Prevalence of chronic kidney disease and cardiovascular comorbidities in adults in 31 remote First Nations communities in Northwest Ontario.

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Introduction

Chronic kidney disease (CKD) is a precursor to end stage renal disease (ESRD) with its significant effects on mortality, quality of life of those affected, their families, and cost to Canada's universal health care system (1-3). Indigenous Canadians experience a high burden of CKD (4-6). Recent screening in Canadian First Nations communities suggest an adult estimate up to 30%.(4-7).

Comorbid cardiovascular conditions often accompany CKD. Diabetes, hypertension and dyslipidemia are more prevalent in Indigenous populations, contributing to cardiovascular disease (CVD) the leading cause of death in this population (8-13).

Complications from these comorbidities are also more common. First Nations Canadians are more likely to go on to ESRD and CKD-related mortality is 77% higher (14-17). Presence of diabetes, a major risk for progressive CKD, is high in Indigenous populations, occurs at a younger age and is associated with increased mortality, cardiovascular disease and lower limb amputations (18- 20).

Hypertension can both initiate and result from CKD, creating a vicious cycle of progressive kidney damage, particularly with coexisting diabetes and dyslipidemia (21, 22). The increased CVD risk experienced by CKD patients is reduced with lipid-lowering strategies.

In response to rising rates of ESRD and CKD, First Nations community chiefs in northwest Ontario requested a better understanding of the disease burden of CKD and related cardiovascular comorbidities. Knowing the prevalence of these conditions and clustering in individual patients is critical for effective management programs.

The purpose of this study is to document the prevalence of CKD and concurrent diabetes, hypertension, and dyslipidemia in a First Nations population in northwest Ontario.

Methods

This observational study used retrospective clinical data from a regional electronic medical record (EMR) system over a three-year period, May 2014 to May 2017. The database included all community residents accessing provincially-funded medical services.

The setting was Northwest Ontario, where 31 remote First Nations communities are supported in primary care by the Sioux Lookout First Nations Health Authority (SLFNHA) which oversaw the study.

Eligibility was confined to community members over 18 years. CKD was defined as estimated glomerular filtration rate (eGFR) < 60 ml/min per 1.73 m2 or urine albuminuria creatinine ratio (ACR) ≥3 mg/mmol.

Demographic and laboratory data included: age, gender, medications, eGFR, ACR, low density lipoprotein cholesterol (LDL-C) and glycated hemoglobin (A1C). The most recent laboratory value was used to determine CKD. Patients with hypertension were identified by their use of antihypertensive medications. Patients with diabetes were identified by two criteria: A1c ≥ 6.5% or the use of a diabetic medication. Patients with dyslipidemia were identified by elevated low density lipoprotein cholesterol (LDL-C ≥ 2.0 mmol/L) or the use of lipid lowering medication (23).

Electronic data collection followed Canadian Primary Care Sentinel Surveillance Network methods. (24) The age adjusted CKD prevalence was calculated using the adult population as denominator. Comorbid prevalence of DM, HTN and DYS with CKD were calculated using the adult CKD population as denominator. Data is presented as the mean and standard deviation for continuous variables and proportions for discreet variables.

Ownership, control, access and possession of the research data (OCAP) was maintained by SLFNHA (25). Ethics approval was granted by the Sioux Lookout Meno Ya Win Research Review and Ethics Committee (#16-15) and the Lakehead University Research Ethics Board (#161 15-61).

Results

There were 16,170 adults in this regional First Nations population of 24,787. Of these 5,224 (32.2%) patient records had an eGFR and/or ACR testing recorded in the EMR over the 3-year period. (Table 1)

Twenty eight percent of the adult population had at least one eGFR measurement (4,578/16,170) and 15% (2,462/16,170) at least one ACR with overlap between these two groups**.** Abnormal results occurred in 18% (806/4,578) of eGFR and 58% (1,433/2,462) of ACR tests. The resulting age-adjusted CKD prevalence in the adult population (1,859) was 14.7%, with a mean age of 55, fourteen years older than the average adult. Fifty-six percent (2,945/5,224) of those tested were female and they had an equivalent prevalence of CKD (54.4%; 1,021/1,859). (Table 1)

The age adjusted prevalence of advanced CKD (stage 3-5), with decreased renal function (eGFR <60), was 7.0% while albuminuria-related CKD (stage 1-2) was 7.7%. (Table 2)

Table 1. Demographics of total 18+ population, population with renal testing

	N (%)	F (%)	Age (SD)
Adult population (18+)	16,170	8,048 (50.0)	41 ± 16.9
Tested population	5,224 (32.3%)	2,945 (56.4)	50 ± 16.0

Table 2. Age-adjusted CKD prevalence

	Number	Age adjusted prevalence
Stage 1-2	1,053	7.7%
Stage 3-5 CKD	806	7.0%
TOTAL CKD	1,859	14.7%

CKD was diagnosed in 1,053 patients with albuminuria alone **(**stage 1,2). Patients with renal function decline (eGFR < 60 ml/min per 1.73m^2) included 592 stage 3 (30- 60), 149 stage 4 (15-30) and 65 stage 5 patients (<15). (Table 1)

Eighty percent of CKD patients had at least one cardiovascular comorbidity (diabetes, hypertension or dyslipidemia) and 39% had all three. Diabetes was most often co-prevalent (72%) followed by dyslipidemia (71%) and hypertension (59%). (Table 3, Figure 1)

Of the 58% of CKD patients with two cardiovascular comorbidities, 47% had diabetes and hypertension, 58% had diabetes and dyslipidemia, and 49% had hypertension and dyslipidemia. (Table 4).

