacientes y científicos que investigan experimentalmente la enfermedad renal inducida por xenobióticos. Nuestros objetivos serán construir una asociación global de patólogos renales y científicos, alinearse con las características patológicas clave de esta enfermedad única, especular sobre patógenos y desarrollar un esquema descriptivo y un protocolo para la caracterización de la biopsia. Los participantes también involucrarán a científicos clínicos para discutir protocolos clínicos para la identificación temprana de pacientes con enfermedades en desarrollo, enfoques para monitorear a los pacientes para aumentar nuestra comprensión de la progresión de la enfermedad, así como identificar áreas potenciales para la investigación experimental.



Poster Abstracts



1. Accuracy of Two Point-of-Care Devices in Detecting Elevated Serum Creatinine in Individuals at Risk for Mesoamerican Nethropathy	24
2. Pilot Test of the DEGREE Protocol, CKDu Module, and Point-of-care Device Measurements in Outdoor Hispanic Workers	26
3. Evaluation of Renal Function in Residents of Agricultural Communities of El Soconusco.....	28
4. Etiological Fracion de la Insuficiencia Renal Cronica de Causas no Tradicionales (ERCnT) en una Area Agricola de Panama.....	30
5. Dysuria and Medical Events Related to Heat Stress and Muscle Injury Among Male Nicaraguan Sugar Cane Workers	31
6. Clinicopathological Characteristics of Patients with Active Component of Chronic Kidney Disease of Unknown Etiology (CKDu) in Sri Lanka	33
7. Terminal Non-Traditional Chronic Kidney Disease (CKDnT) in Renal Replacement Therapy Units in Panama, 2014- 2017	34
8a. Clinical Criteria for the Diagnosis of Mesoamerican Nephropathy: Results of a Regional Survey of Latin American Society of Nephrology and Hypertension (SLANH)	35
8b. Clinical Characteristics and Treatment Carried out to Patients Cataloged as a Mesoamerican Nephropathy in the Hospital Nacional Rosales, El Salvador.....	37
9. Self-reported CKDu and associated risk factors in Central America. Preliminary results from the Second Central American Survey of Working Conditions and Health	39
10. Geospatial clusters of high rates of morbidity and mortality due to chronic kidney disease (CKD) in Panama	41
11. Prevalence of Chronic Kidney Disease in rural Sri Lanka: A new profile of affected districts reliant on groundwater.....	43
12. Biomarkers of kidney injury among children in Nicaragua.....	45
13. Description of the epidemic of chronic kidney disease affecting the adult population of El Salvador: a cross-sectional study.....	47
14. Chronic Kidney Disease in the High Specialty Regional Hospital (HRAECS) of Soconusco Chiapas, Mexico	49
15. Spatial variation of Chronic Kidney Disease mortality within Mesoamerican countries and association with land use and climate factors.....	51
16. Behavioral Risk Factors and CKDu in Sri Lanka	52
17. Do Agricultural Workers in Eastern North Carolina Have Unexplained CKD? - An Exploratory Study	54
18. Synergy of projects for non-traditional Chronic Kidney Disease research in Panama.....	55

19. Multisectoral Commission for the management of Chronic Kidney Disease of unknown etiology (CKDu) in Guatemala.....	57
20. The MesoAmerican Nephropathy Occupational Study (MANOS) Cohort: Overview and progress.....	58
21. State of the Art in Research on Chronic Renal Failure of Non-Traditional Causes in Mexico and Trends in Morbidity and Mortality	60
22. Cyanotoxins: A Hidden Cause of Chronic Kidney Disease of Uncertain Etiology in Sri Lanka?	62
23. Geospatial analysis of the situation of some chemicals used in the Republic of Panama.....	63
24. Evidence Supporting a Role for Vasopressin in Mesoamerican Nephropathy.....	64
25. Investigating possible infectious causes of chronic kidney disease of unknown etiology in a Nicaraguan mining community.....	65
26. A Total Worker Health® approach to assessing kidney health in sugarcane workers in Guatemala: an opportunity for nutrition intervention.....	66
27. Chronic Kidney Disease of unknown etiology (CKDu) India - Observations and Remedial measurement at community level.....	67
28. Incident kidney injury among Nicaraguan sugarcane workers during harvest - first year intervention assessment.....	68
29a. Lack of evidence regarding an Infectious Etiology of Mesoamerican Nephropathy make it unlikely	70
29b. Does Nickel exposure play a role in the etiology of Mesoamerican Nephropathy?	71
30a. The Occurrence of Chronic Kidney Disease of Unknown Etiology in a Rural Colorado Cohort and the Associated Risk Factors.....	72
30b. The Association between Exposure to Naturally Occurring Metals and Acute Kidney Injury and Chronic Kidney Disease in Rural Colorado.....	73
31. Descriptive analysis of nephrotoxic drinking water contaminants and urinary biomarkers of exposure among sugarcane workers in Guatemala	74
32. Exploration of drinking water arsenic exposure and the risk of Chronic Kidney disease in Costa Rica	76
33. Progress in the Sri Lankan Kidney Progression Project (KiPP)	77
34. Advancing Knowledge of Risk Factors Associated with Chronic Kidney Disease of Uncertain Etiology (CKDu): Recent Research in Sri Lanka and Opportunities for Collaboration	78
35. Investigating Developmental Nephrotoxicity of Agrochemical Mixtures	80
36. Systematic investigation of environmental exposures in young adults with declining kidney function in a population at risk of Mesoamerican Nephropathy (MeN).....	82

37. Flow and Transport Modeling-Based Systems Framework for the Analysis of Potential Toxin Pathways through Surface and Groundwater to Address Some Causal Factors of CKDu in Sri Lanka	83
38. Occupational heat stress health effects - A field study on salt pan workers and renal health in South India	85
39a. Measuring Kidney Function using Serum Cystatin C- and Serum Creatinine-Based Estimates of Glomerular Filtration Rate in a Cross-Section of Salvadoran Workers	87
39b. Characterizing Occupational Heat Exposure in the MesoAmerican Nephropathy Occupational Study (MANOS).....	89
40. The effect of climate on CKDu prevalence in the United States (2010-2014).....	91
41. National Toxicology Program Retrospective Review of Agrochemical Associated Nonneoplastic Kidney Lesions	93
42. A Descriptive Survey in an Endemic Area of Sri Lanka – Characterizing Sociodemographic, Consumption, and Agrochemical Exposure Patterns Associated with Chronic Kidney Disease of Uncertain Aetiology (CKDu)	95
Prevalence of impaired kidney function in the district of Anuradhapura, Sri Lanka: a cross-sectional population-representative survey based on the DEGREE protocol among those at risk of Chronic Kidney Diseases of unknown aetiology.....	97
Multiple Acute Kidney Injuries precede Chronic Kidney Disease in a Large Historic MeN Cohort in Nicaragua	99
Urine testing of community residents in a region of Nicaragua with a high burden of Mesoamerican Nephropathy reveal background systemic inflammatory signs rapidly increase in younger ages.....	100

Poster Exhibition Schedule

Wednesday, March 20.....	posters 1-21
Thursday, March 21.....	posters 22-42

1. Accuracy of Two Point-of-Care Devices in Detecting Elevated Serum Creatinine in Individuals at Risk for Mesoamerican Nephropathy

Miranda Dally, University of Colorado, Denver

Abstract:

Purpose: The purpose of this analysis was to assess the accuracy of two point-of-care creatinine devices, the i-STAT handheld (Abbott, Princeton, NJ, USA) and the StatSensor Xpress (Nova Biomedical, Waltham, MA, USA) in comparison to venipuncture creatinine measures. Additionally, we explored how accurate a previously calculated correction factor for the StatSensor Xpress performed in two independent studies.

Methods: There were 213 paired i-STAT and venipuncture samples collected from a community study in Nicaragua in 2015-2016. An additional 267 paired StatSensor Xpress and venipuncture samples were collected, 158 from a community setting in Nicaragua and 109 from a Guatemala sugarcane worker cohort. Pearson correlation coefficients, Bland-Altman plots, and no intercept linear regression models were used to assess agreement between point-of-care devices and blood samples. The previously calculated correction factor of 0.78 was applied to the StatSensor Xpress data and was compared to the paired blood samples.

Results: The i-STAT performed the most accurately, overestimating creatinine by 0.07 mg/dL (95% CI: 0.02, 0.12) with no evidence of proportional bias. The StatSensor Xpress performed well at low levels of creatinine (Mean (SD): 0.87 (0.19)). Due to proportional bias, the StatSensor Xpress performed worse in the Nicaragua community setting where creatinine values ranged from 0.31 to 7.04, suggesting a correction factor of 0.66 was needed. The previously calculated correction factor of 0.78 performed well with the Nicaragua data when the data was restricted to creatinine ≤ 2.59 mg/dL (Adjusted difference: 0.06 mg/dL; 95% CI: 0.03, 0.09) .

Conclusions: These data suggest that the StatSensor Xpress is less accurate as the values of measured creatinine increase, a consideration when using the point-of-care device for screening individuals at risk for Mesoamerican Nephropathy. The i-STAT handheld is an accurate field alternative to lab tested serum; however, in low-resource settings other considerations such as cost and ease of use must be considered when conducting field research.

Contributing Authors: Miranda Dally, Jaime Butler-Dawson, Juan Jose Amador, Damaris Lopez Pilarte, Alexandra Gero, Joe Kupferman, Dave Friedman, Benjamin Griffin, Lee Newman, Daniel Brooks

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Medical Center. The funders had no role in study design; collection, analysis, and interpretation of data; writing the report; and the decision to submit the report for publication.

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2. Pilot Test of the DEGREE Protocol, CKDu Module, and Point-of-care Device Measurements in Outdoor Hispanic Workers

Erika Figueroa-Solis, The University of Texas Health Science Center at Houston School of Public Health

Abstract:

Introduction: Comparison studies of estimated glomerular filtration rate (eGFR) are limited by lack of protocols using standardized creatinine measurements. Use of Point-of-Care (POC) measurements that require a smaller amount of blood, no transporting of specimens, and can be immediately analyzed in the field is attractive, but their accuracy outside of healthcare settings has been questioned. There is also little standardization on questionnaires designed to gather information on risk factors for "CKD of unknown origin" (CKDu).

Objective: To field test the Disadvantaged Populations eGFR Epidemiology Study (DEGREE) protocol, a CKDu risk factor module from the Second Central American Survey of Working Conditions and Health, and POC testing of renal function with the i-STAT (Abbott Laboratories, Abbott Park, IL)/Chem8+ in outdoor workers in different seasons.

Methods: Cross-sectional study of 55 Hispanic workers in Houston. Inclusion criteria were: 1) ≥ 18 years; 2) working outdoors ≥ 20 hours/week; 3) no prior diagnosis or medications for diabetes, renal or cardiovascular disease. Interviewer-administered DEGREE and CKDu module questionnaires and a urine sample were completed indoors; anthropometrics, blood pressure and paired blood samples for POC and isotope dilution mass spectrometry (IDMS) were completed outdoors during November-December (winter) 2017 and April-May (spring) 2018. Correlations between POC and IDMS were compared between coldest/hottest temperatures, lowest/highest humidity, and lowest/highest heat index.

Results: Outdoor temperatures ranged from 60°F to 90°F, relative humidity from 25% to 99%, and heat index from 34°F to 106°F. Administration of the DEGREE protocol and CKDu module averaged 10 and 5 minutes, respectively; questions were easily understood. Average eGFR was 114.07 ml/min/1.73m² (SD = 15.18) in the winter and 105.81 ml/min/1.73m² (SD = 18.21) in the spring. Hemoglobin measurements were strongly correlated during the coldest temperatures (60°F to 70°F) and lowest heat index reported (34°F to 69°F) ($r=0.97$); in the hottest temperatures (80°F to 90°F) and the highest heat index (90°F to 106°F), this correlation was lower ($r=0.84$). The Bland-Altman plots for hemoglobin showed that, on average, the POC i-STAT results were 3.58% higher than with IDMS. Serum creatinine measurements correlated well ($r=0.93$) and blood urea nitrogen (BUN) ($r=0.96$) across the range of temperatures, humidity levels, and heat index. On average, POC-derived creatinine and BUN values were 0.18% and 0.72% higher than IDMS, respectively. Technical limitations with the POC included "out of range" readings and disabled cartridge testing when temperatures were above 85°F or below 65°F, but these resolved when the instrument was brought indoors for a few minutes.

Limitations with the IDMS method included hemolyzed specimens, which affected glucose, sodium and potassium levels, but minimally affected BUN and creatinine.

Conclusion: Implementation of the DEGREE protocol and CKDu module was straightforward, well understood and conducted in a reasonable period of time. The POC device performed adequately in the field insofar as renal function measurements, but required some adjustment in methods when temperature readings were out of range. Acknowledgement to Grant No. 5T42OH00842109 from the National Institute for Occupational Safety and Health (NIOSH) / Centers for Disease Control and Prevention (CDC) to the Southwest Center for Occupational and Environmental Health (SWCOEH)

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3. Evaluation of Renal Function in Residents of Agricultural Communities of El Soconusco

Norma Edith Rivero Perez, Instituto Nacional de Salud Publica/Centro Regional de Investigacion en Salud Publica

Abstract:

Chronic kidney disease (CKD) has been classified by the WHO as one of the main threats to public health, with an increase in incidence and prevalence worldwide in the last two decades. Chronic degenerative diseases such as diabetes mellitus and hypertension have a higher risk of developing CKD. There are other disorders known as CKD of uncertain etiology, which are not attributed to diseases such as diabetes mellitus, hypertension and other known etiologies. In Mexico there are few CKD studies, but none of them includes Soconusco communities in Chiapas where socioeconomic, environmental, demographic conditions are similar to Central American countries in which CKD has had a negative impact on public health generating social concern. Due to this the objective of this study was to evaluate the renal function of the populations residing in agricultural communities exposed to pesticides in Soconusco, Chiapas. The renal function markers were determined Glucose, Creatinine, Urea, and Serine Albumin, Examination General Urine, hemoglobin and as a biomarker of exposure to pesticides, the activity of the Cholinesterase erythrocytic (AChE) was determined in a population belonging to 4 communities of Soconusco, Chiapas., With inclusion criteria aged 18 to 50 years, being residents of the communities and not present any renal disorder or chronic-degenerative disease. The mean values of the markers of renal function in the entire study population were found within the reference parameters considered normal: Glucose (85.8 + - 13.6 mg / dL), Urea (0.2 + - 0.07 mg / dL), Albumin (4.09 + -0.31 g / dL) and Creatinine (1.03 + - 0.24 mg / dL). Significant differences were detected in the mean values obtained from CrS between men and women (1.09 + - .25 vs 0.9 + - .17 mg / dL respectively, $p = .005$). With respect to protein levels in urine, 55.6% of the entire study population had levels of + - 15 g / L and 5.5% had values above > 30 g / L. The calculation of the glomerular flow rate (GFR) was made with the KCD-EPI formula. The mean value of the GFR for the entire study population was 89.7 + - 22.1 mL / min. There was a significant difference between men and women (92.84 + - 22.49 vs 84.11 + - 20.6 mL / min) respectively, being the women with the lowest GFR. The calculation of the ERC prognosis according to the KDIGO 2012 guideline indicated that 45% of the study population had slightly decreased risk of progression to renal damage. The mean value of the activity of the erythrocyte AChE was 5014.0 + - 2274.0 U / L in the entire study population. The analysis of risk estimation of progression of renal damage showed a statistically significant association with sex ($X^2 = 8.8$, $p = .005$) where the risk estimate indicates that the woman is 3 times more risk (OR = 3.2 95% CI 1.46 - 7.17) to present a decrease in GFR compared to men. With regard to age, an association was found ($X^2 = 12.9$, $p = .000$), where the risk estimate (OR = 2.0; 95% CI 1.3 - 3.07) indicates that with the increase in age increases 2 times the decrease in GFR. With the BMI the association was significant ($X^2 = 5.3$, $p = .021$), where being overweight increased by 1.5 times the risk of a decrease in GFR (OR = 1.5, 95% CI 1.04 - 2.05) . The analysis with the erythrocytic

AChE exposure biomarker did not show an association between the decrease in the activity of AchE and the risk of progression of renal damage ($X^2 = .069$, $df = 1$, $p = .792$).

Keywords: Chronic Kidney Disease, Pesticides, Environmental Exposure

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4. Etiological Fracion de la Insuficiencia Renal Cronica de Causas no Tradicionales (ERCnT) en una Area Agricola de Panama

Olaf Jensen, Faculty of Health Science, University of Panama & Center for Maritime Health and Society, University of Southern Denmark

Abstract:

Titulo: Etiological fracion de la insuficiencia renal cronica de causas no tradicionales (ERCnT) en una area agricola de Panama - En las ultimas decadas se ha notado un aumento importante en la incidencia de enfermedad renal cronica de causas no tradicionales (ERCnT) en Centroamerica, sobre todo en hombres jovenes y agricultores, que no tiene relacion con diabetes, hipertension o uso inadecuados de analgesicos. Se hace necesario dar a conocer la magnitud del problema, con el fin de iniciar investigaciones que permitan conocer las causas e implementar las medidas preventivas. **Objetivo** El primer objetivo es responder a la pregunta ¿Se esta constituyendo la insuficiencia renal cronica de causas no tradicionales, en un problema de salud publica y ocupacional en Panama? - el segundo, es describir la comorbilidad de los pacientes con ERC. **Metodo** Se toma una muestra de 100 expedientes de los pacientes en hemodialisis del departamento de nefrologia del Hospital CSS de Aguadulce. El hospital esta ubicado en una zona agricola de Panama, donde la prevalencia de la ERC es alta. Se toma la informacion de los expedientes: diagnosticos y los valores de laboratorio. Se analizaran los datos y se calculara el porcentaje de casos con ERCnT y la comorbilidad. **Resultados esperados** 1) Conocimientos de la comorbilidad en pacientes con ERC y ERCnT. 2) Si el porcentaje de casos con ERCnT > 10 % es un problema importante de salud que debe ser investigado. A continuacion, se realizaran otros dos estudios previstos: un caso clinico y un estudio caso-control etiologico. Los resultados de estos estudios podrian sumarse al conocimiento cientifico de las etiologias de este problema global y podrian servir para reconocer en nuestro pais la enfermedad, como ocupacional. **Palabras clave** Enfermedad renal cronica, agricultura, comorbilidad, medicina ocupacional.

