

The Burden of Chronic Kidney Disease among the Zuni Indians: The Zuni Kidney Project

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The Zuni Indians of New Mexico are experiencing an epidemic of chronic kidney disease (CKD). The Zuni Pueblo created the Zuni Kidney Project (ZKP) to decrease the burden of CKD in the community. The aim of this study was to estimate the prevalence of CKD among Zuni Indians using National Kidney Foundation Kidney Disease Outcomes Quality Initiative criteria. The ZKP conducted a population-based, cross-sectional survey to estimate the prevalence of CKD and related risk factors among Zuni Indians aged ≥ 20 yr ($n = 1113$). GFR was estimated using equations based on serum creatinine, and urine albumin:creatinine ratio was calculated in a single spot urine sample. ESRD counts were obtained from health care providers. The age- and sex-adjusted prevalence of CKD among the Zuni Indians was >2.5 -fold higher than that among the US composite population. The estimated prevalence of CKD stages 1 and 2 combined was three- to four-fold higher than that of CKD stages 3 and 4 combined. This ratio was significantly higher than that in the US composite population (1.4-fold). The prevalence of CKD stage 5 was eight-fold higher among the Zuni Indians than among the composite US population. The Zuni Indians have an expanded pool of CKD that contributes to the high burden of ESRD. The high prevalence of CKD stages 1 and 2 provides a unique opportunity to develop innovative treatment programs to reduce the burden of CKD in Zuni Pueblo.

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The current epidemic of chronic kidney disease (CKD) among American Indians is characterized by high rates of albuminuria and ESRD (1–3). The age- and gender-adjusted prevalence of ESRD among American Indians (2594 per million population) is second only to that among black individuals (4618 per million population) (4).

The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF K/DOQI) has established guidelines to define five stages of CKD (5). The prevalence and distribution of CKD stages in the US population has been described using the Third National Health and Nutrition Examination Survey (NHANES III) population, a representative sample of noninstitutionalized US adults (6,7). Because of the small number of American Indians who participated in NHANES III, only limited data are available on the prevalence of CKD stages among this high-risk group (7).

The Zuni Indians of New Mexico are experiencing an epidemic of renal disease (8,9). In response to this epidemic, the Zuni Pueblo established the Zuni Kidney Project (ZKP) in collaboration with the University of New Mexico Health Sciences Center (UNMHSC), Southwest Foundation for Biomedical

Research, Indian Health Service (IHS) and Dialysis Clinic Inc. The ZKP was funded by the National Institute of Diabetes and Digestive and Kidney Diseases and by Dialysis Clinic Inc. The ZKP conducted a population-based, cross-sectional survey of the Zuni Pueblo to estimate the prevalence of kidney disease and related risk factors (10). This survey reported high prevalence estimates for albuminuria and hematuria among Zuni Indians with and without diabetes (11,12).

This study was conducted to estimate the prevalence of CKD among the Zuni Indians using K/DOQI criteria (5). To accomplish this, we estimated GFR using equations based on serum creatinine among ZKP survey participants (10). We also estimated the prevalence of albuminuria among survey participants with normal and decreased renal excretory function.

Materials and Methods

Study Population

The Zuni Indians are an American Indian tribe who live in a rural portion of western New Mexico. Rates of emigration and immigration among the Zuni are low. The Zuni Indians raise maize and wheat and engage in sheep herding and jewelry making. Traditional Zuni life is oriented around a matrilineal clan system and a ceremonial system based on a belief in the "ancient ones." In 2000, the Zuni Tribe had approximately 10,000 tribal members, 85% of whom live in the Pueblo (13) and receive their health care through IHS. The median age of the population was 26 yr (13).

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Population Sample

Between January 1999 and April 2002, we recruited 1664 participants in the ZKP population-based, cross-sectional survey (10). The sample was representative of the Zuni Indians, as for age, gender, and education (10–12,14). Participants who were non-Zuni Indians ($n = 54$), aged <20 yr ($n = 483$), or missing variables that are required to estimate GFR ($n = 14$) were excluded from this analyses. Therefore, this study was restricted to 1113 participants, who accounted for 17.9% of the Zuni Indians aged ≥ 20 yr.

