Rates and outcomes of diabetic end-stage renal disease among registered native people in Saskatchewan

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Objective: To determine the rates and outcomes of diabetic end-stage renal disease (ESRD) among registered native people and non-native people in Saskatchewan.
Design: Retrospective population-based study using data from the Canadian Organ Replacement Registry.
Setting: Saskatchewan.
Patients: All patients with diabetic ESRD diagnosed between Jan. 1, 1981, and Dec. 31, 1990.
Main outcome measures: Incidence rates of diabetic ESRD in the general population, rates of diabetic ESRD among patients with diabetes mellitus, nature of initial dialysis treatment, length of survival from start of dialysis, cause of death and renal transplant rates.
Results: The 10-year incidence rates of diabetic ESRD were higher among all age groups among registered native people than among non-native people. The overall relative risk ratio for native people was 16.2. When a higher prevalence of diabetes among native people was taken into account, native diabetic people were still seven times as likely as non-native diabetic people to manifest diabetic ESRD. The median survival from start of dialysis was under 2 years in both groups, but more native people died of stroke and more non-native people died of heart disease. Non-native diabetic people were more likely than native diabetic people to receive renal transplants.
Conclusions: Although the overall incidence of diabetic ESRD in Saskatchewan is increasing, registered native people have a disproportionate risk for this serious complication.

Objectif : Déterminer l'incidence et l'issue de l'insuffisance rénale chronique diabétique au stade ultime (IRSU) chez les autochtones inscrits et les non-autochtones en Saskatchewan.
Conception : Étude stratifiée rétrospective fondée sur des données tirées du Registre canadien des insuffisances et des transplantations d'organes.
Contexte : Saskatchewan.
Patients : Tous les patients atteints d'IRSU diabétique diagnostiquée entre le 1er janv. 1981 et le 31 déc. 1990.
Mesure des résultats : Taux d'incidence d'IRSU diabétique dans la population en général, taux d'IRSU diabétique chez les patients atteints de diabète sucré, nature de la dialyse initiale, durée de la survie à compter de la dialyse initiale, cause du décès et taux de greffe de rein.
Résultats : Les taux d'incidence d'IRSU diabétique calculés sur 10 ans étaient plus élevés, dans tous les groupes d'âge, chez les autochtones inscrits que chez les non-autochtones. Le

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taux de risque relatif global chez les autochtones s'établissait à 16,2. Même en tenant compte de la prévalence plus élevée du diabète chez les autochtones, les diabétiques autochtones étaient sept fois plus susceptibles d'être atteints d'IRSU diabétique que les diabétiques non autochtones. La survie médiane à compter du début de la dialyse était inférieure à 2 ans chez les deux groupes, mais plus d'autochtones sont décédés à la suite d'une attaque et plus de non-autochtones sont décédés à la suite d'une cardiopathie. Les diabétiques non autochtones étaient plus susceptibles de recevoir une greffe de rein que les diabétiques autochtones.

Conclusions : Même si l'incidence globale d'IRSU diabétique en Saskatchewan est à la hausse, les autochtones inscrits présentent un risque disproportionné à l'égard de cette grave complication.

Canadian aboriginal peoples are experiencing an epidemic of non-insulin-dependent diabetes mellitus (NIDDM), a disease that was rare, if not absent, in this population as recently as the early 20th century. Chase[1] reported in 1937 that "Indians are not subject to diabetes" after a survey of 1500 Saskatchewan native people failed to identify a single case. In contrast, Young and associates[2] recently showed that the prevalence of NIDDM is generally higher among native people than among non-native people in Canada and that this difference is most striking where there has been longer exposure to a European lifestyle. Several hypotheses have been offered to explain these observations, including the existence of a "thrifty gene"[3] that may lead to higher rates of obesity. Certainly obesity (particularly central) has paralleled the increasing prevalence of NIDDM among aboriginal people in Canada[4,5] and the United States.[6] Changes in activity levels and differences in carbohydrate metabolism[7,8] may further increase the risk of NIDDM.

Documentation of rates of diabetic complications such as nephropathy in native populations has been largely confined to studies carried out in the southwestern United States. There, 50% of Pima Indians have proteinuria 20 years after the diagnosis of NIDDM;[9] a greatly increased rate of end-stage renal disease (ESRD) is largely attributed to diabetic nephropathy.[10,11] The same is likely true for the Zuni[12] as well as the Hopi and Navajo Indians.[13] Medicare data for 1983–86 show that native people in the United States are at least twice as likely as white people to manifest ESRD from all causes.[14] Data for 1989 that include information for patients both with and without Medicare coverage indicate that this risk ratio is close to four.[15] Furthermore, this increased risk appears to be largely due to diabetic ESRD;[15,16] it is not clear to what extent this can be explained by a higher prevalence of NIDDM.