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5. Dysuria and Medical Events Related to Heat Stress and Muscle Injury Among Male Nicaraguan Sugar Cane Workers

Kate Applebaum, George Washington University, Milken Institute School of Public Health, Department of Environmental and Occupational Health

Abstract:

ABSTRACT Nicaraguan sugar cane workers have an elevated prevalence of chronic kidney disease (CKD). Sometimes referred to as Mesoamerican Nephropathy (MeN), the disease pathogenesis may include recurrent heat stress and muscle injury with subsequent kidney injury in the absence of traditional risk factors. A common urinary symptom among at-risk workers is dysuria. Compared with other job types, cane cutters may be at elevated risk of these potential intermediate events, though longitudinal studies are limited.

METHODS: Using employment data for male workers at a Nicaraguan sugar cane company, we classified active work months as cane cutting or non-cane cutting for each month of follow-up, July 1993 through June 2010. Based on medical records, we determined occurrence of separate outcomes: dysuria, heat-related events, and muscle-related events during the follow-up period. Dysuria was defined as pain upon urination without other explanatory cause. Heat-related events included heat stress or experiencing ≥ 2 heat symptoms. Muscle-related events were defined to identify potential rhabdomyolysis. Associations between cane cutting and each outcome were analyzed using logistic regression based on generalized estimating equations for repeated events, controlling for age.

RESULTS: The 242 workers contributed 13,530 active work months, with 22.4% of person-months classified as time worked in cane cutting. There were 376 dysuria events, 35 heat-related events, and 32 muscle-related events. Cane cutting months exhibited a higher odds of dysuria and heat-related events [dysuria: OR=1.67 (95% CI: 1.18-2.37); heat: 1.97 (0.92-4.22)] compared with non-cane cutting months. The associations with cane cutting strengthened after subjects had worked ≥ 60 months [dysuria: OR=2.70 (95% CI: 1.72-4.24); heat: 3.05 (1.22-7.61)]. No association was observed for muscle-related events.

CONCLUSIONS: Working in cane cutting compared with working in a different job in the sugar cane industry was associated with increased dysuria and heat-related events, supporting the hypothesis that cane cutters are at increased risk of events suspected of inducing or presaging CKD.

Contributing Authors: Tiffany L. Stallings, Alejandro Riefkohl Lisci, Nathan McCray, Daniel E. Weiner, James S. Kaufman, Ann Aschengrau, Yan Ma, Michael P. LaValley, Oriana Ramirez-Rubio, Juan Jose Amador, Damaris Lopez-Pilarte, Rebecca L. Laws, Michael Winter, V. Eloesa McSorley, Daniel R. Brooks, Katie M. Applebaum.

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CONFLICTS OF INTEREST: Dr. Brooks, Dr. Amador, and Ms. Lopez-Pilarte are conducting a study supported in part by a gift from Los Azucareros del Istmo Centroamericano (AICA) to Boston University School of Public Health for research on chronic kidney disease in Central America.

6. Clinicopathological Characteristics of Patients with Active Component of Chronic Kidney Disease of Unknown Etiology (CKDu) in Sri Lanka

Neeraja Kambham, Stanford University

Abstract:

Chronic kidney disease of unknown etiology (CKDu) is a leading cause of kidney disease in Central and North Central provinces of Sri Lanka, and its causation is potentially related to an environmental exposure. Renal biopsy findings indicate a primary tubulointerstitial disease characterized by tubular atrophy and interstitial fibrosis with negative immunofluorescence and no/minimal primary glomerular involvement. A subset of CKDu patients also show an active component of tubulointerstitial nephritis (AIN), indicative of acute/ongoing precipitating injury.

Design: Biopsy confirmed CKDU was diagnosed in 43 patients during the study period (10/2016-9/2017). The activity index (AI: tubulitis and interstitial inflammation in nonatrophic cortex) and chronicity index (CI: global glomerulosclerosis, periglomerular fibrosis, tubular atrophy, interstitial fibrosis) (scale 0-3) were scored. Thirteen patients met our criteria of AI \geq 2 & CI \geq 4 for AIN; 12 had sufficient sample for further clinicopathological evaluation. A subset of AIN biopsies were sent for semiquantitative element analysis using mass spectrometry (n= 4) and electron microscopy (EM) (n=2). Biopsies without CKDu served as controls for histology (n=5) and element analysis (n=2).

Results: CKDu patients with AIN were on average 45 (\pm 10.8) years of age, 9 (75%) were men, all were born in the endemic areas and reported drinking well water as a primary source at work or home. Notably only 4 (33%) reported experiencing dysuria in the past 6 months, but 9 (75%) reported some form of acute symptoms (i.e., fever, back pain, joint pain) in the past 6 months. None had hematuria; 11 (92%) did not have proteinuria on dipstick. Pyuria was present in 5 (42%). Mean serum creatinine was 1.9 (1.1) mg/dL. Silver stained rare dense granules were seen in the tubular epithelial cells of both CKDu cases (8 (67%)) and controls (40%). These granules typically involved a single tubule in the biopsy core and one biopsy had granules in 5 tubules. These granules corresponded to irregular tubular lysosomes on EM. Mass spectrometry revealed no traces of cadmium or arsenic; minimal lead was seen, lower than in control paraffin block (Table 1). Although higher iron and copper were noted in 2 cases, tissue staining for ferric iron and copper was negative.

Conclusions: We confirm an active phase of CKDu in a sub-sample of biopsy patients. Rare tubular atypical lysosomes were noted in both cases and controls. There was no support for lead, cadmium, or arsenic deposition in the tissue samples examined.

Contributing Authors: Kambham N*, Ratnatunga N*, Huie P, Montez-Rath M, Adasooriya D, Wijetunge S, Badurdeen Z, Wazil A, Schensul SL, Vlahos P, Haider L, Bhalla V, Levin A, Bendall SC, Angelo RM, Fire AZ, Anand S[^], Nanayakkara N[^] (*co-first & [^]co-senior authors)

7. Terminal Non-Traditional Chronic Kidney Disease (CKDnT) in Renal Replacement Therapy Units in Panama, 2014- 2017

Jesica E. Candanedo P., Ministry of Health

Abstract:

In the last 10 years it has been described in Panama an increase of cases of Chronic Kidney Disease (CKD). It has also been reported a higher than expected percentage of the of these cases with an unidentified cause. In August 2018, seven of the eighteen Renal Replacement Therapy Units (RRTU) from the public health system in Panama started data collection of basic information from all clinical charts of patients with Chronic Kidney Disease (CKD), needed to characterize clinically and epidemiologically these cases. The objective is to identify the proportion of the cases of CKD stage 5, in order to screen those with unidentified cause for the CKDnT criteria, according to PAHO 2016 case definition. This is an exploratory and descriptive design. The intent is to generate hypothesis for future research that strengthens the knowledge about the causality of CKDnT. The study population are all the living cases of CKD from 2010 to 2017 in seven RRTU, located in a diversity of areas along the country: Bocas del Toro, Coclé, Chiriquí, Panama Oeste y Panama Metro. Once identified the stage 5 CKD cases in seven RRTU, and screened for CKDnT criteria, those classified by the nephrologist as CKDnT cases will be tested for *Leptospira* sp. and Fabry disease if necessary. Also, the clinical-epidemiologic survey with data from the clinical chart will be completed, with the patient. Finally, an interdisciplinary group including nephrologist and public health professionals, will select thirty cases using purposive sampling. The selected will be interviewed and visited to their residences and jobs using a second questionnaire, assessing thoroughly socio-economic, occupational and environmental factors.

8a. Clinical Criteria for the Diagnosis of Mesoamerican Nephropathy: Results of a Regional Survey of Latin American Society of Nephrology and Hypertension (SLANH)

Zulma Trujillo, Universidad de El Salvador

Abstract:

INTRODUCTION: Mesoamerican Nephropathy (NeM) is a new chronic kidney disease (CKD) of undetermined cause. We explored the applicability of the major and minor criteria provided by PAHO/SLANH to confirm cases of NeM.

METHODS: Cross-sectional descriptive study. Data obtained with a closed electronic questionnaire to nephrologists from Central America and Mexico in March-April 2017.

RESULTS: Sixty nephrologists participated, 67% with <10 years of practice, 52% work in urban areas, and 88% work in 2 to 4 sites. Regarding PAHO/SLANH criteria, 3 were used by ≥95% of participants: international criteria to define CKD (95%), ruling out other known causes of CKD (98%) and patients' age between 12 and 60 years (100%). Other criteria: albuminuria A1/non-nephrotic (75%) and mild or no hypertension (88%). Four minor criteria described in ≥95%: male patients (95%), located in the Pacific coast (97%), performing open-air work activities with higher heat perception (98%), and exposed to strenuous physical work (98%). Incidental diagnosis is how the disease is most frequently identified (57%). Respondents were asked in which health care area they identified the largest number of cases: a) In the emergency room with electrolyte abnormalities or exacerbated CKD: always or almost always 26 (43%), rarely 22 (37%), occasionally 9 (15%), never 3 (5%). b) Incidental diagnosis: Always or almost always 34 (57%), occasionally 15 (25%), rarely 8 (13%) and never 3 (5%). c) In the outpatient clinic with already established NeM diagnosis: Always or almost always 24 (40%), occasionally 10 (16%), rarely 19 (32%) and never 7 (12%). d) Diagnosed by community screening: Always or almost always 9 (15%), occasionally 13 (22%), rarely 20 (33%) and never 18 (30%). When exploring the clinical symptoms most frequently observed in these cases, the complete answers are detailed in Table 3; however, those described most frequently or always were: asthenia 33 (55%), adynamia 33 (55%) and asymptomatic 31 (52%). The most frequent clinical signs described by nephrologists as always or almost always were: Normotensión 41 (68%), and for CKD stages G4-5: pallor 48 (80%) and symptoms of uremia 37 (62%). The main electrolyte disorders are: Hypokalemia 39 (65%); hypocalcemia 33 (55%); hyponatremia 29 (48%). Hyperuricemia was reported in CKD stages G1-3 by 33 (55%) and in stages G4-5 by 52 (87%), anemic syndrome by 49 (82%) and metabolic acidosis by 33 (55%). In urine the most important findings were Albuminuria A1 by 41 (68%) and isostenuria by 33 (55%) participants (Table 4). Serum creatinine standardized for IDMS is performed: in all laboratories 7 (12%); in some laboratories 23 (38%); in no laboratory 9 (15%); and does not know 21 (35%). The calculation of albumin / creatinine index in urine is randomized in your country: in all laboratories 8 (13%); in some laboratories 46 (77%); in no laboratory 4 (7%); does not know 2 (3%). Renal ultrasound is

available: always 45 (75%), sometimes 13 (22%); 2 (3%) is not available. Kidneys smaller than 9 centimeters are always or almost always described: 37 (62%) surveyed.

CONCLUSIONS: This first inquiry validates the applicability of the criteria for confirmation of NeM cases provided by PAHO/SLANH. The studied minor criteria require further confirmation.

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5- Past President of the association of nephrology and hypertension of El Salvador, Social Emergency Fund for Health, Canton Tierra Blanca, El Salvador Hemodialysis Center, San Salvador, El Salvador.

6- Vice-president of Region 4 of the Latin American nephrology and hypertension society, Diagnostic Center, Advanced Medicine, Medical conferences and Telemedicine, CEDIMAT, Dominican Republic.

8b. Clinical Characteristics and Treatment Carried out to Patients Cataloged as a Mesoamerican Nephropathy in the Hospital Nacional Rosales, El Salvador

Zulma Trujillo, Universidad de El Salvador

Abstract:

METHODS: descriptive, retrospective, statistical analysis in excel and SPSS.

RESULTS: A total of 368 patients was obtained: 123 classified as Mesoamerican Nephropathy (NeM) was compared with 123 with a history of diabetic nephropathy (DN) and 122 with a history of hypertensive nephropathy (HN). the male gender predominated in MeN (n 117) compared to DN (n 39) HN (n 59) p0.000; the mean (x) age in NeM was 45.5 year (y), DN 62,8 y and HN 68,8 y (p 0.000); MeN relation male/female 19/1. The majority of the patients the maximum schooling reached until primary but in MeN 51%, DN 24%, HN 26.2% (p 0.29; the altitude of the house was located according to the address to see how many meters above sea level (m.a.s.l) they live and work the media in MeN was 390 masl, DN 640 masl, HN 622 masl, We investigated the work carried out in the open or in an environment with greater thermal perception of heat in MeN 96,7%, DN 26%, HN 43% p 0.000. The following risk factors were statistically significant in MeN in relation with the other Nephropathies the history of alcoholism, smoking, NSAID consumption and exposure to agrochemicals. Episodes of acute kidney injury documented in the file MeN 44%, DN 28.4%, HN 25%. Symptoms with statistical significance in MeN with respect to the other nephropathies were: cramp, dysuria, paresthesia, lumbago, dizziness, headache, dry skin, thirst, irritability, adynamia, nausea and lower limb edema. The blood pressure was found at normal values in MeN 74%, DN 21%, in no patient with hypertensive nephropathy was normal (p 0.000). In the laboratory analyzes it was found with statistical significance for NeM with respect to the other nephropathies hyperuricemia, hypokalemia, hypochloremia, normoglycemia, hypertriglyceridemia. Results of serum creatinine (mg/dl) of patients with MeN was 2.7 ± 0.97 sd, eGFR using CKD-EPI 37.8 ± 21.02 sd. (ml/min/1.73 m²sc); DN 1.69 ± 1.07 sd, eGFR 63.08 ± 38.63 sd; HN 2.05 ± 1.05 sd. eGFR 45.32 ± 23.1 . Protein in urine 24 h (mg/vol) media

INTRODUCTION: The objective of the study is to identify the clinical characteristics of the laboratory and the findings on ultrasound kidney of patients cataloged as Mesoamerican nephropathy compared to Diabetic and Hypertensive Nephropathy in patients of the Hospital Nacional Rosales. NeM 519 ± 606 sd; DN $1,171 \pm 2,311$, HN 736 ± 1261 ; MeN/DN p 0.006; MeN/HN p 0.388. In renal ultrasound, the highest percentage of small kidneys smaller than 8.9 cm is found in patients with NeM 51.2%, DN 36.6% , HN 42.6%.

RESULTS: The diabetic and hypertensive nephropathy is the most frequent worldwide, however when compared with NeM in the patients of the Rosales National Hospital we can observe a different clinical presentation that predominates male gender, young people with low education, who live and work at a lower height at 500 meters above sea level and working in

open spaces or in an environment with a greater thermal perception of heat. NeM presents with a greater episode of Acute Kidney Injury, symptoms of thermal stress than in the other nephropathies and a more advanced stage of renal damage with small kidneys by ultrasound in a relatively young population.

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9. Self-reported CKDu and associated risk factors in Central America. Preliminary results from the Second Central American Survey of Working Conditions and Health

David Gimeno Ruiz de Porras, The University of Texas Health Science Center at Houston School of Public Health

Abstract:

Introduction: In Central America, chronic kidney disease of undetermined cause (CKDu) is associated with occupational and environmental exposures affecting young men working in lowland agricultural settings, primarily in sugar cane workers, but there are likely to be other at-risk groups who share similar exposures. Suspected causes include a combination of exposure to high temperatures and humidity, inadequate hydration, high physical demands and concomitant use of nephrotoxic nonsteroidal anti-inflammatory agents (NSAIDs), among others.

Objective: To identify the prevalence of CKDu risk factors, self-reported CKDu and work-related CKDu by geographic location, occupation, and industry in the six Spanish-speaking Central American countries: Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama.

Methods: Interviewer-administered survey of a nationally representative sample of 9,032 (~1,500 per country) workers, the Second Central American Survey of Working Conditions and Health, conducted in 2018. The survey included a panel of items on putative risk factors for CKDu (heat/humidity exposure, hydration, physical exertion, analgesic use, agrochemical use), self-reported CKDu and self-reported work-related CKDu.

Results: The prevalence of CKDu risk factors and self-reported CKDu varied across countries, occupations, and industries. Exposure to high temperatures ranged from 25% in Costa Rica to 54% in El Salvador. Exposure to high humidity ranged from 7% in El Salvador to 27% in Panama. Costa Rica had the highest prevalence of participants not drinking water during work (9%); Panama had the highest physically demanding work (48%). Use of NSAIDs ranged from 11% to 30% across countries, but was relatively consistent across industries (14% to 20%). Exposure to agrochemicals was highest in Panama (12%). Self-reported CKDu ranged from 17% in El Salvador to 55% in Nicaragua. Among workers reporting CKDu, the percentage who felt it was work-related ranged from 30% in Guatemala to 71% in Nicaragua. By industry, the highest prevalence of CKDu (24%) and work-related CKDu (62%) were in agriculture and construction, respectively. By occupation, prevalence of CKDu (7%) and work-related CKDu (56%) were highest in agricultural workers and construction workers, respectively.

Conclusion: This preliminary analysis of a large population-based study identifies a broad distribution of suspected CKDu risk factors and self-reported CKDu across Central America, supporting the need to broaden epidemiological research beyond the sugar cane industry. Partially supported by Grants IL-29677-16-75-K-48 from the United States Department

of Labor (USDOL). GD and DG were partially funded by the Southwest Center for Occupational and Environmental Health (SWCOEH), a National Institute for Occupational Safety and Health (NIOSH) Education and Research Center at The University of Texas Health Science Center at Houston School of Public Health, and awardee of Grant No. 5T42OH008421 from the (NIOSH)/Centers for Disease Control and Prevention.

