

Prevalence of Chronic Kidney Disease and Survival among Aboriginal People

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ABSTRACT

Globally, it is known that the incidence of end-stage renal disease is higher among Aboriginals, but it is unknown whether this is due to an increased prevalence of chronic kidney disease or other unidentified factors. We studied 658,664 people of non-First Nations and 14,989 people of First Nations and found that the age- and sex-adjusted prevalence of chronic kidney disease was significantly higher among those of non-First Nations compared to those of First Nations (67.5 versus 59.5 per 1000 population; $P < 0.0001$). However, severe chronic kidney disease (estimated glomerular filtration rate <30 ml/min per 1.73 m²) was almost two-fold higher among people of First Nations ($P < 0.0001$). Cox proportional hazards models suggested that compared to people of non-First Nations, those of First Nations with chronic kidney disease had a 77% increased risk of death after adjusting for age, gender, diabetes and baseline eGFR. In conclusion, whether the higher incidence of end-stage renal disease among people of First Nations is due to suboptimal management of chronic kidney disease and its associated comorbidities, more rapid loss of kidney function, or other unidentified factors remains to be determined.

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Aboriginal people in North America and the Antipodes experience ESRD at rates two to four times higher than non-Aboriginal people.^{1–6} The burden of ESRD among Aboriginal people is believed to be influenced by the rising incidence of diabetes,^{7,8} with $>60\%$ of Aboriginal patients with ESRD developing kidney failure as a result of diabetes, a proportion three times higher than among non-Aboriginals.^{2,6} That Aboriginal people *without* diabetes are still two to three times as likely to develop ESRD compared with non-Aboriginal people suggests that other factors must account for these increased rates.⁹ An increase in the prevalence of severe chronic kidney disease (CKD) that progresses to ESRD requiring dialysis is one plausible and likely explanation; however, data from the United States suggest a lower prevalence of CKD

among minority populations, including black and Mexican American individuals compared with white individuals.¹⁰ To the best of our knowledge, the literature has not yet explored this paradox in detail; in particular, no studies have examined the prevalence of CKD among Aboriginal people specifically.

The use of outpatient laboratory data and serum

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creatinine measurements to estimate GFR allows a unique opportunity to identify individuals with CKD.^{11,12} The use of these data sources for defining and comparing the presence of measured CKD in two populations, however, assumes that the likelihood of renal function testing (*i.e.*, obtaining serum creatinine measurements) is similar for the groups being compared.

The purpose of this study was to use laboratory data from a defined geographic region to determine the presence of measured CKD for First Nations and non-First Nations people. As a first step, we sought to determine whether the likelihood of obtaining a serum creatinine measurement was similar for the two groups of interest. We then determined the prevalence of measured CKD among First Nations and non-First Nations and assessed whether there was an association between race and survival for individuals with CKD.

RESULTS

A total of 676,660 individuals had at least one outpatient serum creatinine measurement between July 1, 2003, and June 30, 2004. We excluded 129 (0.02%) individuals who had a serum creatinine <25 μmol/L, 2139 (0.3%) who were on long-term dialysis, and 739 (0.1%) who had a kidney transplant before their index date, for a final study population of 673,653. The majority of the population, 658,664 (97.8%), were non-First Nations people; 14,989 (2.2%) had First Nations status.

Likelihood and Frequency of Serum Creatinine Measurements

Overall, a greater proportion of non-First Nations (36.6%) compared with First Nations (32.3%) people had least one

outpatient serum creatinine measurement in the 1-yr period ($P < 0.001$); however, after adjustment for age and gender, this trend was reversed, with 40.4% of First Nations and 38.0% of non-First Nations people having had at least one serum creatinine measurement ($P < 0.001$). For both groups, the proportion who had a serum creatinine measured increased with age (χ^2 test for trend, $P < 0.001$ for First Nations and $P < 0.001$ for non-First Nations). Compared with non-First Nations, First Nations people had an increased likelihood of having a serum creatinine measurement across all age groups (Figure 1). The median number (interquartile range [IQR]) of outpatient serum creatinine measurements during the 1-yr period was 1 (IQR 1 to 2). Compared with non-First Nations, First Nations people with CKD had a similar frequency of serum creatinine measurements (median [IQR] 2 [1 to 3] versus 2 [1 to 4]; $P < 0.0001$).

