Decreased Kidney Function of Unknown Cause in Nicaragua: A Community-Based Survey

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Background: End-stage kidney disease overwhelms health services in Central America. We determined prevalences of decreased kidney function in distinct populations in the most affected region of Nicaragua.

Study Design: Cross-sectional survey.

Setting & Participants: Total populations aged 20-60 years of 5 villages in Northwest Nicaragua: mining/subsistence farming (elevation, 100-300 m above sea level), banana/sugarcane (100-300 m), fishing (0-100 m), services (0-100 m), and coffee (200-675 m); 479 men and 617 women (83% response).

Predictor or Factor: Village; participant sex, age, and occupation; conventional chronic kidney disease risk factors.

Outcomes: Serum creatinine (SCr) values greater than laboratory reference range for sex, estimated glomerular filtration rate <60 mL/min/1.73 m^2, proteinuria stratified in the low (dipstick protein excretion, 30-300 mg/dL) and high (>300 mg/dL) range.

Results: Prevalences of abnormal SCr levels: 18% (of all men) and 5% (of all women); in the mining/subsistence farming village, 26% and 7%; banana/sugarcane, 22% and 6%; fishing, 13% and 4%; services, 0% and 1%; and coffee, 7% and 0%. Prevalences of estimated glomerular filtration rate <60 mL/min/1.73 m^2: 14% (of all men) and 3% (of all women); in the listed villages, 19% and 5%, 17% and 4%, 10% and 2%, 0% and 0%, and 7% and 0%, respectively. Proteinuria, predominantly in the low range, affected 14% and 11% of all men and women without marked differences between villages. By occupation, abnormal SCr levels occurred in 31% and 24% of male and female agricultural workers at 100-300 m above sea level, but not at higher altitudes, and also was high in male artisans (43%), construction workers (15%), and miners (14%). In logistic regression models, for the banana/sugarcane and mining/subsistence farming villages, high blood pressure and age were significant predictors of abnormal SCr levels in men, and for mining/subsistence farming, age in women.

Limitations: Causality is not addressed.

Conclusions: In some Nicaraguan villages and population segments, men in particular show a high prevalence of decreased kidney function of unknown origin, possibly environmental or occupational.

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INDEX WORDS: Serum creatinine; chronic kidney disease (CKD); glomerular filtration rate (GFR); prevalence; Central America; occupation; agriculture.

Chronic kidney disease (CKD) is a worldwide public health problem with increasing numbers of patients in need of renal replacement therapy.[1-7] Knowledge regarding the prevalence or incidence of early-stage CKD nonetheless is scarce. Epidemiologic studies from industrialized countries have identified primarily aging, diabetes, hypertension, and use of nephrotoxic drugs as CKD risk factors.[1,4,5,7-10] Although some developing countries show similar patterns,[11,12] others have identified occupational and environmental causes.[13,14] The natural substances aristolochic acid and ochratoxin A have been related to CKD outbreaks,[15-19] and long-term exposures to heavy metals have been revealed as causes of renal damage.[20-24]

Nicaragua recently has witnessed an increasing number of renal replacement therapy patients

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and CKD mortality. Data from the Nicaraguan Ministry of Health (MINSA) show that in 1992-2002, the crude national mortality rate increased from 4 to 9 deaths/100,000 inhabitants. Most affected is the Northwest Pacific region, where mortality increased from 13 to 36 deaths/100,000 inhabitants, with a male-to-female ratio of 5:1.[25] Unpublished studies in Nicaragua[26-28] and other studies from Central America[14,25,29,30] have suggested increased risks for agricultural workers, in particular, sugarcane workers, and have noted that kidney disease decreases at higher altitudes.

The available information is insufficient to understand the extent of this public health threat or its causes. The aim of this study is to investigate the prevalence of decreased kidney function in men and women of 5 villages of Northwestern Nicaragua, differentiated by their main economic profiles and occupations of their inhabitants. We investigated the extent to which conventional CKD risk factors may explain the prevalence of decreased kidney function and tried to substantiate or decrease the likelihood of agricultural work as a risk indicator and high altitude as a protective indicator for renal damage.