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10. Geospatial clusters of high rates of morbidity and mortality due to chronic kidney disease (CKD) in Panama

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Abstract:

Introduction: Chronic kidney disease (CKD) is a global problem affecting in its final stage 19.7 million people around the world in 2017. During the period from 1990 to 2017 the mortality rate increased for all the countries of Central America. In Panama, workers of rice fields and canaverales in the south of the province of Cocolé, have been pointing out the existence of a high number of cases and deaths due to chronic renal failure since at least the 1990s. Independent studies carried out among residents of this have registered that, if there is a high number of cases, without establishing what could be the risk factors associated, or determine with certainty the magnitude of the impact of chronic kidney disease in the population.

Objectives: Confirm or rule out the existence of clusters of mortality and morbidity due to chronic kidney disease in Panama, characterizing the affected population and the magnitude of the clusters identified with respect to national rates.

Methods Mortality data compiled by the INEC between 2001-2015 and the patient database in Units were used. of Hemodialysis, provided by the Social Security Fund. The data were georeferenced at corregimiento level, using the politico-administrative division of 2003. Mortality and morbidity rates were adjusted and spatially smoothed for CKD using the Geoda software; subsequently, an analysis of atypical and group values was performed using ArcGIS (Moran Local Anselin), which allowed to identify hot spots, cold spots and atypical values, the results were mapped by the geographic information software QGIS. Results In the Republic of Panama, between From 2001 to 2015, some 4,441 deaths were recorded, while a total of 2,343 patients were registered in hemodialysis rooms. The adjusted mortality rate increased from 6.3 per 100 thousand inhabitants in 2001 to 14.4 per 100 thousand inhabitants in 2015, with a global rate for the entire period of 7.7 per 100 thousand inhabitants. The rate adjusted for age and sex for patients in the hemodialysis units between 2001 and 2015 was 7.73 patients per 100 thousand inhabitants, being higher for men (8.6 patients per 100 thousand inhabitants, than for women (6.3 patients per each 100 thousand inhabitants.) As for the specific rates, it is possible to identify that between 15 and 19 years, the specific rates for men and women are similar, but that from here the specific rate for each age group in the men began to be greater than the specific rate of women (0.8 patients per 100 thousand inhabitants for both sexes). Chronic kidney disease in Panama affects mainly the male population (70% of deaths), in occupations with extenuating conditions as, agricultural workers, street vendors and construction workers and factories (70%), are the ones that register the highest number of deaths. The distribution of corregimiento clusters with mortality rates, includes part of the provinces of Panama West, Cocolé, Herrera, Los Santos, Veraguas and Chiriquí. In the case of

morbidity, the cluster includes all the provinces mentioned above, with the exception of the province of Veraguas.

Conclusions: The existence of corregimiento clusters with high rates of morbidity and mortality due to chronic kidney disease could be verified, with the southern area of Cocre having the highest rates, which exceed three or four times the national rate.

11. Prevalence of Chronic Kidney Disease in rural Sri Lanka: A new profile of affected districts reliant on groundwater

Ted Horbulyk, International Water Management Institute (IWMI)

Abstract:

The hypothesized connection between groundwater use and chronic kidney disease of unknown etiology (CKDu) in Sri Lanka has not, until now, been well supported by data that connect historical and sustained use of groundwater sources with meaningful measures of disease prevalence at the household level. Ongoing research reported here provides a clear and up-to-date snapshot of the current situation. A carefully designed household survey across ten affected districts of Sri Lanka provides new information on households with and without household members who in the past ten years have been clinically diagnosed with chronic kidney disease (CKD). Data collection is from in-person interviews with 8,049 households conducted in the third quarter of 2018. A rigorous sample design supports the extrapolation of the characteristics of this sample to rural populations in areas that have the greatest number of affected households. Statistical tests employing these data indicate whether or not the reported instances of CKD vary by age, gender or location in a statistically significant manner. This information updates historical estimates of the prevalence of chronic kidney disease (including CKDu) in rural areas of Sri Lanka. Historically, estimates of disease prevalence have been derived from other methods, such as from individual health care records, clinical records or from smaller field surveys. Sri Lanka reports high and growing rates of CKDu in specific districts, but the definitions and distinctions between diagnoses of CKD and CKDu have not always been clear, especially when CKD is accompanied by diabetes or hypertension. To avoid including or excluding arbitrarily any of the surveyed households, the current study reports on any CKD as certified by a doctor of western medicine, as well as reporting on coexisting diabetes and hypertension. This study employs a simplified survey instrument that documents the historical reliance of affected and non-affected households on groundwater for household consumption. This approach classifies symptomatic individuals—whether currently alive or deceased in the past decade—by gender, age (current age if alive, at the time of death if deceased), residency and other self-reported health indicators. Households are classified according to whether or not they have used groundwater (from household wells, agro-wells or springs) as their primary source for drinking or cooking purposes in at least five of the past 20 years. More than 98% households reported to have consumed groundwater as their primary source, but the pattern varies across districts and divisional secretariats. The share of affected households that consumed groundwater for at least five years in the last 20 years is higher than that for non-affected households. These results characterize demographic and other similarities and differences between symptomatic and non-symptomatic individuals. This includes information about each symptomatic individual's age, gender, residency, whether this individual also reports symptoms of diabetes and hypertension, and whether this individual is still alive. There is a significantly higher incidence of CKD among females compared to males. The incidence of diabetes and hypertension among individuals with CKD does differ across districts and divisional secretariats but no such difference exists by gender of the symptomatic individual. These findings can guide public health programs directed at prevention, diagnosis

and treatment of individuals or at provision of broader social support to affected communities. They will also inform the design of future research exploring (multifactorial) hypotheses about the causes of CKDu in those rural areas with a high historical reliance upon groundwater for household use.

Contributing Authors:

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12. Biomarkers of kidney injury among children in Nicaragua

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Abstract:

Chronic kidney disease of unknown etiology (CKDu) is a leading cause of mortality in Central America, particularly in Nicaragua and El Salvador. High incidence of CKDu is notably observed among workers in agricultural industries along the Pacific coast, although the disease is not exclusive to these occupational groups or regions. Efforts to understand the etiology of CKDu are largely focused on occupational populations that experience highest mortality, however community-level exposures, which may occur throughout the lifecourse, may also play a role in disease initiation. We hypothesize that CKDu is initiated in part due to environmental or genetic factors that predispose individuals to kidney disease as young adults. The goal of this study was to assess whether early evidence of kidney injury will be evident in children in the region.

Methods: We assessed five urinary biomarkers of kidney injury (NGAL, IL-18, YKL-40, MCP-1 and KIM-1) in a subset of children enrolled in a 2016 study in Nicaragua (n=210). These biomarkers have been associated with acute kidney injury or early CKD in prior research. Participants ranged from 7-17 years, with 36% (n=76) younger than 12 years, and boys and girls were enrolled in equal number. Children were recruited from three high-risk CKD regions in Nicaragua (Chichigalpa, Mina El Limon, and La Paz Centro) as well as from a lower-risk region as referents (Managua). Biomarker concentrations were standardized to urinary creatinine and log transformed for analysis. Multivariable linear regression was used to evaluate risk factors for biomarker concentrations.

Results: Median and IQR for each urinary biomarker concentration were: NGAL (median: 9.0 ng/g; IQR: 4.0-24.0 ng/g; YKL-40 (median: 487.5 pg/mg; IQR: 320.6-705.8 pg/mg); IL-18 (median: 30.8 pg/mg; IQR: 21.7-44.5 pg/mg); MCP-40 (median: 141.5; IQR: 101.6-198.9 pg/mg); KIM-1 (median: 812.5 pg/mg; IQR: 474.9-1269.9 pg/mg). We observed statistically significantly higher biomarker concentrations in girls compared to boys across all markers tested ($p < 0.001$). Approximately 40% of children had at least one urinary biomarker concentration greater than the sample mean plus one standard deviation, suggestive of an elevated level. Girls had more than five times the odds of having elevated urinary concentrations of >1 biomarker using this designation compared to boys (OR: 5.3; $p < 0.001$; 95% CI: 2.8, 10.4). In adjusted models, urinary NGAL concentration was significantly higher in older children, while YKL-40 and IL-18 concentrations were higher in younger children, and KIM-1 and MCP-1 concentrations were not associated with age. High-risk municipality, eGFR and family history of CKD were not associated with increased concentrations of any of the biomarkers.

Conclusion: Biomarker analyses may provide early insight into kidney injury prior to CKDu diagnosis and may have utility in identifying youth at risk for the disease or pre-occupational risk factors. Forty percent of children in our study had urinary concentrations of at least one biomarker that were elevated compared to other children in this sample, however we did not observe a strong effect by region, age or family CKD history. The observation of girls having

significantly higher levels of biomarker concentrations than boys is consistent with our prior study of adolescents, and may indicate community-level environmental exposures or behaviors, or sex-linked biological differences. Trends in biomarker concentrations over time are needed to identify biomarkers associated with reductions in eGFR or serum creatinine.

Contributing Authors: Jessica H. Leibler, Oriana Ramriez Rubio, Juan Jose Amador, Damaris Lopez-Pilarte, Wassim Obeid, Chirag R. Parikh, and Daniel R. Brooks

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13. Description of the epidemic of chronic kidney disease affecting the adult population of El Salvador: a cross-sectional study

Carlos Orantes, Nephrologist. NCD Directorate, MINSAL

Abstract:

INTRODUCTION The start of the present century has witnessed the outbreak of an epidemic of chronic kidney disease (CKD) in several Central American countries. In El Salvador the epidemic is a serious health problem. CKD is the second leading cause of death among men, the fifth among people aged over 18 years, and the third leading cause of hospital deaths among the adult population. Knowledge about the condition is fragmentary, particularly as concerns the subtype not attributable to traditional causes, basically diabetes and hypertension.

OBJECTIVE Estimate the extent of the epidemic of chronic renal disease affecting the adult population of El Salvador, considering both the prevalence of the condition by type and the presence of its potential risk factors across the country and in the most relevant subpopulations.

METHODS A descriptive cross-sectional study was conducted based on the results of the Survey of Non-Communicable Diseases in the Adult Population of El Salvador, completed in 2015 (ENECA-ELS 2015), which was applied to a two-staged probabilistic cluster sample with stratification of first-stage units. The survey addressed 19 of the 118 primary variables included in the original study. Collection of data about 4 817 adults (questions and measurements) was performed between October 2014 and March 2015. Statistical analysis focused on point estimation of prevalence rates and means describing risk factors. Both biological or non-traditional (such as poor hydration or exhausting working hours) and toxic-epidemiological risk factors were looked into. A separate analysis was performed to determine the prevalence of CKD of non-traditional causes. Estimation of the corresponding confidence intervals was made with the appropriate weighting factors.

RESULTS Hypertension was found to be the most common biological risk factor (37.0%). "Non-traditional" and toxic-epidemiological risk factors included high intake of sugared beverages (81.0%) and poor hydration (65.9%), as well as the fact that one out of every 10 people are intensely exposed to agrochemicals (12.6%) while doing their job. Overall CKD prevalence was 12.8% (18.0% for men and 8.7% for women), whereas the prevalence of non-traditional causes was 3.9% (6.1% for men and 2.2% for women). 13.1% of the CKD sufferers are aged 40 years or under.

CONCLUSIONS An epidemic of chronic kidney disease of large proportions is currently underway El Salvador. Data depict a public health tragedy affecting not only elderly men, but also young people of both sexes. Results corroborate the findings of previous research conducted in some Salvadoran farming communities. A relevant, alarming fact is the high degree of exposure to agrochemicals by the population, a situation deserving more detailed analysis, regardless of its potential impact on chronic kidney disease.

KEYWORDS chronic kidney disease, prevalence, risk factors, epidemic, El Salvador, CKDu, CINAC, MeN

14. Chronic Kidney Disease in the High Specialty Regional Hospital (HRAECS) of Soconusco Chiapas, Mexico

Antonio Trejo Acevedo, Instituto Nacional de Salud Publica/ Centro Regional de Investigacion en Salud Publica

Abstract:

The Soconusco region is made up of 15 municipalities, which includes the border zone between Mexico and Guatemala. This area is considered as the main agricultural area of the state of Chiapas. The communities that live in this region have population, socioeconomic and epidemiological characteristics similar to the countries of Central America and Sri Lanka, where the CKD has caused concern about the increase in the number of patients with this condition. Hence the importance of conducting research in the Soconusco to know the causes and origin of CKD. This is the first study that addresses CKD in the Soconusco region, showing the frequency of patients diagnosed with CKD at the Regional Hospital of High Specialty of the Health City (HRAECS) of Tapachula, Chiapas, Mexico. A retrospective, cross-sectional and descriptive study was carried out, which consisted in carrying out the review of records of patients with a diagnosis of CKD registered in the HRAECS Nephrology specialty from January 1, 2008 to December 31, 2017. A database was generated, with the numbers of files, name, age, sex, place of origin and address. With the information obtained, thematic maps were generated by location, municipality and year to locate and observe the areas of incidence of CKD in the municipalities of the state of Chiapas. After each file, the telephone number of the patients or relatives was obtained, who were contacted and obtained the informed consent to review their file in the HRAECS clinical file. Results: The number of patients registered and treated in the specialty of Nephrology during the study period was 620 records with a diagnosis of RD. Of the total of cases, 510 cases were located in the municipalities of the Coast of the State of Chiapas, representing 82.26%. Of which 436 were located in municipalities of El Soconusco, corresponding to 70.32% of the total cases of RE registered in the State of Chiapas. Within the municipalities that comprise the Coast of Chiapas, it was observed that the municipality of Tapachula was the one that presented the largest number of cases with 242 patients. Followed by the municipalities of Pijijiapan (35), Tuxtla Chico (25), Mapastepec and Huehuetan (22 records each). While the municipalities of Suchiate and Frontera Hidalgo presented 21 cases, Cacahoatan registry 20 and Acapetahua 18 cases. The rest of the municipalities presented a lower number of cases. To the analysis by sex I throw that 52.55% are men and 47.45% women. With respect to the age of the patients, the age group of 21 to 30 years old presented the highest number of RD with 30 cases, followed by the group of 31 to 40 years with (24) and the one of 41 to 50 years with (26) , being these three age groups from 21 to 50 years the highest frequency of patients diagnosed with CKD, representing 65.4% of the cases registered in the period. The occupations reported by the patients were 44% housewives, 20% have no employment, 16% employed 9.6% peasants. 34.4% reported having 3-6 months with CKD and 4.8% <3 months. We carried out the confirmation of the diagnosis of the patients admitted to the HRAECS comparing the diagnosis of the physical file versus the electronic file, finding that the main causes of CKD in the HRAECS were Diabetes, Hypertension, structural, autoimmune,

glomerulonephritis and 20% of the total of the cases are of unknown causes. There are few studies of CKD in Mexico. This is the first study conducted in the south-southeast that describes the situation of CKD, to understand the dynamics and determinants involved in the prevalence of CKD. Key words: Renal Disease, Soconusco

Contributing Authors: Trejo-Acevedo A1; Rivero-Perez NE1; Mugerza-Lara A2; Sandoval-Bautista MA1; Moreno-Banda GL3; Cetina Diaz H2; Sepulveda-Delgado J2; Perez-Tirado JM2; Danis-Lozano R1 1.- Instituto Nacional de Salud Publica. Centro Regional de Investigacion en Salud Publica 2. Hospital Regional de Alta Especialidad Ciudad Salud. 3. Instituto Nacional de Salud Publica. Centro de Investigacion en Salud Poblacional.

15. Spatial variation of Chronic Kidney Disease mortality within Mesoamerican countries and association with land use and climate factors

Erik Hansson, Gothenburg University

Abstract:

Introduction: Previous studies have shown that CKD burden has a substantial subnational spatial heterogeneity in Mesoamerica. Differences in data sources, analysis methods and covariate handling limit comparability of the findings of spatial determinants of CKD burden from different Mesoamerican countries.

Method: CKD mortality or admissions data from registries or previously published studies were collected from all countries from Mexico to Colombia except Belize (pending) and Honduras (unavailable). Bayesian spatial regression models were used to estimate the underlying risk surface from the raw data to reduce the noise in small-area data and identify significant clusters of increased risk. After descriptive analysis, Bayesian regression models were also used to analyze associations between CKD burden and area-level risk factors for each country - so far focusing on heat and sugarcane cultivation and the interaction between these.

Results: Maps of spatial variation of CKD burden identify CKD hotspots on the Pacific coast of southernmost Mexico, Guatemala, El Salvador, Nicaragua, Costa Rica and Panama, and one in the Mexican state of Veracruz, but identify no clusters in Colombia. There was a clear association between CKD and increasing temperatures, especially in areas with intense sugarcane cultivation. Conversely, there was no association between CKD risk and sugarcane cultivation intensity in colder areas. An area-level association between lower CKD burden and adverse socioeconomic conditions in some countries raises questions on differences in data capturing within countries.

Discussion: This project is ongoing and findings preliminary, but congruent with the hypothesis that intense physical efforts in heat is a significant cause of CKD in Mesoamerica. We welcome collaboration on further stages of this project, in which we aim to analyze area-level associations between CKD and pesticides, drinking water properties and infectious disease.

