Prevalence and risk factors for chronic kidney disease among brickmaking workers in La Paz Centro, Nicaragua

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Abstract

Rationale & Objective: In Central America there is high prevalence of chronic kidney disease (CKD) of non-traditional etiology often observed among agricultural workers. Few studies have assessed CKD prevalence among workers in non-agricultural occupations, which was the objective of this investigation.

Study Design: Prospective cohort study.

Setting & Participants: Male and female workers (n=224) employed by artisanal brickmaking facilities in La Paz Centro, Nicaragua.

Predictors: Age, sex, education, smoking status, body mass index, alcohol consumption, water consumption, first degree relative(s) with CKD, years worked, hours worked per week, job category, study visit (baseline and follow-up), self-reported hypertension and diabetes.

Outcomes: CKD defined as estimated glomerular filtration rate eGFR<60 mL/min/1.73m^2 at two time points, four months apart and CKD stage.

Analytical Approach: Linear regression for repeated measures with an unstructured covariance matrix to evaluate the association between demographics, occupational risk factors and eGFR at baseline. The interaction between risk factors and time with change in eGFR was also evaluated. Multivariable logistic regression models were used to evaluate the predictors of CKD.

Results: The prevalence of CKD was 12.1% (n=27), 100% of the cases were male, 30% had stage 5 CKD (eGFR<15 mL/min/1.73m^2), and 22% were < 35 years of age. The proportions of participants with eGFR <60 mL/min/1.73m^2 at baseline and at follow-up were 13.8% and 15.2%, respectively. Linear regression analysis demonstrated significant predictors of lower kidney function at baseline including oven work, older age, lack of education. and having an immediate family member with CKD. Predictors of CKD identified using logistic regression analysis included oven work and lack of education.

Limitations: crude job classification measures, loss to follow-up, self-reported exposures

Conclusions: Prevalence of CKD is high in this population of brick workers, suggesting the epidemic of CKD affecting Mesoamerica is not limited to agricultural workers. These results are consistent with the hypothesis that occupational heat exposure is a risk factor for kidney disease in this region.

Index words: Chronic Kidney Disease (CKD), Mesoamerican Nephropathy (MeN), Brickmaking, Heat exposure, Nicaragua

Summary: Chronic Kidney Disease (CKD) of non-traditional etiology is a leading cause of death in Nicaragua. Most prevalence studies have focused on agricultural workers. This study included 224 artisanal brick and tile workers in Northwestern Nicaragua, where CKD rates are high. We measured kidney function at two time points to determine the prevalence of CKD according to international guidelines. We also examined social, economic and occupational factors that may influence kidney health. Prevalence of CKD was high among these workers and was not evenly distributed. Kidney function was lower at baseline among oven workers, workers with low education, and among workers who had a family member with CKD. Oven workers and workers who lacked education were more likely to develop CKD.

Introduction

A chronic kidney disease of non-traditional etiology (CKDnt) has been documented in Central America over the past two decades. Also called Mesoamerican Nephropathy (MeN), its cause is unknown, but it is characterized by high mortality rates among young, adult males who often have a history of manual labor in agriculture and live along the lowlands of the Pacific coast. Traditional risk factors of chronic kidney disease (CKD) such as diabetes, hypertension, obesity and proteinuria are not typically present in CKDnt.[1-7]

Excess mortality from CKD is considerably higher in El Salvador and Nicaragua compared to other Central American countries. In 2013, the age-standardized mortality rates from CKD were 36.7 per 100,000 population in Nicaragua and 47.4 in El Salvador, compared to 6.6 in Costa Rica.[8] The male-specific CKD mortality rates far exceed rates among women in both Nicaragua and El Salvador.[3, 8] CKDnt in this region is thought to be multi-factorial, likely with environmental, occupational, genetic, social, and economic risk factors. Risk factors that have been associated with decreased kidney function include living at low altitude, job task and occupation, heat stress, family history of CKD, alcohol consumption, lack of education, increased consumption of water, and male sex.[1, 2, 7, 9-22]

Most epidemiologic studies to date have been cross-sectional, determined estimated glomerular filtration rate (eGFR) or serum creatinine at a single time point[1, 2, 9-18, 23] and have focused on populations that are employed in agriculture.[9, 12] However, high serum creatinine has also been measured among workers in construction, mining and fishing.[9, 10]

This study reports on CKDnt in a population employed in brickmaking. The objectives of this study were to (1) determine the prevalence of CKD among workers in the artisanal brick industry in La Paz Centro, Nicaragua; (2) examine whether kidney function changed over the study period; (3) identify risk factors for decreased eGFR and CKD and; (4) identify risk factors associated with decreasing eGFR over time.

