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RESEARCH ARTICLE

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Characteristics of End-Stage Kidney Disease in a Cohort of Indigenous and Non-Indigenous Adults in Northwestern Ontario, Canada

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SUMMARY

Background: In Canada, the prevalence of chronic kidney disease is two-fold higher among Indigenous than non-Indigenous people. Direct comparisons of clinical characteristics between Indigenous and non-Indigenous end-stage kidney disease (ESKD) patients have not been previously conducted. We compared demographic and clinical characteristics of Indigenous and non-Indigenous adults with ESKD receiving dialysis at the primary hospital serving a region with 20% Indigenous population.

Methods: During 4 years, 186 adults with ESKD were recruited for a clinical trial to analyze the response to pneumococcal immunization. Demographic and clinical data, including age, sex, residency, dialysis characteristics, etiology for chronic kidney disease, comorbidities, history of infections and prior pneumococcal immunization were compared between 91 Indigenous and 94 non-Indigenous individuals.

Results: Indigenous participants were significantly younger than non-Indigenous, both at the time of the study and initiation of dialysis; they had a longer history of dialysis and lower vaccination rates with the recommended pneumococcal vaccine. The most prevalent cause of the disease was diabetes, with a higher prevalence of type 2 diabetes among Indigenous than non-Indigenous. Glomerulonephritis was also more common among Indigenous participants due to a higher prevalence of IgA nephropathy. Renal vascular, chronic heart, joint diseases, and malignancies were more common among non-Indigenous participants.

Conclusions: Indigenous individuals were greatly overrepresented among adults with ESKD receiving dialysis, with a younger age of disease onset and a more severe disease course. Despite a recognized risk of pneumococcal disease, adults with ESKD were under-immunized with the recommended pneumococcal vaccine, with the lowest immunization rates among Indigenous individuals.

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KEYWORDS

Canadian Indigenous People, End-Stage Kidney Disease, Clinical Characteristics.

Abbreviations

EMR: Electronic medical record

ESKD: End-stage kidney disease

GFR: glomerular filtration rate

TBRHSC: Thunder Bay Regional Health Sciences Center

US: United States

Introduction

Chronic kidney disease is a medical issue of global significance estimated to affect almost 700 million people in 2017 based on epidemiological data collected from 195 countries [1]. Chronic kidney disease is defined as either kidney damage or a decreased glomerular filtration rate (GFR) less than 60 mL/min/1.73 m2 for 3 or more months. The most severe form, end-stage kidney disease (ESKD) or chronic renal failure, is characterized by GFR < 15 mL/min/1.73 m2 and requires renal replacement therapy, such as hemodialysis, peritoneal dialysis or kidney transplantation [2]. Both early and late stages of chronic kidney disease are associated with high morbidity and hospitalization rates [3]. Patients who receive dialysis have an increased risk of mortality, particularly from cardiovascular disease and infections, with the highest mortality rates observed among the older patients [4]. According to the US Renal Data System Report, patients with chronic kidney disease who initiate dialysis have an overall 1-year mortality rate of 20% and a 5-year mortality rate exceeding 60%. The rates of all-cause mortality (adjusted for gender and race) are 6.7-8.5 times higher for patients receiving dialysis than their general population counterparts [4].

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Globally, Indigenous populations in high-income countries experience a greater burden of chronic kidney disease and ESKD than the general population [5-13]. According to the 2016 Census data, 4.9% Canadians (1.673 million) identify themselves as Indigenous, a diverse population comprised of First Nations (0.977 million), Métis (0.587 million), and Inuit (0.065 million) [14]. In Canada, the prevalence of chronic kidney disease is two-fold higher among Indigenous compared to non-Indigenous people [5-7]. This excess disease burden is primarily due to the high prevalence of type 2 diabetes resulting in diabetic nephropathy [15, 16]. Indigenous people also experience an excess burden of non-diabetic chronic kidney disease, mainly explained by a high rate of glomerulonephritis [17].