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16. Behavioral Risk Factors and CKDu in Sri Lanka

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Abstract:

Chronic Kidney Disease of Unknown Etiology (CKDu) is found in tropical and sub-tropical regions of the world, where agriculture is the predominant mode of production. In Sri Lanka, where the proposed project will be carried out, CKDu is common among farmers engaged in paddy and slash and burn cultivation. Mean age is which is 39.1 years (Jayatilake et al. 2013) is significantly younger than the mean age of CKD in industrialized countries, where the primary cause of CKD is diabetes or hypertension. This indicates that we need to investigate what risk factors trigger disease risk in rural agricultural communities. In this research, I shall use a life course approach to examine the connection between CKDu and behavioral risk factors. Such behavioral risk factors include drinking water from shallow wells, canals, and tanks, living in unhygienic conditions, working as paddy laborers, manually spraying chemicals and fertilizers often without protective gear, working under the hot sun, drinking locally brewed alcohol, smoking, and chewing beetle and tobacco. Such people often subject to snake bites, another risk factor for CKDu. The other variables in this perspective include a family history of involuntary resettlement, malaria, poor nutrition, malnutrition during childhood, low birth weight, high infant and maternal mortality. Hantavirus infection and leptospirosis, which are risk factors for CKDu are reported. People get such infections due to working in inundated paddy fields with contaminated water and living in substandard housing infested with urine and other fluids of rodents and cows. Field data will be collected from three different communities. 1) high-risk endemic community with many CKDu affected families with patients identified moderate to advanced CKDu (estimated glomerular filtration rate [eGFR] of 20- 59 ml min⁻¹ 1.73 m⁻², based on hospital data and recent mass blood surveys), 2) a low-risk community with fewer or no CKDu patients, and 3) a middle-income community where such behavioral forms are not present as described above but carry out paddy agriculture. Data on hantavirus infection and incidents of leptospirosis will be collected from hospital records and past medical histories of people, which will also reveal malnutrition, birth weight and incidents of malaria in the sample. Urine dipstick and serum creatinine testing will be conducted on all residents above 12 years of age in all three sample populations. Biometric data including age, sex, height, weight, and body mass index, and blood pressure will be measured, collected and recorded. Past medical history of all members will be extracted. Data on sociocultural variables will be collected using a semi-structured interview schedule. The project will have three phases. During the first phase (exploratory phase) qualitative information will be collected to identify the necessary variables. Participant observation, open-ended interviews, and other anthropological methodologies will be used to explore a sequence of socially defined events and roles that the individual enacts over time and identifying related variables. During the second phase, the variables that are identified in the exploratory phase will be measured. In the third phase, data will be analyzed, interpreted, and published. Data will be recorded in an online platform using iPad as the instrument for data collection. Data will be analyzed using standard statistical procedures. In addition, a predictive model will be developed using machine learning

algorithms. This predictive model can be used to predict if a person has CKDu or not or has the tendency to get CKDu. The project will introduce a new perspective to look at CKDu as a behaviorally induced disease with a new theoretical approach.

17. Do Agricultural Workers in Eastern North Carolina Have Unexplained CKD? - An Exploratory Study

Guillermo Hidalgo, East Carolina University

Abstract:

Chronic kidney disease (CKD) often results in lifelong dialysis and early death. An epidemic of unexplained chronic kidney disease (CKDu) is occurring throughout Central America and Mexico (CAM). CKDu manifests without classical hallmarks of traditional CKD. Annually, North Carolina (NC) hosts ~75,000 migrant and seasonal farmworkers (MSFWs) from CAM. Many MSFWs, US citizens and adolescent children of diverse ethnic ancestries labor in Eastern NC farm fields. The presence of CKD and CKDu occurring in agricultural workers in Eastern NC is unknown. Environmental exposures, heat stress and dehydration are leading hypotheses contributing to this preventable disease.

Goal: This exploratory study aims to estimate the distribution of eGFR and biomarkers for genetic, occupational and environmental exposures in a convenience sample of 200 agricultural workers (ages 13-55) in 5 contiguous counties in eastern NC (Pitt, Greene, Lenoir, Wayne, and Duplin Counties) and Buncombe county during harvest season (September and October 2020).

Methods: Agricultural workers and adolescents will be identified through existing farmworker health programs, grass roots community groups and local clinics. Crops include strawberries, sweet potatoes, and tobacco. The North Carolina Agro-medicine Institute located at ECU has strong collaborations with USDA agricultural extension offices and local primary care clinics. eGFR will be measured according to definitions articulated in DEGREE and CKiD study (Caplin et al 2017, Furth et al 2009). Measures of family history of CKD, diabetes status, hypertension, and BMI will be obtained concurrently with personal interviews (English and Spanish) obtaining occupational (pesticide exposure, land altitude), hydration, non-steroidal anti-inflammatory drugs and alcohol intake as well as dietary information. For eGFR below 60 ml/min, urine and blood biomarkers, and biopsy material will be collected and classified by blinded genetics, proteomics and renal histopathology teams. Participants will be offered follow-up care and treatment. The primary outcome of this exploratory study is the prevalence of reduced renal function in agricultural workers (Caplin et al 2017).

References. What do epidemiological studies tell us about chronic kidney disease of undermined cause in Meso America? A systematic review and meta-analysis. Gonzalez Quiroz, M. Pearce, N. Caplin, B. and Nitsch, D. Clin. Kidney J. 2018 Aug;11(4):496-506
Longitudinal formulas to estimate glomerular filtration rate in children and adolescents with chronic kidney disease. Abraham, AG. Schwartz GJ. Furth, S. Warady, BA. Munoz, A. Clin J. Soc. Nephrol. 2009;4(11): 1724-30

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18. Synergy of projects for non-traditional Chronic Kidney Disease research in Panama

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Abstract:

Since 2005, the SALTRA-Panama team attempted to investigate Chronic Kidney Disease (CKD) in Panama, however, it was not feasible. After the SALTRA Workshop in Nicaragua (October 2013) in which this topic of research in the region was prioritized, it was retaken. In January 2015, the Ministry of Health formalized the group and supported the search for funds. The II SALTRA National Meeting held in May 2015 dedicated one day to developing the ERC theme with international guests: Dr. Tord Kjellstrom (New Zealand), Dr. Jennifer Crowe (Costa Rica) and Dr. Agnes Soares (PAHO, Washington). In October 2016 the agreement between the Ministry of Health, the University of Panama and the National Secretariat of Science, Technology and Innovation (SENACYT) was signed for the development of the Joint Research Project "COMPREHENSIVE EVALUATION OF CHRONIC RENAL DISEASE NON-TRADITIONAL CAUSE (ERCnT) IN PANAMA" with a financing of US \$ 350,000.00. The objectives of the project are: to articulate the institutional and sectoral resources to face the serious problem of the increase of patients with CKD in Panama; develop the analysis of the integral situation of the ERC in Panama; carry out scientific research activities that generate evidence for the determination of the causality of the ERCnT, its alternative solutions and decision making; strengthen the installed capacity through processes to support the training, updating and training of human resources for research and the provision of health services to meet the high demand for patients with CKD and promote the implementation of health interventions, based on scientific evidence , that support the prevention of premature deaths by ERCnT. The inter-institutional team, coordinated by SALTRA-Panama, has been made up of officials from the Ministry of Health, the Social Security Fund, the Statistics and Census Institute of the General Comptroller's Office of the Republic, the Gorgas Memorial Institute for Health Studies, of the Nephrology and Hypertension Society of Panama, the Specialized University of the Americas and the University of Panama. In 2018, it was associated, as a synergistic project, with Project PAN0008 - Strengthening the Capacity to Improve the Use of Nuclear Applications for Development - under the coordination of the Ministry of Foreign Affairs. It is a technical cooperation project for an amount of 273,909 EUROS financed by the International Atomic Energy Agency. The objective is to increase the capacity in the management of nuclear technology and strengthen national human resources. It includes scholarships, visits by experts, training courses, scientific visits, work meetings and teams. The following working groups are available: occupational health / health, water, air, soil / sediment, food and meteorology with members of the Technological University of Panama, the Ministry of Environment, the Ministry of Agricultural Development, the Institute of Agricultural Research , the Public Services Authority, the Aquatic Resources Authority, the Nutrition Institute of Central America and Panama (INCAP). There is a team of researchers at the national level and another at the local level of the most affected region, the province of Coclé. Determinations of pesticides and heavy metals will be made in water, food, soil / sediments. In air, ozone, nitrogen dioxide, lead, mercury and cadmium will be determined in PM 2.5 and PM10 particles. Both projects will provide information on a topic of

great impact on public health and have been based on cooperation, the exchange of information and the transfer of knowledge with the support of experts.

19. Multisectoral Commission for the management of Chronic Kidney Disease of unknown etiology (CKDu) in Guatemala

Gerardo Arroyo, Departamento de Citohistología, Universidad de San Carlos de Guatemala

Abstract:

In 2013, the Pan American Health Organization, on his resolution CD52.R10, recommended to promote alliances within all sectors involved in management of CKDu. In June 2018, the University of San Carlos of Guatemala (USAC) and Guatemalan Social Security Institute (IGSS) organized a National Seminar on CKDu which concluded with the implementation of a Multisectoral Commission for the study of CKDu in Guatemala, and included representatives of the government, from the medical assistance sectors, and IGSS, and representatives from the sugar cane production sectors. This is the first time that such an alliance comes to play a role in finding solutions for a common problem. This Commission signed an agreement with the goal of implementing a research agenda, which came from recommendations given at the National Seminar on CKDu, at three discussion tables: Social and economic aspects of CKDu, the Environment and kidney diseases and Public Health in CKDu. The five following topics have been prioritized: 1. Formulation, preparation and distribution of a hydrating beverage for agricultural workers of sugar cane crops 2. Prevalence and risk factors for developing CKDu in Guatemala 3. Working conditions of agricultural and other workers in the south coast of Guatemala 4. Metals in water sources for human consumption, in areas with high numbers of patients on hemodialysis 5. Biomarkers for evaluation of renal tubular function Other activities included the advocacy for the creation of the National Dialysis and Transplants Registry through a Ministerial Agreement and the organization of the II National Seminar on CKDu which will be held in June 2019. Sources for financing research projects as well as meetings will be procured by the Commission. This represents a unique approach for solving a relevant problem in the area.

20. The MesoAmerican Nephropathy Occupational Study (MANOS) Cohort: Overview and progress

Sinead Keogh, Boston Univeristy

Abstract:

The epidemic of Mesoamerican Nephropathy, also known as CKDu, continues to adversely impact communities throughout Central America. While there are many theories regarding the causes of CKDu, identifying specific risk factors has been difficult, in part due to design limitations of previous cross sectional studies and reliance upon self-reported exposures. To address these limitations, we established the Mesoamerican Nephropathy Occupational Study (MANOS), a prospective cohort study of workers from multiple industries in El Salvador and Nicaragua. The goal of MANOS is to investigate the role of occupational and environmental exposures, including heat stress, glyphosate, and heavy metals, on the initiation and progression of CKDu in Central America.

Methods: Recruitment of workers and baseline exposure assessment took place from January through May 2018 in both countries. The MANOS study teams, led by physicians with extensive occupational health and research expertise, coordinated with industries and worker cooperatives to conduct initial workshops to provide interested individuals with an overview of study aims and design. Eligibility criteria included males age 18-45, work in current industry for at least one season, and no prior diagnosis of CKD or other related health outcomes. At baseline, MANOS team members conducted an extensive interview with enrolled participants regarding demographics, current and past job tasks and schedule, work and home agrochemical use, personal protective equipment, medical history, current medical symptoms and medication use, hydration practices, diet, alcohol and tobacco use, and family history of CKD. For the following three consecutive workdays, participants were monitored during their work shift to measure core body temperature, heart rate and physical exertion. Pre- and post-shift questionnaires were also administered. Pre- and post-shift urine samples were collected on all three days, with pre- and post-shift blood collected on the last day only. Samples will be analyzed for indicators of kidney function (serum creatinine and cystatin-c), urinary biomarkers of kidney damage, and exposures to heavy metals and glyphosate. Saliva samples are also being collected for genetic analysis. The MANOS cohort will be followed every approximately six months for three years, to administer a detailed follow-up questionnaire and collect urine and blood samples.

Results: A total of 569 workers (279 from El Salvador and 290 from Nicaragua) were recruited into the MANOS cohort and completed baseline monitoring. In El Salvador, participants represent sugarcane (40%), corn (40%), and road construction (20%) industries. In Nicaragua, they represent sugarcane (43%), plantain (20%), and brick making (37%) industries. Sugarcane workers in both countries are cane cutters and/or pesticide applicators. Preliminary data indicate that, despite exclusion criteria of diagnosis with CKD, 9.3% of the MANOS cohort had an eGFR <60 mL/min/1.73 m² at baseline monitoring. To date, we have completed two rounds

of data collection and are beginning the third round. Participant follow-up in round 2 was highly successful, with ~90% retention.

Discussion: Using a longitudinal cohort design and gold-standard exposure assessment and laboratory methods to evaluate exposure to glyphosate, heavy metals, and heat stress, the MANOS cohort will enable us to investigate the potential role of key risk factors for the development of CKDu, including potential gene-environment interaction. The cohort will also provide insight into early disease and progression factors by monitoring both CKDu diagnostic outcome markers (eGFR and serum creatinine) as well as biomarkers indicative of early kidney injury over time.

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21. State of the Art in Research on Chronic Renal Failure of Non-Traditional Causes in Mexico and Trends in Morbidity and Mortality

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Abstract:

Introduction: Chronic kidney disease (CKD) is a global problem affecting in its final stage 19.7 million people around the world in 2017. During the period from 1990 to 2017 the mortality rate increased for all the countries of Central America. In Panama, workers of rice fields and canaverales in the south of the province of Cocolé, have been pointing out the existence of a high number of cases and deaths due to chronic renal failure since at least the 1990s. Independent studies carried out among residents of this have registered that, if there is a high number of cases, without establishing what could be the risk factors associated, or determine with certainty the magnitude of the impact of chronic kidney disease in the population.

Objectives: Confirm or rule out the existence of clusters of mortality and morbidity due to chronic kidney disease in Panama, characterizing the affected population and the magnitude of the clusters identified with respect to national rates.

Methods: Mortality data compiled by the INEC between 2001-2015 and the patient database in Units were used. of Hemodialysis, provided by the Social Security Fund. The data were georeferenced at corregimiento level, using the politico-administrative division of 2003. Mortality and morbidity rates were adjusted and spatially smoothed for CKD using the Geoda software; subsequently, an analysis of atypical and group values was performed using ArcGIS (Moran Local Anselin), which allowed to identify hot spots, cold spots and atypical values, the results were mapped by the geographic information software QGIS. Results In the Republic of Panama, between From 2001 to 2015, some 4,441 deaths were recorded, while a total of 2,343 patients were registered in hemodialysis rooms. The adjusted mortality rate increased from 6.3 per 100 thousand inhabitants in 2001 to 14.4 per 100 thousand inhabitants in 2015, with a global rate for the entire period of 7.7 per 100 thousand inhabitants. The rate adjusted for age and sex for patients in the hemodialysis units between 2001 and 2015 was 7.73 patients per 100 thousand inhabitants, being higher for men (8.6 patients per 100 thousand inhabitants, than for women (6.3 patients per each 100 thousand inhabitants.) As for the specific rates, it is possible to identify that between 15 and 19 years, the specific rates for men and women are similar, but that from here the specific rate for each age group in the men began to be greater than the specific rate of women (0.8 patients per 100 thousand inhabitants for both sexes). Chronic kidney disease in Panama affects mainly the male population (70% of deaths), in occupations with extenuating conditions as, agricultural workers, street vendors and construction workers and factories (70%), are the ones that register the highest number of deaths. The distribution of corregimiento clusters with mortality rates, includes part of the provinces of Panama West, Cocolé, Herrera, Los Santos, Veraguas and Chiriquí. In the case of

morbidity, the cluster includes all the provinces mentioned above, with the exception of the province of Veraguas.

Conclusions The existence of corregimiento clusters with high rates of morbidity and mortality due to chronic kidney disease could be verified, with the southern area of Coclé having the highest rates, which exceed three or four times the national rate.

22. Cyanotoxins: A Hidden Cause of Chronic Kidney Disease of Uncertain Etiology in Sri Lanka?

Pathmalal Manage, Department of Zoology, University of Sri Jayewardenepura

Abstract:

Chronic Kidney Disease (CKD) is a growing global public health concern representing the 7th most common cause of death according to WHO (2012), and in hot spots around the globe, CKD of Uncertain etiology (CKDu) is a leading non-communicable disease and cause of death. In Sri Lanka, there is an alarming increase of CKDu in the dry zone of rural farming communities. Existing evidence favors a multi-factorial aetiology, but research over the last few decades has failed to recognize the specific risk factors. One understudied area of research is whether cyanotoxin formation from algal blooms may be a risk factor for people living in endemic-areas. The objective of this initial research focus is to evaluate whether cyanotoxins contribute to CKDu in Sri Lanka. Our hypothesis is that cyanotoxin presence is elevated CKDu-endemic areas compared to non-endemic areas, and drinking water exposure from affected wells or surface water reservoirs may contribute in part to altered kidney function and CKDu development. Our recent research identified cyanobacteria in 75% of freshwater bodies tested in endemic areas compared to 40% of freshwater bodies in non-endemic areas. Recent findings also reveal toxin-producing cyanobacteria in a majority of drinking water reservoirs including *Microcystis aeruginosa*, *Cylindrospermopsis* sp. and *Anabaena* sp. Additionally, surface and dug well water in CKDu-endemic areas significantly correlate between cell density of cyanobacteria and cyanotoxins. The occurrence of multiple cyanobacteria with elevated cyanotoxin concentrations [*Cylindrospermopsis* (CYN) (1.0 ± 0.01 to $5.3 \pm 0.02 \mu\text{gL}^{-1}$) and *Microcystin-LR* (MC-LR) (1.0 ± 0.01 to $7.6 \pm 0.34 \mu\text{gL}^{-1}$)] in commonly used dug wells show that ingestion of well water is a likely source of cyanotoxin exposure. Indeed, our ongoing study demonstrates a high concentration of CYN (1000 ± 10 to $860102 \pm 260 \mu\text{gL}^{-1}$) and MC-LR (200 ± 10 to $240102 \pm 120 \mu\text{gL}^{-1}$) in urine samples collected from 248 CKDu patients in the North Central Province, compared to control samples (72) (below the detection limit $50 \mu\text{gL}^{-1}$) collected from Agunukolapallassa, a non-endemic area in the Southern Province. Further research includes the development of rat model and cell culture studies to investigate the effects of cyanotoxins on kidneys. Future work that includes cyanotoxins as one potential risk factor in a global, multi factorial study would help corroborate these research findings. Keywords: Cyanotoxins, *Cylindrospermopsis* (CYN), *Microcystin-LR* (MC-LR), Well water, Human Urine, Exposure

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23. Geospatial analysis of the situation of some chemicals used in the Republic of Panama

Maria Ines Esquivel, Ministerio de Salud

Abstract:

Exposure to chemicals may cause acute or chronic effects. These effects can be: direct, systemic; Awareness Combined the health effects of chronic exposure to heavy metals such as lead, cadmium and mercury are widely documented, but there is little data on the renal impact of low environmental exposure to these metals. In Central America and Panama is studying chronic renal disease and chronic non-traditional renal disease, which are the cause of an epidemic in some countries that are in the strip of Ecuador. In this process of analysis of possible causal factors of non-traditional renal disease, in the Republic of Panama is being done analysis of the existing data in government institutions to better visualize the situation of some chemicals in the country. The risk factors (susceptibility, initiation and/or progression) associated with chronic non-traditional renal disease, the known environmental causes of chronic renal disease and different epidemiological studies have led to the thought that etiology It could be multifactorial. There are a variety of causal hypotheses such as: Exposure to heat and intense work, exposure to heavy metals such as cadmium, or arsenic, agrochemicals, diseases systemic infections such as leptospirosis, the use chronic of drugs potentially Nefrotoxicos, such as non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, or aminoglucosidos antibiotics. This paper presents a mapping of the existing information on crops and some pesticides that have been used or used for their production, as well as the analysis of the monitoring data of some fertilizers for the control of input quality that is done by the Competent authority. The objective is to visualize in maps the possible risks of exposure to chemicals, using the existing official data, to have an objective guide to direct other studies related to chemicals. As a methodology was carried out a survey of the official information that exists in the web of the institutions, like crops and recommended inputs; Data of cancer mortality, data of morbidity where some diseases were selected that the literature mentions as caused by disrupting substances of the endocrine system. This information was selected and is mapped according to the cultures by province. Then, cases of cancer mortality were mapped by province, and cases of morbidity. The expected result is that the possible risks can be easily visualized by the community in general, besides that the maps can serve as guide for further deeper studies.