Prevalence of Measured CKD and Participant Characteristics

The crude prevalence of measured CKD (per 1000 population) was significantly higher in non-First Nations compared with First Nations people (59.1 versus 25.5; $P < 0.0001$). After adjustment for age and gender, the prevalence of measured CKD (per 1000 population) was less disparate but remained significantly higher among the non-First Nations group (67.5 versus 59.5; $P < 0.0001$); however, when further stratified by stage of CKD, we found that the prevalence of more severe CKD was approximately two-fold higher among First Nations compared with non-First Nations people (Table 1). The crude prevalence of measured CKD increased with advancing age similarly for both First Nations and non-First Nations people (Figure 1, proportion measured and eGFR <60).

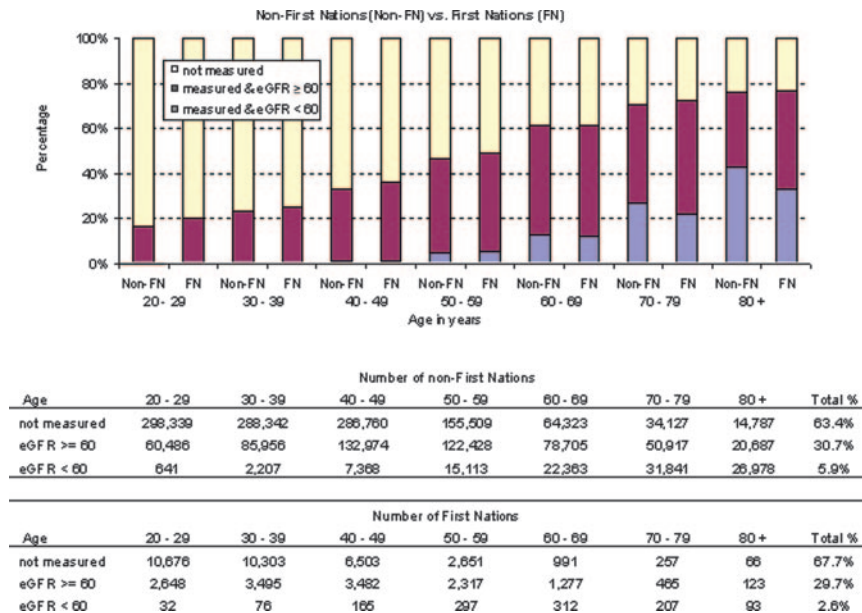


Figure 1. Proportion of population with at least one outpatient serum creatinine measurement and prevalence of CKD, by age and First Nations status.

Compared with non-First Nations people with CKD, First Nations people with CKD were significantly younger and more commonly lived in rural neighborhoods in the lowest household income quintile (Table 2). First Nations people were also more likely to have diabetes and more severe kidney dysfunction compared with non-First Nations people.

All-Cause Mortality

A total of 10,974 individuals died during the study period, for an overall mortality rate of 18.4 per 1000 person-years. The crude mortality rate was lower in First Nations (16.4 per 1000 person-years) compared with non-First Nations people (18.4 per 1000 person-years), and in unadjusted analyses, First Nations status was associated with a lower risk for all-cause mortality (hazard ratio [HR] 0.89; 95% confidence interval [CI] 0.81 to 0.97); however, given the difference in the age distribution between the two groups, after adjustment for age and gender, the mortality rates were consistently higher for First Nations compared with non-First Nations people across all levels of baseline kidney function (Table 3). After adjustment for age, gender, diabetes, and baseline eGFR, compared with non-First Nations people, First Nations people with CKD (eGFR <60 ml/min per 1.73 m²) had a 77% increased risk for death (HR 1.77; 95% CI 1.47 to 2.13). Results

were similar in a sensitivity analysis, which also adjusted for household income and rural location of residence.

DISCUSSION

Despite the higher incidence of ESRD among First Nations compared with non-First Nations people, somewhat surprising, we found that the prevalence of measured CKD (eGFR <60 ml/min per 1.73 m²) was lower in the First Nations population. The proportion of the First Nations population who had at least one outpatient serum creatinine measurement was higher than that of the non-First Nations population, suggesting that our finding of a lower prevalence of measured CKD is not due to a lower probability of having a serum creatinine measurement. Notably, though, First Nations people had a higher prevalence of more severe CKD (eGFR <30 ml/min per 1.73 m²) compared with non-First Nations people. With regard to survival, we found that the level of kidney function did not modify the association between race and survival, with consistently higher adjusted mortality rates for First Nations compared with non-First Nations people across all levels of baseline kidney function.

