Population Estimates of GFR and Risk Factors for CKD in Guatemala

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Introduction: Chronic kidney disease (CKD) is an emerging public health priority in Central America. However, data on the prevalence of CKD in Guatemala, Central America's most populous country, are limited, especially for rural communities.

Methods: We conducted a population-representative survey of 2 rural agricultural municipalities in Guatemala. We collected anthropometric data, blood pressure, serum and urine creatinine, glycosylated hemoglobin, and urine albumin. Sociodemographic, health, and exposure data were self-reported.

Results: We enrolled 807 individuals (63% of all eligible, 35% male, mean age 39.5 years). An estimated 4.0% (95% confidence interval [CI] 2.4–6.6) had CKD, defined as an estimated glomerular filtration rate (eGFR) less than 60 ml/min per 1.73 m^2. Most individuals with an eGFR below 60 ml/min per 1.73 m^2 had diabetes or hypertension. In multivariable analysis, the important factors associated with risk for an eGFR less than 60 ml/min per 1.73 m^2 included a history of diabetes or hypertension (adjusted odds ratio [aOR] 11.21; 95% CI 3.28–38.24), underweight (body mass index [BMI] <18.5) (aOR 21.09; 95% CI 2.05–217.0), and an interaction between sugar cane agriculture and poverty (aOR 1.10; 95% CI 1.01–1.19).

Conclusions: In this population-based survey, most observed CKD was associated with diabetes and hypertension. These results emphasize the urgent public health need to address the emerging epidemic of diabetes, hypertension, and CKD in rural Guatemala. In addition, the association between CKD and sugar cane in individuals living in poverty provides some circumstantial evidence for existence of CKD of unknown etiology in the study communities, which requires further investigation.

The CKD epidemic is rising rapidly. The global prevalence has increased 29.3% from 1990 to 2017 and CKD-related disability is disproportionately concentrated in low- and middle-income countries.[1] Furthermore, within these countries, the burden of disease is unequally distributed. For example, CKD ranked as the 12th leading cause of death globally, but second in Central Latin America, including Guatemala.[1] This unequal distribution is likely driven primarily by a rapid increase in the prevalence of type 2 diabetes and hypertension, coupled with fragile public health systems. In addition, access to evidence-based preventive strategies, early diagnosis, treatment to prevent disease progression, and renal replacement therapy are extremely limited, leading to higher disease morbidity and mortality.[1–6]

In addition to traditional CKD, CKD of unknown etiology (CKDu) has also been rising in Central America.[7–10] First noted in a case series in El Salvador in 2002, CKDu is not associated with diabetes and hypertension and has been described mainly in young men and agricultural (especially sugar cane) workers.[11–21] Leading hypotheses for CKDu include recurrent exposure to heat stress and dehydration, heavy metal and pesticide exposures, infectious diseases, and genetic factors.[8,22,23]

In Guatemala, given the international and regional interest, most CKD research to date has focused on CKDu among agricultural workers.[24–27] Despite the

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importance of this research, population-level data on overall CKD prevalence and on diabetes and hypertension is for the most part lacking.[28,29] Furthermore, most of the rural population is indigenous Maya and suffers from some of the highest rates of child undernutrition and low birthweight worldwide, both factors associated with a higher risk for CKD later in life.[30–33] Consequently, obtaining population-level data on CKD, diabetes, and hypertension is an important priority for Guatemala. In this article, we address this gap in the literature by reporting results from a population-based survey of eGFR and CKD risk factors in 2 rural, indigenous communities in Guatemala.

METHODS

Study Design and Setting

We conducted a representative, cross-sectional survey in 2 rural agricultural municipalities: Tecpán (85,000 estimated population), and San Antonio Suchitepéquez (52,000 estimated population). Tecpán is a cool climate highland municipality at 2100 m above sea level. The warmest month is April, with an average high temperature of 22°C/72°F. Major agricultural crops are corn and vegetables. San Antonio Suchitepéquez is a hot climate, lowland municipality at 350 m above sea level. The warmest month is April, with an average high temperature of 33°C/92°F. Sugar cane is the most common crop grown. Age and sex distributions are similar in both municipalities. These 2 communities were chosen for the differences in climate and agricultural work thought to be associated with differences in the distribution of CKD and CKDu in Guatemala.

The work was conducted in collaboration with Maya Health Alliance, a primary health care organization with clinics in both municipalities. The study was approved by the institutional review boards of Maya Health Alliance (WK 2018 001), the Institute for Nutrition of Central America and Panama (CIE REV 075/2018), and Partners Healthcare (2017P002476). STROBE guidelines were used in preparing this manuscript.[34] The study design followed guidelines provided by the *Disadvantaged Populations eGFR Epidemiology Study* Core Protocol.[35]

Participant Selection and Study Size

Participants were nonpregnant adults (≥18 years of age) living in randomly selected households. The sample frame was generated using Epicentre's Geo-Sampler tool (https://epicentre.msf.org/), which allows for a selection of spatially random points centered on human structures using satellite imaging.