Northwestern Ontario is a large geographic area, with the second-largest proportion of Indigenous Canadians after the Northern Territories. The region has a population of 231,690, including 20% Indigenous people, primarily First Nations [14]. The primary hospital in the region is the Thunder Bay Regional Health Sciences Center (TBRHSC), which serves Thunder Bay and the geographic region of Northwestern Ontario. The hospital has 395 acute care beds and includes the Dialysis Unit [18].

Recent studies have found that adults living in Northwestern Ontario First Nations communities are disproportionally affected by chronic kidney disease, with a prevalence of stage 3-5 disease double that of the general population; however, direct comparisons of clinical characteristics between Indigenous and non-Indigenous patients have not been conducted in these studies [19]. Our study objective was to directly compare demographic and clinical characteristics of Indigenous and non-Indigenous adults with ESKD receiving dialysis through the TBRHSC over the past 5 years. We intended to identify potentially modifiable factors to alleviate excess morbidity and mortality among Indigenous patients with ESKD.

Materials and Methods

Study Design and Setting

We recruited study participants from individuals receiving dialysis through the TBRHSC between May 15, 2015, and February 15, 2019, as part of a vaccine clinical trial analyzing the effects of previous pneumococcal immunization with PNEUMOVAX®23 on the immune response to Prevnar®13 [20]. As this study provided an opportunity to investigate detailed characteristics of individuals receiving dialysis in Northwestern Ontario, we expanded the clinical trial objectives by collecting specific demographic and clinical data from the study participants to summarize the latter data in a descriptive study. To gather the data, we used the following approach. In the clinical trial recruitment process, individuals receiving dialysis who consented to participate in the vaccine clinical trial also consented to have their medical information collected and used for research purposes. As outlined in our clinical trial protocol, we used the following inclusion criteria: minimum age of 18 years, a diagnosis of ESKD, and written informed consent to participate in the clinical trial and share demographic and medical history data. After reviewing the medical history, we applied the following exclusion criteria for participation in the clinical trial and immunization with the study vaccine: immunization with PNEUMOVAX®23 within the past 12 months; any suspected or confirmed immunodeficiency condition; history of allergic disease or reactions likely to be exacerbated by any component of Prevnar®13; history of immunosuppressive therapy for more than 14 days and within six months of vaccination; administration of immunoglobulins or blood products during the study period or within the three months preceding the study vaccine; administration of any vaccine one month prior the study vaccine; pregnancy. The exclusion criteria were applied according to the clinical trial protocol, with the goals of preventing adverse reactions to the vaccine and ensuring that the immunogenetic effect of the study vaccine, Prevnar®13, was not misinterpreted [20].

We collected demographic data at recruitment for all study participants and performed retrospective data analysis to examine the demographic characteristics and medical histories for a total of 186 individuals. Out of this total, we immunized 132 participants with the study vaccine and followed them for one year post-immunization (Figure 1).