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24. Evidence Supporting a Role for Vasopressin in Mesoamerican Nephropathy

Jaime Butler-Dawson, Center for Health, Work, & Environment, University of Colorado

Abstract:

Early identification and understanding of mechanisms related to subclinical kidney dysfunction are important steps in detecting and protecting populations at risk for chronic kidney disease of unknown origin (CKDu). The aim of this study was to examine whether the vasopressin pathway, as measured by copeptin, contributes to kidney dysfunction, and to determine whether increasing fluid intake can reduce circulating copeptin and thereby preserve kidney health among healthy agricultural workers exposed to hot and potentially dehydrating conditions. **Methods:** We conducted two longitudinal studies of sugarcane workers in southwest Guatemala to examine relationships between hydration indices, copeptin concentrations, and kidney function markers. For both studies, urine and blood samples were collected at the end of work shift from a combined total of 302 participants at three time points during the 6-month harvest. For each study independently, we calculated β estimates and 95% confidence intervals of each kidney function marker using multivariable linear mixed-effect models for repeated measures. In addition, we examined whether baseline copeptin concentrations increased the odds of having developed $< 60 \text{ mL/min/1.73 m}^2$ estimated glomerular filtration rate (eGFR). **Results:** In multivariable cross-sectional analyses, copeptin concentration was positively associated with serum creatinine (β : 0.01, 95% CI: 0.003, 0.03), cystatin C (β : 0.02, 95% CI: 0.001, 0.04), and neutrophil gelatinase-associated lipocalin (NGAL) (β : 1.69, 95% CI: 1.24, 2.14) and inversely associated with eGFR (β : -1.10, 95% CI: -2.03, -0.17). In addition, as workers improved their hydration (measured by a decrease in urinary specific gravity), copeptin was suppressed, and copeptin suppression was associated with an increase in kidney function (measured by an increase in eGFR). Elevated baseline copeptin concentrations were associated with increased odds for $< 60 \text{ eGFR}$ in one study (OR = 1.12, 95% CI 1.01-1.24) after adjusting for pre-employment eGFR, HbA1c, age, systolic and diastolic blood pressure. **Conclusion:** Elevated copeptin is associated with markers of kidney dysfunction. From this study, it appears that a potential pathway to preserve kidney function in agricultural workers could be accomplished by lowering vasopressin through increasing fluid intake.

Salary support was provided in part by Pantaleon, an agribusiness in Guatemala. University of Colorado and Pantaleon are separate, independent organizations. University of Colorado employed appropriate research methods in keeping with academic freedom, based conclusions on critical analysis of the evidence and reported findings fully and objectively. The terms of this arrangement have been reviewed and approved by the University of Colorado in accordance with its conflict of interest policies.

25. Investigating possible infectious causes of chronic kidney disease of unknown etiology in a Nicaraguan mining community

Katherine Yih, Dep't of Population Medicine, Harvard Medical School

Abstract:

A chronic kidney disease of unknown etiology (CKDu) has been killing workers in Central America. Occupational heat stress is thought to play an important role. Leptospirosis and hantavirus have been suggested as additional possible risk factors. In a case-control study in a Nicaraguan mining community, a structured survey was administered to adults, and biological measurements and specimens were taken. Serum was analyzed for antibodies to *Leptospira* and hantavirus. Prior to statistical analysis, a board-certified nephrologist determined final case and control status based on serum creatinine and other laboratory values. Multi-variable analysis was by logistic regression. In sensitivity analyses, cases were restricted to those diagnosed with CKDu in the previous 3 years. Of 320 eligible participants, 112 were classified as presumptive cases, 176 as controls, and 32 as indeterminate. The risk of CKDu in those ever having worked in mining or construction was 4.4 times higher than in other participants (odds ratio=4.44, 95% CI: 1.96-10.0, $p=0.0003$). Eighty-three (26%) of the 320 participants were seropositive for at least one tested strain of *Leptospira*. No evidence of a causal link between leptospirosis or hantavirus and CKDu was found. The sensitivity analyses provide some evidence against the hypotheses that leptospirosis or hantavirus leads to CKDu within a few years. A major limitation was the impossibility of determining the absolute or relative timing of infection and CKDu onset. A prospective cohort design, with repeated collection of specimens over several years, could yield clearer answers about infections as potential etiologic agents in CKDu.

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26. A Total Worker Health® approach to assessing kidney health in sugarcane workers in Guatemala: an opportunity for nutrition intervention

Lyndsay Krisher, Center for Health, Work & Environment, Colorado School of Public Health, University of Colorado Denver

Abstract:

A Total Worker Health® approach to assessing kidney health in sugarcane workers in Guatemala: an opportunity for nutrition intervention The Center for Health, Work & Environment (CHWE) began a collaborative project to address Total Worker Health® (TWH) with Pantaleon, a Guatemala sugarcane agribusiness. TWH is a systematic approach to promote the wellbeing of workers as well as preventing workplace injuries and illnesses. One of the project aims is to address risk factors for kidney injury, which has led to the development, implementation and evaluation of enhanced preventive activities and interventions to protect workers. During a 2017-18 research study, anthropometric and body composition characteristics of 154 sugarcane cutters were measured over the harvest (November to April). The mean change in weight, BMI, body fat percentage, skinfolds of the triceps, subscapular and chest, body density, fat mass and fat free mass were measured or calculated. All measures significantly declined across the harvest. The majority of workers lost body weight (78%), body fat (91%), and fat mass (92%). Over half lost muscle (fat free) mass. On average about 4% of body mass was lost during the season. Results differed by worker origin (highland vs. coastal). Urinalysis was conducted to assess proteinuria and ketones. The data suggest that workers may be hypocaloric; poor nutrition may put workers at increased risk for kidney function decline. Based on the preliminary findings, CHWE and Pantaleon are collaborating to assess worker food security and the efficacy of the current nutrition benefits provided by Pantaleon to workers (3 meals per day and snacks) to design an enhanced nutrition intervention program. In conclusion, findings from research coupled with quality improvement initiatives can be utilized to implement interventions that directly benefit workers.

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Support was provided in part by Pantaleon. University of Colorado employed appropriate research methods in keeping with academic freedom, based conclusions on critical analysis of the evidence and reported findings fully and objectively. The terms of this arrangement have been reviewed and approved by the University of Colorado in accordance with its conflict of interest policies.

27. Chronic Kidney Disease of unknown etiology (CKDu) India - Observations and Remedial measurement at community level

Gangadhar Taduri, Professor&Head, Department of Nephrology, Nizams Institute of Medical Sciences

Abstract:

Introduction:CKDu incidence and prevalence is increasing in various parts of India. Various etiological theories have been proposed. There are no community intervention studies available.

Material & Methods: Based on reports from patients coming from the region and data from hospital, community study was carried out in three regions of the state of Andhra Pradesh over a period of 10 years. The 3 regions screened were Nellore District 2006-2010 (4 villages), Prakasam District 2008-2010 (15 Villages) and Srikakulam- Uddanam 2013 - 2016 (13 Villages). Two adjacent control regions were chosen Prakasam District (2 Villages) and Srikakulam-Uddanam (7 Villages). Community awareness was created for screening; Screening included biochemistry (Blood Urea Nitrogen, Serum Creatinine, Total Cholesterol and Random Blood Sugar), Complete Urine Examination and 3 part Complete Blood Examination. Community intervention by changing source of drinking water to surface from bore well water was carried out in Prakasam District region and Nellore District.

Results: Total population screened in 32 villages of 3 regions was 6956 from a total population of 57000. Percentage prevalence of kidney disease in the screened population Nellore District (11 - 41.13), Prakasam District (6.17 - 24.32) and in Srikakulam- Uddanam region (6.3 - 33.8). The percentage prevalence range in control regions Prakasam District (3.15 - 5.48) and Srikakulam- Uddanam (0.6 - 1.3). In short term (06 months) follow up with surface drinking water at Prakasam District there is no difference in the renal function (Scr - 2.043 + 0.39 mg/dl vs 2.011 + 0.56 mg/dl; p=0.76) but the endothelial function (as measured by Augmentation Index and Augmentation Pressure Sphygmocor, Australia) improved statistically. (Augmentation pressure- (10.4 + 6.93 vs 3.3 + 3.17: P=<0.0001), aortic augmentation index -(24.7 + 11.11 vs 11.5 +11.27 : P=<0.0001). In long term intervention (08 years) with surface drinking water at Uchapally Village (1800 population) of Nellore district the prevalence reduced to 7% (screened 136) in 2014 from 41.13% screened population 51) in 2006.

Conclusions: Kidney disease prevalence is high in various parts of India and CKDu is contributing to the disease significantly. Surface water intervention appears to be best possible remedial measure to prevent the CKDu.

28. Incident kidney injury among Nicaraguan sugarcane workers during harvest - first year intervention assessment

David Wegman, University of Massachusetts Lowell

Abstract:

Introduction: Previous studies document high risk of incident kidney injury (IKI) during harvest among sugarcane workers that may progress to CKD in a substantial proportion of cases. Limiting dehydration and heat exposure by adequate rest, water and shade could reduce IKI and ultimately the onset and progression of CKD among sugarcane workers. This study describes the results from year one of an ongoing study evaluating work practices at a sugarcane mill committed to improving working conditions. We also map workers to assess if those with IKI tend to cluster in certain neighborhoods.

Methods: A cohort with four different types of sugarcane field workers (burned cane cutters, seed cutters, drip irrigation repair workers and field support staff) was followed during one harvest with biological sampling (including serum creatinine (SCr)) and questionnaires before and at the end of harvest. A convenience sample of administrative staff at the same sugarcane mill unexposed to environmental heat at work served as a comparison group. Only men with SCr ≤ 1.3 mg/dL and women with SCr ≤ 1.2 mg/dL were hired as field workers. Those with a SCr increase of >0.3 mg/dL when retested or reporting sick leave or leaving work due to creatinine elevation were considered to have IKI. Cohort dropouts were approached after harvest and interviewed on reason for leaving. Multi-level Bayesian regression models with spatially correlated random effects were used to estimate the spatial variation of neighborhood IKI risk, controlling for age, sex and occupation.

Results: Seven percent of those measured at end of harvest had IKI. A substantial proportion of workers quit working during harvest or missed follow-up measurements for other reasons (113/545), but 87% of these could be contacted afterwards. Creatinine elevation was reported among 32% as reason for sick leave or quitting, giving an overall IKI incidence of 12%. Occupation was the strongest determinant of IKI incidence and appeared associated with physical effort required: 27% among burned cane cutters (extreme physical effort), 8% among seed cutters (high physical effort) and 2% among irrigation repair workers and field support staff (lighter physical effort). All groups had similarly high environmental heat exposure. The age- and sex adjusted rate ratio comparing burned cane cutters with drip irrigation repair workers and field support staff was 11.2 (95% confidence interval 3.78-33.3). One 41 yo administrative worker (2%) developed IKI during the harvest period. This individual had hypertension at baseline, a condition very rare in the cohort. Elevated C-reactive protein (CRP) levels, decreased hematocrit and reporting recent fever, headache or weakness were associated with IKI, as was reduced baseline kidney function. The vast majority (96%) of followed-up workers could be mapped to 105 different neighborhoods. The median odds ratio (MOR) between a lower and higher risk neighborhood decreased from 2.96 (95% CI 1.67-5.70) to 1.70 (1.19-3.12) when adjusting for job, considerably smaller than the risk ratio seen for burned cane cutters (11.2). Statistically, the MOR cannot be below one.

Discussion: A healthy worker effect must be considered in similar studies. The strong association seen between increasing physical efforts and IKI is consistent with intense physical efforts in heat as a cause of IKI and CKD in this setting. Efforts to reduce heat exposure and dehydration should be intensified, especially for the most heat exposed workers. The symptoms and inflammatory markers associated with IKI may be heat-related and deserve further investigation. There was little variation in IKI incidence between neighborhoods, indicating that occupational rather than residential exposure influences IKI risk.

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29a. Lack of evidence regarding an Infectious Etiology of Mesoamerican Nephropathy make it unlikely

Rebecca Fischer, Texas A&M Health Science Center & Baylor College of Medicine

Abstract:

Infectious diseases are an important cause of interstitial nephritis in low- and middle- income countries. A longstanding hypothesis about the etiology of the unexplained kidney disease in Central America, Mesoamerican Nephropathy (MeN), is an infectious agent. Leptospirosis and Hantavirus infection have been suggested as the most likely culprits.

Methods: In 2015, we began surveillance for acute MeN at a large private hospital serving workers at an agricultural estate in western Nicaragua, a hotspot for MeN, in which individuals with AKI or elevated serum creatinine are prospectively identified. As part of this surveillance, urine and serum were collected in order to test for exposure to potential pathogens, and renal biopsies were collected on a small subset of classically-presenting patients. We tested serum from 199 acute MeN patients for IgM antibodies to *Leptospira* and Hantavirus; for a subset (n=10), urine, serum, and renal tissue underwent high throughput nucleic acid (RNA and DNA) sequencing methods to probe for patterns consistent with potential pathogens. Paired, acute and convalescent phase, sera were tested for n=90 individuals in order to ascertain seroconversion.

Results: In this population of agriculture workers, the prevalence of antibodies to *Leptospira* was 25% (IgM and 0% IgG), with seroconversion in 16%. Antibodies to hantavirus were observed in 12% (19% IgG and 3% IgM), with seroconversion in 7%. Nucleic acid sequencing suggested no pathogen of interest common to multiple subjects.

Conclusion: This study among acutely ill renal patients in a high-risk population of agriculture workers in a MeN hotspot, and high proportion of the population exhibits exposure to *Leptospira*, but circulating *Leptospira* were not detected within serum, urine, nor renal tissue. Hantavirus, while an important finding in this population, was not implicated as a cause of MeN. Advanced molecular methods to look for potential pathogens did not raise any alerts to commonalities or possible causative agents. In this analysis, infections were not implicated in the acute disease process of MeN patients.

29b. Does Nickel exposure play a role in the etiology of Mesoamerican Nephropathy?

Rebecca Fischer, Texas A&M Health Science Center & Baylor College of Medicine

Abstract:

Clinical evidence suggests a toxic, inflammatory etiology of Mesoamerican Nephropathy (MeN). Trace metals have not been fully explored as a cause of MeN, although several metals are known to cause interstitial nephritis, are implicated in oxidative stress, and disrupt immune and inflammatory processes. The goal of this analysis was to measure exposure to metals and evaluate a metal toxicity as a possible cause of MeN.

Methods: Toenail clippings were collected from 18 individuals with elevated creatinine who were presumptively diagnosed with acute MeN (cases) and 36 healthy controls who lacked evidence or history of renal impairment. Cases are individuals detected during MeN surveillance (AKI, elevated creatinine, and CKD) at a large agriculture estate in western Nicaragua. Cases were enrolled in the MeN cohort, and toenails were aseptically collected approximately 6 months after acute presentation; controls were recruited at health screenings from the same worker population. Zinc, Aluminum, Iron, Copper, Manganese, Selenium, Nickel, Cobalt, Mercury, Vanadium, Chromium, Arsenic, Lead, Cadmium, and Uranium concentrations were measured using by ICPMS.

Results: Toenails on 18 cases (median age 26.9 years) and 36 (median age 29.5 years) were tested. Relative concentrations among cases were:

Al>Zn>Fe>Cu>Mn>Ni>Hg>Co>Se>Cr>As>Pb>V>Cd>U; controls had:

Zn>Al>Fe>Cu>Mn>Se>Ni>Co>Hg>V>Cr>As>Pb>Cd>U. Nickel was the only element common to all cases but was detected in only 58% of controls ($p=0.001$), and nickel concentrations were higher in nails from cases (1.55mg/kg, 0.17-42.65; $p=0.003$).

Conclusions: Nickel exposure was significantly associated with having temporally proximal episode of acutely elevated creatinine, presumed to be acute MeN. Clinical events in Ni toxicity can mirror what is observed during acute MeN. In the case of Ni-induced acute interstitial nephritis, Ni accumulates in kidneys, causing focal inflammatory damage at the corticomedullary junction, and leukocytosis, anemia, nausea, and vomiting are common. Ni should be thoroughly explored through human and environmental investigations to assess its role in MeN, particularly through repeat or chronic exposures, even at low levels. Geogenic and anthropogenic sources of nickel and other metals posing hazards to human and animal health in this region should be further investigated.