Using ArcGIS 10.15.1, we created polygon shape-files, imported into Geo-Sampler (version 0.1.0.47), which selected random points centered on buildings in Google Earth satellite images (image dates January 9, 2018) with a buffer of 15 m. Selected points (latitude and longitude) were converted to a keyhole markup language file, which was uploaded to Google Earth and provided to study data collectors. Navigation to each selected household used the Google Earth interface on Android-based smartphones.

We generated a list of 350 randomly selected structures and 300 supplemental structures for replacement if needed. Data collectors approached structures and determined whether they were households. If so, residents were invited to participate. If not, the nearest household to the selected structure was approached. If no households were nearby, a structure from the supplemental list was chosen.

Our *a priori* sample size calculation estimated that 700 participants from 350 households were required to estimate the point prevalence of CKD with a margin of error of 0.35, assuming 10% refusals, a design effect of 2 to account for household clustering in buildings, an expected 10% prevalence of CKD taken from a global meta-analysis, and at least 2 eligible residents per household based on data from the latest Demographic and Health Survey.[36,37] We also planned for a nested case-control analysis to explore risk factors for CKD. Based on an estimated CKD prevalence of 10%, we calculated that our sample size would have sufficient power to detect differences in proportions as low as 12% at $\alpha = 0.05$ or 9% at $\alpha = 0.1$ in the case-control analysis.

Data and Sample Collection and Processing

Data were collected from June 2018 to October 2019 in parallel in both communities. All data were collected by field nurses with training in phlebotomy, anthropometry, and survey techniques. Anthropometric data were collected in triplicate using standard methods developed by the Institute for Nutrition of Central America and Panama.[38] Anthropometric data were collected with subjects wearing undergarments and a light paper examination gown. Seca portable stadiometer Models 123 and 2013 (www.seca.com) and Tanita portable digital scales Model BC-558 (www.tanita.com) were used. Seated arterial blood pressure was obtained in triplicate after 15 minutes of rest with an Omron 7 digital oscillometric automated cuff (www.omron.com). Blood pressure was then estimated as the mean of the 3 measurements.

Blood and urine were placed in a field cold pack immediately after obtaining each sample. Blood samples were centrifuged at 1500*g* for 15 minutes, and serum aliquots removed, within 4 hours of obtaining the samples. Serum aliquots and urine were frozen at −20°C. Cold samples were then transported in

batches to the reference laboratory at the Institute for Nutrition of Central America and Panama. Glycosylated hemoglobin and serum and urine creatinine were measured using the Roche Cobas C111 analyzer (www.roche.com). Creatine assays used a colorimetric kinetic assay based on the Jaffe method. Creatinine assays and calibrators were traceable to an isotopic dilution mass spectrometry standard. Urine albumin was measured on the Shenzhen New Industries Biomedical Engineering Co. Maglumi 1000 analyzer (www.snibe.com) using a competitive chemiluminescent immunoassay technique.

A demographic and exposure survey was developed after review of previously published data from Central America. The survey (Supplementary File S1) included questions on sociodemographics, health care access, occupation, agricultural and manual labor exposures, corn consumption, alcohol, tobacco and drugs, personal and family medical history, pesticide exposure, and nonsteroidal anti-inflammatory drug (NSAID) use. We included a question about childhood orthopedic fractures as a negative control to help assess presence of recall and selection biases.[39] All surveys were conducted within the subject's home in a private location. Interviews were conducted in either Spanish or a Mayan language, based on the participant's preference.

Confirmatory Testing

For individuals with a first abnormal eGFR <90 ml/min per 1.73 m^2 or albumin/creatinine ratio in urine greater than 30 mg/g, confirmatory testing was planned after 3 months. However, conclusion of the first round of laboratory analyses corresponded with the onset of the global COVID-19 pandemic, and follow-up field visits were suspended due to widespread restrictions on movement and concerns for staff and participant safety, so confirmatory tests were available in only a small subsample of participants, as described later in this article.

Variable Definitions

We calculated eGFR using the Chronic Kidney Disease–Epidemiology Collaboration equation.[40] We classified individuals using the Kidney Disease: Improving Global Outcomes system.[41] For the statistical analysis, we defined CKD as an eGFR < 60 ml/min per 1.73 m^2 with or without proteinuria. We defined stunting as measured height of less than −2 standard deviations below the mean on 2007 WHO Reference Standards for 19-year-olds.[42] We defined hypertension as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg and diabetes mellitus as a glycosylated hemoglobin ≥6.5%.