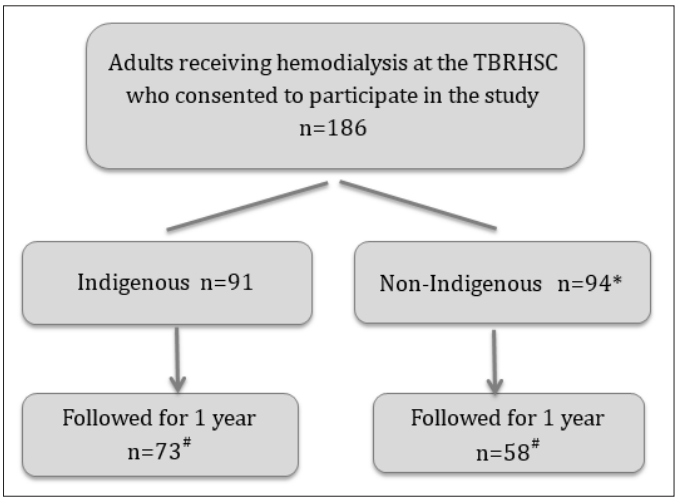

Figure 1: Study Participants

*One did not disclose ethnicity

The remaining had exclusion criteria to participate in the clinical trial

TBRHSC, Thunder Bay Regional Health Sciences Center

Data Sources

The demographic information we collected included age, sex, urban or rural residency, and ethnicity, all self-reported at recruitment. Ethnicity and residency data were exclusively self-reported; the remaining demographic data were verified with the electronic medical record (EMR). We collected medical history data, including current and prior dialysis modalities, etiology for ESKD (classified according to the Canadian Organ Replacement Register) and comorbidities, which we obtained from consultation notes on the EMR [21]. Participants self-reported pneumococcal immunization history, which we verified with the EMR and, if required, with physician offices.

We contacted participants who were immunized with the study vaccine on day 365 post-immunization with Prevnar®13, to determine end-of-study disposition, including study completion, lost-to-follow-up, or death and to assess for any infectious episodes. We also reviewed the EMR for any infection-related hospital admissions or emergency department visits. We collected this information to check our hypothesis that participants who had previously been immunized with a pneumococcal vaccine, PNEUMOVAX®23, might develop fewer infectious episodes during the follow-up period than those without prior pneumococcal immunization.

Ethics Approval and Consent to Participate

This study was registered at ClinicalTrials.gov (NCT 02370069, February 24, 2015) and approved by the research ethics boards of Lakehead University (Romeo #1464206) and the Thunder Bay Regional Health Sciences Centre (REB #2014124). The study has been conducted according to the World Medical Association Declaration of Helsinki and compliant with the Tri-Council Policy Statement 2 for research involving the First Nation, Inuit and Métis Peoples of Canada. All participants provided informed written consent.

Statistical Analysis

We performed a descriptive statistical analysis of the dataset, including 186 participants in the overall analysis and 132 in the immunized subset (Table). We calculated the mean ± standard deviation (SD) for continuous variables and percentages for categorical variables. We then compared the data between the 91 Indigenous and 94 non-Indigenous participants (with one participant excluded because they declined to disclose their ethnicity). For data analysis on participants immunized with the study vaccine, there were 73 Indigenous and 58 non-Indigenous individuals (Figure 1). We used Student's t-test to compare independent continuous variables and $\chi 2$ test of independence with Yates correction for categorical variables, with a significance level of $\alpha<0.05$.

Table: Demographic and clinical characteristics of patients with end-stage kidney disease (ESKD) who received dialysis through the Thunder Bay Regional Health Sciences Centre between May 15, 2015 and February 15, 2019

Characteristics	Patients, n (%)*			
	Indigenous n = 91	Non-Indigenous n = 94	P values	All n = 186&
Age, yr, mean ± SD (range)	52.2 ± 14.3 (20 - 80)	66.1 ± 14.4 (20 - 96)	<0.001	59.3 ± 15.9 (20 - 96)
Female sex	40 (49.9)	42 (44.7)	0.91	82 (44.1)
Rural residency	17 (18.7)	10 (10.6)	0.17	27 (14.5)
Cause of ESKD				
Diabetes mellitus†	48 (52.7)	35 (37.2)	0.048	83 (44.6)
Glomerulonephritis/autoimmune disease‡	28 (30.8)	11 (11.7)	0.003	40 (21.5)
Renal vascular disease§	3 (3.3)	15 (16.0)	0.008	18 (9.7)
Congenital/hereditary renal disease¶	4 (4.4)	9 (9.6)	0.27	13 (7.0)
Nephropathy, drug Induced‡‡	0 (0)	2 (2.1)	N/A	2 (1.1)
Other§§	7 (7.7)	15 (16.0)	0.17	22 (11.8)
Unknown	9 (9.9)	18 (19.1)	0.11	27 (14.5)
Multiple causes	13 (14.3)	16 (19.1)	0.69	29 (15.6)
Comorbidity				
Hypertension	62 (68.1)	68 (72.3)	0.64	131 (70.4)
Diabetes mellitus††	65 (71.4)	45 (47.9)	0.002	111 (59.7)
Chronic heart disease	22 (24.2)	39 (41.5)	0.019	62 (33.3)
Coronary artery disease	20 (22.0)	31 (33.0)	0.13	52 (28.0)
Dyslipidemia	22 (24.2)	30 (31.9)	0.31	52 (28.0)
Joint disease	14 (15.4)	30 (31.9)	0.013	44 (23.7)
Peripheral vascular disease!	20 (22.0)	21 (22.3)	0.91	41 (22.0)
Chronic lung disease	11 (12.1)	20 (21.3)	0.14	31 (16.7)
Malignancy¶¶	6 (6.6)	24 (25.5)	0.001	31 (16.7)
Mental health disorder	19 (20.9)	10 (10.6)	0.09	29 (15.6)
Cerebrovascular disease	8 (8.8)	14 (14.9)	0.29	22 (11.8)
Obesity	10 (11.0)	10 (10.6)	0.17	20 (10.8)
Thyroid disease	8 (8.8)	9 (9.6)	0.94	17 (9.1)