METHODS

Setting and Study Population

This cross-sectional survey established the prevalence of decreased kidney function in populations aged 20-60 years of 5 villages in Northwest Nicaragua. The villages were selected by convenience, with a maximum of 800 inhabitants to be manageable, and represent distinct economic profiles and locations at different altitudes: gold mining and subsistence farming (200-300 m above sea level), large-scale banana and sugarcane production (100-200 m above sea level), small-scale fishery near the Pacific Ocean (0-100 m above sea level), small-scale coffee farming (at 675 m above sea level and a minor part at 200 m above sea level), and services (0-100 m above sea level). The study was approved by the Ethical Committee for Biomedical Research of the National Autonomous University of Nicaragua at León (UNAN-León).

Data were collected from September to December 2007 on weekends to guarantee maximum participation. University personnel with village representatives performed a census in each village, registering members of each household independently of being in the village or not. All houses were georeferenced. Two weeks after the census, a survey was carried out using a questionnaire and clinical measurements, lasting 2-5 weekends. Participants were contacted in their houses and, if not at home, revisited at the end of the data collection in their village. All participants signed an informed consent.

Variables, Data Sources, and Measurements

We used serum creatinine (SCr) level greater than the laboratory reference range as an indicator for decreased kidney function: >1.2 mg/dL for men and >0.9 for women. In addition, we estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 based on the isotope dilution mass spectrometry (IDMS)-traceable 4-variable Modification of Diet in Renal Disease (MDRD) Study equation.[31]

Trained medical we agree, the change is acceptable students visited every house applying the questionnaire covering demographic information, lifestyle, diseases, and medications. Subsequently, participants went to a mobile laboratory located in the health center, community house, or a village leader's home. Here, we measured blood pressure using a previously calibrated digital sphygmomanometer and weight and height using a calibrated clinical scale and obtained blood and urine samples.

Participants gave a morning random urine sample (50 mL) in a sterile collector and a nonfasting blood sample (20 mL) in 2 tubes, 1 with and 1 without anticoagulant. Two laboratory technicians performed within 30 minutes tests for glucosuria (glucose levels ≥100 mg/dL considered positive) and 2 different degrees of proteinuria (protein excretion >30 and >300 mg/dL) using reactive strips for chemical analyses (Urine-10; Cypress Diagnostics, www.diagnostics.be/frame_cl_uri.html). Blood samples without anticoagulant were centrifuged within the hour. Serum was transferred to 2 separate tubes, placed in an icebox, transported at the end of the day to the laboratory at UNAN-León, frozen, and kept at −20°C. Within 7 days, 1 of the serum sample tubes was transported on ice to the Central Laboratory of MINSA, where SCr was measured using Cobas Integra 400 (Roche Diagnostics, www.labsystems.roche.com/content/products/integra_400plus/introduction.html), automated equipment, using the Jaffé compensated method.[32-34] The remaining serum and full blood samples, as well as part of the urine samples, were stored for future analyses of nephrotoxins (heavy metals and pesticides). For quality control, 10% of the urine samples handled by each of the 2 technicians were reanalyzed by the other, with 97% of samples coinciding in all test parameters. For SCr measurements, every day an intralaboratory control was performed on the automated equipment according to its own reference values, and in addition, each batch of samples transferred to the MINSA laboratory included at least 2 spiked samples. Deviations were at all times within 1 standard deviation. The MINSA laboratory takes part in an international interlaboratory quality control program.

Hypertension was defined as either systolic blood pressure ≥140 mm Hg, diastolic pressure ≥90 mm Hg, or self-reported medical history. Diabetes mellitus was defined as glucosuria (glucose excretion ≥100 mg/dL) using a urine stick or self-reported medical history of diabetes mellitus. Obesity was defined as body mass index ≥30 kg/m^2. Urinary and renal illness was limited to self-reported medically diagnosed urinary tract infections in the previous year and history of renal lithiasis versus no such conditions. Use of nonsteroidal anti-inflammatory drugs (NSAIDs) was defined as consuming at least 1 NSAID in the previous year for >7 consecutive days combined with a self-reported history of chronic joint pain.