Statistical Analysis

We used Stata Version 15 (www.stata.com) for all analyses. Most variables are reported as weighted population estimates, given as means (for continuous variables) or proportions (for categorical variables) with 95% CIs. Sampling weights and household and individual response weights were applied to all population estimates and analyses, with further

Table 1. Weighted prevalence estimates and error bounds of sociodemographic and occupational characteristics by site and by gender

| Characteristic[a] | All | Estimates by site | | Estimates by gender | |
		Tecpán	San Antonio Suchitepéquez	Male	Female
Age, y	39.5 (37.5–41.4)	38.7 (36.4–41.0)	41.3 (37.5–44.9)	41.0 (39.0–42.9)	39.3 (37.9–40.7)
Below national poverty line, %	14.3 (10.5–18.1)	9.9 (6.6–13.4)	23.5 (15.4–31.5)[b]	20.6 (16.1–25.1)	17.4 (14.3–20.5)
Education higher than primary school, %	39.4 (33.3–45.8)	39.7 (32.2–47.8)	38.6 (28.9,49.2)	43.1 (37.3–49.1)	32.9 (28.9–37.3)
Self-identifies as indigenous, %	80.4 (73.3–86.0)	85.7 (76.2–91.8)	69.2 (57.1–79.2)[b]	77.4 (70.9–82.9)	75.3 (69.8–80.1)
In a couple/union, %	70.1 (74.5–75.1)	69.7 (62.1–76.4)	70.5 (63.6–76.8)	68.7 (63.1–73.8)	68.7 (64.6–72.5)
Wage labor outside the home, %	50.2 (45.3–55.1)	50.3 (43.8–56.8)	50.1 (43.8–56.3)[b]	84.7 (79.6–88.7)	31.6 (27.5–36.0)[b]
Any lifetime agriculture or construction, %	52.5 (46.1–58.8)	58.4 (49.8–66.5)	39.1 (32.0–46.8)[b]	74.3 (68.2–79.6)	35.2 (30.6–40.1)[b]
If any lifetime agriculture, predominant crop[c]:					
Sugar cane, %	10.1 (6.1–16.5)	0.2 (0–1.4)	44.1 (28.8–60.6)[b]	17.3 (11.6,24.9)	8.8 (5.2–14.6)[b]
Banana, %	2.6 (0.8–7.8)	1.1 (0.1–7.9)	7.5 (2.0–24.2)	2.5 (0.7–7.9)	2.3 (0.9–6.1)
Coffee, %	3.3 (1.9–7.5)	3.2 (1.6–6.4)	3.6 (1.6–7.6)	3.1 (1.3–7.2)	10.0 (6.2–15.8)
Vegetables, %	27.1 (20.2–35.3)	34.6 (25.2–45.3)	1.6 (0.4–6.1)	18.5 (12.9,25.7)	35.3 (27.9–43.5)
Corn, %	50.0 (40.0–60.0)	54.1 (42.7–65.0)	35.9 (20.4–55.0)	52.4 (44.0,60.1)	34.7 (27.5,42.7)
Other, %	6.8 (4.0–11.4)	6.7 (3.4–12.7)	7.2 (3.4–14.5)	6.1 (3.3–11.1)	8.8 (5.2–14.6)
Typical daily hours worked in predominant crop labor[c]	7.4 (8.8–8.2)	6.9 (6.3–7.4)	9.3 (7.9–10.6)[b]	8.6 (8.0–9.3)	6.7 (6.3–7.2)[b]
Typical days/week worked in predominant crop labor[c]	4.6 (4.3–5.0)	4.4 (4.0–4.7)	5.6 (5.1–6.2)[b]	5.2 (4.9–5.5)	4.6 (4.3–4.9)
Any lifetime agricultural pesticide exposure, %[c]	37.3 (31.5–43.6)	37.9 (31.9–44.3)	35.4 (20.7–53.6)	52.3 (44.5–59.9)	32.0 (25.3–39.6)[b]
Grows own corn for consumption, %	31.1 (22.6–41.1)	44.2 (32.2–57.0)	3.7 (1.4–9.5)[b]	–	–

[a]All characteristics given as mean or percentage, with 95% confidence intervals in parentheses. Estimates of totals are provided for the site distribution using the overall sampling weights; separate gender-specific post-estimation weights are used for the gender estimates and comparisons.
[b]$P < 0.05$.
[c]Numbers pertain to $n = 352$ subjects who reported any lifetime agricultural work.

details given in Supplementary File S2. We used Stata's *svy* commands to produce population-representative means and proportions with 95% CIs and robust variance estimates using Taylor linearization. Total estimates by study municipality used the overall sampling weights, whereas separate gender-specific post-estimation weights were used for the gender-stratified estimates and comparisons to decrease potential biases due to differential response rates (Tables 1 and 2). For overall comparisons by gender, we calculated post-estimation weights by combining the reported populations for Tecpán and San Antonio Suchitepéquez by gender and age older than 18. We assessed the association of risk factors with CKD through logistic regression. Factors identified in univariable analysis as statistically significant at an alpha of 0.2 were considered for inclusion; final models were developed using adjusted Wald tests to compare full and reduced models. We tested for interactions in the variables included in the final model. We conducted regression diagnostics including plots of deviance and predicted values to assess highly influential patterns and Archer-Lemeshow tests of goodness of fit for the final models.