Drug abuse	10 (11.0)	5 (5.3)	0.25	15 (8.1)
Current smoker	6 (6.6)	5 (5.3)	0.95	11 (5.9)
Dialysis characteristics**				
Length of dialysis, months, mean ± SD (range)	38.7 ± 51.1 (1 - 228)	26.5 ± 37.5 (1 - 202)	0.034	32.7 ± 45.1 (1 - 228)
Age when started dialysis, yr, mean ± SD (range)	49.3 ± 15.9 9 - 79	64.1 ± 14.9 19 - 96	<0.001	56.6 ± 17.0 9 - 96
Current hemodialysis	87 (95.6)	92 (97.9)	0.65	180 (96.8)
Current peritoneal dialysis	4 (4.4)	2 (2.2)	0.65	6 (3.2)
Prior kidney transplantation	3 (3.3)	3 (3.2)	0.71	6 (3.2)
Vaccinated with PNEUMOVAX®23	30 (33.0)	49 (52.1)	0.013	79 (42.5)
End of study disposition***				
Infectious episodes#	29 (39.7)	22 (37.9)	0.98	51 (38.6)
Lost-to-follow-up	1 (1.4)	1 (1.7)	0.58	2 (1.5)
Death	11 (15.0)	15 (24.8)	0.27	26 (19.7)
Age at death, yr, mean ± SD (range)	57. 73 ± 10.64 (35 – 69)	70.0 ± 9.42 (59 – 87)	0.015	64.8 ± 11.73 (35 – 87)

Note: SD = standard deviation

*Unless otherwise indicated

&Ethnicity for one patient was unknown

† Type 1, *n* = 6; type 2, *n* = *77*

‡ Including IgA nephropathy (*n* = *10*), post-strep glomerulonephritis (*n* = *7*), focal glomerulosclerosis (*n* = *4*), membranoproliferative glomerulonephritis (*n* = *3*), Wegener's granulomatosis (*n* = *3*), mesangial proliferative glomerulonephritis (*n* = *2*), membranous nephropathy (*n* = *2*), lupus erythematosus (*n* = *2*), and other conditions present in single patients

§ Including hypertension (*n* = *7*), ischemic nephropathy (*n* = *6*), renal vascular, type unspecific (*n* = *4*), and atheroembolic (*n* = *3*) diseases, multiple conditions (*n*=*2*)

¶ Including polycystic kidney disease (*n* = *3*), congenital renal hypoplasia (*n* = *3*), and other conditions present in single patients

‡‡ Caused by lithium, non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors

§§ Including pyelonephritis/interstitial nephritis (*n* = *8*), acute tubular necrosis (*n* = *4*), pyelonephritis due to acquired obstructive nephropathy (*n* = *3*), and other conditions present in single patients