In Canada Young and collaborators[17] showed that native Canadians have an incidence of ESRD that is at least 2.5 times higher than the national rate, and Wilson and colleagues[18] found that James Bay Cree have a prevalence of ESRD 3.2 times the national rate. Both studies suggest that diabetic nephropathy is largely responsible for these findings, but, again, it is not clear whether this is due to a higher prevalence of NIDDM or whether native people with diabetes are more likely to manifest diabetic ESRD.

In this paper we report the first detailed study of diabetic ESRD in a large population of Canadian native people, including an adjustment for an increased prevalence of diabetes mellitus.

Methods

Serial data for all Saskatchewan patients with ESRD diagnosed between Jan. 1, 1981, and Dec. 31, 1990, were submitted annually to the Canadian Organ Replacement Register. Information subsequently retrieved included birth date, sex, race, cause of ESRD, date and nature of first treatment of ESRD, dates and nature of subsequent changes in ESRD treatment and, if applicable, the date and cause of death. For this study ESRD was defined as the date when long-term treatment with dialysis was started or transplantation done.

A person was considered to have diabetic ESRD if that was the diagnosis submitted to the register by the attending nephrologist. We did not differentiate between insulin-dependent diabetes mellitus (IDDM) and NIDDM because an initial review of the data showed that many patients with NIDDM had been misclassified as having IDDM.

Because of the difficulty in identifying the total number of people with native ancestry in Saskatchewan, the difficulty in defining a native person and possible errors in race designation in the data from the organ replacement register, we limited our study of native people to those with registered status (such people are not necessarily of predominantly native ancestry). They were identified on the basis of a designation attached to their Saskatchewan Health Services Plan number; self-reporting of registered status was used to identify the few people for whom this number was not available. Although the prevalence of diabetes may vary among the different tribal groups within Saskatchewan, we were unable to examine these differences.

Descriptive epidemiologic data in respect to overall numbers of cases, sex, cause of ESRD, nature of initial treatment and cause of death were compiled for native and non-native patients and were compared by means of χ^2 analysis when possible differences appeared.

In calculating initial rates for the two groups we used as denominators the annual populations for 1981–90 of registered native people in Saskatchewan (region 5), available from the federal government, and

the annual provincial populations covered by the Saskatchewan Hospital Services Plan minus the corresponding year's population of registered native people (Table 1).

We calculated age- and sex-specific 10-year incidence rates of diabetic ESRD for the two groups by using their estimated mid-interval (1985) populations as the denominators. The age-adjusted relative risk was used to compare the incidence of diabetic ESRD between the two groups. Age adjustment is imperative in comparing these two populations since a much larger proportion of native people are in lower age groups. The overall age-adjusted risk ratios and their 95% confidence intervals were obtained by combining the age-specific ratios on a logarithmic scale. Statistical tests of the significance of differences between the two groups in the age-adjusted risk ratios were based on the Mantel–Haenszel statistic available through the BMDP 4F program.[19] This method yields pooled risk ratios that place greater weight on larger age subgroups.

Since annual incidence rates of diabetic ESRD for the two populations varied because of small numbers, we calculated the average annual incidence of this complication for two 5-year periods, 1981–85 and 1986–90, to study trends.

Because only diabetic people are at risk for diabetic ESRD and because a difference in the prevalence of diabetes mellitus between native and non-native people might explain a difference in rates of diabetic ESRD, we calculated age- and sex-specific rates of diabetic ESRD for the diabetic populations for the 10-year period. We used the number of new cases of diabetic ESRD in each population from 1981 to 1990 as the numerators and the estimated number of cases of diabetes mellitus in each population in mid-1990 (Table 1) as the denominators. (Only 1990 prevalence data for cases of diabetes are known. This will have underestimated our rates of diabetic ESRD, particularly for native people, since the number of diabetic native people probably increased more rapidly than the number of diabetic non-native people during the study period.) We estimated the number of diabetic native people in Saskatchewan on June 1, 1990, using data from a point prevalence study of known cases of diabetes mellitus on Saskatchewan reserves (Maggie Pioro, Medical Services Branch, Health Canada: personal communication, 1992). These data were obtained from reserve health centres and were presented at the First International Conference on Diabetes Among Native Peoples, held in Minneapolis Nov. 7 to 10, 1990. The number of diabetic non-native people was estimated from information for the three Prairie provinces available from the Canadian Heart Health Surveys Group (Dr. Bruce A. Reeder, Department of Community Health and Epidemiology, University of Saskatchewan: personal communication, 1992) and later summarized.[20] To compare groups, risk ratios and 95% confidence intervals were calculated as for the total populations.