Sensitivity Analyses

For the subset of individuals with confirmatory testing, we performed a classification analysis using Krippendorf's alpha to determine the proportion of those whose CKD classification changed on repeat testing. In addition, we assessed the relationship between the negative control question, the primary outcome (eGFR <60 ml/min per 1.73 m^2), and selected risk factors (history of diabetes, hypertension, stunting, lifetime tobacco use) to check for recall bias.

RESULTS

Results of Sampling and Enrollment

Figure 1 summarizes the community-based recruitment and enrollment. Of 652 structures identified for the sample (350 + 300 supplemental, with 2 duplicate coordinates that enrolled different houses), 104 were not residences. We enrolled participants from 347 residences and identified 1281 eligible adults (54% female). Of these, 807 participated in the study (63%

Table 2. Weighted prevalence estimates and error bounds of clinical characteristics by site and by gender

| Characteristic[a] | All | Estimates by site | | Estimates by gender | |
		Tecpán	San Antonio Suchitepéquez	Male	Female
Systolic BP, mm Hg	110 (108–112)	108 (106–110)	117 (114–120)[b]	118 (115–120)	109 (107–110)[b]
Diastolic BP, mm Hg	74 (73–75)	73 (71–75)	76 (74–77)[b]	76 (74–77)	73 (72–74)[b]
Hypertension, %[c]	8.6 (6.3–11.7)	7.0 (4.6–10.4)	12.4 (7.6–19.5)[d]	12.8 (9.4–17.2)	8.2 (6.1–10.9[b])
Hypertension, or self-report history of hypertension, %[e]	20.7 (17.4–24,4)	21.8 (17.8–26.4)	18.2 (12.9–25.0)	20.1 (15.9–25.1)	21.0 (17.7–24.7)
Glycosylated hemoglobin ≥6.5%, %	9.3 (7.1–12.2)	8.2 (5.5–11.9)	11.9 (8.1–17.0)	10.7 (7.5–15.0)	13.6 (10.9–16.8)
Glycosylated hemoglobin, if ≥6.5%	10.0 (9.3–10.7)	10.2 (9.2–11.3)	9.6 (8.9,10.4)	10.1 (9.1–11.1)	9.6 (9.0–10.1)
Glycosylated hemoglobin ≥6.5% or self-report of diabetes, %[f]	12.3 (9.4–15.8)	11.4 (7.9–16.2)	14.2 (10.2–19.5)	14.0 (10.4–18.6)	15.7 (12.9–19.0)
Height, cm	150.7 (149.8–151.6)	149.8 (148.7–150.9)	152.7 (151.3–154.1)[b]	158.6 (157.7–159.5)	146.5 (145.9–147.1)[b]
Body mass index (BMI)	27.1 (26.6–27.6)	27.2 (26.6–27.7)	27.0 (25.9–28.1)	25.7 (25.1–26.3)	28.0 (27.4–28.5)[b]
Obese (BMI ≥ 30), %	25.1 (21.0–29.7)	23.7 (18.9–29.2)	28.3 (21.2–36.6)	14.0 (10.2–19.0)	33.5 (29.4–37.7)[b]
Overweight (BMI ≥ 25, < 30), %	39.3 (32.8–46.1)	41.2 (32.5–50.4)	34.9 (28.8–41.5)	43.2 (37.0–49.5)	33.3 (29.2–37.6)
EGFR					
<60 ml/min per 1.73 m², %[g]	4.0 (2.4–6.6)	2.7 (1.1–6.2)	7.0 (3.7–12.8)[d]	3.3 (1.7–6.2)	3.3 (2.1–5.1)[b]
≥ 60, <90, %	20.6 (17.0–24.7)	22.7 (18.0–28.1)	16.3 (11.8–22.2)	25.8 (21.0–31.3)	16.3 (13.1–20.0)
Any lifetime ethanol consumption, %	56.0 (50.5–61.6)	56.6 (49.1–63.8)	54..7 (48.8–60.5)	71.7 (65.8–77.0)	45.8 (41.0–50.7)[b]
Any lifetime tobacco use, %	25.4 (21.9–29.2)	25.3 (21.1–30.0)	25.5 (19.6–32.4)	58.4 (52.3–64.2)	8.1 (6.1–10.7)[b]
Any prolonged NSAID use, %[h]	93.0 (89.7–95.3)	91.0 (86.4–94.1)	97.6 (92.8–99.2)	94.5 (91.1–96.6)	93.2 (90.5–95.1)
Family history of diabetes or hypertension, %	54.9 (49.0–60.7)	57.6 (50.4–64.5)	48.8 (39.0–58.6)	57.5 (50.8–63.8)	54.8 (49.8–59.6)
Self-reported history of diabetes or hypertension, %	21.4 (18.0–25.2)	23.9 (19.4–29.1)	15.7 (11.8–20.7)[b]	19.5 (15.3–24.6)	21.8 (18.4–25.4)
Self-reported history of child malnutrition or prematurity, %	6.3 (4.2–9.3)	7.7 (4.7–12.1)	3.7 (2.1–6.5)[d]	5.4 (3.2–9.1)	6.4 (4.5–9.0)

