The growing volume of diabetes-related dialysis: a population based study

Charmaine E. Lok¹,², Matthew J. Oliver³, Deanna M. Rothwell² and Janet E. Hux²,³

¹Division of Nephrology, University Health Network, Toronto General Hospital, ²Institute for Clinical Evaluative Sciences and ³Department of Medicine, Sunnybrook & Women’s College Health Sciences Centre, Toronto, Ontario, Canada

Abstract

Background. End-stage renal failure requiring dialysis is one of the most serious complications of diabetes mellitus, and diabetes is the most common cause of end-stage renal failure. The aim of this large, observational study is to describe the population-based incidence and prevalence rates and outcomes of diabetic individuals in Ontario, Canada who require dialysis therapy.

Methods. Two cohorts of patients, those with diabetes and those without, were created between April 1, 1994 and March 31, 2000 (total of ~8.4 million) and followed until March 31, 2001 using several large, linked administrative databases at the Institute for Clinical Evaluative Sciences. The incidence, prevalence and mortality on dialysis for each cohort were determined. A multivariate Cox proportional hazards analysis, adjusting for age, sex and co-morbidity, was used to determine the independent impact of diabetes on patient survival.

Results. The average annual incidence rate of dialysis was 12 times greater in persons with diabetes (130 per 100,000) vs without diabetes (11 per 100,000). By 1999–2000, diabetic patients comprised 51% of the incident dialysis population. The average annual prevalence rate was 10 times greater in the diabetic cohort. Patients with diabetes had more co-morbidities at the start of dialysis and poorer 3 year survival (55 vs 68%; P < 0.0001).

Conclusions. The incident and prevalent rates of dialysis for patients with diabetes mellitus are many times the rates of those without diabetes. Patients with diabetes mellitus often start dialysis with significant co-morbidities, which may contribute to the relatively high rate of mortality on dialysis.

Keywords: diabetes; dialysis; population study; survival

Introduction

Renal failure remains one of the most serious complications of diabetes mellitus (DM) and can ultimately require renal replacement therapy with dialysis or transplantation. The risk of developing end-stage renal disease (ESRD) has been reported to be up to 13-fold higher in men with DM than those without [1,2]. Furthermore, the lifetime risk of developing DM is high. Of individuals born in the year 2000, an estimated 32.8% of men and 38.5% of women [3] will develop diabetes. It is currently the most common cause of ESRD in North America, contributing to over one-third of new cases [4,5].

While dialysis imposes a burden of reduced quality of life on patients, the burden on the health care system is also important. Dialysis units, and requirements for related services such as interventional radiology, can pose a significant challenge to hospital resources. Accordingly, accurate data on trends in dialysis requirements are essential for health planners evaluating state/provincial and local capacity to deliver dialysis therapy. The purpose of this population-based study is to describe the incidence, prevalence and outcomes of persons in the province of Ontario, Canada with DM and ESRD who require dialysis therapy.

Subjects and methods

This study was approved by the local Research Ethics Board. The study period was from April 1, 1994 to March 31, 2001, representing fiscal years 1994/95 to 2000/01.
Population-based cohort definition

Ontario residents aged 20 years and older were identified using the Registered Persons Database (RPDB), which contains a unique numeric identifier, date of birth, sex, postal codes and death dates (where applicable) for all Ontario residents with a valid health card. For each year of the study, we classified the population into two cohorts: those with DM (incident or prevalent in that year) and a corresponding non-diabetic (non-DM) cohort. The DM cohort was identified using the Ontario Diabetes Database (ODD), an administrative data-derived registry of all persons in Ontario diagnosed with diabetes. The creation and validation of the ODD have been described previously [6].

Data extraction, definitions and analysis

Dialysis use was identified from claims to the Ontario Health Insurance Plan. Nephrologists providing dialysis care in the Quinte/Kingston/Rideau District Health Council region are reimbursed under an alternative funding programme that does not generate OHIP claims, so individuals in this region (4% of the Ontario population) were excluded from analysis.

Duration of dialysis was calculated as the time between the first and last dialysis claims. Gaps longer than 21 days were subtracted from the total dialysis duration to exclude episodes of acute renal failure or dialysis for acute indications, such as intoxications. Chronic dialysis (hereafter referred to as dialysis) was defined as total treatment for >90 days.

Dialysis starts (incident cases) were attributed to the fiscal year in which the first claim occurred. Prevalent cases (period prevalence) were defined as those individuals who met the above definition of dialysis and who had at least one dialysis billing claim in a given year. Dialysis billing records were examined for the years before and after the study period to ensure that prevalent patients at the beginning of the study, and incident patients at the end of the study period, were included.