Table 3. Characteristics of CKD population

Characteristic	*CKD Population, n= 1,859*
eGFR n, (%)	
not tested	*299 (16)*
≥60	*754 (41)*
30-59	*592 (32)*
15-29	*149 (8)*
<15	*65 (4)*
ACR n, (%)	
not tested	*357 (19)*
<3	*69 (4)*
3-300	*936 (50)*
>300	*497 (27)*
Comorbidities	
Diabetes, n (%)	*1,332 (72)*
Hypertension, n (%)	*1,098 (59)*
Dyslipidemia, n (%)	*1,313 (71)*
Average A1c	8.3
Average LDL	2.1
LDL <2.0	688 (37)
Statin Rx, n (%)	980 (53)
ACE-I/ARB Rx, n (%)*	619 (33)

**ACE-I/ARB: Angiotensin converting enzyme inhibitors/Angiotensin receptor blocker*

Table 4. Prevalence of multiple comorbidities in CKD population

Total CKD n, (%)	1859 (100)
CKD + 3 comorbidities DM, HTN, DYS	716 (39)
CKD + 2 comorbidities	1,078 (58)
DM, HTN	877 (47)
DM, DYS	1,069 (58)
HTN, DYS	852 (49)

DM = diabetes mellitus, HTN = hypertension, DYS = dyslipidemia

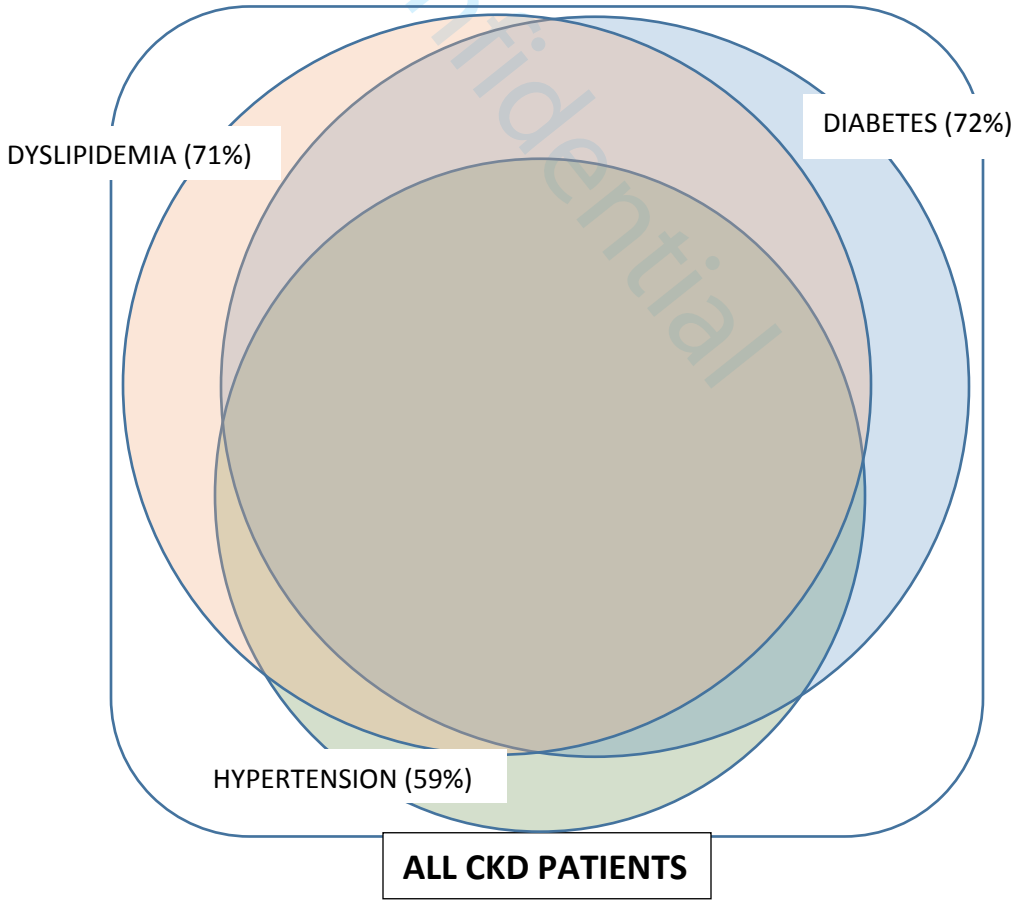

Figure 1. Comorbidities in CKD patients

Discussion

This is the first study assessing the prevalence of CKD and cardiovascular comorbidities in the First Nations population of northwest Ontario. At 14.7%, our age-adjusted prevalence of CKD is higher than the estimated Canadian prevalence of 12.5% (5) but lower than recent screening reported from other Canadian First Nations communities of 25% (6, 7). This is likely due to limited ACR testing. Fifteen percent of the population had ACR testing, which often detected (68%) CKD. Early stage CKD constitutes most cases detected in screening studies, without robust ACR testing, our study likely underestimates total CKD prevalence.