Data Collection

We collected data from the following sources: (1) ZKP population-based, cross-sectional survey, which has been previously described ($n = 1664$) (10); (2) Zuni Dialysis Unit, which provided de-identified information on Zuni ESRD patients maintained on hemodialysis ($n = 83$) or peritoneal dialysis ($n = 6$); and (3) UNMHSC Transplant Services, which provided de-identified information on Zuni patients who received renal transplantation ($n = 9$). The study was approved by the Human Research Review Committee of the UNMHSC, the Zuni Tribal Council, and the institutional review board of the IHS. Participants were asked to sign an informed consent before entering the study.

Laboratory Methods

Creatinine in serum and urine and serum glucose were measured by colorimetric methods (15). During a 28-mo period, the median coefficients of variation of the serum creatinine standards were 3.6% (interquartile range [IQR] 2.2) for creatinine values in the normal range (approximately 1.0 mg/dl; $n = 3146$ measurements) and 1.4% (IQR 0.4) for values in the high range (approximately 5.8 mg/dl; $n = 3200$ measurements). Glycosylated hemoglobin (HbA_{1c}) was measured by latex immunoagglutination inhibition. Urine albumin was measured in spot urine samples by rate nephelometry and expressed as urine albumin to creatinine ratio (UACR) (16,17).

Estimation of GFR

No specific prediction equation is available to estimate GFR among American Indians. Therefore, we estimated GFR using two serum creatinine–based equations: (1) MDRD-C (18): Estimated GFR (eGFR; ml/min per 1.73 m²) = $186.3 \times [\text{serum creatinine (mg/dl)}]^{-1.154} \times \text{age (years)}^{-0.203} \times (0.742 \text{ if female})$; and (2) MDRD-AI: eGFR (ml/min per 1.73 m²) = $186.3 \times [\text{serum creatinine (mg/dl)}]^{-1.154} \times \text{age (years)}^{-0.203} \times (0.742 \text{ if female}) \times 1.106$.

The MDRD-C equation is the four-variable equation developed by the Modification of Diet in Renal Disease (MDRD) Study for white individuals (18). The MDRD-AI equation is the four-variable MDRD equation modified for American Indians. The rationale for this modified equation is based on studies that were conducted by Nelson *et al.* (19) among the Pima Indians. These investigators compared GFR as measured by iothalamate clearance (iGFR) with GFR estimates that were obtained with the four-variable MDRD equation with and without the black term. The measured GFR were intermediate between the estimates that were obtained with and without the term for black race. Specifically, eGFR as estimated using the MDRD formula without the black term underestimated iGFR by a median of 11%, and the equation with the black term overestimated iGFR by a median of 8%. Therefore, we used a multiplicative term of 1.106 that is halfway between the MDRD term for white race (1.0) and that for black race (1.212).

Classification of Participants

CKD was defined according to the NKF K/DOQI guidelines as (1) presence of markers of kidney damage in urine or blood or (2) eGFR

<60 ml/min per 1.73 m² (5). CKD stages were defined according to NKF K/DOQI guidelines: Stage 1, kidney damage with normal or increased GFR (≥ 90 ml/min per 1.73 m²); stage 2, kidney damage with mildly decreased GFR (60 to 89 ml/min per 1.73 m²); stage 3, moderately decreased GFR (30 to 59 ml/min per 1.73 m²); stage 4, severely decreased GFR (15 to 29 ml/min per 1.73 m²); and stage 5, kidney failure (GFR <15 ml/min per 1.73 m² or renal replacement therapy) (5).

Albuminuria was classified according to the American Diabetes Association recommendations (normal: UACR <0.03; microalbuminuria: $0.03 \leq \text{UACR} < 0.3$; macroalbuminuria: UACR ≥ 0.3) (20). Because of its cross-sectional design, results from the ZKP survey did not allow us to determine whether the microalbuminuria was persistent. To estimate the persistence of microalbuminuria over time, we examined agreement in UACR findings in a subset of survey participants ($n = 228$) who were enrolled in a subsequent ZKP case-control study. A second urine sample was collected after a median period of 130 d (25th percentile 84 d; 75th percentile 287 d). Among participants who had microalbuminuria during the initial survey, the proportion with micro- or macroalbuminuria at follow-up was 68% (95% confidence interval [CI] 55.4 to 78.2). We then used a 0.68 factor to compute the prevalence of persistent microalbuminuria among participants who had an eGFR ≥ 60 ml/min per 1.73 m² (6).