30a. The Occurrence of Chronic Kidney Disease of Unknown Etiology in a Rural Colorado Cohort and the Associated Risk Factors

Katherine A James, University of Colorado, Anschutz Medical Campus

Abstract:

Acute kidney injury and chronic kidney disease are global public health concerns which can lead to end stage renal disease. We will present preliminary findings from our study investigating the presence of chronic kidney disease of unknown origin (CKDu) (also known as Mesoamerican nephropathy and heat stress nephropathy), which is seen in regions that have experienced temperature extremes in other parts of the world. We will present preliminary findings showing higher levels of metal exposure (inorganic arsenic, tungsten, lead, manganese, cadmium), occupational profiles (agriculture, mining, outdoor laborer, construction) and hydration levels in people with CKDu compared to other CKD profiles and those without kidney injury. We defined CKDu conservatively based on absence of any indication of hypertension (repeated blood pressure measurement, history of any hypertension diagnosis, medication use), diagnosis of diabetes (repeated measures of fasting glucose levels and hemoglobin A1C) and age less than 55 years.

30b. The Association between Exposure to Naturally Occurring Metals and Acute Kidney Injury and Chronic Kidney Disease in Rural Colorado

Katherine A James, University of Colorado, Anschutz Medical Campus

Abstract:

Acute kidney injury and chronic kidney disease are global public health concerns which can lead to end stage renal disease. Known risk factors (diabetes mellitus and hypertension) have been unable to account for all the variability in kidney injury and chronic kidney disease risk especially in tropical areas where an emerging epidemic of chronic kidney disease of unknown etiology is occurring. Therefore, research has expanded into examining environmental exposures as potential risk factors, including climate factors (heat stress and dehydration), drinking water quality (metals, hardness, silica, and fluoride), pesticide exposure (2,4 dichlorophenoxyacetic acid and glyphosate), and health risk behaviors (smoking and non-steroidal anti-inflammatory drug use). In several area of the world (Sri Lanka, Guatemala, and western United States), exposure to metals has been well characterized and identified as associated with kidney outcomes. We will present findings from our investigation of the association between environmental exposure to naturally occurring metals (arsenic, cadmium, lead, manganese, molybdenum, uranium, thallium, and tungsten) and clinical and preclinical indicators of acute and chronic kidney disease in the San Luis Valley Diabetes Study cohort. This cohort has extensive longitudinal clinical, demographic, and behavioral data. Metals exposure was estimated through urinary biomarker analysis of historically collected repeated samples and kidney injury was determined as acute or chronic using estimated glomerular filtration rate equation (eGFR) based on serum creatinine levels that were verified by eGFR based on cystatin C levels measures in concurrently collected serum samples. In a smaller sample (n=700) we investigated the association between urinary metals exposure and the preclinical indicators Neutrophil gelatinase-associated lipocalin (NGAL) and Kidney Injury Molecule-1 (KIM-1). Our modeling also accounts for other pathophysiologic and confounding factors including age, sex, race/ethnicity, diet, smoking, physical activity, family history, diabetes mellitus, hypertension, specific drug use, occupation, hydration level, and other contributing medical factors. Findings from this study of an identified association between exposure environmentally relevant metals and clinical and preclinical kidney disease, can help elucidate the pathophysiology with possible linkage to the emerging epidemic in tropical regions. Completed under NIEHS 1 R21 ES026433-01A1.

31. Descriptive analysis of nephrotoxic drinking water contaminants and urinary biomarkers of exposure among sugarcane workers in Guatemala

Diana Jaramillo, Center for Health, Work, & Environment, University of Colorado

Abstract:

Statement of Purpose: The role of environmental exposures such as nephrotoxic heavy metals and agrochemicals has not been established in Central America, a region with increased prevalence of chronic kidney disease of unknown etiology (CKDu). The purpose of this study was to characterize the nephrotoxic contamination in drinking water sources at a Guatemalan sugarcane worksite and assess urinary biomarkers of exposure in a cohort of workers.

Methods: We sampled 36 drinking water sources from a large sugarcane plantation. Five nephrotoxic heavy metals were analyzed: arsenic (As), cadmium (Cd), lead (Pb), mercury (Hg), and uranium (U), and two agrochemicals: 2, 4-Dichlorophenoxyacetic acid (2,4-D) and Glyphosate. During the prior harvest urine samples were collected and analyzed for As, Cd, U, 2, 4-D and Glyphosate from 42 sugarcane workers at two different time points. We compared urinary contaminant concentrations to a representative national sample of Mexican-Americans participating in the National Health and Nutrition Examination Survey (NHANES). In addition, we evaluated differences in contaminant urinary levels by home of residence, which provides information about different exposure pathways.

Results: Concentrations of heavy metals in the water samples were found to be either below the limit of detection or under WHO provisional guideline values (PGV). 2, 4-D was present in all water sources and found to be below PGV except in one site where PGV was exceeded. Detectable levels of glyphosate were found in all water samples, with a median of 28.10 parts per trillion (PPT) and maximum of 94.10 PPT. We found that, on average, urinary heavy metal concentrations were not elevated in this population, specifically uranium, cadmium, and arsenic. While the average levels of arsenic were lower in this study population than the NHANES population, we did find that six workers (16%) had levels higher than 95% of the NHANES population. In addition, the mean urinary 2, 4-D concentrations were higher than the NHANES geometric mean. We found that coastal region workers had significantly higher cadmium and arsenic levels than the migrant highland region workers. Possibilities for this difference include water source, tobacco smoke, diet, and poor air quality. Since arsenic and cadmium exposure can occur through tobacco, we examined the workers' cotinine levels in their urine. Cotinine levels were significantly correlated with urinary cadmium and arsenic levels.

Conclusions: Metals were within WHO permissible limits in the sampled drinking water. Detectable levels of agrochemicals were found in all water samples. A small proportion of workers had higher heavy metal and 2, 4-D urinary concentrations than a representative NHANES population. Renal effects from chronic low-level exposures to contaminants warrant investigation, as does the potential for interaction with other risk factors for CKDu.

Support was provided in part by Pantaleon, an agribusiness in Guatemala. University of Colorado employed appropriate research methods in keeping with academic freedom, based conclusions on critical analysis of the evidence and reported findings fully and objectively. The terms of this arrangement have been reviewed and approved by the University of Colorado in accordance with its conflict of interest policies.

32. Exploration of drinking water arsenic exposure and the risk of Chronic Kidney disease in Costa Rica

Nicole Villegas, cencam member

Abstract:

Introduction:In multiple sites worldwide, the problem of arsenic exposure has been described by the natural contamination of water sources for human consumption and the associated health effects. In Costa Rica, total arsenic concentrations have been identified in supply systems above the national standard (10 µg / L), which oscillate up to 187 µg / L in the period from 2009 to 2011; available at the time of doing this research.

Objective:To explore the risk of getting Chronic Kidney Disease (CKD) in Costa Rica associated with exposure to arsenic in drinking water.**Methods:**An Ecological design was made, consisting of three parts:1. A spatial analysis from 2003 to 2011, in which a thematic map was made through a Geographical Information System, representing a risk indicator for each district throughout the country2. A temporal analysis was carried out for three years (from 1991 to 2011) in the districts in which there was at least one arsenic result ≥ 11 µg / L.3. Classification by exposure zones: Not exposed: corresponds to the districts in which arsenic results were not detected. Low: in which at least one result was found between 3 µg / L and 10 µg / L. Medium to high: at least one result ≥ 11 µg / LFor all three parts, the Standardized Morbidity Index (SMI) by age was calculated with the indirect method, the accuracy of the results was carried out at 95% confidence and the raw morbidity per 1000 persons.

Results:1. In the spatial analysis we observed a spatial pattern defined in the northwest and south of the country. We found 8 districts out of 10 with presence of arsenic on the norm and excesses of risk of illness from 2003 to 2011, three of them statistically significant.2. With respect to the time series, it was identified that Los Chiles district presented a temporary trend of increase over time 3. In relation to the classification by exposure zones, excluding the 161 districts of the country without arsenic data at the time of this research, it was found that the areas of low 1.16 (1.08-1.24) and median at high 3.59 (3.04-4.13) exposure they present excess risk of getting sick due to CKD from 2003-2011 compared to the national average.

Conclusions:Information was observed that could serve as an input to investigate future hypotheses about the relationship between the CKD epidemic and exposure to arsenic.Information on classification by exposure zones should be handled with caution, due to the number of districts excluded from the analysis for which no exposure information was available.

Key words: drinking water, arsenic ,Chronic Kidney Disease, Costa Rica. $\geq\geq$

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33. Progress in the Sri Lankan Kidney Progression Project (KiPP)

Penny Vlahos, Associate Professor - University of Connecticut

Abstract:

KiPP is a two year longitudinal study that tracks 296 participants that have been diagnosed with chronic kidney disease of unknown etiology (CKDu) in the Wilgamuwa region of the north-central Sri Lankan dry zone. KiPP integrates clinical, behavioral and environmental components of each participant's micro and macro environment. The study is targeted for completion in summer 2019. Here we present the results of the environmental sampling components of KiPP including inorganic trace metals, complex ions and measurements of organic agrochemicals in the well waters of each participant. Results indicate that inorganic species including metals in shallow drinking wells do not appear to occur at concentrations above thresholds of concern though persistent concentrations of organic agrochemicals were detected. The goal is to identify exposure patterns as associated with CKDu progression.

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34. Advancing Knowledge of Risk Factors Associated with Chronic Kidney Disease of Uncertain Etiology (CKDu): Recent Research in Sri Lanka and Opportunities for Collaboration

Jill Lebov, RTI International

Abstract:

Sri Lanka recently transitioned from a low to middle income nation, with an accompanying epidemiological transition from a high prevalence of infectious diseases to an increased prevalence of non-communicable diseases. The recent emergence of chronic kidney disease of unknown or uncertain etiology (CKDu) has produced a public health crisis in Sri Lanka, where endemic CKDu occurs predominantly in rural regions with a dry, hot climate. Despite concentrated research efforts over the past decade, no study has been able to pinpoint the likely causes of CKDu in Sri Lanka. While most studies in Sri Lanka have focused on individual concerns (e.g., arsenate pesticides), based on the findings of CKDu studies globally, we hypothesize that the causes may be complex and multifactorial. The purpose of this current work is to assess environmental exposures as a potential contributing risk factor to CKDu. Ultimately, we aim to facilitate development of a collaborative and harmonized international research study that addresses critical knowledge gaps and holistically evaluates the global CKDu crisis.

Methods: In 2016, we completed a limited regional geochemical analysis in Sri Lanka to screen the heavy metal and trace nutrient concentrations in biological, environmental, and food samples collected from two towns in the CKDu-endemic North Central Province. Results identified levels of specific constituents above current health benchmarks, including cadmium, lead, mercury (human blood or hair); arsenic and chromium (soil); fluoride and lead (drinking water). To follow-up on these findings, we are currently completing a regional case/control study (N=320 participants) to identify CKDu environmental risk factors in the North Central Province. Biological (blood and urine) and environmental (drinking water, soil, and rice) media were collected. A brief questionnaire was developed to obtain demographic and lifestyle data from study participants. Samples were shipped to RTI for analysis using advanced laboratory techniques to evaluate biomarkers of kidney function, agrochemicals, and trace and heavy metals. Laboratory analysis will also include evaluation of perfluorinated compounds in water and urine samples and non-targeted analysis of other organic contaminants or metabolites. Data from cases and controls will be compared to determine statistically significant risk factors, and data clusters will be plotted to visualize geographic differences.

Discussion: Addressing the complex environmental health issue of CKDu requires multidisciplinary engagement, unbiased selection of study participants and areas of environmental media collection, and harmonized analytical processes that can generate accurate and standardized clinical and environmental results. We expect the results of our current research to inform a more comprehensive study in several countries with identified CKDu hotspots. Such a study could facilitate cross-cutting comparisons of sociodemographic,

biological, occupational, and environmental factors that contribute to the development of CKDu. We postulate that CKDu etiology is multifactorial, involving some combination of genetic predisposition, nutritional/dehydration status, environmental nephrotoxin exposure, and behavioral/lifestyle factors. An international network of local monitoring programs with strategic laboratory capacity-building could enable the collection of robust, scientifically defensible datasets and improve the likelihood of identifying the predominant risk factors associated with CKDu in Sri Lanka and other hot spots globally.

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35. Investigating Developmental Nephrotoxicity of Agrochemical Mixtures

Nishad Jayasundara, University of Maine

Abstract:

Studies on chronic kidney disease of uncertain etiology (CKDu) in Sri Lanka and India have highlighted a key role for environmental contaminants in initiation and progression of this disease. This research also emphasizes a critical gap in (i) evaluating a role of chemical mixtures underlying CKDu, and (ii) available methods to comprehensively characterize chemical composition of environmental samples. To this end, our studies focus on determining nephrotoxicity of chemical mixtures derived in the laboratory and from the environment (lakes, paddy fields, and drinking water wells) from two CKDu affected regions in Sri Lanka. Notably, a recent study in Sri Lanka showed that kidney dysfunction is affecting ~9% of the children (5-11 years of age) in endemic regions in Sri Lanka, suggesting a developmental onset for CKDu. Therefore, we particularly examine developmental effects of exposure to chemical mixtures. We utilized zebrafish *Danio rerio* as a model to evaluate developmental renal toxicity of chemical mixtures derived from lakes and drinking-water wells from CKDu regions. Zebrafish are a prominent model in kidney disease research and a number of tools are available to quantify kidney damage and dysfunction in these fish. A key advantage of this model is that they enable high throughput toxicity assays to determine temporal effects of multiple chemical mixtures. In addition to toxicity studies, we characterized the chemical composition of environmental samples using an ICP-MS analysis for metals and a novel non-targeted LC-MS analysis for organic compounds. In concordance with previous studies, our results show that chemical compounds in environmental samples are present at levels that are considered safe for human consumption under current guidelines. However, based on gene expression analyses and kidney-specific mitochondrial oxidative stress studies, toxicity data show mixture-specific effects on kidney development and injury and suggest protective effects when arsenic is present in the mixture. Based on these results, our long-term goals are to (a) determine gene-regulatory networks underlying kidney development and how environmental contaminants affect these processes that may have persistent later-life effects, and (b) to develop rapid screening approaches to quantify nephron-toxicity of environmental mixtures to identify at risk communities—a critical need to mitigate the spread of this disease.

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36. Systematic investigation of environmental exposures in young adults with declining kidney function in a population at risk of Mesoamerican Nephropathy (MeN)

Evangelia Smpokou, University College London

Abstract:

Objectives: There is an epidemic of Mesoamerican Nephropathy (MeN) in Central America causing the death of tens of thousands of young agricultural workers, an area where sugarcane production is prominent. Numerous causes have been proposed, but to date there is limited evidence to support any one hypothesis. A nested case-control study using biosamples from a rural, community-based follow-up study of 350 young adults from Northwest Nicaragua at risk of MeN, was conducted with the aim of characterising the associations between urinary concentrations of metals, pesticides and mycotoxins, and decline in kidney function.

Methods: Urine samples collected at baseline (pre-sugarcane harvest) and at the first 6-month follow-up (post-sugarcane harvest) visit were tested. Twelve metals and metalloids were analysed by Inductively-Coupled Plasma-Mass Spectrometry. Eleven pesticide metabolites, ochratoxin A (OTA) and citrinin (CIT) were analysed by Liquid Chromatography coupled to mass spectrometry. Differences in the creatinine-corrected urinary concentrations of the measured exposures between outcome groups (men experiencing rapid decline in kidney function versus men with stable function over a 2-year follow-up period) were examined.

Results: Across the population, elevated levels of aluminium and total arsenic as well as a number of pesticide metabolites were detected. No statistical differences were identified between the rapidly declining and stable groups in the levels of metals or pesticide metabolites tested. Levels of OTA and CIT were below the limit of detection.

Conclusions: These findings suggest that exposure to the tested metals, metalloids, pesticides and mycotoxins, are unlikely to be the primary cause(s) of MeN in Nicaragua.

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37. Flow and Transport Modeling-Based Systems Framework for the Analysis of Potential Toxin Pathways through Surface and Groundwater to Address Some Causal Factors of CKDu in Sri Lanka

Tissa Illangasekare, Center for the Experimental Study of Subsurface Environmental Processes (CESEP), Colorado School of Mines

Abstract:

Since first identified in the early 1990s, the chronic kidney disease of unknown etiology (CKDu) has markedly increased in the North Central Province (NCP) in the dry zone of Sri Lanka. CKDu has been recognized as a global health issue in more than a dozen countries in Asia, South America, and the Middle-East. Sri Lanka is the most affected with the highest cases of CKDu patients and mortality rates. The drinking water of the CKDu-affected farming communities in affected areas of Sri Lanka comes from the irrigation canals, deep-bored wells, shallow regolith water table aquifers recharged by canal seepage and from precipitation. Many contributing factors and hypotheses have been presented and discussed. These include: Arsenic (As) in groundwater from impurities in agrochemicals, Cadmium (Cd) from triple superphosphate, fluoride in the groundwater reacting with other ionic constituents in water such as Ca, Na and Mg, genetic links, effect of Glyphosate in hard water, Cd in food, Cyanobacterial toxins, pesticide, and misuse and abuse of agrochemicals, and heat stress, among others. The suspected environmental exposure pathways are through water and air. Even though extensive data on water quality exists, no systematic investigations have been conducted to identify, study and analyze how pathways develop through the water storage and distribution systems from sources to the receptors where human exposure occurs. The possibility of using a systems-based approach to study this multifactorial problem is explored. The systems approach has been defined for a diversity of problems in engineering, management, social sciences among many others. Use of systems thinking and modeling and system approach for public health practice also has been reported. What is fundamental to the systems approach is that in addition to studying a specific process, phenomenon or mechanism within each system, how the system interacts with other systems are studied to predict the behavior of the whole system. In the case of CKDu epidemic, the goal is to understand and identify the most significant causal factors to eliminate them or reduce their impact. Using this approach, how the system as a whole behaves in reducing CKDu risk through various decisions, choices, behavioral and management strategies could be determined. Five sub-systems that form the whole system are identified: (1) social/behavioral, (2) human health, (3) environmental/water, (4) economic and (5) climate. The linkages of the inputs and outputs from these sub-systems define the behavior of the whole system allowing for the study of CKDu causal factors based on a multidisciplinary framework. Numerical models simulating water flow and the fate and transport of naturally occurring toxins and agrichemicals and their geo-bio-chemical transformation products in surface and groundwater allow for the integration of the outputs from the of the social/ behavioral, economic, and climate sub-systems to the environmental/water sub-system to predict stresses on the human health to determine CKDu risk. The modeling tools should be designed to incorporate characterization parameters of the

surface water storage and distribution systems, and relevant geo-bio-chemical processes, hydrogeologic data for both the shallow and deep aquifers, water quality data, geographical information system (GIS) framework, epidemiological data, and climate drivers. Innovations in numerical modeling could be used to down-scale climate and regional hydrological model simulation data to evaluate exposure pathways at local scales (e.g., villages) under different climate scenarios and uncertainties.