Methods

Study design

The study population included workers employed by 44 brickmaking facilities in La Paz Centro, a municipality in northwestern Nicaragua in the Department of León. All study participants were at least 18 years old and provided informed consent. The Institutional Review Boards at the National Autonomous University of Nicaragua, León (UNAN-León) and Boston University Medical Campus approved this study.

The municipal office of La Paz Centro provided the study team with 2014 census data, including a list of the 97 brickmaking facilities in the area; each employing three to thirty workers, with six workers per facility on average. Investigators randomly selected 45 facilities to participate, ultimately working with 44 (Figure 1). Workers were eligible to participate if they were (1) currently a brick worker, had been employed in brickmaking for at least one year and; (2) between the ages of 18 and 60. We also required that workers had not been working for more than two hours at the time of recruitment and collection of biological samples. If workers expressed interest in participating and met the inclusion criteria, but had already worked more than two hours on that day, they were recruited on the following day, prior to the start of their shift. Of those invited to participate (N=300), 14% (n=43) did not participate due to disinterest or concerns about reduced productivity (daily wages correspond with production) (Fig. 1). Study participants (n=257) were enrolled at baseline (February 2016). Four months later (June 2016), we conducted a follow-up assessment with 224 of the 257 originally recruited workers at their workplace or at home if the participant was not working (see Figure 1).

The baseline assessment was conducted at the workplace and included the collection of blood and urine, a physical exam including height and weight, and administration of a questionnaire on personal characteristics, medical and occupational history, work practices, and habits. Blood and urine were collected in the morning prior to (or no more than two hours after the beginning of) their work-shift. At the follow-up visit, we obtained blood and urine samples, weight, and administered an abbreviated questionnaire. As at baseline, participants provided biological samples prior to (or no more than 2 hours after the beginning of) their work-shift, or during the early morning hours for those participants who were not working at the time of follow-up.

All workers enrolled in this study performed brickmaking outdoors. Job tasks performed by brick workers can include more than one task per day and can vary daily. The final study population reflects workers who completed six different job tasks on the day prior to the field visits: oven loader, oven operator, mixer, molder, supervisor, or other activity. Workers who had not worked the prior day were also included. Working practices vary between facilities, but most operations involve workers manually mixing clay, ash and water and elaborating their product with handheld molds as well as with their bare hands and feet. Most workers begin their shift in the early morning when still dark (e.g. 5:00 AM), but may work until mid-day. Based on observation and conversations with management and workers (who asserted that the oven workers were the most likely to get kidney disease), we hypothesized that workers who performed tasks involving the oven were at a higher risk of heat exposure and of CKD. The ovens are large brick structures, which must be manually lit, and the fire stoked and stocked with wood. Oven workers must maintain the fire at temperatures sufficient to cook the bricks, often for long periods of time. In most shops the ovens are located at a distance from other aspects of brick-making. Thus, we grouped the job tasks into three mutually exclusive job exposure categories for our analyses. If the job task(s) reported by a participant at the baseline *and* follow-up assessments included oven loading or oven operating, their job category was classified as (1) oven work at both visits; if the job task(s) reported by a participant at either the baseline *or* follow-up assessments included oven loading or oven operating, their job category was classified as (2) oven work at one visit; and if the job task(s) did not include oven loading or oven operating, their job category was classified as (3) oven work at neither visit.

Laboratory analysis of biomarkers of kidney function

Spot urine samples were collected in 50mL collection cups, and blood samples were collected in vacuum tubes with clot activator and gel for serum separation. Following collection, all samples were immediately transported to the local health center on ice packs (4°C). Urine samples were analyzed using reactive strips (Combur 10 UX™) and an automated reader (Urisys 1100, Roche Diagnostics, Germany). Blood samples were centrifuged at 3500 RPM for five minutes, subsequently separated into aliquots and stored at -20ºC at the Research Centre on Health, Work and Environment (CISTA) at UNAN-León. Within 48 hours, serum aliquots were transported to the Biochemistry Laboratory at UNAN-León, where serum creatinine (SCr) and serum uric acid were measured (ChemWell® 2910, Awareness Technology, United States). SCr was measured via the Jaffe method and uric acid by enzymatic colorimetric method (PAP-method). For each batch of samples at least two duplicates were included for quality control. The biochemistry laboratory participates in an international inter-laboratory quality control program where measurements are compared to a laboratory standard (Serodos Plus Human Diagnostics, Wiesbaden, Germany) daily. Measured SCr and uric acid values in the samples were all within the accepted limits of the method.