Participants were classified as having diabetes when they had a history of diabetes (excluding gestational diabetes), random glucose ≥ 200 mg/dl, or HbA_{1c} >7.0% (20,21). Among the Pima Indians without a previous diagnosis of diabetes, the probability of having diabetes was 50% for individuals with HbA_{1c} of 6.0 to 6.9% and 98% for individuals with HbA_{1c} of 7.0 to 7.9% (22). Therefore, we classified participants with HbA_{1c} between 6.0 and 7.0%, a random glucose <200 mg/dl, and no history of diabetes as having an indeterminate diabetes status.

Data Quality

Participants with an implausibly high eGFR (eGFR >200 ml/min per 1.73 m²; $n = 1$) were assigned a maximum value of 200 ml/min per 1.73 m² (6). Participants with eGFR <15 ml/min per 1.73 m² ($n = 2$ by MDRD-C equation; $n = 1$ by MDRD-AI equation) were likely not to be in steady state with regard to serum creatinine and were not included in eGFR distributions. When prevalence of decreased eGFR was stratified by diabetes, we excluded 24 participants who were missing diabetes status and 67 participants with indeterminate diabetes status. When we estimated the prevalence of CKD, we excluded participants who did not have a UACR determination ($n = 17$).

Statistical Analyses

Prevalence estimates of decreased eGFR and CKD were expressed as percentages with 95% CI. Estimates of the variances and covariances were first obtained using Taylor series linearization to adjust for dependencies that were created by sampling within families. Because these results were very similar to those without adjustment for the sampling design and some proportions were very small, exact binomial proportions were used instead. When appropriate, estimated prevalence of decreased eGFR and CKD were age-adjusted (4-yr intervals) using the 2000 Zuni Tribal Census, with variance estimates adjusted by the finite population correction factor because >10% of the eligible population was enrolled in the survey (13). Estimated prevalence of decreased eGFR and CKD were also adjusted to the 2000 US census to allow comparison with NHANES III data (6,23). Statistical analyses were carried out in SAS (SAS Institute, Cary, NC) and SUDAAN (RTI, Research Triangle Park, NC) to account for the complex study design. The level of statistical significance was $P < 0.05$.

Table 1. Demographic and clinical characteristics of study participants

Characteristic	Female (n [%]) (n = 616)	Male (n [%]) (n = 497)	Total (N = 1113)
Age (yr)			
20 to 39	339 (55.0)	331 (66.6)	670 (60.2)
40 to 59	209 (33.9)	123 (24.8)	332 (29.8)
≥60	68 (11.0)	43 (8.6)	111 (10.0)
Diagnosis of diabetes ^a			
yes	164 (26.9)	75 (15.7)	239 (22.0)
indeterminate	38 (6.2)	29 (6.0)	67 (6.2)
no	408 (66.9)	375 (78.3)	783 (71.9)

^aYes = participants with history of diabetes, random glucose ≥200 mg/dl, or glycosylated hemoglobin (HbA_{1c}) > 7.0%; indeterminate = participants with no history of diabetes, random glucose <200 mg/dl, and HbA_{1c} between 6.0 and 7.0%; no = participants with no history of diabetes, HbA_{1c} <6.0%, random glucose <200 mg/dl.

Results

Demographic Characteristics of ZKP Survey Participants

The demographic characteristics of ZKP survey participants are shown (Table 1). Female participants (median age 38 yr; IQR 22 yr) were older than male (median age 35 yr; IQR 16 yr) participants (*P* < 0.002). As we previously reported, prevalence of diabetes was higher among female (27.9%; 95% CI 23.6 to 30.6) than male (15.7%; 95% CI 12.4 to 18.9) participants (*P* < 0.001) (11,14).

Distribution of Serum Creatinine Concentrations

The distributions of serum creatinine concentrations among female and male survey participants are shown (Figure 1). Serum creatinine was slightly skewed toward higher values among both female and male participants. The median serum creatinine concentration was lower among female (0.8 mg/dl; IQR 0.2 mg/dl) versus male (0.9 mg/dl; IQR 0.1 mg/dl) participants (*P* < 0.001).

Distribution of eGFR

The distributions of eGFR that were obtained from the MDRD-C and MDRD-AI estimating equations are shown in Figure 2. Regardless of the prediction equation used, eGFR was slightly skewed toward higher values. Because of the multipli-

cative correction factor of 1.106 incorporated in the MDRD-AI equation, the eGFR values that were obtained using the MDRD-C equation were lower compared with those that were obtained by MDRD-AI equation (median eGFR difference -9.5 ml/min per 1.73 m² [IQR 3.1] for female and -10.2 ml/min per 1.73 m² [IQR 2.4] for male participants).