Yearly incidence and prevalence rates of dialysis were calculated for patients with and without DM. For persons with DM, numerators were persons in the ODD who were receiving dialysis and denominators were the ODD population for that year. For persons without DM, numerators and denominators were drawn from persons in the RPDB but not in the ODD during the given year. Rates were adjusted for age and sex by direct standardization to the 1996 Ontario population aged 20 years or older. Rates will be presented as number of individuals initiating or on dialysis per 100 000 individuals per year for each fiscal year.

Patient co-morbidities at dialysis initiation were identified from hospital discharge records [data from the Canadian Institute for Health Information (CIHI)] and are reported individually and using the Charlson–Deyo Comorbidity Index [7]. CIHI discharge abstracts were reviewed for the 5 years before dialysis initiation and up to 3 months afterwards. In a sensitivity analysis, we excluded the first 3 months after dialysis initiation to limit acquisition bias, where greater co-morbidity may be detected due to a greater number of hospitalizations occurring within the first few months after dialysis initiation.

Mortality rates were determined for the DM and non-DM study cohorts and compared using the Kaplan–Meier method with censoring at the time of kidney transplant or study end date (if alive). Survival was also adjusted for age, sex, presence of diabetes and the Charlson index using a Cox model. A sensitivity analysis was performed that replaced the Charlson index with the individual covariates that comprise the index plus hypertension. All statistical analyses were performed using SAS (version 8.0, Cary, NC); two sided P-values of <0.05 were deemed statistically significant.

Results

Incidence and prevalence of chronic dialysis in people with and without diabetes

There were 528 874 people in the DM cohort and 7 876 752 in the non-DM cohort in 1999/00 (Table 1). The incident dialysis rate in the DM cohort (133 per 100 000) was 12 times that of the non-DM cohort (11 per 100 000). For men initiating dialysis in the DM cohort in 1999/00, the incident rate was 167 per 100 000 (age unadjusted) while for women it was 144 per 100 000 (age unadjusted). The observed average annual increase in rate of dialysis was 4.6% in the DM population but reduced to 0.1% when adjusted for age and sex. In the non-DM population, the observed average and adjusted annual increases were 0.1 and 0.5%, respectively.

There were 8344 incident dialysis patients whose demographics are presented in Figure 1. A consistent increase in the absolute numbers of diabetic patients starting dialysis was seen (Table 1). There was an 8-fold increase in the average annual rate of dialysis growth of the population with DM (13.2%) compared with non-DM (1.6%). The greatest growth occurred in those older than 75 years of age for patients with and without DM (Figure 1). Diabetic patients comprised 51% of the incident dialysis population by 1999/00.

The average age/sex-adjusted dialysis prevalence rate was also substantially higher among patients with DM than among those without (449 vs 46 per 100 000) (Table 2). The average annual growth of prevalent dialysis cases increased by 15% in the DM and 5% in the non-DM population. During the study period, 8.5% of patients who initiated dialysis without diabetes developed diabetes.

Co-morbidity and survival

Diabetic patients have significantly more co-morbidity compared with non-diabetic patients. The mean Charlson index at dialysis initiation for patients with and without DM was 3.8 and 2.4, respectively (P < 0.0001) (Table 3). Even when diabetes and renal disease are removed from the Charlson index, the mean was 2.3 for the DM cohort and 1.7 in the non-DM cohort (P < 0.0001). Patients with DM were more likely to start dialysis with a past history of hypertension, myocardial infarction, congestive heart failure, peripheral vascular disease and cerebrovascular disease (Table 3). The sensitivity analysis that excluded co-morbidities
Table 1. Age/sex-adjusted incidence of chronic dialysis per 100,000 individuals per year with/without DM aged ≥20 years, 1994/95–1999/00

<table>
<thead>
<tr>
<th>Fiscal year</th>
<th>Ontario population (n)</th>
<th>Age/sex-adjusted incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diabetes</td>
<td>No diabetes</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>Incidence rate</td>
</tr>
<tr>
<td></td>
<td>Observed</td>
<td>Adjusted</td>
</tr>
<tr>
<td>1994/95</td>
<td>356 112</td>
<td>7 359 527</td>
</tr>
<tr>
<td>1995/96</td>
<td>389 404</td>
<td>7 446 921</td>
</tr>
<tr>
<td>1996/97</td>
<td>421 661</td>
<td>7 538 458</td>
</tr>
<tr>
<td>1997/98</td>
<td>457 162</td>
<td>7 630 051</td>
</tr>
<tr>
<td>1998/99</td>
<td>493 165</td>
<td>7 749 891</td>
</tr>
<tr>
<td>1999/00</td>
<td>528 874</td>
<td>7 876 752</td>
</tr>
<tr>
<td>Average annual growthb, %</td>
<td>8.2</td>
<td>13.2</td>
</tr>
</tbody>
</table>

*All fiscal years are from April 1 to March 31.