Statistical analysis

The biochemistry laboratory reported non-IDMS-calibrated SCr (mg/dL), therefore recorded values were multiplied by 0.95 in order to use the Chronic Kidney Disease epidemiology collaboration equation (CKD-EPI)[24, 25] for IDMS-traceable SCr to calculate eGFR. Race was categorized as "non-black." Based on KDIGO guidelines,[23] CKD was defined as an eGFR<60 ml/min/1.73m^2 at baseline and follow-up (the second measurement 4 months apart from the baseline), and was classified in three stages (stage 3 to 5). Urinary protein was measured semi-quantitatively via reactive strip, and albuminuria was not quantified. Consequently, we did not classify CKD cases in stage 1 or 2, which is reliant on both eGFR and proteinuria.

We first determined the prevalence of CKD in the final study population by stage, sex, age, family history of CKD and ever hypertension/diabetes status. We then used multivariable logistic regression models to evaluate the association between job type and CKD. We then used a marginal linear model for repeated measures with an unstructured covariance matrix estimated by maximum likelihood allowing complete flexibility of the correlation over time to analyze the association between socio-demographic characteristics, occupational risk factors and kidney function at baseline. The interaction between risk factors and time on change in eGFR was also evaluated.

Variables considered as potential predictors of eGFR and change in eGFR were job, study visit (baseline, follow-up—for change in eGFR only), age (continuous), sex, educational attainment (none, primary, secondary/university), years worked in brickmaking (continuous), smoking status (current/former/never), alcoholic drinks consumed per week (using US Dietary Guidelines 2015-2020 categorized as none, moderate, excess),[26] first degree relative(s) with CKD (yes/no), current hours worked per week (>48/≤48), water consumption yesterday (<3, 3-6, and >6 liters), self-reported hypertension (ever/never), self-reported diabetes (ever/never), and body mass index (BMI) (BMI ≥ 30 (obese), < 30). Data were analyzed using SAS (version 9.4, Cary, NC, USA).

For the logistic regression model, we used a two-step approach to create a parsimonious model. First, we excluded variables that were likely to be on the causal pathway between job type and CKD, such as water consumption and number of hours worked. We then sequentially added variables whose inclusion resulted in a meaningful change in the estimate of the association between job type and CKD. We arrived at a 5-variable model (job, age, education, relative with CKD, and alcohol consumption). Sex was not included as a potential predictor because all cases occurred among males. Because age and years worked in brickmaking were correlated (Pearson correlation=0.71), we also constructed a second logistic regression model where years brickmaking was substituted for age.

Results

Study participant characteristics

The mean age was 33.9 years (standard deviation (SD) ± 11.07 years) and the majority of workers recruited were male (86%) and had a BMI less than 30 (90%) (Table 1). Most participants (76%) had an occupational history of working in brick for between >6 years and almost half had worked for >11 years. Most workers reported consuming ≥3 liters of water the day prior (71%), 15% of men and 16% of women reported performing oven work at both visits, and 47% of participants did not report performing oven work at either visit. Oven workers at both visits reported the longest work shift on average (8.6 hours) and some oven workers reported working 24-hour shifts. Non-oven workers reported shifts of 7.4 hours on average, and did not report a shift exceeding 16 hours (Table S1). Workers who reported some oven work were also 6.2% more likely to report having exceeded a 48-hour workweek as compared to workers who reported none (Table S2). Thirty-one percent of workers reported having at least one first-degree family member with CKD and most workers reported consuming one or more alcoholic drinks per week (63%) (Table 1). Eleven percent of workers had hyperuricemia (uric acid >7mg/dL serum) and 4% had proteinuria at baseline. About 3% reported ever having had diabetes and 15% reported ever having hypertension.