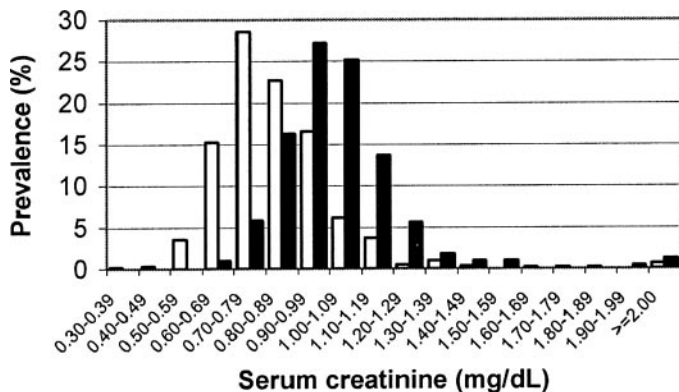


Figure 1. Distribution of serum creatinine among female (□) and male (■) survey participants.

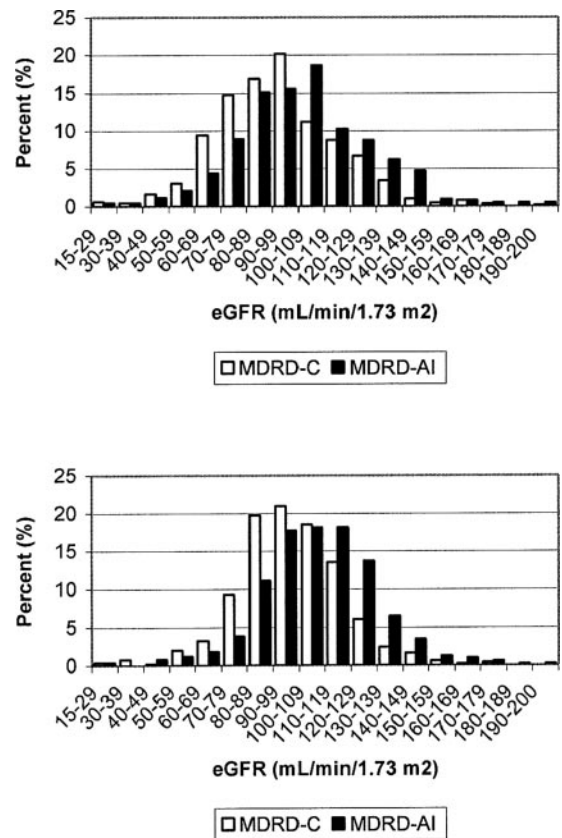


Figure 2. Distribution of GFR estimated using the Modification of Diet in Renal Disease equation for white individuals (MDRD-C; □) and MDRD equation for American Indians (MDRD-AI; ■) among female (top) and male (bottom) participants. eGFR, estimated GFR; MDRD-C, no correction factor; MDRD-AI, correction factor = 1.106.

Prevalence of Decreased eGFR

The prevalence of decreased eGFR that was obtained using the MDRD-C and MDRD-AI equations, stratified by gender and age (Table 2) and by gender and diabetes status (Table 3), are shown. Regardless of the prediction equation used to estimate GFR, the prevalence of decreased eGFR increased with age. The proportion of study participants with diabetes increased with advancing stages of CKD.

Prevalence of CKD

The prevalence estimates for CKD stages 1 through 5 are shown in Table 4. The prevalence of CKD stages 1 and 2 combined (eGFR ≥ 60 ml/min per 1.73 m² and persistent microalbuminuria or overt proteinuria) was 15.7% using the MDRD-C equation and 16.4% using the MDRD-AI equation. The prevalence of CKD stages 3 and 4 combined (eGFR 15 to 59 ml/min per 1.73 m²) was 5.4 and 3.8% using the MDRD-C and the MDRD-AI equation, respectively. The overall prevalence of CKD (all stages combined) was similar regardless of the equation used. The proportion of participants who were classified as having CKD on the basis of decreased eGFR alone (eGFR < 60 ml/min with normal albuminuria) was 3.9% (95% CI 1.3 to 8.9) among participants with diabetes and 7.6% (95% CI 3.8 to 13.1) among participants without diabetes.