NSAID, nonsteroidal anti-inflammatory drug.
[a]All characteristics given as mean or percentage, with 95% confidence intervals in parentheses. Total estimates are provided for the site distribution using the overall sampling weights; separate gender-specific post-estimation weights are used for the gender estimates and comparisons.
[b]$P < 0.05$.
[c]Defined as systolic blood pressure (BP) ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg.
[d]$P < 0.10$.
[e]All individuals with measured systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg or self-reported history of hypertension.
[f]All individuals with measured glycosylated hemoglobin ≥6.5% or self-reported history of diabetes.
[g]GFR estimated using the Chronic Kidney Disease–Epidemiology Collaboration equation.
[h]Defined as self-reported daily use for ≥ 3 months.
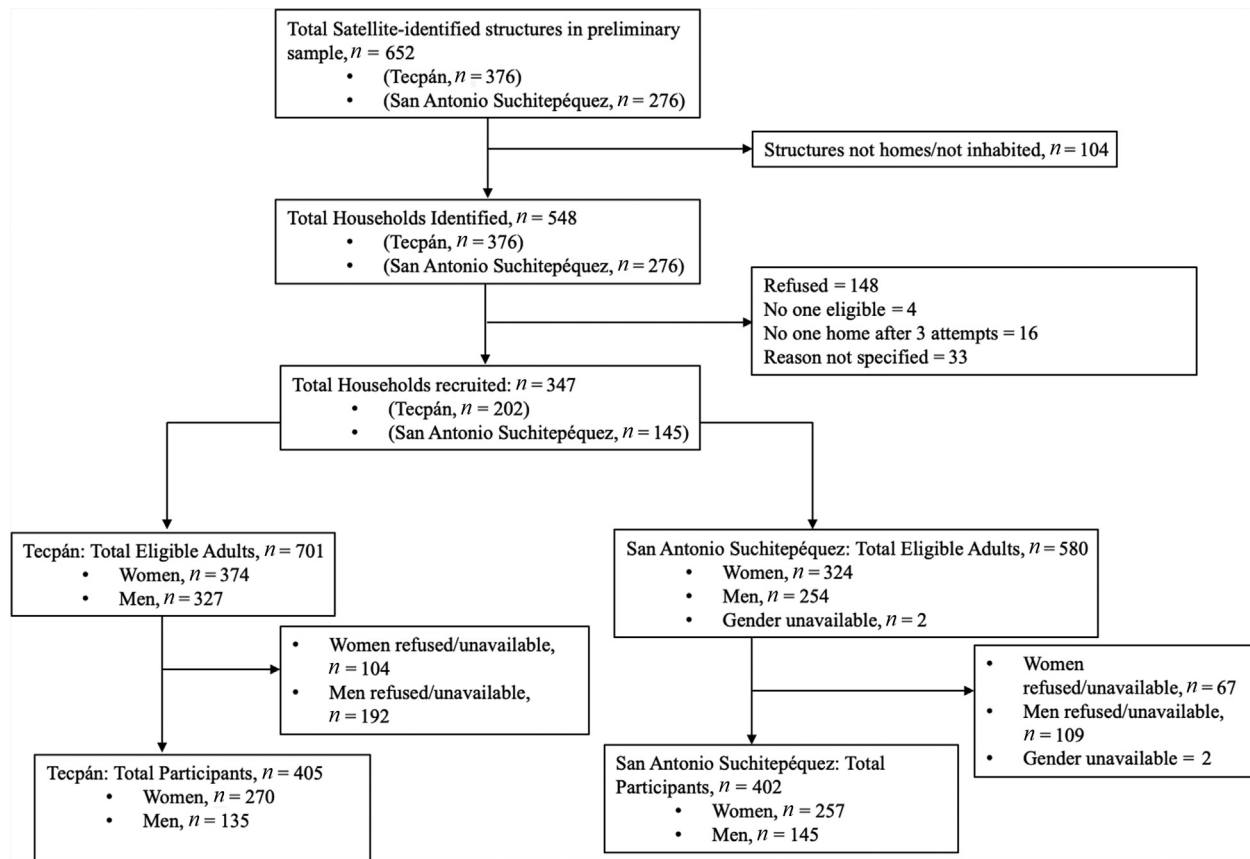
Figure 1. Flow chart of sample recruitment and enrollment.