Prevalence of CKD

The median eGFR at baseline was 110.6 mL/min/1.73m^2 (range of 9.4-154.9 mL/min/1.73m^2). At follow-up, the median eGFR was 107.7 mL/min/1.73m^2 (range of 6.3-149.9 mL/min/1.73m^2). The percentage of participants with eGFR<60 mL/min/1.73m^2 was 13.8% at baseline and 15.2% at follow-up. Of the thirty-one participants who had eGFR<60 at baseline, four participants improved at follow-up from kidney function consistent with Stage 3a CKD to normal function. Of the thirty-four participants who had an eGFR<60 at follow-up, five participants had declined from normal at baseline to having an eGFR consistent with Stage 3a CKD and two participants had declined to an eGFR consistent with Stage 3b.

The prevalence of CKD (eGFR<60 ml/min/1.73m^2) was 12.1%, including 4.9% with stage 3, 3.6% with stage 4, and 3.6% with stage 5 (Table 2). CKD was seen exclusively among men and prevalence was five times higher in 25-34 year-old participants (8.1%) and ten times higher in 35-44 year-old participants (16.7%) as compared to 18-24 year-old participants (1.7%), respectively. Of those workers who developed CKD one reported having ever had diabetes and seven reported having ever had hypertension.

Risk factors for decreased eGFR

Linear models explored risk factors associated with lower eGFR at baseline as well as factors associated with a decrease in eGFR over time between study visits (Table 3). Oven operation, lack of education, increasing age and having an immediate family member with CKD were associated with having a lower eGFR at baseline. Workers who performed oven work at both baseline and follow-up had an eGFR that was on average 15.52 mL/min/1.73m^2 lower at baseline as compared to workers who did not report work with the oven at either visit (95% CI: -26.02, -5.01). Workers who had no formal education had an eGFR that was on average 14.17 mL/min/1.73m^2 lower at baseline as compared to workers who had a secondary or university education (95% CI: -24.30, -4.05). Workers who had at least one first degree relative with CKD had an average eGFR that was 7.66 mL/min/1.73m^2 lower at baseline as compared to workers who had no relatives with CKD (95% CI: -15.17, -0.14) and per every decade of aging, eGFR was 9.5 mL/min/1.73m^2 lower than among younger workers (95% CI: -1.42, -0.47). After exploring various interactions in the linear model, we observed no significant associations between oven work, education, age or family history of CKD and eGFR over time. However, drinking less than 3 liters of water at work (β:-11.28, 95% CI: -21.06, -1.51) and working for more than 48 hours a week (β:-7.65, 95% CI:-15.00, -0.30) were associated with a significant decrease in eGFR over time.

The multivariable logistic regression model (Table 4) indicated that workers who performed oven work at both time points had 5.47 (95% CI: 1.40 – 21.34) greater odds of having CKD compared to workers who did not perform oven work at either time point. Age, having no formal education, excess or moderate consumption of alcohol, and having a first-degree relative with CKD were also associated with increased prevalence of CKD. The odds ratio for the association between job type and CKD was virtually identical when years worked in brickmaking replaced age in the model.

Discussion

This study assesses the prevalence and predictors of CKD in a population of brick workers at risk for CKDnt. Prevalence of CKD in this population of brick workers was 12.1%. The estimated prevalence of CKD was higher when based on measurements of SCr at one time point (i.e. 13.8% at baseline; 15.2% at follow-up) versus both time points (12.1%). However, even based on two time points, the prevalence of CKD stage 3-5 is higher than expected in this predominantly young population. For a crude comparison, in the U.S., prevalence of stage 3-5 CKD based on a single time point among NHANES participants (2011-2014) aged 20-39, was 0.3%, and among ages 40-59, the prevalence was 3.3%.[27] A cross sectional study conducted in León, Nicaragua estimated prevalence of eGFR<60ml/min/1.73m² at 14% among men and 6% among women aged 18 to 60. Risk factors were age, living and working in rural areas, low education, and increasing years of agriculture work.[19] Only two other studies have examined CKDnt prevalence in this region using two measures of SCr at least 3 months apart.[16, 28] The first study (N=775) in the Bajo Lempa region of El Salvador (a rural area comprised primarily of agricultural communities) estimated CKDnt prevalence to be 18% (stages 1-5). When restricted to stages 3-5 as measured in our study, the prevalence was 10%.[16] The second study (N=2,388), conducted by the same group among Salvadoran agricultural communities showed similar results.[28] Of particular interest, both studies reported prevalence of 12% and 14% among women with stages 3-5, while there were no cases among women in our study. These differences may be due to the small number of women in our study (n=32), as well as the differences in the nature of the study population (occupational vs. community-based). Of note, only 0.5% of the El Salvador population had eGFR consistent with stage 5 CKD compared to 3.6% in our study.