*bAnnual growth refers to growth from previous year in that group, not growth rate of people with DM relative to those without DM.

Table 2. Age/sex-adjusted prevalence of chronic dialysis per 100,000 individuals per year with/without DM ≥20 years 1994/95–1999/00

<table>
<thead>
<tr>
<th>Fiscal year</th>
<th>Diabetes</th>
<th>No diabetes</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Prevalence rate</td>
<td>n</td>
</tr>
<tr>
<td></td>
<td>Observed</td>
<td>Adjusted</td>
<td></td>
</tr>
<tr>
<td>1994/95</td>
<td>1480</td>
<td>415.6</td>
<td>437.9</td>
</tr>
<tr>
<td>1995/96</td>
<td>1708</td>
<td>438.6</td>
<td>439.4</td>
</tr>
<tr>
<td>1996/97</td>
<td>1931</td>
<td>458.0</td>
<td>435.2</td>
</tr>
<tr>
<td>1997/98</td>
<td>2265</td>
<td>495.5</td>
<td>450.6</td>
</tr>
<tr>
<td>1998/99</td>
<td>2614</td>
<td>530.1</td>
<td>454.1</td>
</tr>
<tr>
<td>1999/00</td>
<td>2983</td>
<td>564.0</td>
<td>474.4</td>
</tr>
<tr>
<td>Average annual growthd, %</td>
<td>15.1</td>
<td>5.2</td>
<td>8.9</td>
</tr>
</tbody>
</table>

*All fiscal years are from April 1 to March 31.

*dRates are age/sex adjusted to the Ontario 1996 population aged 20 and over.

*Total prevalent patients cannot be calculated from adding yearly prevalences; the same patient can be prevalent in more than one year.

*dAnnual growth refers to growth from previous year in that group, not growth rate of people with DM relative to those without.

Fig. 1. Growth rate of incident dialysis patients by age from 1994/5 to 1999/00. aPercentage of men with DM/percentage of men without DM by age group and year. bThe median age of women with and without DM initiating dialysis in 1999/00 was 66 years old, 5 years older than the median age in 1994/95. The median age of men with and without DM initiating dialysis in 1999/00 was 65 and 64 years old, respectively. This is 4 and 6 years older than the median age in 1994/95 for men with and without DM, respectively. c82.9% of the Ontario population was Caucasian, 3.3% Black, 9.7% Asian, and 4.1% of other ethnicity.
detected 3 months after dialysis initiation did not change the results. Only 3.6% of diabetic patients did not require hospitalization in the 5 years prior to initiating dialysis vs 8.8% of the non-diabetic cohort. Co-morbidity scores were set to zero for these individuals since no data were available for construction of the Charlson index.

A survival difference was observed between the DM and non-DM cohorts (Figure 2). The 3-year survival was 55 and 68% in patients starting dialysis with and without DM, respectively (Figure 2). The unadjusted hazard ratio for death for patients with DM starting dialysis was 1.52 [95% confidence interval (CI) 1.41–1.63]. After adjustment for age, sex and Charlson co-morbidity index, the hazard ratio was 1.36 (95% CI 1.27–1.47). Co-morbidity adjustment that used individual co-morbidities (instead of the index) yielded a hazard ratio of 1.37 (95% CI 1.27–1.48).

**Discussion**

The rapid increase in demand for dialysis services over the past 6 years has been driven largely by the growing burden of diabetes in the population. Almost 3000 people with DM in Ontario were treated with chronic dialysis in 1999/00, and >800 new patients with DM started dialysis that year compared with numbers of 1500 and 450, respectively, 5 years earlier.

This is a large, population-based study that reports the rate of growth of dialysis according to diabetes status. Several previous studies lacked generalizability because they examined populations that were genetically high risk for diabetes [8,9] or were limited by studying men only [1]. Thus, our study may have particular significance for health care planners for resource allocation to pre-dialysis clinics and end-stage renal replacement programmes.

The incidence rate of dialysis in this current study was 12 times greater in persons with diabetes compared with those without. A previous large cohort study of 323,544 men who participated in the Multiple Risk Factor Intervention Trial (MRFIT) [1] found an incidence rate of 199.0 per 100,000 person years in diabetic patients vs 13.7 per 100,000 in non-diabetic patients. In MRFIT, diabetes was identified by the presence or absence of medication use to control diabetes at a baseline study visit. This could possibly lead to a number of patients being misclassified and to
a smaller denominator in the diabetes group and a larger numerator in the non-DM group, cumulating in a slightly higher, but comparable incidence rate than in our study. The male population studied may also have contributed to the slightly higher incidence rates, as men are known to have a higher rate of progression of renal disease [4]. Our study also supports this observation with an incident rate of 23% higher in diabetic men (167 per 100,000) compared with diabetic women (136 per 100,000) (Figure 1).