†† Type 1, *n* = *6*; type 2, *n* = *105*

! Including limb amputations due to non-healing diabetic ulcers (*n* = 23)

¶¶ Including history of renal (*n* = 11), bladder (*n* = 5), colorectal (*n* = 4) cancers, multiple myeloma (*n* = *3*), breast cancer (*n* = *2*), and others present in single patients

#Including skin/soft tissue (*n* = *29*), respiratory infections (*n* = *24*), sepsis/bacteremia (*n* = *6*), gastrointestinal (*n* = *3*), and genitourinary infections (*n* = *2*)

**Analyzed in *n* = *181*

***Indigenous n = 73; non-Indigenous n = 58; all n = 132

Results

Demographic and medical history data are summarized in Table. Nearly half of the individuals with ESKD self-identified as Indigenous (49%); men (56%) were prevalent over women. Despite an overall wide age distribution of 20 to 96 years, the mean age of Indigenous participants (52.2±14.3 years) was significantly lower than that of non-Indigenous (66.1±14.4 years, p<0.001). In both ethnic groups, a minority indicated rural residency (14.5%).

The primary cause of chronic kidney disease was diabetes, with a greater prevalence of type 2 diabetes in Indigenous (n=47, 51.6%) than non-Indigenous (n=30, 31.9%) study participants (p=0.01). Type 2 diabetes was present as a comorbidity in 64 (70.3%) Indigenous and 40 (42.6%) non-Indigenous patients (p<0.001). There was no significant difference in the prevalence of type 1 diabetes between the groups. The second most common primary diagnoses fell within the category of glomerulonephritis/ autoimmune diseases, with a significant difference between the groups attributed to the higher prevalence of IgA nephropathy in Indigenous (n=9, 9.9%) than non-Indigenous (n=1, 1.1%) participants (p=0.020). In contrast, the prevalence of renal vascular disease was higher among non-Indigenous participants (p=0.008). Congenital/hereditary renal diseases and drug-induced nephropathy were less common. In participants with multiple etiologies, type 2 diabetes or hypertension were most frequently observed in combination with others (n=15, 8.0% and n=5, 2.7%, correspondingly).

Indigenous study participants were less likely to have chronic heart, joint or malignant diseases than non-Indigenous. The prevalence of other comorbidities did not significantly differ between the two groups. The length of dialysis was significantly longer for Indigenous than non-Indigenous participants. In 79 (43.9%), the length of dialysis was <1 year; in 68 (37.6%), it was 1 year - 4 years and 11 months; in 20 (11.1%), it was 5 years - 9 years and 11 months; 13 (7.2%) had been on dialysis for >10 years. At the start of dialysis, Indigenous participants were significantly younger than non-indigenous (49.3±15.9 vs 64.1±14.9 years, p<0.001). At the time of recruitment, nearly all study participants were on hemodialysis (n=180, 96.8%); 17 (9.4%) had previously been on peritoneal dialysis. Six had received kidney transplantation in the past, including one individual who received two unique kidney transplants. The transplant rate was nearly identical among Indigenous and non-Indigenous participants. Less than half of the study participants had been vaccinated with PNEUMOVAX®23, the recommended vaccine for people with chronic kidney disease, with a lower immunization rate among Indigenous than non-indigenous participants (33% vs 52%, p=0.013).

During a one-year follow-up, 51 (38.6%) participants experienced at least one, and 18 (13.6%) experienced ≥ 2 infectious episodes, with no significant differences between Indigenous and non-Indigenous individuals. Twenty-six individuals died during the follow-up period. Cardiac disease was the most common cause of death (n=11, 42.3%), followed by sepsis (n=3, 11.5%), respiratory failure (n=2, 7.7%), and malignancy (n=2, 7.7%). The cause of death could not be identified in 8 (30.7%) cases. Age at time of death was significantly lower for Indigenous than non-Indigenous patients (57.7±10.6 vs 70.0±9.4 years, p=0.015).