One reason that we observed higher prevalence of stage 5 CKD in this sector may be due to the difference in worker protection and screening. Within the formal sector of the sugarcane industry in the region, employers often conduct a pre-employment health screening which includes measurement of SCr, as described by Laws et al. 2015.[29] Workers that have elevated SCr are often not hired. Given that brickmaking is comparatively informal relative to the sugarcane industry in this region, it is likely that more brick workers with kidney damage are occupationally active. This is a significant public health concern that should be addressed in this highly active population; over a quarter (n=68) of the workers in this study reported exceeding the standard 48-hour workweek in Nicaragua, and working more than 48 hours a week was associated with a decline in kidney function over time.

At baseline, increasing age, performing oven work, and having immediate family members with CKD were associated with having lower eGFR while education appeared to be protective. Similarly, oven work and lack of formal education were predictive of having CKD. However, it is notable that the same proportion of women performed oven work at both visits as men, and none had CKD; the effect of oven work at both visits on kidney function was only observed among men. Additionally, although men had an average eGFR that was lower than women at baseline and over time, the association was insignificant.

In the present study, eGFR increased by 3.91 mL/min/1.73m^2 on average over the study period. Although inconsistent with longitudinal studies conducted among sugarcane workers in Nicaragua (which found that kidney function declined over 6 months and 9 weeks of the sugarcane harvest season[29, 30]), the phenomenon of partial recovery of kidney function following the end sugarcane harvest season has also been observed.[31] Similar to sugarcane, one possible reason for the increase in eGFR observed in the present study is that the follow-up visit occurred at the beginning of the rainy season when brickwork (an outdoor occupation) is less intense due to inclement weather.

Our results indicate that brick workers have a high prevalence of CKD and share risk factors for CKDnt that are similar to those observed among agricultural workers in the region, including occupation and low education.[1, 2, 7, 9-22] In the present study a medical history of hypertension or diabetes was infrequent and neither was associated with CKD, consistent with the presentation of CKDnt in the region. Sugarcane and brick makers in this region of Nicaragua live in predominantly rural areas where their respective industries are the primary economic activity and, as such, define the lifestyle of the surrounding communities. This may include less emphasis on or opportunity for formal education. Insufficient hydration and volume depletion events may also be risk factors shared by these populations. At baseline, the association between self-reported water consumption and eGFR was insignificant while lower water consumption was associated with a decrease in eGFR over time. This may suggest that the effect of hydration habits on kidney function is dependent on time but, given the limitations of self-report, merits additional investigation. Having at least one first degree relative with CKD was significantly associated with having lower eGFR at baseline and was associated with CKD, which is consistent with previous studies among communities employed in sugarcane.[16, 32] Given that 48% of participants with CKD in the present study (all men) reported at least one immediate family member with known disease, a future study evaluating genetic markers or familial clustering of CKD may be warranted. Based on our observations, brickmaking can be a familial operation in which immediate relatives work at the same or a nearby facility, suggesting that a participant's family may be exposed to similar risk factors.

A strength of this study is the focus on workers in a non-agricultural sector in the region at high risk for CKDnt. Additionally, CKD prevalence data was based on two time points, adding longitudinal evidence to the current body of cross-sectional literature on MeN.

A limitation of this study is a crude job classification metric. Our classification of oven worker at both, one or neither visit was not based on an exposure assessment. We also used job task as a proxy for heat exposure and metabolic expenditure, and relied on self-reported water consumption as a measure of hydration status. An exposure assessment of brickmaking job tasks and working conditions would contribute to a more robust job exposure metric. Observations and quantitative measures of exposure (e.g., temperatures) and outcomes (e.g. metabolic expenditure) could also better characterize volume depletion events.