Explanations for these seemingly paradoxical findings of similar measured CKD prevalence yet higher ESRD incidence among First Nations people are comparable to those postulated for the observed growth in ESRD in general.^{13,14} First, the likelihood of accepting dialysis may be higher for First Nations people. Second, First Nations people may experience improved survival from competing causes, resulting in a greater proportion of First Nations people with CKD surviving to develop ESRD. Third, the First Nations population may have a higher risk profile at any given stage of CKD, such as diabetes, severe hypertension, and proteinuria, resulting in faster kidney function loss and an in-

Table 1. Age- and gender-standardized prevalence of measured CKD per 1000 population by First Nations status

eGFR Stage (ml/min per 1.73 m ²)	Non-First Nations per 1000 Population	First Nations per 1000 Population	P ^a
30 to 59	63.1	50.7	<0.0001
15 to 29	3.8	5.9	<0.0001
<15	0.6	2.9	<0.0001

^aχ² test.

Table 2. Baseline characteristics of individuals with CKD, by First Nations status

Characteristic	Non-First Nation (n = 106,511)	First Nations (n = 1182)	P ^a
Age (yr; median [IQR])	71 (60 to 80)	60 (50 to 70)	<0.0001
Female (%)	67,741 (63.6)	743 (63.0)	NS
eGFR (median [IQR])	52 (44 to 57)	50 (38 to 56)	<0.0001
eGFR stage (ml/min per 1.73 m ² ; %)			<0.0001
30 to 59	99,594 (93.5)	1014 (85.8)	
15 to 29	5907 (5.6)	105 (8.9)	
<15	1010 (1.0)	63 (5.4)	
Diabetes (%)	19,929 (18.7)	500 (42.3)	<0.0001
Household income level (%) ^b			<0.0001
first quintile (lowest)	20,613 (20.1)	566 (53.7)	
second quintile	20,948 (20.5)	198 (18.8)	
third quintile	21,231 (20.7)	143 (13.6)	
fourth quintile	18,931 (18.5)	73 (7.0)	
fifth quintile (highest)	20,634 (20.2)	74 (7.0)	
Rural residence (%)	14,208 (13.3)	550 (46.5)	<0.0001

^aRank-sum test was performed when comparing medians; χ² when comparing proportions.

^bSample size = 103,411.

Table 3. All-cause mortality by First Nations status and eGFR

eGFR (ml/min per 1.73 m ²)	Age- and Gender-Adjusted Mortality Rate per 1000 person-Years (95% CI)		HR (95% CI) ^a	HR (95% CI) ^b
	Non-First Nations	First Nations		
>90	13.9 (13.3 to 14.4)	24.0 (21.0 to 27.6)	1.68 (1.46 to 1.93)	1.48 (1.27 to 1.72)
60 to 89	4.4 (4.2 to 4.6)	8.3 (7.1 to 9.6)	1.75 (1.50 to 2.04)	1.53 (1.29 to 1.80)
30 to 59	7.5 (7.0 to 8.0)	11.5 (9.1 to 14.1)	1.58 (1.26 to 1.98)	1.32 (1.03 to 1.69)
<30	60.9 (53.7 to 69.2)	73.0 (52.5 to 101.5)	1.69 (1.22 to 2.33)	1.70 (1.21 to 2.37)

^aHR associated with First Nations status, adjusted for age, gender, and diabetes.

^bHR associated with First Nations status, adjusted for age, gender, diabetes, household income, and rural residence.

creased likelihood of developing ESRD. Fourth, First Nations people may have reduced access to therapies that slow the rate of kidney function loss. Finally, given that entry into the cohort required a serum creatinine measurement, we cannot exclude the possibility that “unmeasured” CKD was more prevalent among First Nations people. Difference in acceptance of dialysis treatments is possible, although it is unlikely to account for the magnitude of the difference in ESRD rates between First Nations and non-First Nations people. The increased mortality among First Nations compared with non-First Nations people with CKD reported in this study, as well as higher mortality rates in general,^{15,16} does not support improved survival as a possible explanation for our results. Also, the similar frequency of serum creatinine testing in the two populations makes “unmeasured” CKD less likely as an explanation; therefore, we speculate that differences in the underlying risk profile of the First Nations population, including more severe CKD, high-risk characteristics, and other factors including lack of access to proven therapies, may result in more rapid loss of kidney function among First Nations people and may explain their higher rates of ESRD requiring dialysis.

Similar to our study, data from the United States also suggest that black individuals have a lower prevalence of CKD yet higher rates of ESRD compared with white individuals.¹⁰ Social, personal, and environmental factors all have been identified as potentially contributing to more rapid progression of kidney dysfunction among black individuals, conceivably contributing to their higher rates of ESRD.¹⁷ Similar factors may be present in the Aboriginal population; in particular, decreased access to specialized medical care^{18,19} and insufficient or ineffective primary care^{20,21} may result in suboptimal use of therapeutic approaches that have been shown to slow the progression of kidney failure.^{22–26} Barriers in access to care for patients with CKD are not unique to the Aboriginal population; ethnic minorities with CKD in general are much less likely than white individuals to be referred to a nephrologist.²⁷ Although estimates of the prevalence of CKD in these groups are unknown, these ethnic groups have also been shown to have higher rates of ESRD,^{6,28,29} suggesting that management of CKD among ethnic minorities in general warrants further investigation.