38. Occupational heat stress health effects - A field study on salt pan workers and renal health in South India

Robin Lennqvist, Sahlgrenska Academy, Gothenburg University, Sweden

Abstract:

Introduction: There is a growing body of research suggesting a link between occupational heat stress and chronic kidney disease in manual workers without the common risk factors such as hypertension or diabetes. With increasing temperatures due to global warming, the problem can only be predicted to be aggravated in the absence of countermeasures. We have performed a cross-sectional study in salt pan workers in Tamil Nadu, South India, investigating heat stress and prevalence of decreased kidney function. Salt pan workers, coming from a vulnerable population and working unprotected under the sun in a tropical climate, have never been studied before.

Methods: Two locations with in total five salt pans and 116 workers were surveyed during the Indian summer in 2018. Environmental heat was assessed through wet bulb globe temperature (WBGT). A questionnaire covered demographics and perceptions about heat stress, symptoms, and mitigative measures. Physiological measurements (heart rate, blood pressure, core body temperature) and urinary dipstick and specific gravity were measured pre-and post-shift. S-creatinine and blood uric acid was measured once, and eGFR (estimated Glomerular Filtration Rate) was calculated with the CKD-EPI formula. Continuous data on WBGT, and physiological measurements were collected for a subset of workers.

Results: Almost all WBGT measurements were above the TLV (threshold limit value) for the corresponding work intensity. There were notable temperature differences between the two locations during data collection, mean WBGT for location A was 30,3°C and location B 28,9°C, presumably due to different wind speeds at the arrival of the monsoon. Questionnaire data showed that workers in location A (n=63, mean age 49) perceived heat stress as a problem for a longer time of the year and reported more symptoms, compared to workers from B (n=62, mean age 48). Physiological and urinary data did not change significantly over the day in any of the locations. Proteinuria was rare at around 5%. There were no major differences between men and women. Continuous measurements of heart rate in 26 workers indicated moderate work load (75th percentile for heart rate 97 bpm). Unexpectedly, the prevalence of eGFR <60ml/min/1.73m² was markedly different between locations, 17% at A and 1,6% at B.

Conclusion: Heat exposure is a problem among salt pan workers, demonstrated by measured WBGT index and workers' perceptions. Self-pacing is likely taking place, as there were no changes in physiological parameters cross-shift. There was a higher than expected incidence of impacted kidney function in location A, but not in B, which is intriguing since the work conditions were seemingly the same. Further studies are necessary, preferably population-based prevalence studies in the communities where the workers live. Climate change, bringing even higher temperatures, will have an impact on these groups that are already in the risk of having their health affected by heat stress.

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39a. Measuring Kidney Function using Serum Cystatin C- and Serum Creatinine-Based Estimates of Glomerular Filtration Rate in a Cross-Section of Salvadoran Workers

Zoe Petropoulos, Boston University School of Public Health

Abstract:

Chronic kidney disease (CKD) is typically diagnosed based on estimated glomerular filtration rate (eGFR). Measurement of actual GFR is complicated, so epidemiological studies estimate GFR using various formulas (such as CKD-EPI, MDRD, Cockcroft-Gault, etc) that are based on various combinations of serum creatinine levels, race, age, sex, and weight, with CKD-EPI considered the most accurate in persons who do not already have CKD. Although definitions vary, $eGFR < 60 \text{ mL/min/1.73 m}^2$, is often used to define CKD. The inaccuracies of creatinine-based eGFR measurements have more recently been highlighted in the literature, with some international guidelines recommending the use of serum cystatin C in addition to serum creatinine in the eGFR calculations. Serum creatinine measures are influenced by muscle mass, and may contribute to inaccurate eGFR values for workers who experience extreme physical exertion and are either especially muscular or lean. As a result, the addition of cystatin C to the equation for eGFR may be particularly relevant in the context of Central American agricultural workers. We analyzed serum creatinine and serum cystatin C for a subset of Salvadoran participants in the MesoAmerican Nephropathy Occupational Study (MANOS). We measured serum creatinine in all participants in El Salvador ($n=279$) and serum cystatin C in 105 of these participants. For all 105 participants in this subset, we estimated GFR in Round 2 using the CKD-EPI equations for serum creatinine and cystatin C separately, as well as the equation that combines both serum creatinine and cystatin C. The resulting GFR estimates from each equation were highly correlated with one another (range: 0.85 - 0.97, all significant at $p < 0.0001$). The mean difference between eGFR calculated from serum creatinine and the eGFR calculated from cystatin C was 7.17 (interquartile range: 19.62). The mean difference between eGFR calculated from serum creatinine and eGFR calculated from both biomarkers was 4.69 (interquartile range: 10.85). We identified 13 participants for whom the results of the creatinine-based eGFR and cystatin C-based eGFR were discordant using a threshold of estimated $GFR < 60 \text{ mL/min/1.73m}^2$. For 11 of these 13 participants, the creatinine-based eGFR was higher than the cystatin C-based estimate. We identified 8 participants for whom the results of the creatinine-based eGFR and combined biomarker-based eGFR were discordant using a threshold of estimated $GFR < 60 \text{ mL/min/1.73m}^2$. For 7 of these 8 participants, the creatinine-based eGFR was higher than the combined estimate. We performed additional analyses to identify potential predictors of discordance between these two measures. We will share these analyses and other ongoing work comparing serum creatinine and cystatin C and their diagnostic and predictive value for understanding kidney function in the MANOS cohort.

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39b. Characterizing Occupational Heat Exposure in the MesoAmerican Nephropathy Occupational Study (MANOS)

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Abstract:

There is a growing body of evidence to support the hypothesis that heat stress plays a critical role in the epidemic of Mesoamerican Nephropathy (MeN). Studies have documented that workers in warmer, lowland, coastal regions of Central America, and workers performing more strenuous job tasks experience higher risk of developing the disease. Heat stress may be related to extracellular fluid volume depletion and/or muscle damage, both of which may increase the risk of kidney damage and acute kidney injury. To better understand the relationship between occupational heat stress and volume depletion, muscle damage, kidney injury, and kidney disease, we seek to improve our metrics for assessing individual-level exposures and outcomes in the MesoAmerican Nephropathy Occupational Study (MANOS), a longitudinal study of agricultural and non-agricultural workers in El Salvador and Nicaragua. New exposure assessment technologies, such as ingestible sensors, allow researchers to collect core body temperature for individuals, potentially providing a more accurate assessment of heat stress than using ambient temperature or wet bulb globe temperature (WBGT). Core body temperature among workers in the same workplace can differ because of the level of physical exertion and individual characteristics (e.g. acclimatization). Capturing core body temperature during a work shift among workers at risk of developing MeN accomplishes multiple objectives: 1) providing more detailed and individualized exposure data for epidemiologic research than WBGT, which reduces the risk of exposure misclassification; 2) allowing for research on the relationships between core body temperature and intermediate sequelae (volume depletion, muscle damage, acute kidney injury); and 3) predicting risk for dangerous core body temperatures and informing potential intervention strategies. At baseline, we collected core body temperature, physical activity, and heart rate (HR) during work shifts using CorTemp pills, ActiGraph wGT3X-BT devices, and heart rate monitors, respectively, for 569 workers. In addition to CorTemp pills, we collected tympanic temperature for workers before their work shift and used wet bulb globe thermometers to capture WBGT at the worksite during the shifts. These variables will allow us to better understand and predict core body temperature, and compare results to other studies that use WBGT and to government and industry occupational heat guidelines. We plan to analyze concordance between these metrics of heat exposure. Changes in HR reflect the body's response to heat and can be used to assess heat tolerance. HR and core body temperature will be used to calculate a previously-published metric of heat strain. The ActiGraph devices will be used to estimate active energy expenditure throughout the work shift in kcals/hr. We plan to use the aforementioned exposure data to analyze the associations between occupational heat stress and acute kidney injury and long-term kidney function, through potential intermediate outcomes of volume depletion and muscle damage. This poster will summarize the available data for measuring occupational heat exposure and describe future analyses that will be conducted with the longitudinal kidney function data that is being collected for the MANOS participants.

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40. The effect of climate on CKDu prevalence in the United States (2010-2014)

Francesca Macaluso, University of Colorado, Anschutz Medical Campus, Colorado School of Public Health

Abstract:

Objective: The goal of this analysis was to evaluate the association between CKDu prevalence and climate across the U.S.

Methods: CKDu prevalence was calculated using United States Renal Data System estimates and U.S. Census Bureau population estimates for 2010 - 2014. 2010 prevalence estimates were used as a baseline level. Climate data was obtained from Daymet weather projections and from The North American Regional Reanalysis. Simple regression analyses were conducted to assess the relationship between CKDu prevalence by year and annual averages of various climate indicators, such as precipitation, SWE (snow water equivalent), longwave and shortwave radiation, and relative humidity, controlling for 2010 CKD prevalence. Climate data were evaluated during the year of CKD prevalence, at a 1-year lag, and in previous 3-year, 5-year, and 10-year averages. Regression analyses were stratified by age group (20-64 and 65-85). Stepwise selection was used to finalize climate variables included in the models.

Results: The average CKDu prevalence for all U.S. states in 2010 was 0.13027 ($\sigma = 0.049$). There was a statistically significant increasing trend in CKDu prevalence over the five-year study period from 2010-2014 (Kendall tau β $p < 0.0001$). At baseline, the states with the highest CKDu prevalence in adults age 20-64 were West Virginia, Kentucky, and Mississippi. West Virginia, Kentucky, and Mississippi were among the top five states for CKDu prevalence for all five years of the study period. Many climate indicators, such as relative humidity, maximum and minimum temperature, shortwave radiation, and WBGT fluctuated significantly in the U.S. between the years of 2000 and 2014 (Kendall tau β $p < 0.0001$). Longwave radiation increased significantly from 2000-2009, then decreased significantly from 2009-2014 (Kendall tau β $p < 0.0001$). Precipitation increased significantly from 2000-2006, then decreased significantly from 2006-2014 (Kendall tau β $p < 0.0001$). Significant predictors of CKD prevalence differed by year and by age group. Annual average relative humidity was positively associated with CKDu prevalence in adults aged 20-64 in 2011 and 2012 when considered in the same year, in the prior year, and as the prior 3, 5, and 10-year averages. Shortwave radiation was negatively associated with CKDu prevalence in adults age 20-64 in 2013 when considered as the prior 3, 5, and 10-year averages. Maximum temperature was negatively associated with CKDu prevalence in adults age 20-64 in 2013 when considered in the prior year, but was not as an average of the previous 3, 5, or 10-year values. 2014 CKDu prevalence in adults age 20-64 was negatively associated with only the 2014 longwave radiation average. The 2010 and 2011 WBGT averages were positively associated with CKDu prevalence in adults age 65-85 in 2011, but not when considered as a 3, 5, or 10 year averages. The previous 3, 5, and 10-year minimum temperature was positively associated with 2011 CKDu prevalence in adults age 65-85. WBGT was positively associated with 2012 CKDu prevalence in adults age 65-85 when considered in

the same year, in the prior year, and as the prior 3, 5, and 10 year averages. There were no significant predictors of CKDu in either age group in 2014.

Conclusion: CKDu prevalence increased in the U.S. between the years of 2010 and 2014. Some climate indicators were significantly associated with CKDu prevalence in that time frame, suggesting that climate change may significantly impact human health outcomes. Understanding long-term patterns in climate factors may help us predict increases in prevalence of health conditions, such as CKDu, and apply necessary interventions. Future analyses should explore this relationship in individual states and over longer time periods.

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41. National Toxicology Program Retrospective Review of Agrochemical Associated Nonneoplastic Kidney Lesions

Susan Elmore, National Institute of Environmental Health Sciences and National Toxicology Program

Abstract:

Chronic kidney disease of unknown origin (CKDu) is an unexplained epidemic that is prevalent in agricultural workers in southern Mexico, Guatemala, El Salvador, Nicaragua, Honduras, Costa Rica and other countries such as Sri Lanka and India. The cause is unknown but may be multifactorial (e.g., agrochemicals, heat load, work load, dehydration, medication, mineral exposure, infectious disease). The US National Toxicology Program (NTP)/NIEHS is partnering with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the global community to better understand the pathology of this disease and explore potential etiologies and mechanisms. Since 1978, the NTP has played a critical role in generating, interpreting, and sharing toxicological information about potentially hazardous substances in the environment. To date, the NTP has evaluated more than 2800 environmental agents for potential human health effects. Materials (tissues, paraffin blocks, slides) from mouse and rat studies are housed at the NTP Archives and the corresponding technical reports are available on the NTP public website. Applying this resource to the context of CKDu, we searched the NTP website for agrochemical-related substances that field workers in the affected regions may have been exposed to, and that also resulted in treatment-related renal nonneoplastic lesions. We have currently identified 47 chemicals with renal lesions in subchronic and/or chronic (2-year) studies. Renal lesions include tubular necrosis, degeneration, regeneration, hyperplasia, atrophy, dilation, casts, mineralization, and epithelial cell cytomegaly; glomerulosclerosis; hydronephrosis; pigmentation and hemosiderosis; α 2u-globulin nephropathy; rodent chronic progressive nephropathy; toxic nephropathy; renal papillary degeneration and necrosis; renal pelvis hyperplasia; and chronic inflammation. Our goal is to further explore any similarities in renal histomorphology and pathogenesis between rodent and human pathologies. This work allows us to utilize the unique and publicly available NTP resources to provide insight into CKDu etiology. While links between chemical effects and CKDu should also be evaluated in human studies that measure important comorbidities, work conditions and relevant risk factors, these data provide a rationale for identifying important chemical candidates. Where exposure data indicate presence of chemicals that have not been previously tested, prospective collection of relevant toxicology data on chemicals of concern in the affected population can also be considered. We welcome partnership with the global pathology, epidemiology, clinical and public health communities to explore these options further. (Supported by the Intramural Research Program of NIH.)

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42. A Descriptive Survey in an Endemic Area of Sri Lanka – Characterizing Sociodemographic, Consumption, and Agrochemical Exposure Patterns Associated with Chronic Kidney Disease of Uncertain Aetiology (CKDu)

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Starting in the mid-1990s, Chronic Kidney Disease of uncertain aetiology (CKDu) was reported among the rice farmers in the North Central Province (NCP) of Sri Lanka. CKDu is now an endemic disease in NCP and neighbouring provinces in the Northwestern, Eastern, Uva, and certain areas of Central Province. It is considered as multi-factorial in etiology but the exact cause for CKDu is still under debate. The objective of this descriptive survey was to obtain information on the sociodemographic, consumption, and agrochemical exposure patterns for adults living in Padaviya Divisional Secretariat (PDS) in the North Central Province (NCP), an area with a reportedly high prevalence of CKDu. In total, 92 participants (47 CKDu and 45 control participants) were enrolled in the study based on convenient sampling. The survey was completed with face-to-face interviews to collect primary data. Survey questions related to sociodemographics (gender, age, farming age, socioeconomic status, educational background), eating and drinking habits (drinking water consumption and sources, food consumption, alcohol intake), and agrochemical exposure (pesticide and fertilizer use, personal protection, water consumption on farm).

Of CKDu participants, 60% are males and 40% are females. Among control participants, 53% are males and 47% are females. Mean individual age of CKDu versus control participants was 61 ± 11 years and 46 ± 8 years, respectively. Both CKDu and control participants live in a farming community and work as full-time farmers for most of their adult years (55% of CKDu participants for 37 ± 15 years; 44% of control participants for 26 ± 16 years). Overall, 94% of the study population own their own paddy land. A family history of CKDu was positive for 30% ($n=14$) of participants and 11% ($n=5$) of control participants. It is notable that 45% of CKDu participants do not attend regular clinics and checkups conducted by government health care providers. Family income was below LKR 10,000/month (\$56 USD) in 58% of CKDu participants, compared to 20% for controls. Regarding education level, 15% (Ordinary Level) and 6% (Advanced Level) of CKDu participants completed secondary education, and 11% of CKDu participants never attended school.

Water consumption questions indicate that that 90% of CKDu participants have consumed dug well and tubewell water for a period of ten years. After being diagnosed with CKD or CKDu, 72% of people changed their drinking water well to Reverse Osmosis (RO) water and pipe-borne water. However, 42% of people still consume water from dug wells for cooking purposes. While working, 68% of farmers consume water from the wells situated in paddy fields, while approximately 32% bring water from home. Average water consumption during working time was 3.0 ± 0.54 L. Average consumption of freshwater fish was twice a week. Rice is the staple food and 98% consume rice from their own cultivation. Agrochemical exposure questions

indicate that 90% of farmers use pesticide and fertilizer for paddy cultivation several times per year without wearing personal protective equipment. This survey highlights the patterns associated with CKDu participants in an endemic area of Sri Lanka. Additional studies are needed to identify whether changing certain patterns, such as drinking filtered water, could reduce prevalence of CKDu..