of all eligible). Refusal and lack of availability was higher for men than for women, with 48% of eligible men and 76% of eligible women agreeing to participate.

Descriptive Characteristics of Study Participants

Table 1 details the survey-weighted estimates of sociodemographic and occupational characteristics by municipality and gender. Most respondents self-identified as indigenous Maya, although the proportion was higher in Tecpán (85.7%, 95% CI 76.2–91.8) than in San Antonio Suchitepéquez (69.2%, 95% CI 57.1–79.2). In addition, a higher proportion of individuals were below the national poverty line in San Antonio Suchitepéquez (23.5%, 95% CI 15.4–31.5) than in Tecpán (9.9%, 95% CI 6.6–13.4). Approximately half the respondents were engaged in manual labor, with a higher proportion of lifetime work in agriculture or construction in Tecpán than in San Antonio Suchitepéquez. Corn cultivation was common in both communities, but intensive tropical crops (sugar cane and banana) were more frequent in San Antonio Suchitepéquez than in Tecpán. Overall, men were more likely to be engaged in manual labor, especially agriculture and construction (74.5%, 95% CI 68.4–79.9), than women (35.1%, 95% CI 30.5–40.1).

For those in agriculture, labor intensity (hours per day or days per week) and pesticide exposure were higher in men than in women.

Clinical Characteristics of Study Participants

Table 2 details the survey-weighted estimates of clinical characteristics of the sample by municipality and gender. The estimated proportion of individuals with an eGFR less than 60 ml/min per 1.73 m^2 was 4.0% (95% CI 2.4–6.6) with a trend toward more individuals in San Antonio Suchitepéquez. Most cases (88.4%) were associated with diabetes and/or hypertension. In addition, 20.6% (95% CI 17.0–24.7) of individuals had an eGFR between 60 and 90 ml/min per 1.73 m^2.

We classified participants into CKD risk categories using the Kidney Disease: Improving Global Outcomes classification system (Figure 2).[43] Notable here was the overall low prevalence of albuminuria. Even among those individuals with an eGFR less than 60 ml/min per 1.73 m^2, most did not exhibit albuminuria >30 mg/g.

Overall, 9.3% (95% CI 7.1–12.2) demonstrated an elevated glycosylated hemoglobin (Table 2). Among these, glycemic control was poor, with a mean glycosylated hemoglobin of 10.0% (95% CI 9.3–10.7). In addition, 20.7% (95% CI 17.4–24.4) reported a history of hypertension or were found to be hypertensive on

				Albuminuria categories		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				< 30 mg/g	30–299 mg/g	≥ 300 mg/g
GFR categories (ml/min Per 1.73 m²)	G1	Normal or high	≥ 90	599 (73.3%)	16 (2.0%)	0
	G2	Mildly decreased	60–89	160 (19.7%)	7 (1.0%)	0
	G3a	Mild to moderately decreased	45–59	16 (2.0%)	0	0
	G3b	Moderately to severely decreased	30–44	8 (1.0%)	1 (0.1%)	0
	G4	Severely decreased	15–29	2 (0.2%)	<1	0
	G5	Kidney failure	< 15	0	6 (0.7%)	0

Figure 2. Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Risk Classification for study population. All numbers are survey-weighted counts and frequencies. GFR, glomerular filtration rate.

clinical examination. Overweight or obesity (BMI ≥25) was 64.4% (95% CI 58.6–69.8) overall. Mean height was lower in Tecpán than San Antonio Suchitepéquez (Table 2). A key significant difference between genders was the higher prevalence of overweight or obesity in women (66.9%, 95% CI 62.5–71.0) compared with men (57.0%, 95% CI 50.5–63.2).