The marked rise in the number of diabetic patients starting dialysis is largely explained by the increasing prevalence of diabetes, which rose by 48.5% between 1994/95 and 1999/00 (Table 1), and by an apparent broadening of eligibility criteria for dialysis. This increased acceptance of dialysis in patients with diabetes and in the elderly has occurred worldwide. For example, in 1982, only 11% of all patients receiving renal replacement therapy in the UK were over 65 and only 8% had diabetes, in contrast to 47 and 19%, respectively, in 1998 [10].

Of note, the difference in the observed (4.6%) and age/sex-adjusted (0.1%) average annual increase of diabetic patients initiating dialysis across the diabetic population in Ontario suggests that the growth in dialysis was not due to a higher proportion of persons with DM reaching ESRD, and is unlikely to be attributed to a decline in the quality of DM care.

The result of the age/sex adjustment suggests that the increasing age of the prevalent diabetic population accounts for the majority of the increase in yearly dialysis incidences. The near quadrupling number of new starts in diabetic patients over 75 years old highlights the contribution of age. Conversely, the rates of dialysis in persons under the age of 65 remained relatively steady.

The high dialysis incidence and prevalence in diabetic individuals highlight the importance of proven therapies in delaying the progression of renal disease. Excellent glucose [11] and blood pressure [12] control and the use of angiotension-converting enzyme inhibitors [13] and angiotension receptor blockers [14] in managing patients with DM should be emphasized. The cost effectiveness of intervention has been documented [15].

Once on dialysis, patients with DM have significantly lower rates of survival than those without DM. Our findings are consistent with the Canadian Organ Replacement Register that reported 3-year survival (December 1, 1991–December 1, 1999) of 52% for those with DM and 65% for those without [3]. The 5-year survival reported in Australia is 42% (DM) and 60% (non-DM) [16]. The Japanese 5-year survival data are also similar to ours at 47% for diabetic persons [17].

Similar to other reports [18, 19], our survival differs from that of the USA overall, unadjusted 5-year survival of 32% [4]. This study was not designed to explore reasons for this difference, which remain controversial. Our survival analysis suggests that the increased mortality of diabetic patients on dialysis may be due to factors other than diabetes itself, since the elevated risk associated with diabetes was significantly reduced after adjustment for other confounding factors [20].

**Limitations**

A small portion (<5%) of the Ontario population was excluded from analysis. However, the provincial dialysis rates were unaffected because people from this region were removed from both the numerator and denominator of the reported rates.

Due to the nature of these administrative data, we could not determine whether diabetic nephropathy was the cause of ESRD in incident patients with DM. Administrative data also probably underestimate disease severity and total co-morbidity (determined by hospital discharge abstracts), since not all patients were hospitalized and not all co-morbidities are noted at the time of hospitalization. Lastly, other important factors that may affect dialysis patients such as ethnicity, dialysis adequacy, nutritional status and other variables requiring laboratory data (biochemistry, haematology) were not examined.

The strengths of our study include its large, diverse ethnic population base of both genders, and wide range of ages and socio-economic class. The crude, unadjusted rate provides an ‘as is’ snapshot of growth in a prospering Canadian province. This can assist health policy makers and resource planners in Ontario and other industrialized states/countries. For example, our data on the rate of increase in dialysis in the ageing, diabetic population with increasing co-morbidity may trigger planning of programmes directed to this type of patient. Resources can be allocated to try to achieve an appropriate balance of establishing both satellite units which are appropriate for independent, agile patients who can do their own dialysis (usually younger patients), and nursing homes or rehabilitation centres that offer multidisciplinary care and dialysis for these other complex patients. It also reinforces the importance of and need for greater involvement of diabetic nurse specialists, endocrinologists and other diabetes care workers in the care of dialysis patients who have diabetes, rather than leaving the primary diabetes care to the nephrologist, who may or may not be providing complete diabetes care. The challenges put forward by our study are to provide the necessary capacity to accommodate current growth and to limit the rapid growth of ESRD in patients with diabetes.

**Conclusions**

This population-based epidemiological study demonstrated a rapidly growing number of Ontarians with diabetes requiring dialysis. These trends will need to be monitored on an ongoing basis to assist in capacity planning and resource allocation. The high rates of dialysis among patients with DM serve as a pointed
reminder of the importance of aggressive primary management of DM, its complications and the associated risk factors for renal impairment.

Acknowledgements. This work was presented as an abstract at the American Society of Nephrology International Expo, San Diego, 2003.

Conflicts of interest statement. None declared.

References

9. UK Renal Registry Report. UK Renal Registry, Bristol

Received for publication: 11.6.04
Accepted in revised form: 16.9.04