Prevalence of ESRD

Prevalence estimates of CKD stage 5 (patients on hemodialysis or peritoneal dialysis, transplant recipients, and participants with eGFR < 15 ml/min per 1.73 m²) are shown in Table 5. Among Zuni Indians who were aged ≥ 20 yr, the age-adjusted prevalence of ESRD was 13.0- and 12.7-fold higher than that of female and male individuals in the composite US population, respectively.

Discussion

This study demonstrates that the age- and gender-adjusted prevalence of CKD among the Zuni Indians is > 2.5 -fold higher than that among the US composite population (6). Surprising, among the Zuni Indians, the estimated prevalence of CKD stages 1 and 2 combined was three- to four-fold higher than that of CKD stages 3 and 4 combined, whereas among the US composite population, this ratio is 1.4-fold (6). However, the prevalence of CKD stage 5 was significantly higher among the Zuni Indians compared with that among the composite US population (6). The absence of an expanded pool of CKD stages 3 and 4 in a population with a high prevalence of ESRD is in concert with the findings among black individuals in NHANES III (6).

Several possible factors may have contributed to these findings. First, high levels of anxiety and poor functional status among patients with CKD stages 3 and 4 may have led to significant selection bias with underrepresentation of these CKD groups (10,11,14). Furthermore, as postulated by Coresh *et al.* (6), anxiety and illness may also lead to nonparticipation and underrepresentation of patients with CKD stage 5. However, we minimized this risk by estimating the prevalence of ESRD from the records of the Zuni Dialysis Unit and the UNMHSC

Table 2.

Prevalence of decreased eGFR estimated using the MDRD-C or MDRD-AI equations, stratified by gender and age^a

Age (yr)	eGFR Category (% [95% CI])												
	60 to 89 ml/min per 1.73 m ²				30 to 59 ml/min per 1.73 m ²				15 to 29 ml/min per 1.73 m ²				
	Female		Male		Female		Male		Female		Male		
MDRD-C													
20 to 39	339	331	36.9 (31.7 to 42.2)	27.2 (22.5 to 32.3)	1.8 (0.6 to 3.8)	0.3 (0.0 to 1.7)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)
40 to 59	209	122	46.4 (39.5 to 53.4)	40.2 (31.4 to 49.4)	2.4 (0.8 to 5.5)	5.7 (2.3 to 11.5)	0.5 (0.0 to 2.6)	0.5 (0.0 to 2.6)	0.5 (0.0 to 2.6)	0.5 (0.0 to 2.6)	0.5 (0.0 to 2.6)	0.5 (0.0 to 2.6)	0.5 (0.0 to 2.6)
≥ 60	67	43	46.3 (34.0 to 58.9)	48.8 (33.3 to 64.5)	31.3 (20.6 to 43.8)	16.3 (6.8 to 30.7)	4.5 (0.9 to 12.5)	4.5 (0.9 to 12.5)	4.5 (0.9 to 12.5)	4.5 (0.9 to 12.5)	4.5 (0.9 to 12.5)	4.5 (0.9 to 12.5)	4.5 (0.9 to 12.5)
All ^b	615	496	41.5 (37.7 to 45.4)	33.0 (28.7 to 37.3)	5.9 (3.9 to 7.9)	3.7 (1.8 to 5.6)	0.5 (0.0 to 1.0)	0.5 (0.0 to 1.0)	0.5 (0.0 to 1.0)	0.5 (0.0 to 1.0)	0.5 (0.0 to 1.0)	0.5 (0.0 to 1.0)	0.5 (0.0 to 1.0)
All ^c	615	496	41.9 (37.3 to 46.5)	36.1 (30.9 to 41.2)	11.7 (7.1 to 16.3)	5.9 (2.9 to 8.9)	1.0 (0.0 to 1.9)	1.0 (0.0 to 1.9)	1.0 (0.0 to 1.9)	1.0 (0.0 to 1.9)	1.0 (0.0 to 1.9)	1.0 (0.0 to 1.9)	1.0 (0.0 to 1.9)
MDRD-AI													
20 to 39	339	331	20.1 (15.9 to 24.7)	12.7 (9.3 to 16.8)	0.9 (0.0 to 2.6)	0.3 (0.0 to 1.7)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)	0.0 (0.0 to 1.1)
40 to 59	209	122	37.3 (30.8 to 44.3)	18.0 (11.7 to 26.0)	1.9 (0.6 to 4.8)	4.1 (1.3 to 9.3)	0.0 (0.0 to 1.8)	0.0 (0.0 to 1.8)	0.0 (0.0 to 1.8)	0.0 (0.0 to 1.8)	0.0 (0.0 to 1.8)	0.0 (0.0 to 1.8)	0.0 (0.0 to 1.8)
≥ 60	68	43	42.6 (30.7 to 55.2)	44.2 (29.1 to 60.3)	23.5 (14.1 to 35.4)	9.3 (2.6 to 22.1)	4.4 (0.9 to 12.4)	4.4 (0.9 to 12.4)	4.4 (0.9 to 12.4)	4.4 (0.9 to 12.4)	4.4 (0.9 to 12.4)	4.4 (0.9 to 12.4)	4.4 (0.9 to 12.4)
All ^b	616	496	28.8 (25.2 to 32.4)	17.6 (14.1 to 21.1)	3.9 (2.3 to 5.6)	2.6 (1.0 to 4.2)	0.6 (0.0 to 1.2)	0.6 (0.0 to 1.2)	0.6 (0.0 to 1.2)	0.6 (0.0 to 1.2)	0.6 (0.0 to 1.2)	0.6 (0.0 to 1.2)	0.6 (0.0 to 1.2)
All ^c	616	496	32.3 (27.8 to 36.8)	21.3 (16.6 to 26.0)	7.5 (4.0 to 11.1)	4.2 (1.5 to 6.8)	1.4 (0.0 to 3.2)	1.4 (0.0 to 3.2)	1.4 (0.0 to 3.2)	1.4 (0.0 to 3.2)	1.4 (0.0 to 3.2)	1.4 (0.0 to 3.2)	1.4 (0.0 to 3.2)