Our sample comprised approximately 44% of the brick worker population according to 2014 census data. We recruited 257 brick workers and 13% were lost to follow-up. On average, those lost were younger than the final study sample, and had worked fewer years than the study average. Twelve of those lost emigrated for work, suggesting that they remained occupationally active at the time of follow-up. The remaining fifteen were either known to have moved or could not be located. Of those lost to follow-up, 12% (n=4) had an eGFR<60 at baseline. Although we were not able to confirm CKD case status at follow-up for those four participants, even if their loss to follow-up was a result of CKD, our estimated prevalence would likely remain unchanged.

Another limitation of our study was that blood samples were collected either prior to the start of the work shift or within two hours of the work shift beginning. Ideally, samples would have been collected prior to the start of work for all participants. Given that start times were variable within and between brick facilities, this presented a logistical challenge. Additionally, given that our follow-up occurred in June (the beginning of the rainy season) some participants had recently transitioned from intensive brickwork to infrequent shifts or other employment, which required us to follow-up with them at home. Lastly, we were not able to establish the prevalence of stage 1 and 2 CKD (we did not quantify albuminuria), preventing us from comparing early stage CKD in this population to existing literature.

In conclusion, CKD prevalence was high among the brick workers in La Paz Centro, Nicaragua and comparable to estimates reported in other regional studies of agricultural workers. These results provide further evidence that the CKD epidemic in Central America known as Mesoamerican Nephropathy is not limited to sugarcane or agricultural workers. In addition, CKD risk within the brickmaking industry was substantially higher among oven workers, who also experience the greatest heat exposure. Our results are consistent with the hypotheses that occupational heat exposure and socioeconomic conditions may be contributing factors to MeN.

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Chronic Kidney Disease (CKD)

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Table 4. Multivariable Logistic Regression of CKD

Statistically significant at alpha=0.05

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Table 1. Characteristics of study population at baseline (n=224)

Age	**N**	**%**
18-24 years	62	27.7
25-34 years	61	27.2
35-44 years	59	26.3
45-60 years	42	18.8
Sex		
Male	192	85.7
Female	32	14.3
Education		
None	60	26.8
Primary	106	47.3
Secondary or university	58	25.9
Smoker		
Current	106	47.3
Former	18	8.0
Never	100	44.7
Alcohol*		
Non-drinker	84	37.5
Moderate (1-14 drinks/week)	105	46.9
Excessive (≥ 15 drinks/week)	35	15.6
Immediate family with CKD		
No	154	68.8
Yes	70	31.2
Years worked in brickmaking industry		
1-5	54	24.1
6-10	60	26.8
11-19	52	23.2
20-47	58	25.9
Job category based on baseline and follow-up visit (n=224)		
Oven work at both visits	34	15.2
Oven work at one visit	86	38.4
Oven work at neither visit	104	47.4
Proteinuria at Baseline		
Urine Protein ≥2+	9	4.0
Negative	215	96.0
Hyperuricemia at Baseline		
Uric acid ≥7 mg/dL (all men)	25	11.2
Uric acid < 7 mg/dL	199	88.8
Body Mass Index (BMI)		
Underweight (<18.5)	9	4.0
Normal (BMI 18.5 – 24.9)	141	63.0
Overweight (BMI 25 – 29.9)	52	23.2
Obese (BMI ≥ 30)	22	9.8
Self-reported Hypertension		
Ever	33	14.7
Never	191	85.3
Self-reported Diabetes		
Ever	6	2.7
Never	218	97.3
Water consumed yesterday		
<3 liters	65	29.0
3-6 liters	119	53.1
>6 liters	40	17.9
Current hours per week worked		

≤ 48 hours	156	69.6
>48 hours	68	30.4

Table 2. Prevalence of CKD by sex, age group and immediate family with previous diagnosis among brick workers in La Paz Centro (n=224)

	# of participants diagnosed with CKD	n	Prevalence of CKD (%)
CKD (all stages, 3-5) (eGFR < 60 ml/min/1.73m^2 at both visits)	27	224	12.1
CKD (by stage)			
Stage 3A: Mild to moderate (45 ≤ eGFR < 60 ml/min/1.73m^2)	3	224	1.3
Stage 3B: Moderate to severe (30 ≤ eGFR < 45 ml/min/1.73m^2)	8	224	3.6
Stage 4: Severe (15 ≤ eGFR < 30 ml/min/1.73m^2)	8	224	3.6
Stage 5: Kidney failure (eGFR < 15 ml/min/1.73m^2)	8	224	3.6
Sex			
Male	27	192	14.1
Female	0	32	0.0
Age at follow-up			
18-24	1	60	1.7
25-34	5	62	8.1
35-44	10	60	16.7
45-61	11	42	26.2
Immediate Family Member with CKD			
Yes	13	70	18.6
No	14	154	9.09
Self-reported Hypertension			
Ever	7	33	21.2
Never	20	191	10.5
Self-reported Diabetes			
Ever	1	6	16.7
Never	26	218	11.9