Discussion

Analysis of demographic and clinical data collected from adults receiving dialysis through the TBHSC over the past 5 years indicated that approximately half of the individuals with ESKD self-identified as Indigenous. The hospital serves a population comprising 20% Indigenous people, indicating a substantial overrepresentation of Indigenous people among those requiring dialysis. Our observations agree with previous data from other parts of Canada, showing that Indigenous people experience a higher burden of chronic kidney disease, particularly advanced stages, compared to the general population [5]. However, such data were mainly collected from Manitoba, Alberta, and Saskatchewan, which are regions with smaller proportions of Indigenous people [5, 6, 15-17, 22, 23]. A nationwide study, which addressed hospitalization rates in patients undergoing dialysis (excluding Manitoba and Quebec) in 2005-2014, included merely 4.6% Indigenous people [24]. According to that study, Indigenous patients had a higher risk of hospitalization than Caucasians (hazard ratio: 1.20, 95% CI: 1.12-1.28) [24]. We identified one study on the prevalence of chronic kidney disease in Northwestern Ontario among 26 remote First Nations communities. The study identified a 7% prevalence rate of stage 3-5 chronic kidney disease, double the rate of the general Canadian population [19].

Our findings confirm that ESKD affects Indigenous Canadians at an earlier age, takes a more severe course, and is associated with earlier death than that of the general population. Indeed, Indigenous participants were significantly younger than non-Indigenous, both at the time of enrolment into our study and initiation of dialysis. Although the proportion of deceased study participants did not significantly differ between the two groups, the age at death for Indigenous individuals was more than 10 years younger than in non-Indigenous. In addition, Indigenous participants had a longer history of dialysis. Comparison between Indigenous and non-Indigenous participants in our settings revealed similar trends found by other Canadian studies. In the Prairie Provinces, age-adjusted death rates after initiation of dialysis were higher in Indigenous than Caucasian patients [22]. In Saskatchewan, in comparison to non-First Nations, First Nations people had a higher proportion of ESKD, earlier onset of chronic kidney disease, and higher rates of ESKD secondary to type 2 diabetes [23]. In that study, the difference in the average age at death between First Nations and non-First Nations patients undergoing dialysis (13.7 years) was similar to our data (12.3 years).

Type 2 diabetes was both the most prevalent cause of ESKD and the most common comorbidity among Indigenous participants in our study, in agreement with the high prevalence rates seen in Canadian Indigenous peoples [16, 25-27]. Type 2 diabetes was also identified as the most common cause of ESKD in non-Indigenous study participants, however, the prevalence was lower. Other etiologies, such as renal vascular disease, including

hypertension, were more commonly identified in non-Indigenous individuals. In addition, certain comorbidities, including chronic heart disease, joint disease, and malignancy were more frequently observed in non-Indigenous than Indigenous study participants. This observation may be attributed to the older mean age of the former group.

We observed a significantly higher prevalence of IgA nephropathy in Indigenous than non-Indigenous study participants. Genomic studies identified several susceptibility loci for IgA nephropathy, which may explain an increased prevalence of this disease in specific populations and geographic areas [28, 29]. Earlier studies reported a 10 times higher prevalence of IgA nephropathy in Indigenous compared to non-Indigenous children in Manitoba [30]. In addition, an increased prevalence of IgA nephropathy was observed in Indigenous populations of New Mexico [31]. The Indigenous people of Canada are made up of distinct and diverse populations, including First Nations, Inuit and Métis. It remains unknown if genetic, environmental, or socioeconomic factors underlie North American Indigenous populations' increased susceptibility to this disease [32-34].