^aMDRD-C, Modification of Diet in Renal Disease equation, no correction factor; MDRD-AI, Modification of Diet in Renal Disease equation, correction factor = 1.106.

^bAdjusted to the 2000 Zuni Census (13).

^cAdjusted to the 2000 US Census (23).

Table 3. Prevalence of diabetes, stratified by gender and eGFR category^a

Parameter	eGFR Category (% [95% CI])											
	≥90 ml/min per 1.73 m ²		60 to 89 ml/min per 1.73 m ²		30 to 59 ml/min per 1.73 m ²		15 to 29 ml/min per 1.73 m ²					
	Female	Male	Female	Male	Female	Male	Female	Male				
MDRD-C diabetes indeterminate diabetes status	163	74	26.9 (22.2 to 32.1)	13.4 (9.8 to 17.7)	22.7 (17.7 to 28.4)	14.8 (9.6 to 21.4)	51.6 (33.1 to 69.9)	60.0 (32.3 to 83.7)	75.0 (19.4 to 99.4)	50.0 (1.3 to 98.7)	25.0 (0.0 to 80.6)	0.0 (0.0 to 84.2)
	38	29	4.6 (2.6 to 7.5)	5.6 (3.3 to 8.8)	8.0 (4.9 to 12.0)	7.8 (4.1 to 13.1)	2.4 (0.8 to 5.5)	5.7 (2.3 to 11.5)				
MDRD-AI diabetes indeterminate diabetes status	164	74	24.4 (20.3 to 28.8)	13.2 (10.0 to 17.0)	28.0 (21.5 to 35.3)	20.2 (12.0 to 30.8)	54.6 (32.2 to 75.6)	60.0 (26.2 to 87.8)	100.0 (29.2 to 100.0)	50.0 (1.3 to 98.7)	0.0 (0.0 to 29.2)	0.0 (0.0 to 84.2)
	38	29	8.0 (4.4 to 13.1)	10.1 (12.0 to 30.8)	8.0 (4.4 to 13.1)	10.1 (4.5 to 19.0)	13.6 (2.9 to 34.9)	0.0 (0.0 to 30.8)				

^aParticipants were classified as having diabetes when they had a history of diabetes, random glucose ≥200 mg/dl, or HbA_{1c} >7.0%; participants with HbA_{1c} between 6.0 and 7.0%, random glucose <200 mg/dl, and no history of diabetes were classified as having an indeterminate diabetes status.