Table 3. Linear regression models of eGFR (n=224)

Variable	eGFR (mL/min/1.73m²)					
	Mean difference	**(95% CI)**	**P-value**	**Coefficient from time interaction**	**(95% CI)**	**P-value**
Age	**-0.95**	**(-1.42, -0.47)**	**0.0001**	0.07	(-0.27, 0.41)	0.7
Sex (Male vrs Female)	-5.24	(-17.02, 6.54)	0.4	-2.22	(-10.88, 6.45)	0.6
*Body Mass Index (*BMI ≥ 30 vrs BMI <30)	-2.28	(-12.85, 8.29)	0.7	-0.77	(-9.38, 7.85)	0.9
Education (Reference category: Secondary/University)						
None	**-14.17**	**(-24.30, -4.05)**	**0.006**	-1.98	(-9.29, 5.32)	0.6
Primary	-3.9	(-12.50, 4.69)	0.2	-5.7	(-11.88, 0.47)	0.07
Immediate family member with CKD (Yes vrs No)	**-7.66**	**(-15.17, -0.32)**	**0.05**	-1.64	(-7.14, 3.86)	0.6
Study visit (Reference category: Round 1)						
Round 2 (follow-up)	3.91	(-11.07, 18.88)	0.6			
Job (Reference category: No oven work)						
Oven work at both visits	**-15.52**	**(-26.02, -5.01)**	**0.004**	7.1	(-0.59, 14.79)	0.07
Oven work at one visit	0.54	(-7.02, 8.10)	0.9	3.82	(-1.69, 9.32)	0.2
Years worked in brickmaking industry	-0.41	(-0.90, 0.08)	0.1	0.15	(-0.20, 0.50)	0.4
Hours worked per week (Greater than 48 vrs *48 or less)*	3.47	(-1.70, 8.64)	0.2	**-7.65**	**(-15.00, -0.30)**	**0.04**
Water intake yesterday (Reference category: >6 liters)						
<3 liters	**7.74**	**(0.49, 14.99)**	**0.04**	**-11.28**	**(-21.06, -1.51)**	**0.02**
3-6 liters	6.29	(-0.07, 12.65)	0.05	**-11.55**	**(-20.61, -2.50)**	**0.01**
Ever hypertension (Yes vs No)	-7.29	(-17.54, 2.97)	0.2	-3.59	(-11.02, 3.84)	0.3
Ever diabetes (Yes vrs No))	5.07	(-16.84, 26.98)	0.6	-3.67	(-19.52, 12.18)	0.6
Alcohol (Reference category: Non-drinker)						
Excess	-4.84	(-16.49, 6.81)	0.4	1.53	(-6.87, 9.93)	0.7
Moderate	-8.08	(-16.81, 0.64)	0.07	2.58	(-3.71, 8.87)	0.4
Smoking status (Reference category: Never)						
Current	-2.37	(-10.44, 5.71)	0.6	2.92	(-2.92, 8.77)	0.3
Former	-3.81	(-17.66, 10.04)	0.6	3.56	(-6.46, 13.59)	0.5

Table 4. Multivariable Logistic Regression of CKD (n=224)

Variable	**Chronic Kidney Disease (CKD)**		
	Odds Ratio	**(95% CI)**	**P-value**
Age	**1.06**	**(1.02, 1.11)**	**0.006**
Education *(Reference category: Secondary/University)*			
None	**8.00**	**(1.57, 40.75)**	**0.002**
Primary	1.90	(0.37, 9.81)	0.5
Immediate family member with CKD *(Yes vrs No)*	2.20	(0.88, 5.53)	0.09
Job *(Reference category: No oven work)*			
Oven work at both visits	**5.47**	**(1.40, 21.34)**	**0.02**
Oven work at one visit	1.30	(0.47, 3.63)	0.2
Alcohol *(Reference category: Non-drinker)*			
Excess	4.70	(1.15, 19.23)	0.08
Moderate	2.84	(0.90, 8.95)	0.6