Product-limit survival analysis employing the BMDP 1L and 2L programs[19] was used to compare patient survival from start of treatment of ESRD.

Results

During the study period ESRD was diagnosed in 645 Saskatchewan residents: 89 (14%) were registered native people, and most of the remainder (552/556) were classified as white. Fifty (56%) of the native people had diabetic ESRD, as compared with 135 (24%) of the non-native people ($p < 0.001$). Among those with diabetic ESRD there was a reversal in the male:female ratio between the study groups: 19 male and 31 female native people had this complication, as compared with 97 male and 38 female non-native people (Table 1). The mean age of the native people with diabetic ESRD at the time of diagnosis of ESRD was 55.9 years, as compared with 50.6 years for their non-native counterparts; no patient was under 20 years of age.

There were minor differences between the native

Table 1: Populations of registered native people and non-native people in Saskatchewan in 1981–90*

Population	Men	Women	Both
Total population aged ≥ 20 yr			
Native	13 802	14 516	28 318
Non-native	332 917	335 342	668 259
Estimated no. of people with diabetes mellitus			
Native	774	1 333	2 107
Non-native	19 065	22 581	41 646
No. of diabetic people with end-stage renal disease (ESRD)			
Native	19	31	50
Non-native	97	38	135

*See the Methods section for the sources of the data.

and non-native groups in initial treatment of diabetic ESRD. For 18% of the native people and 22% of the non-native people the initial treatment was chronic ambulatory peritoneal dialysis, and 46% of the native people and 42% of the non-native people were first treated with in-hospital hemodialysis. The remainder initially underwent in-hospital peritoneal dialysis.

Fig. 1 shows the age-specific incidence rates of diabetic ESRD per 10 000 in the general Saskatchewan population aged 20 years or more for 1981–90. Among native people there was a progressive increase in the incidence of diabetic ESRD, which peaked among those aged 60 to 69 years. In contrast, the rates for non-native people were much lower and were relatively stable. Fig. 2 shows the age-specific 10-year rates of diabetic ESRD among native and non-native people with diabetes (the lower age groups have been collapsed into one category because of small numbers). Even when a higher prevalence of diabetes mellitus in the native population was taken into consideration, differences in the rates of diabetic ESRD persisted.

The age-adjusted 10-year incidence rates of diabetic ESRD in the general populations by sex are shown in Fig. 3. Native women had a higher incidence of diabetic ESRD than native men; however, this sex difference disappeared when a higher prevalence of diabetes mellitus among native women was taken into consideration (Fig. 4). In fact, although the small number of patients in some subgroups allowed only a prediction of possible trends, diabetic native men were at higher risk for diabetic ESRD than diabetic native women in all age groups except among those aged 60 to 69 years (Fig. 5). The difference in rates of diabetic ESRD between native and non-native men with diabetes increased with increasing age.

Table 2 summarizes the risk ratios for diabetes mellitus and diabetic ESRD for native and non-native people. Overall, native people were more than 16 times as likely as non-native people to manifest diabetic ESRD; for native women the risk ratio was over 30. Na-

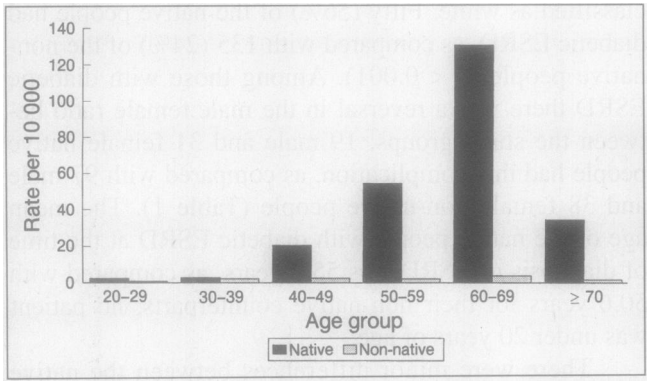

Fig. 1: Incidence rates of diabetic end-stage renal disease (ESRD) among registered native people and non-native people aged 20 years or more in Saskatchewan in 1981–90 by age.