Transplant Services, where virtually all Zuni Indians with ESRD receive their care. Second, kidney function of Zuni Indians with CKD stages 3 and 4 may deteriorate rapidly, so the duration of these stages is short and their prevalence is low. Among the Pima Indians with overt albuminuria, the mean rate of GFR loss was three-fold higher than that reported among MDRD participants (24,25). Therefore, because disease progression is faster among patients with diabetic *versus* nondiabetic CKD, it is likely that, overall, the Zuni Indians have a faster progression because of the high prevalence of diabetic kidney disease (26). Third, the mortality rate among Zuni Indians with CKD stages 3 and 4 may be high, resulting in a lower prevalence of these CKD stages than expected. In fact, it is well established that CKD is associated with an excess risk for cardiovascular disease (CVD), even after adjustment for traditional CVD risk factors (27). Strong Heart Study investigators reported high rates of albuminuria and increased CVD mortality among American Indians (2,28). Fourth, the IHS, the Zuni Diabetes Program, and the ZKP all have increased the awareness of kidney disease; this may have led to better control of risk factors for progression of CKD (*e.g.*, blood glucose, arterial BP) and, potentially, to slow disease progression. Finally, it should be noted that American Indians with ESRD have improved survival compared with non-Hispanic white individuals; this may have contributed to the observed high prevalence of CKD stage 5 (4).

The decision to use the four-variable MDRD equation to assess eGFR was based on several cultural and logistic reasons. The use of radioactive tracers for research purposes is not culturally acceptable to the Zuni Indians. The remote setting of the Zuni Pueblo practically precludes the possibility to measure GFR with unlabeled iothalamate (29). Finally, serum cystatin C measurements were not widely available at the time the survey was conducted (30). We acknowledge that the MDRD equation has not been validated in the following settings: (1) Among American Indians, (2) in the full range of eGFR expected in a population, and (3) among individuals with diabetes. However, Nelson *et al.* (19) demonstrated that, among the Pima Indians, the four-variable MDRD equation adequately predicted GFR as measured by the clearance of unlabeled iothalamate. Because no validated formula is available to estimate eGFR among American Indians, the use of a modified MDRD equation is reasonable. Recently, Poggio *et al.* (31) demonstrated that the four-variable MDRD equation performs well among individuals with diabetes but underestimated by 9.0 ml/min per 1.73 m² the GFR as measured by iothalamate clearance in individuals with normal GFR. Furthermore, the lack of standardization of our creatinine assay to the MDRD laboratory assay may have led to errors in estimating GFR between -5.5 and -8.1 ml/min per 1.73 m², with larger errors at higher levels of eGFR (32). This may have resulted in underestimation of GFR in this study. However, because the majority of participants with eGFR between 60 and 69 ml/min per 1.73 m² had either persistent microalbuminuria or overt proteinuria, a bias in eGFR of 9.0 ml/min per 1.73 m² would only minimally affect the estimated prevalence of CKD. It should be noted that a small proportion of participants with CKD had only a decreased

Table 4. Prevalence of CKD stages 1 through 5 defined according to NKF K/DOQI guidelines (5)^a