Risk Factor Analysis

We conducted logistic regression using applicable survey and response weights to explore the relationship between selected covariates and eGFR <60 ml/min per 1.73 m² (Table 3). After multivariable adjustment, a personal history of diabetes or hypertension was strongly associated with an eGFR below 60 ml/min per 1.73 m² (aOR 11.21, 95% CI 3.28–38.24), as was low BMI (aOR 21.09, 95% CI 2.05–217.0). Odds of CKD also were higher with increasing age (aOR 1.12, 95% CI 1.06–1.19) but decreased at higher poverty levels (aOR 0.93, 95% CI 0.87–0.99). An interaction existed between poverty and history of sugar cane agriculture, in that sugar cane history was associated with increased odds of CKD in individuals with higher poverty levels (aOR 1.10, 95% CI 1.01–1.19), but this sugar cane–related risk was not observed in individuals with lower poverty scores.

Sensitivity Analyses

Confirmatory testing was available for 63 individuals at an interval of more than 3 months. For these individuals, we examined eGFR on confirmatory tests (Figure 3). Overall, eGFR class worsened for 8% and improved for 24%; 14 individuals with an eGFR of 60 to 89 ml/min per 1.73 m² had an eGFR of ≥90 ml/min per 1.73 m² on repeat testing. Overall agreement between initial and confirmatory testing was 68% (Krippendorf's alpha 0.47). We also assessed for recall bias. To do this, we confirmed that responses to the negative control item (*Have you ever had a broken bone*

Table 3. Logistic regression analysis for factors associated with any abnormal eGFR <60 ml/min per 1.73 m²

Characteristic	Unadjusted OR	Adjusted OR
Lives in hot climate (San Antonio Suchitepéquez)	2.78 [0.94–8.25]	–
Age, y	1.10 [1.06–1.14][a]	1.12 [1.06–1.19][a]
Below national poverty line	1.01 [0.99–1.03]	0.93 [0.87–0.99][a]
Agricultural experience		
- Sugar cane	10.25 [2.89–36.29][a]	0.57 [0.06–5.17]
- Banana	4.55 [0.45–46.45]	–
- Coffee	6.03 [1.29–28.18][a]	–
- Vegetables	1.28 [0.27–5.97]	–
- Corn	0.60 [0.17–2.20]	–
Interaction between poverty and history of employment in sugar cane		1.10 [1.01–1.19][a]
History of diabetes or hypertension[b]	7.20 [1.89–27.35][a]	11.21 [3.28–38.24][a]
Weight status		
- Underweight (BMI < 18.5)	5.82 [0.80–42.08][c]	21.09 [2.05–217.0][a]
- Overweight/Obese (BMI ≥ 25)	0.52 [0.16–1.65]	0.72 [0.25–2.06]
Any lifetime tobacco use	3.05 [0.92–10.12][c]	–

BMI, body mass index; eGFR, estimated glomerular filtration rate; OR, odds ratio
[a]$P < 0.05$.
[b]All individuals with measured systolic blood pressure (BP) ≥140 mm Hg or diastolic BP ≥90 mm Hg, measured glycosylated hemoglobin ≥ 6.5%, or self-reported history of hypertension or diabetes
[c]$P < 0.10$.

in childhood?) were not statistically significantly associated with GFR or important risk factors, such as history of diabetes, hypertension, stunting, or tobacco use, suggesting that recall bias is unlikely to be an important factor in interpreting the results.

DISCUSSION

Globally, the burden of CKD is rising rapidly and is disproportionately concentrated in particular countries, among them Central America and Mexico.[1] To our knowledge, our findings are the first estimates of CKD in a rural population-based sample in Guatemala. The prevalence of CKD in our sample (4%) is similar to that reported for a recent population-based study in southwestern Nicaragua with a similar demographic age structure (5%).[44] By contrast, metanalyses have estimated the overall global prevalence of CKD at approximately 11%.[36,45] Central American countries

			Confirmatory Testing		
	GFR categories (ml/min Per 1.73 m²)		≥ 90²	60–89	< 59
Initial Testing	≥ 90		19 (30%)	2 (3%)	--
	60–89		14 (22%)	19 (30%)	3 (5%)
	< 59		1 (2%)	1 (2%)	5 (8%)

Figure 3. Glomerular filtration rate (GFR) classification on confirmatory testing. Confirmatory testing was available for 63 subjects. Cells are color-coded as green (no change in GFR classification), blue (improved GFR classification), and yellow (worsened GFR classification).

have among the youngest population age structures in the world, which likely accounts for these differences.