This is the first study, to our knowledge, to estimate the prevalence of CKD using serum creatinine measurements among Aboriginal people; however, other studies have documented high rates of albuminuria among Aboriginal people both with and without diabetes compared with non-Aborigi-

nal people.^{30–32} Whether these increased rates of albuminuria are also associated with reduced eGFR, which may represent earlier stages (stages 1 and 2) of CKD, is not reported. The results of our study demonstrating a higher prevalence of more severe CKD suggest that not all of the earlier stages of CKD progress, or, if they do, they may not have adequate follow-up and testing of their kidney function.

A limited number of studies have reported the prevalence of measured CKD in the general population. Similar to our results in the non-First Nations population, a Canadian-based study also using a laboratory-based assessment reported a prevalence of measured CKD among the general population of 5.0%.¹¹ Results from the United States, based on the National Health and Nutrition Examination Survey (NHANES IV) have also reported similar CKD prevalence rates.¹⁰

The results of our study should be interpreted in context of the study limitations. First, by using outpatient serum creatinine measurements to identify our study cohort, we included a group of patients who had access to the health care system and had obtained a serum creatinine measurement, which may limit the generalizability. This may also result in a possible selection bias if the likelihood of having a serum creatinine measurement for patients with CKD varied by racial status. That the likelihood of obtaining renal function testing was similar for First Nations and non-First Nations people is reassuring. Our prevalence estimates of measured CKD for the non-First Nations population were similar to those reported in the United States using a population-based screening study,¹⁰ as well as a Canadian-based study using a similar laboratory-based assessment,¹¹ which also adds validity to our results; however, verification of these estimates of CKD among First Nations people would require a population-based screening study.

Second, we did not directly calibrate our serum creatinine measurements to the Cleveland Clinic, where the Modification of Diet in Renal Disease (MDRD) eGFR equation was derived, or validate the MDRD eGFR equation in a local population. We have, however, implemented a province-wide standardization of serum creatinine measurements that have been indirectly calibrated to the isotope dilution mass spectrometry reference standard using the new modified MDRD equation.³³ The similarity of our prevalence estimates to those reported in Ontario,¹¹ which also used a laboratory-based method of screening, as well as the United States¹⁰ supports the validity of our results. Lack of direct calibration would not have a differ-

ential impact on the prevalence rates for these two groups; therefore, comparison of CKD prevalence rates is valid given the common metric applied to both First Nations and non-First Nations people. Third, we were not able to identify Métis people and non-Registered First Nations people, which may result in misclassification of some Aboriginal patients with CKD in the non-First Nations group; however, given that the majority of the Aboriginal population in Alberta are Registered First Nations and given the size of the non-First Nations population, this potential misclassification would have minimal impact on the study results. Finally, we did not have an assessment of urine protein, which may be a potential confounder in determining the association between CKD and mortality, although we were able to adjust for presence of diabetes.

To the best of our knowledge, this study is the first to assess the burden of measured CKD among First Nations people and provides new insight into understanding kidney disease in this population. The results of our study suggest that the higher incidence rates of ESRD among the First Nations population is not simply explained by an increased prevalence of CKD. Rather, these higher rates of ESRD may be driven by more rapid progression of kidney dysfunction among individuals with more severe CKD, perhaps as a result of higher risk characteristics such as heavier proteinuria as well as genetic and environmental factors. In addition, lack of access to proven therapies may contribute to the rate of loss of kidney function and the development of ESRD. Studies confirming rates of progression of kidney function loss in this population, as well as predictors of rapid progression, are required and would have important implications for development of strategies to decrease ESRD rates in the First Nations population.

CONCISE METHODS

Study Population and Variable Definition

We used computerized laboratory data from six of the nine geographically defined Regional Health Authorities (geographic regions responsible for delivery of health services within their region) in the province of Alberta. These six Regional Health Authorities contained >80% of the 3,091,831 provincial residents in 2003. Eligible individuals were residents of Alberta who were aged ≥ 20 yr and had one or more outpatient serum creatinine measurements during a 1-yr period between July 1, 2003, and June 30, 2004. Individuals with a clinically implausible serum creatinine measurement ($< 25 \mu\text{mol/L}$) were excluded. Because we were interested in stable CKD and to avoid episodes of acute renal failure, we also excluded laboratory measurements associated with a hospital admission. The date of the first serum creatinine measurement was used to define the index date.