Testing with eGFR was more common (28%) with a lower yield of abnormal results (18%). Despite limited testing, our prevalence of advanced stage CKD of 7.0% is more than double that of the Canadian population (3.1%) and Manitoba First Nations (3.3%) and higher than southern Ontario First Nations (4.9%). (6, 7) Since patients with advanced CKD (eGFR<60) carry the highest risk for cardiovascular disease and progression to ESRD, these results are concerning. (26, 27)

Women constituted 56.4% of the tested population; CKD was detected in 55.4%, similar to estimates in the general Canadian population (5).

Diabetes

Since diabetes in highly prevalent in First Nations populations and the leading cause of end stage renal disease (ESRD), a high (72%) co-prevalence of CKD and DM is not surprising. (28-30) (Table 3) This is higher than Komenda's Manitoba screening study, where 60% of CKD patients also had diabetes (6). Gao's retrospective study of medical records of Alberta First Nations patients with advanced CKD (eGFR<60) also identified (42%) comorbid diabetes (14).

Dyslipidemia

In this CKD cohort, 71% had coexisting dyslipidemia. (Table 3) The co-prevalence of dyslipidemia in First Nations adults (without CKD) has been estimated at 32% (10, 11) The general Canadian population prevalence is estimated at 14-36% (31).

The 2016 CCS guidelines for the management of dyslipidemia now includes CKD as 'high risk' for cardiovascular disease, with an indication for statin therapy to lower the LDL-C to < 2 mmol/L, the benchmark used in our study (13). The average LDL-C value in CKD patients was 2.1mmol/L, lower than the average of 2.43 mmol/L observed in the 2012 national CIRCLE study of 885 First Nations people with diabetes (4).

Almost one third (29 %) of the study cohort was not screened for lipids during the 3-year study period. Only 53% of patients with CKD in our study were receiving a statin and only 37% met the recommended LDL goal.

Hypertension

We found a 59% co-prevalence of HTN and CKD, higher than the 27% identified in the 2016 Manitoba study (6). Ashton's 2011 study of 555 First Nations community members in southern Ontario, found a 29.5% prevalence of HTN and CKD but co-prevalence was not determined (7).

Only 56% (619/1,098) of our CKD patients with hypertension were receiving treatment with ACE-I/ARBs. This represents suboptimal utilization considering Diabetes Canada and Kidney Disease: Improving Global Working Group (KDIGO) recommendations (31, 32).

Multiple Cardiovascular risk factors

The prevalence of other chronic diseases with CKD confers additional CVD risk. A significant cohort of CKD patients (39%) suffered all three cardiovascular comorbidities. (Table 4, Figure 1) The 2012 Circle study noted progression from albuminuria to advanced CKD was associated with duration of diabetes and co-prevalence with hypertension and dyslipidemia in First Nations patients (4).

While only a small proportion (<1%) of patients with CKD progress to ESRD, their risk of all-cause and cardiovascular mortality is at least ten-fold higher (33). The higher rate of CKD in Indigenous Canadians is an important signal of the need for assessment of comorbidities for CVD risk management (14, 26).

Diabetes and hypertension both affect renal function and our study found both present in 47% of CKD patients. This contrasts with the 20% (9/45) of patients identified with advanced CKD (eGFR<60) and HTN and DM in the 2017 Manitoba study (6).

Limitations

Our study has limitations because of the real-world nature of the data, with relevant testing of only 32% of the population. This cohort may not be representative of the total adult population, as higher risk patients were more likely to both seek medical attention and receive renal function testing. Comparing results to universal screening studies is also problematic. Screening studies include many well, volunteer subjects, while our participants were actively undergoing treatment or clinical investigation, with limited well-person screening. Studies also used a variety of denominators in calculating prevalence: the screened population (6,7) or sampling which excluded Indigenous or rural communities (5) or the total adult population, used in this and Gao's Alberta study (14) Our noted prevalence of CKD is likely an underestimation when compared to screening studies with universal ACR and eGFR testing (6,7). ACR urine testing gives the highest yield of CKD detection but is not universally used in general practice and was ordered in only 13% of the adult population. Urine screening at point of care testing (dipstick) is commonly used but not systematically recorded in this EMR (available in clinical notes only). Our study is therefore limited in providing an estimate of overall CKD, but the high prevalence of advanced CKD in this population is notable, with only 28.3% having eGFR testing.

Interpretation

We document a high prevalence of advanced CKD and associated cardiovascular comorbidities in this First Nations population. Co-prevalence of these major chronic diseases in this population increases cardiovascular risk and robust assessment is warranted. These findings will help health care providers identify people at high risk for cardiovascular disease and progressive kidney disease.

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