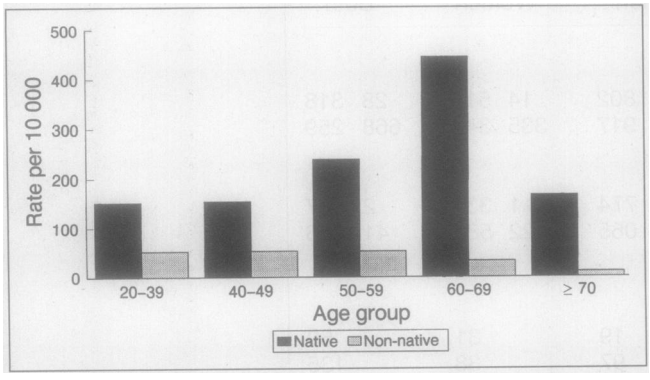

Fig. 2: Rates of diabetic ESRD among diabetic people in the two populations for 1981–90 by age.

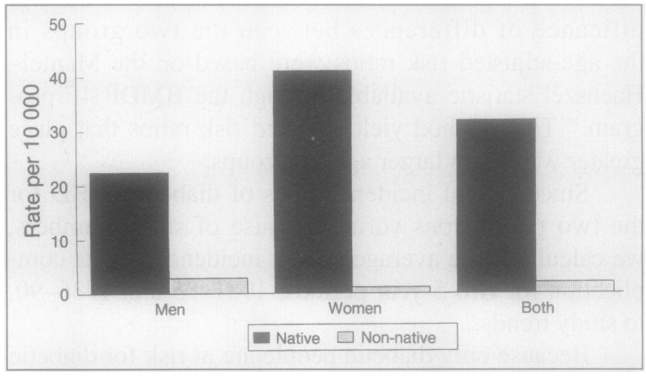

Fig. 3: Age-adjusted incidence rates of diabetic ESRD in the two populations for 1981–90 by sex.

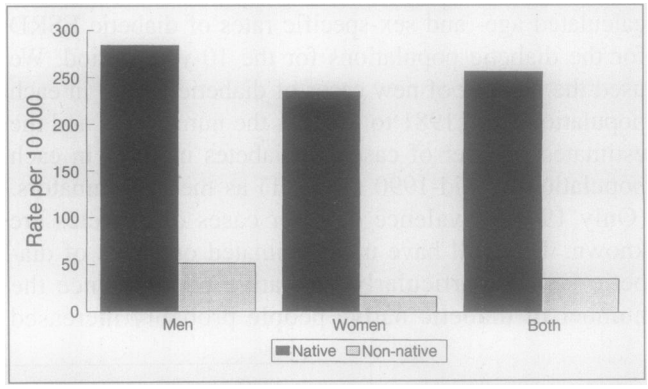

Fig. 4: Age-adjusted rates of diabetic ESRD among diabetic people in the two populations for 1981–90 by sex.

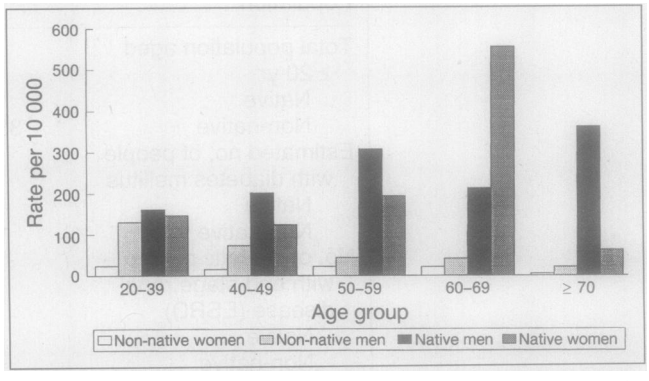

Fig. 5: Rates of diabetic ESRD among diabetic people in the two populations for 1981–90 by age and sex.

tive people (particularly women) in the province were also more likely than non-native people to have diabetes mellitus. This finding accounts only partially for the differences in risk for diabetic ESRD in the general populations: native people with diabetes were seven times as likely as their non-native counterparts to manifest ESRD.

The average annual crude incidence rates of diabetic ESRD rose for both groups between 1981–85 and 1986–90. For native people the rate increased from 1.2 to 2.2 per 10 000 people in the general population, and for non-native people the rate increased from 0.16 to 0.24 per 10 000.

Outcomes

During the study period 34 (68%) of the 50 native people and 76 (56%) of the 135 non-native people with diabetic ESRD died. The overall median survival from the time that dialysis was started was less than 2 years for both groups, although younger people and those who received a renal transplant survived longer. There were no differences in survival between the study populations either in the overall (crude) survival analysis or when survival analysis was adjusted for age, sex, suspected type of diabetes and ESRD treatment.