The cohort was linked to provincial administrative health data to identify First Nations status and health care use. First Nations status in the Alberta Health Care Insurance Plan Registry file is defined as any individual registered under the Federal Indian Act. The Registry file was searched from April 1, 1993, to March 31, 2005, and any individual with a First Nations indicator at any time point was classified as

“First Nations” with all others classified as “non-First Nations.” Aboriginal people in Alberta who were not registered within the Indian Act, such as unregistered First Nations and Métis, were included in the non-First Nations comparison group. According to the 2001 census, approximately 70% of the Alberta Aboriginal population is Registered First Nations.³⁴

Individuals with a kidney transplant before their index date, as determined from the Provincial Renal Program databases, were excluded. Using a previously developed algorithm,³⁵ we identified and excluded individuals who were on long-term dialysis before their index date, defined as a period of continuous dialysis treatment of at least 90 d (based on physician billing claims *International Classification of Diseases, Ninth Revision* codes 13.99A, 13.99B, 13.99C, 13.99D, and 13.99O). Individuals with diabetes were identified using a validated administrative data algorithm.³⁶ Socioeconomic status was estimated using the neighborhood income per person equivalent, which is an estimate of household income that is adjusted for the size of the household on the basis of data provided by the 2001 Canadian census.³⁷ Location of residence, based on community size, was also obtained from census data with rural location of residence defined as a community size of $< 10,000$. Finally, the cohort was linked to the Alberta Vital Statistics Death Registry to determine date of death (all-cause mortality) for individuals who died during the follow-up period ending December 31, 2005.

Measure of Kidney Function

We estimated GFR (eGFR) using the abbreviated MDRD prediction equation, which includes variables for age, gender, black race, and serum creatinine.³⁸ Although data on race were not available from the data sources, $< 1\%$ of the Alberta population is black; therefore, the impact at the population level of eliminating race from the equation was expected to be minimal. Preliminary studies have validated this equation in the Aboriginal population³⁹ and a community-based population without kidney disease.⁴⁰ Serum creatinine measurements from laboratories across the province were standardized to a single central laboratory, with a correction factor applied when necessary to ensure a province-wide standardization of values. As an indirect calibration, we also compared the eGFR estimates obtained based on this method with those from one of the largest laboratories in the province using an isotope dilution mass spectrometry reference standard and the new modified MDRD study equation,³³ with similar estimates obtained. The first serum creatinine measurement during the 1-yr accrual period (July 1, 2003, to June 30, 2004) was used to determine the eGFR. We categorized eGFR according to the Kidney Disease Outcomes Quality Initiative classification (≥ 90 , 60 to 89, 30 to 59, 15 to 29, and $< 15 \text{ ml/min per } 1.73 \text{ m}^2$).⁴¹ CKD was defined as an eGFR $< 60 \text{ ml/min per } 1.73 \text{ m}^2$.

Statistical Analyses

χ^2 and rank-sum tests were used to compare baseline characteristics for First Nations and non-First Nations people. To determine whether there was a difference in the likelihood of renal function testing, we initially calculated the crude as well as the age- and gender-standardized proportion of the First Nations and non-First Nations people who had at least one creatinine measurement between July 1,

2003, and June 30, 2004. The 2001 Canadian population and the direct method were used to obtain age- and gender-standardized estimates. Age- and gender-standardized prevalence rates of CKD stages, for First Nations and non-First Nations, were then calculated using the number of people with measured CKD as the numerator and the total population in the six Regional Health Authorities (as determined from provincial administrative data) as the denominator. We refer to these estimates as the prevalence of “measured” CKD, because they are based on individuals who had a serum creatinine measurement obtained. Poisson regression was used to calculate the age- and gender-adjusted mortality rates for First Nations and non-First Nations people, stratified by baseline eGFR, with individuals followed from their index date until December 31, 2005. Finally, the association between race and survival was assessed using Cox proportional hazards analyses, adjusting for age, gender, diabetes, and baseline eGFR. In a sensitivity analysis, we also adjusted for household income and rural location of residence, variables not included in the primary analysis because they may be considered a component of ethnicity and result in overadjustment.⁴² Assumptions for the Cox and Poisson regression models were tested and met. Analyses were conducted using Stata 9 (Stata Corp., College Station, TX) and SAS 9.1.3 (SAS Institute, Cary, NC). The study was approved by the institutional review board of the University of Calgary.

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DISCLOSURES

None.

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