Next, we estimated the prevalence of diabetes and hypertension (12.3% and 20.7%, respectively) in our population and the relationship with CKD (Table 2). Most cases of CKD were associated with diabetes and hypertension. Importantly, nearly a third (29%) of respondents with elevated glycosylated hemoglobin (≥6.5%) did not already carry a diagnosis of diabetes. Many prior studies on CKD and CKDu in Central America have relied on self-report of diabetes or hypertension.[15,44,46] Our findings suggest that in the context of rural populations with limited access to health care and high prevalence of diabetes or hypertension, self-report is unlikely to yield the true prevalence of these conditions and may lead to classification errors, for example, between traditional CKD and CKDu cases.[47]

The presence of CKD in some respondents without diabetes and hypertension, the very low prevalence of proteinuria in those with CKD (Figure 2), and the association between CKD and sugar cane agriculture among participants with high poverty levels all are circumstantial evidence for the likely existence of at least some CKDu in our sample. Unfortunately, the overall low prevalence of CKD in our sample did not allow us to examine CKDu risk factors independently. It also reinforces the fact that even in rural communities in Guatemala where CKDu may occur, much disease will still be related to diabetes and hypertension. In these settings, study designs that enrich for hypothesized risk factors, such as occupational health studies with sugar cane workers, are more likely to provide insights into CKDu specifically than population-representative samples such as ours.[26,27]

Other findings from the multivariate regression deserve brief mention. First, the strong association between CKD and low BMI may be a reflection of severe poverty (e.g., food insecurity and the burden of catastrophic health care spending for chronic illness). In Guatemalan rural communities, we have observed a wasting phenotype in very poor individuals with diabetes or other chronic illnesses that precedes progressive kidney disease.[48] Some studies have evaluated the association between BMI and progression of CKD.[49–54] Studies from China and Taiwan, for example, have found that low BMI is an independent risk factor for disease progression in individuals with CKD.[49,50] In the United States and Sweden, higher BMI has been commonly associated with CKD progression, but at least one large cohort study has shown U-shaped associations between BMI and CKD progression and mortality.[22,51–54]

Second, although poverty was a risk factor for CKD in those working in sugar cane agriculture, it was otherwise slightly protective against CKD. This discrepancy may represent difficulties in accurately measuring the multidimensional nature of poverty in rural settings, or residual confounding for risky lifestyle factors found primarily in those with higher income levels.[55]

Third, according to the developmental CKD origins hypothesis, we anticipated that the very high rates of low birthweight and childhood malnutrition in rural Guatemala might be reflected in adult CKD.[56–59] However, we did not observe this association in our regression model. It is possible that early childhood exposures lead to subtle decrements in kidney function that, in a relatively young adult population, do not manifest as frank CKD. Along these lines, the large proportion of individuals with an eGFR between 60 and 90 ml/min per 1.73 m^2 (nearly 21%) is notable and will be an important area of future study. However, given the lack of validation studies of GFR estimating equations in our population and the inability to obtain confirmatory testing in most participants, we did not conduct this analysis here.

Our study has several limitations. First, women are overrepresented among respondents. However, our estimates use gender-specific post-stratification response weights designed to decrease bias due to nonresponse and underrepresentation of men. In addition, if certain groups (e.g., male agricultural workers) were less likely to participate, selection bias may have occurred. However, we compared our sample structure to the proportions of younger male agricultural workers from the recent population-based Demographic and Health Survey, and found no significant differences. Therefore, selection bias is unlikely to have been a serious issue.[37] Second, the numbers of individuals with an eGFR less than 60 ml/min per 1.73 m^2 in our sample was small, and thus our power to assess risk factors in this population is limited. However, this was an exploratory aim in our study protocol, and the sample size was large enough to detect differences in some important and well-known risks. Third, our assessment of several important risk factors and exposures relied on self-report, with a risk for misclassification. Finally, we lack confirmatory testing for most participants due to the COVID-19 outbreak, which introduces some uncertainty into our CKD classification, although in our sensitivity analysis this largely affected individuals with an eGFR of more than 60 ml/min per 1.73 m^2.

In conclusion, in this first population-based survey of eGFR in rural areas of Guatemala, the overall

prevalence of CKD was similar to that recently documented in the neighboring country of Nicaragua. Most CKD cases identified were associated with diabetes and hypertension. The association between CKD and sugar cane agriculture in high-poverty individuals is suggestive of CKDu in the population.

DISCLOSURES

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AUTHOR CONTRIBUTIONS

ACM designed the study, conducted primary analysis, critically revised all versions and co-wrote the final version of the manuscript. ET coordinated data collection, conducted primary analysis, and critically revised the manuscript. ED and LS coordinated data collection and critically revised the manuscript. DRT advised on sample selection, calculation of survey weights, and critically revised the manuscript. DF, PG, JB, and CMM designed the study and critically revised the manuscript. PR designed the study, conducted primary analysis, and wrote the first and final drafts of the manuscript.

DATA AVAILABILITY

Original deidentified study data will be made available on a case-by-case basis to researchers with an institutional review board–approved study protocol, and requests can be made directly to the corresponding author. Study instruments are included as Supplemental Files to the manuscript.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)
File S1. Structured Participant Survey
File S2. Description of Sample Weighting Procedures
STROBE Statement

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