Table 3 shows the cause of death for those with diabetic ESRD. Cardiac disease was the single most common cause in both groups, but more native than non-native people died of a variety of abdominal problems and of stroke.

Whereas nondiabetic native people with ESRD were almost as likely as their non-native counterparts to receive a transplant (28% v. 35%), native people with diabetes were only half as likely as non-native diabetic people to receive a renal graft (14% v. 27%). This finding appeared to be due to a larger proportion of younger people with IDDM in the non-native diabetic population.

Discussion

Although our population data may have slightly underestimated the true populations of registered native people and non-native people in the province, they represent the best information available. A more important factor in our analysis is the inclusion of a large number of unregistered native people in the non-native population; this will have tended to reduce any differences in rates between the native and non-native groups.

Our results show that native people in Saskatchewan are at increased risk for diabetic ESRD and that this is only partly caused by a higher prevalence of diabetes. Because most diabetic native people have NIDDM we were not surprised to find that the biggest differences in rates of diabetic ESRD occurred in the higher age groups; however, we also found that younger native people with diabetes had a higher rate of diabetic ESRD. Given the small numbers used in rate calculations for these lower age groups, further study is needed to substantiate this finding. Although we were not able to distinguish accurately between NIDDM and IDDM we believe that most young native people with diabetes have NIDDM.[21]

There are several plausible explanations for our findings. First, a larger proportion of native people with diabetes may manifest diabetic glomerulosclerosis, the process that eventually leads to renal failure. Since chronic hyperglycemia seems to be the common underlying factor leading to diverse diabetic complications[22] and since hypertension may also play a causative role in diabetic nephropathy,[23] either late diagnosis of diabetes or poorer glycemic/hypertensive control in native people known to have diabetes may contribute to increased rates of diabetic nephropathy. Our finding that native diabetic people with ESRD are more likely to die from stroke is consistent with differences in hypertension con-

Table 3: Causes of death for native and non-native diabetic people with ESRD in 1981–90

Cause of death	Group; % of patients: Native (n = 34)	Non-native (n = 76)
Cardiac disease	8 (24)	32 (42)
Abdominal problem	6 (18)	4 (5)
Stroke	4 (12)	5 (7)
Infection	3 (9)	4 (5)
Dialysis stopped	3 (9)	7 (9)
Malignant disease	1 (3)	2 (3)
Other	9 (26)	22 (29)

Table 2: Native:non-native risk ratios for diabetic ESRD in 1981–90

Variable	Sex; risk ratio (and 95% confidence limits): Men	Women	Both
Diabetic ESRD in general population	8.5 (5.0, 14.2)	33.7 (20.0, 56.8)	16.2 (11.5, 22.9)
Diabetes mellitus in general population	1.5 (1.4, 1.6)	2.1 (1.9, 2.2)	1.8 (1.7, 1.9)
Diabetic ESRD in diabetic population	5.3 (3.1, 8.9)	14.0 (8.3, 23.6)	7.0 (4.9, 9.9)

trol. Differences in the availability and use of medical services as well as in cultural attitudes and understanding about disease may also be important issues. In regard to genetic factors, diabetic nephropathy can occur in family clusters,[24,25] and its occurrence in such instances may also be related to the presence of hypertension.[23]

A second possible explanation for our findings is that we may have greatly underestimated the number of native people with diabetes mellitus in Saskatchewan; however, this is unlikely to account for a sevenfold difference in rates of diabetic ESRD.

A final consideration is that glomerulosclerosis may be more likely to progress to ESRD in native people with diabetes than in non-native people with diabetes. Although diabetic glomerulosclerosis virtually always progresses, it is conceivable that native diabetic people with nephropathy may be less likely than non-native diabetic people to die before dialysis is necessary. A more rapid course from onset of diabetic glomerulosclerosis to diabetic ESRD, for example, could be associated with fewer interim deaths from other causes.

We believe that the eventual solution to this very serious problem lies in the development of native community-initiated programs designed to prevent NIDDM. In the meantime, secondary prevention of diabetic glomerulosclerosis and delay of its progression are achievable. Greater efforts must be directed toward the early recognition and treatment of NIDDM and hypertension in this high-risk group. Although an optimum screening program for this population has not been determined, obese native people of any age and those over age 40 should probably undergo annual testing for diabetes and hypertension to permit early therapeutic intervention. For those with diabetic glomerulosclerosis early nephrologic evaluation can lead to programs designed to slow the rate of progression and, possibly, arrest the process. These measures should be considered a priority public health concern not only because of the devastating effects of diabetic ESRD on patients and families but also because of the costs and often limited success of its treatment.

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