Keywords: CKDu, Sri Lanka, Sociodemographic, consumption, agrochemical exposure, survey, interviews, patterns, personal protective equipment

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Prevalence of impaired kidney function in the district of Anuradhapura, Sri Lanka: a cross-sectional population-representative survey based on the DEGREE protocol among those at risk of Chronic Kidney Diseases of unknown aetiology

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Abstract:

Over the last 20 years there have been reports of a form of chronic kidney disease of unknown cause (CKDu) affecting rural communities in the North Central Province of Sri Lanka. Valid prevalence estimates, using a standardised methodology, are needed to assess the burden of disease, assess secular trends, and perform international comparisons.

Methods: Given the public health importance of the issue of CKDu for global health, and to promote the generation of comparable evidence across studies in various countries with uniform measures that ensure the quality of data, an international group has been formed to address these issues, the Disadvantaged Populations eGFR Epidemiology (DEGREE) collaboration. The present survey was undertaken using the DEGREE protocol which was developed by the above group, to estimate the prevalence and geographical distribution of low eGFR in the district of Anuradhapura which is the district which records the highest numbers of patients with CKDu in Sri Lanka. All the adults above the age of 18 years whose main place of residence for the past 6 months was in one of the five study areas were included in the study. Exclusion criteria were pregnant women and patients undergoing treatment for cancers. Serum creatinine and urine protein: Creatinine ratios were tested in the laboratory of the Anuradhapura Teaching Hospital in a single batch. Serum creatinine was measured using assays calibrated utilizing quality controls traceable to isotope dilution mass spectrometry (IDMS) standards. In the laboratory, samples of serum (total of 2 ml stored as a single aliquot) and urine (2ml in one aliquot) were separated for bio-banking purposes and frozen (-20oC). We used a proxy definition of CKDu involving a single measure of impaired kidney function (eGFR<60mL/min/1.7m², using the CKD-Epi formula) in the absence of hypertension, diabetes or heavy proteinuria.

Results: A total of 4803 participants (88.7% of those invited) took part in the study. Nearly half of the study participants were less than 44 years old and a majority were females (68.2%). Most males (85.7%) had been occupied in farming with equal proportions reporting full-time (42.6%) and part-time (43.1%) engagement. Among females, the proportion ever occupied in full-time farming was similar to males (48.5%) while those who reported part-time farming were lower (21.9%). A total of 1262 (26.3%, 95% CI 25.0 - 27.5) of the study population had hypertension, while the 470 had diabetes mellitus (9.7%, 95% CI 8.9 - 10.6). A total of 110 who were found to be suffering from heavy proteinuria, also suffered from diabetes or hypertension. We observed that a total of 202 of the 4803 study participants had a low eGFR in the absence of hypertension, diabetes and heavy proteinuria thus meeting the criteria for proxy CKDu. The

age-standardized prevalence of proxy CKDu was 6.0% (95% CI 5.2-6.8). The age-standardized proportion of males (11.2%; 95% CI 9.2 - 13.1) with CKDu were triple than the females (3.7%; 95% CI 2.9 - 4.5).

Conclusions: These data, collected using a standardised methodology demonstrate a high prevalence of impaired kidney function, not due to known causes of kidney disease, in this region of Sri Lanka. There is a need for longitudinal studies to describe the natural history and to characterise risk factors for the decline in kidney function.

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Multiple Acute Kidney Injuries precede Chronic Kidney Disease in a Large Historic MeN Cohort in Nicaragua

Rebecca Fischer, Texas A&M Health Science Center & Baylor College of Medicine

Abstract:

Although historically referred to as a chronic kidney disease (CKD) of unknown etiology, recent evidence documents an acute disease process in Mesoamerican Nephropathy (MeN). Acute MeN has been reported as acute kidney injury with systemic inflammation that can progress rapidly to CKD. A clinical case definition of acute MeN has been proposed but is not yet validated. Our goals with this analysis were to (1) describe the initial, acute clinical presentation in a large cohort of historic MeN CKD cases and (2) document the occurrence of an acute scenario in historic cases.

Methods: We conducted a retrospective study at a large sugar estate in Nicaragua, where CKD surveillance began in the 1995. Hospital medical records were reviewed on 746 individuals diagnosed with MeN CKD from 1995 to 2013, and we abstracted clinical, demographic, and medical history data. We documented clinical signs at the first recorded above-range serum creatinine level for each patient.

Results: Data were available on 746 cases, diagnosed at various stages of CKD: 18% Stage 1, 40% Stage 2, 30% Stage 3, and 12% Stage 4-5. Patients were male (98%) and young (median 33 years). The mean acute serum creatinine level was 2.0 ± 1.3 mg/dL and sometimes coincided with back pain (26%), fever (21%), leukocytosis (35%), neutrophilia (53%), anemia (74%), hyperuricemia (50%), electrolyte imbalance (34%), leukocyturia (99%) and leukocyte casts (17%). 20% were recorded as being asymptomatic. Prior diabetes (2%) and hypertension (8%) were rare. Prior AKI was determined in 84% of patients (AKIN criteria), with average of 2 (1 to 8) AKI episodes over a mean 3.2 years before CKD diagnosis.

Conclusions: This evidence confirms AKI as a precedent for CKD in most MeN cases, some with systemic inflammation. Importantly, we document a high frequency of asymptomatic acute MeN. Other important findings include exceedingly high prevalence of anemia. This study underscores rapidity of progression from acute to chronic MeN. Further understanding of the disease process and baseline physiology may indicate opportunities to intervene in disease progression or suggest susceptibility factors that may be addressed to prevent AKI and progression to CKD in MeN.

Urine testing of community residents in a region of Nicaragua with a high burden of Mesoamerican Nephropathy reveal background systemic inflammatory signs rapidly increase in younger ages

Rebecca Fischer, Texas A&M Health Science Center & Baylor College of Medicine

Abstract:

A large and ongoing epidemic of kidney disease of unknown etiology affects the rural poor from Mexico to Panama and has resulted in greater than 50,000 deaths. Mesoamerican nephropathy (MeN) is a devastating and rapidly progressing disease that affects primarily young agriculture workers who are otherwise healthy and lack traditional risk factors for kidney disease. Very little is known about renal function in the community-at-large, especially among children.

Methods: Urine specimens were collected from individuals of all ages at health fairs in 4 rural, agricultural communities in the Pacific lowland areas of Nicaragua, a region heavily affected by MeN and where morbidity and mortality due to the epidemic has more than quadrupled since its emergence. Semi-quantitative dipstick and microscopic analysis were performed on fresh specimens. We generated descriptive statistics and tested for differences by age and community by Chi-squared and ANOVA in Stata 15.

Results: Urine from 471 community residents, ages 3 months to 89 years (median 21 years) were analyzed. Almost all individuals (99%) were shedding leukocytes, many (21%) with >5 per field. Renal cell shedding (11%), hematuria (13.4%) were also noted. Proteinuria was rare (3.2%). Hematuria and leukocytosis varied by locale ($p < 0.05$).

Conclusion: In this community-based sample, clinical urine specimens indicate an underlying prevalence of markers of impaired renal function. Further investigations into MeN should target populations other than agricultural workers and should specifically look at renal function in children. Geographic differences in clinical indicators may also point to the highest risk communities.



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World Café: Facilitator

Miranda Dally

University of Colorado
USA
Primary WG: Heat/dehydration
World Café: F - 1

George Delclos

The University of Texas Health Science Center at
Houston
USA
Primary WG: Heat/dehydration
World Café: D - 12

Iris Delgado

Boston University
USA
Primary WG: Epidemiology
World Café: E - 13

Carl-Gustaf Elinder

Karolinska Institutet
Sweden
Primary WG: Biomarkers
World Café: E - 10

Susan Elmore

National Institute of Environmental Health
Sciences
USA
Primary WG: Pathology
World Café: L - 10

Jose Escamilla

Pan American Health Organization (PAHO)
USA
Primary WG: Surveillance
World Café: Facilitator

Monica Espinoza

Medicina familiar
Costa Rica
Primary WG: Epidemiology
World Café: L - 9

Maria Ines Esquivel

Ministerio de Salud
Panama
Primary WG: Surveillance
World Café: F - 5

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The University of Texas Health Science Center at
Houston
USA
Primary WG: Heat/dehydration
World Café: A - 1

Rebecca Fischer

Texas A&M University Health Science Center
and Baylor College of Medicine
USA
Primary WG: Surveillance
World Café: G - 1

Nora Franceschini

University of North Carolina, Chapel Hill
USA
Primary WG: Molecular
World Café: L - 13

David Friedman

Beth Israel Deaconess Medical Center
USA
Primary WG: Molecular
World Café: Facilitator

Stephanie Garbanzo Bolivar

Agencia Costarricense de Investigaciones
Biomedicas (ACIB)
Costa Rica
Primary WG: Clinical
World Café: B - 8

Ramon Garcia Trabanino

Centro de Hemodialisis / Fondo Social de
Emergencia de Tierra Blanca
El Salvador
Primary WG: Clinical
World Café: Facilitator

Nelson Garcia-Salazar

H. Espana-Chinandega
Nicaragua
Primary WG: Clinical
World Café: G - 4

David Gimeno Ruiz de Porras

The University of Texas Health Science Center at
Houston
USA
Primary WG: Heat/dehydration
World Café: I - 10

Jason Glaser

LIN
USA
Primary WG: Heat/dehydration
World Café: F - 7

Daniel Goldstein

Bayer CropScience
USA
Primary WG: Pesticides/Metals
World Café: M - 12

Marvin Antonio Gonzalez Quiroz

CISTA UNAN-León and National Autonomous
University of Nicaragua
Nicaragua
Primary WG: Epidemiology
World Café: Facilitator

Carlos Gordon

Universidad de Panama
Panama
Primary WG: Epidemiology
World Café: A - 9

Nalika Gunawardena

World Health Organization Country Office for
Sri Lanka
Sri Lanka
Primary WG: Surveillance
World Café: Facilitator

Carolina Guzman-Quilo

USAC Facultad de Ciencias quimicas y Farmacia.
SALTRA
Guatemala
Primary WG: Pesticides/Metals
World Café: Facilitator

Erik Hansson

Gothenburg University
Sweden
Primary WG: Surveillance
World Café: -

Alison Harrill

National Institute of Environmental Health
Sciences
USA
Primary WG: Molecular
World Café: I - 6

Chula Herath

Sri Jayewardenepura General Hospital
Sri Lanka
Primary WG: Clinical
World Café: L - 3

Guillermo Hidalgo

East Carolina University
USA
Primary WG: Clinical
World Café: D - 2

Christer Hogstedt

Karolinska Institutet
Sweden
Primary WG: Epidemiology
World Café: F - 10

Ted Horbulyk

International Water Management Institute (Sri Lanka) and University of Calgary
Canada
Primary WG: Epidemiology
World Café: B - 9

Asela Iddawela

Presidential Task Force for Chronic Kidney Disease Prevention
Sri Lanka
Primary WG: Heat/dehydration
World Café: J - 3

Tissa Illangasekare

Colorado School of Mines
USA
Primary WG: Surveillance
World Café: B - 5

Kristina Jakobsson

University of Gothenburg
Sweden
Primary WG: Epidemiology
World Café: Moderator

Katherine James

University of Colorado
USA
Primary WG: Pesticides/Metals
World Café: D - 1

Diana Jaramillo

University of Colorado
USA
Primary WG: Epidemiology
World Café: K - 10

Emmanuel Ricardo Jarquin Romero

AGDYSA
El Salvador
Primary WG: Pesticides/Metals
World Café: H - 4

Channa Jayasumana

Rajarata University of Sri Lanka
Sri Lanka
Primary WG: Pesticides/Metals
World Café: F - 13

Nishad Jayasundara

School of Marine Sciences Graduate School of Biomedical Science and Engineering
USA
Primary WG: Molecular
World Café: A - 11

Roberto Jimenez

Nicaragua
Primary WG:
World Café: L - 5

Bonnie Joubert

National Institute of Environmental Health Sciences
USA
Primary WG: Pesticides/Metals
World Café: Facilitator

Neeraja Kambham

Stanford University
USA
Primary WG: Pathology
World Café: B - 11

Sinead Keogh

Boston University School of Public Health
USA
Primary WG: Epidemiology
World Café: D - 11

Paul Kimmel

National Institute of Health
USA
Primary WG: Molecular
World Café: Facilitator

Lyndsay Krisher

University of Colorado
USA
Primary WG: Epidemiology
World Café: E - 1

Suzanne Lea

East Carolina University
USA
Primary WG: Epidemiology
World Café: J - 13

Jill Lebov

RTI International
USA
Primary WG: Epidemiology
World Café: E - 5

Jessica Leibler

Boston University School of Public Health
USA
Primary WG: Epidemiology
World Café: C – 1

Ricardo Leiva

Hospital Nacional Rosales
El Salvador
Primary WG: Clinical
World Café: M - 8

Robin Lennqvist

Gothenburg University
Sweden
Primary WG: Heat/dehydration
World Café:

José David León Rivas

National Autonomous University of Nicaragua,
León UNAN León
Nicaragua
Primary WG: Heat/dehydration
World Café: D - 1

Damaris Lopez

Escuela de Salud Publica Universidad de Boston
Nicaragua
Primary WG: Epidemiology
World Café: B - 6

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Nephrology Institute of Havana
Cuba
Primary WG: Pathology
World Café: I - 13

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Biomedicas (ACIB)
Costa Rica
Primary WG: Clinical
World Café: D - 7

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University of Colorado
USA
Primary WG:
World Café: D - 5

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Costa Rican Health Care and Social Security
System
Costa Rica
Primary WG:
World Café: X - x

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Instituto Nacional de Cardiologia
Mexico
Primary WG: Surveillance
World Café: Facilitator

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University of Sri Jayewardenepura
Sri Lanka
Primary WG: Pesticides/Metals
World Café: G - 3

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Medico
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Primary WG: Heat/dehydration
World Café: C - 12

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National Institute of Diabetes and Digestive and
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USA
Primary WG: Clinical
World Café: Facilitator

José Miranda

COMISCA
Costa Rica
Primary WG:
World Café: B – 3

Edmundo Morales Galindo

National Institute of Public Health
Mexico
Primary WG: Heat/dehydration
World Café: M - 2

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Brown University
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Primary WG: Surveillance
World Café: H - 6

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Teaching hospital, Kandy, Sri Lanka
Sri Lanka
Primary WG: Molecular
World Café: A - 3

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Cedars-Sinai Medical Center
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World Café: A - 6

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Primary WG: Surveillance
World Café: G - 7

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Ministry of Health of El Salvador
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Primary WG: Surveillance
World Café: C - 4

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Primary WG: Surveillance
World Café: H - 10

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Primary WG: Epidemiology
World Café: A - 5

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Metropolitan Hospital Complex
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Primary WG: Clinical
World Café: M - 5

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Pan American Health Organization (PAHO)
Costa Rica
Primary WG:
World Café: K - 5

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World Café: F - 11

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Costa Rica
Primary WG: Epidemiology
World Café: M - 6

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University of Maryland
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Primary WG: Pesticides/Metals
World Café: H - 7

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University
USA
Primary WG: Clinical
World Café: J - 2

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Boston University School of Public Health
Spain
Primary WG: Epidemiology
World Café: L - 8

Ana Rivera

Inciensa
Costa Rica
Primary WG: Epidemiology
World Café: K - 6

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National Institute of Public Health/Regional
Center for Public Health Research
Mexico
Primary WG: Biomarkers
World Café: C - 11

Andres Robles

ING.
Primary WG: Heat/dehydration
World Café: H - 11

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CropLife Latin America
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Primary WG: Pesticides/Metals
World Café: K - 13

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USA
Primary WG: Heat/dehydration
World Café: A - 8

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Universidad Nacional
Costa Rica
Primary WG: Epidemiology
World Café: J - 9

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Escuela Ciencias del Movimiento Humano y
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Costa Rica
Primary WG: Heat/dehydration
World Café: H - 9

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World Café: G - 8

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Primary WG: Pesticides/Metals
World Café: J - 6

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USA
Primary WG: Epidemiology
World Café: K - 7

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Sciences
USA
Primary WG: Molecular
World Café: C - 8

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MINSA / Panama
Panama
Primary WG: Surveillance
World Café: F - 4

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University of Florida
USA
Primary WG: Epidemiology
World Café: K - 2

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Primary WG: Pesticides/Metals
World Café: A - 2

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Primary WG: Surveillance
World Café: Facilitator

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World Café: J - 4

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Paradox Found, LLC
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World Café: G - 13

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Primary WG: Epidemiology
World Café: G - 11

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Primary WG: Clinical
World Café: B - 2

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Primary WG: Epidemiology
World Café: D - 8

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Primary WG: Clinical
World Café: L – 12

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Primary WG: Pesticides/Metals
World Café: E - 11

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Sciences
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World Café: Facilitator

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Hospital Nacional Rosales
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World Café: C - 5

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The Houston Methodist Hospital, Renal
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USA
Primary WG: Pathology
World Café: I - 7

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Costa Rica
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World Café: F - 8

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Sri Ramachandra University
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Primary WG: Heat/dehydration
World Café: B - 4

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Consortium on the Epidemic of Nephropathy in
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Primary WG: Epidemiology
World Café: G - 6

Penny Vlahos

University of Connecticut
USA
Primary WG: Pesticides/Metals
World Café: H - 3

Kamani Wanigasuriya

University of Sri Jayawardenepura
Sri Lanka
Primary WG: Biomarkers
World Café: M - 3

David Wegman

University of Massachusetts Lowell
USA
Primary WG: Epidemiology
World Café: J - 10

Ilana Weiss

La Isla Network
USA
Primary WG: Heat/dehydration
World Café: E - 7

Annika Wernerson

Karolinska Institutet
Sweden
Primary WG: Pathology
World Café: C - 9

Catharina Wesseling

Karolinska Institutet / La Isla Network
Costa Rica
Primary WG: Pesticides/Metals
World Café: I - 9

Julia Wijkstrom

Karolinska Institutet
Sweden
Primary WG: Pathology
World Café: G - 10

Katherine Yih

Harvard Medical School
USA
Primary WG: Molecular
World Café: F - 3



**Third International Workshop on
Chronic Kidney Diseases of Uncertain/Non-Traditional
Etiology in Mesoamerica and Other Regions**