eGFR (ml/min per 1.73 m ²)	n	Prevalence of eGFR Category (5)	CKD Stage	Prevalence of Albuminuria		Prevalence of CKD Based on Overt Albuminuria	Prevalence of CKD Based on Persistent Microalbuminuria	Prevalence of CKD
				Incipient	Overt			
MDRD-C								
≥90	633	56.0 (53.1 to 58.9)	1	19.6 (16.6 to 22.9)	3.2 (1.9 to 4.8)	1.8 (1.0 to 2.6)	7.7 (6.4 to 9.0)	9.5 (8.0 to 11.0)
60 to 89	410	37.0 (34.2 to 39.9)	2	15.4 (12.0 to 19.2)	5.4 (3.4 to 8.0)	2.4 (1.3 to 3.2)	4.0 (3.0 to 4.9)	6.2 (4.9 to 7.5)
30 to 59	47	4.8 (3.4 to 6.2)	3	32.6 (19.5 to 48.0)	32.6 (19.5 to 48.0)	—	—	4.8 (3.4 to 6.2)
15 to 29	6	0.6 (0.1 to 1.0)	4	0.0	83.3 (35.9 to 99.6)	—	—	0.6 (0.1 to 1.0)
<15 or ESRD	100	1.6 (1.4 to 1.9)	5	—	—	—	—	1.6 (1.4 to 1.9)
All ^b	1196	—	—	—	—	—	—	22.7 (20.2 to 25.2)
All ^c	1196	—	—	—	—	—	—	29.9 (25.9 to 33.8)
MDRD-AI								
≥90	804	71.4 (68.8 to 74.1)	1	18.5 (15.9 to 21.4)	3.4 (2.2 to 4.8)	2.5 (1.5 to 3.4)	9.3 (8.0 to 10.7)	11.8 (10.2 to 13.5)
60 to 89	255	23.5 (20.6 to 25.7)	2	17.2 (12.8 to 22.5)	6.7 (3.9 to 10.5)	1.8 (0.9 to 2.6)	2.8 (1.9 to 3.6)	4.6 (3.4 to 5.8)
30 to 59	33	3.3 (2.1 to 4.4)	3	28.1 (13.7 to 46.7)	43.8 (26.4 to 62.3)	—	—	3.2 (2.1 to 4.4)
15 to 29	5	0.6 (0.0 to 1.1)	4	0.0	100.0 (47.8 to 100.0)	—	—	0.6 (0.0 to 1.1)
<15 or ESRD	99	1.6 (1.3 to 1.8)	5	—	—	—	—	1.6 (1.3 to 1.8)
All ^b	1196	—	—	—	—	—	—	21.8 (19.4 to 24.2)
All ^c	1196	—	—	—	—	—	—	28.4 (24.6 to 32.2)

^aCKD, chronic kidney disease; NKF K/DOQI, National Kidney Foundation Kidney Disease Outcomes Quality Initiative.

^bAdjusted to the 2000 Zuni Census (13).

^cAdjusted to the 2000 US Census (23).

eGFR. In fact, the prevalence of CKD reported in this study, which is based on both UACR and eGFR, is similar to what we previously reported using albuminuria alone (11).

We acknowledge that a cross-sectional survey with a single spot urine sample cannot accurately assess the prevalence of persistent microalbuminuria. This limitation may have significantly decreased the precision of our estimated prevalence of CKD stage 1. However, when microalbuminuria was measured twice in a subset of survey participants, the persistence rate (68%) was similar to that reported by Coresh *et al.* (6) among a subset of the NHANES III population. Furthermore, we recently reported that among the Zuni Indians, there is an excellent agreement between the classification of albuminuria using one *versus* three spot urine samples (33).

We recognize that some Zuni Indians with glomerulonephritis may present with intermittent hematuria (8,9). However, we decided not to include hematuria as an indicator of CKD for the following reasons: (1) Using isolated hematuria as a marker for CKD may have significantly biased the precision of our prevalence estimates (12), (2) medical chart review often did not provide sufficient evidence to exclude a urologic cause for isolated hematuria, and (3) dipstick analysis is only semiquantitative and not specific.

We acknowledge that by not measuring fasting glucose we may have underestimated the proportion of participants with diabetes. However, this may not have had a major impact on the accuracy of our estimates. First, the prevalence of undiagnosed diabetes among the Zuni Indians is relatively low because of increased diabetes awareness (14). Second, most individuals with early diabetes were likely to be classified as undetermined diabetes status, allowing us to obtain conservative estimates among individuals with diabetes and individuals with normal glucose tolerance.

Conclusion

The expanded pool of CKD among the Zuni Indians has significant public health implications. Because the majority of the individuals with CKD are in stage 1 or 2, prevention and early treatment programs will likely succeed in reducing the burden of ESRD among the Zuni Indians. Our findings will support the efforts of this community to develop community-based screening and early implementation of primary and secondary prevention programs.

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Table 5. Prevalence of ESRD stratified by gender and age

Age (yr)	<i>n</i>		ESRD Prevalence (% [95% CI])	
	Female	Male	Female	Male
20 to 39	5	2	0.3 (0.1 to 0.7)	0.1 (0.0 to 0.4)
40 to 59	19	18	1.7 (1.0 to 2.6)	2.1 (1.2 to 3.3)
≥60	33	21	8.2 (5.7 to 11.2)	6.4 (4.0 to 9.7)
All ^a	57	41	1.7 (1.3 to 2.4)	1.4 (1.0 to 1.9)
All ^b	57	41	3.0 (2.2 to 3.8)	2.3 (1.6 to 3.0)

^aAdjusted to the 2000 Zuni Census (13).

^bAdjusted to the 2000 US Census (23).

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Disclosures

None.

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