Individuals with advanced stages of chronic kidney disease undergoing dialysis are at high risk of pneumococcal infection [35-37], and in Canada, they are recommended to receive a publicly funded 23-valent pneumococcal vaccine, PNEUMOVAX®23 [38]. Only 42.5% of all individuals enrolled in our study had received the vaccination, with much lower vaccine coverage in Indigenous than non-Indigenous individuals (33% versus 52%). Prevnar®13, a 13-valent pneumococcal vaccine, was the study vaccine in our clinical trial and is not the current recommended vaccine for people with chronic kidney disease in Canada. The last National Immunization Coverage Survey indicated that the vaccination rates of adults with chronic medical conditions recognized as risk factors for pneumococcal infection were 58% for individuals ≥65 years of age and 25% for those 18-64 years old [39]. As these data are based on a very limited sample, their comparison to our findings would be largely inconclusive; nevertheless, our study participants' immunization rates appear insufficient [39]. Considering that North American Indigenous peoples, in general, have an increased incidence of invasive pneumococcal disease as compared to the general population [40, 41], Indigenous people with ESKD in our region are greatly under-immunized. The reasons for these low pneumococcal immunization rates will require further study. Improvements in vaccination rates will help prevent serious infectious diseases that can aggravate kidney disease and lead to increased hospitalization rates and mortality. Furthermore, it has been reported that pneumococcal immunization improves the survival of patients undergoing hemodialysis [42-44].

Limitations

The main study limitations are related to the inclusion criteria, i.e. informed consent to participate in the clinical trial and share demographic and medical history data. Not all of the individuals receiving dialysis we approached provided consent to participate in the study, and as a result, our analysis does not include 100% of the respective population. The proportion of self-reported rural study participants may inaccurately reflect the demographics of the region's ESKD population because many indigenous people with ESKD have relocated to the urban setting to receive dialysis. In addition, the one-year observation was completed only for those participants who had been immunized with the study vaccine. Exclusion criteria were applied to 54 individuals as per the vaccine clinical trial protocol, which might result in bias. Clinical data were collected using a retrospective review of the EMR and hence limited to the recorded data; this resulted in some unavailable information. Lastly, statistical analysis was complicated by heterogeneity in the studied population regarding causes for kidney disease, comorbidities, and length of dialysis.

Conclusions

Our study is the first to directly compare demographic and clinical characteristics of Canadian Indigenous and non-Indigenous individuals with ESKD, with a study population comprised of approximately 50% Indigenous participants. In the context of Northwestern Ontario regional demographics, we found that Indigenous people appear to be greatly over-represented among individuals receiving dialysis, with a younger age of disease onset and a more severe disease course. As Indigenous people are disproportionally affected by type 2 diabetes, our findings further emphasize the importance of this issue and the urgent need to take an upstream approach to address relevant social determinants of health, such as ensuring access to affordable, nutritious food and consistent access to appropriate health care services. Our study was the first to notice the significance of IgA nephropathy as a cause for ESKD in the Indigenous people of Northwestern Ontario. These findings call for studies to elucidate the role of genetic versus environmental and socioeconomic factors among Indigenous people with increased susceptibility to IgA nephropathy.

Our findings, which are based on a direct comparison between Indigenous and non-Indigenous Canadians residing in the same geographic region and receiving dialysis in the same hospital, are concordant with observations from other parts of the world. Significant differences in the prevalence and outcomes of chronic kidney disease between Indigenous and non-Indigenous populations have been reported across various other high-income countries, including the US, Australia, and New Zealand. Such disparities likely reflect multiple factors, which may negatively affect the health of Indigenous people and remain insufficiently addressed by health care policies. Although diabetic nephropathy is recognized as the primary cause of ESKD in Indigenous people, it may not be the only reason for the excessive burden of this disease. The role of genetic factors predisposing to kidney disease needs to be considered in the context of environmental factors, such as socioeconomic disadvantage or exposure to toxic substances.

Despite a recognized high risk for pneumococcal disease, adults with ESKD are under-immunized with the recommended pneumococcal vaccine, with the lowest immunization rates observed among Indigenous individuals. Improvements to immunization rates will help prevent infectious diseases that may otherwise exacerbate kidney disease, leading to increased hospitalization rates and mortality.

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