The Prevalence of Motor Neurone Disease in the Province of Alberta

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ABSTRACT: Using data from the Alberta Health Care Insurance Plan, the prevalence of motor neurone disease (MND) was estimated for the Province of Alberta, Canada. Between January 1, 1994 and December 31, 1995, 208 cases of MND (125 males, 83 females) were identified from physician billing records giving a period prevalence of 7.38 (8.9 for males, 5.9 for females) per 100,000 population. On prevalence day, July 1, 1995, there were 171 cases (103 males, 68 females) of MND giving a point prevalence estimate of 6.07 (7.3 for males, 4.8 for females) per 100,000 population. Males were more likely to be diagnosed (OR = 1.52, 95% CI 1.1, 2.1) with MND and there was an increased risk of receiving a diagnosis with increasing age ($\chi^2_{trend} = 281$, $p < 0.001$). The mean age of the cases was 59.2 years (58.5 for males, 60.3 for females) and did not differ significantly between the sexes. Geographically, there was no statistically significant difference in the prevalence across regions of the Province. During the study period, 28% of the cases had died (30% of males, 25% of females). The prevalence of MND in Alberta, is among the highest reported in the literature and requires additional investigation to verify these estimates and identify possible causative factors.

RÉSUMÉ: Prévalence de la sclérose latérale amyotrophique en Alberta. Nous avons estimé la prévalence de la sclérose latérale amyotrophique (SLA) dans la province d'Alberta au Canada, au moyen des données du plan albertain d'assurance santé. Entre le premier janvier 1994 et le 31 décembre 1995, 208 cas de SLA (125 hommes et 83 femmes) ont été identifiés à partir des réclamations d'honoraires des médecins, ce qui donne une prévalence de 7.38 (8.9 pour les hommes et 5.9 pour les femmes) par 100,000 de population. Les hommes étaient plus susceptibles de recevoir un diagnostic de SLA (RR = 1.52, IC 95% de 1.1 à 2.1) et le risque d'un tel diagnostic augmentait avec l'âge (χ^2tendance $= 281$, $p < 0.001$). L'âge moyen des patients était de 59.2 ans (58.5 pour les hommes et 60.3 pour les femmes) et n'était pas significativement différent selon le sexe. Au point de vue géographique, il n'y avait pas de différence significative de la prévalence selon les régions de la province. 28% des patients (30% des hommes et 25% des femmes) sont morts pendant la période de l'étude. La prévalence de la SLA en Alberta est parmi les plus hautes rapportées dans la littérature. D'autres études seront nécessaires pour vérifier ces estimés et pour identifier les facteurs en cause.

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Motor neurone disease (MND) is a chronic neurological condition of unknown aetiology characterized by a progressive degeneration of motor neurones leading to weakness, skeletal muscle wasting, and respiratory failure.[1] It represents a group of disorders that include amyotrophic lateral sclerosis (ALS), progressive muscular atrophy, progressive bulbar palsy, and primary lateral sclerosis.[2] ALS accounts for approximately 80-90% of all cases of MND.[3] The prognosis is fatal and in the case of ALS, approximately half of all patients die within 2 to 3 years of initial diagnosis.[4-6]

Considerable variation exists in the reported prevalence of MND world-wide. Emery[7] has estimated the world-wide prevalence of MND at 4.2 per 100,000 population. While high prevalent areas have been identified, MND prevalence has ranged from 0.95 per 100,000 in Hong Kong[8] to 8.5 in Värmland, Sweden.[9]

While some studies report either no sex difference[10] or a minimal difference,[11,12] most report an increased risk among males with male to female ratios of 1.5 or greater.[13-17]

Few Canadian studies exist which describe the epidemiology of MND. Hudson et al.[11] examined MND in south-western Ontario between 1978 and 1982 and estimated the prevalence to be 4.9 per 100,000 population. These authors also noted an increase in prevalence associated with increasing age and significant variation across regions of the province. In the province of

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Nova Scotia, Murray et al.[18] identified 161 cases of ALS over a ten-year period for an average annual incidence of 1.95 per 100,000 population. The authors indicated that the incidence of ALS had been increasing over time and that the rate in Nova Scotia was among the highest reported world-wide at that time.

Most studies of MND have been community or clinic-based and few have assessed the prevalence of MND on a population basis. The Province of Alberta, with its publicly funded universal health care system provides the opportunity to assess the prevalence of MND at a population level. The present study estimates the prevalence and geographic distribution of MND in the Province of Alberta, Canada using a population-based data source. Our objective was to provide baseline information at a population level to assess future incidence and changing prevalence of MND in a well defined area.

METHOD

The Province of Alberta, Canada, is a western province bordering on the Rocky Mountains covering an area of 662,833 square kilometres. Its southern most latitude is 49° and its northern most is 60°. The population of approximately 2.7 million people is divided, administratively, into 17 health regions (Figure 1). For this analysis, the health regions were combined into five areas: South (health regions 1, 2, 3, 5), Calgary (health region 4), Central (health regions 6, 7, 8, 9), Edmonton (health region 10), and North (health regions 11, 12, 13, 14, 15, 16, 17). Health regions 4 and 10 comprise the two major urban centres (Calgary and Edmonton respectively) and account for approximately 58% of the provincial population.

The Province of Alberta has a universal publicly funded health care system in which all residents of the province are eligible for medical services. Registration with the system is mandatory for residents and virtually complete. Using the fee-for-service practitioner claims administrative database from the Alberta Health Care Insurance Plan (AHCIP), all individuals receiving a diagnosis of MND (ICD-9 No. 335.2) from a physician between January 1, 1994 and December 31, 1995 were extracted. The ninth revision of the *International Classification of Diseases*[19] was used for diagnostic coding. Demographic information available included age, sex, and address of the patient. In addition to the AHCIP database, the Alberta Vital Statistics mortality database was also used to identify individuals who had died during the study period with MND recorded as the underlying cause of death. A record linkage, using deterministic strategies,[20] was performed to determine which individuals identified from the AHCIP data had died during the study period.

Prevalence estimates were age-standardized using the direct method to the 1991 Alberta census population.[21] Age- and sex-specific prevalence estimates were calculated for the five regions described above and for the entire province, using the number of individuals registered with the AHCIP as the denominator. Geographic differences were assessed using a χ^2 test for differences among proportions.[21] A χ^2 statistic was used to assess sex differences and age trends.[21] For continuous variables, either a t-test or analysis of variance was used. Odds ratios, and 95% confidence intervals, were calculated to estimate the relative risk of receiving a MND diagnosis by age and sex.[21]

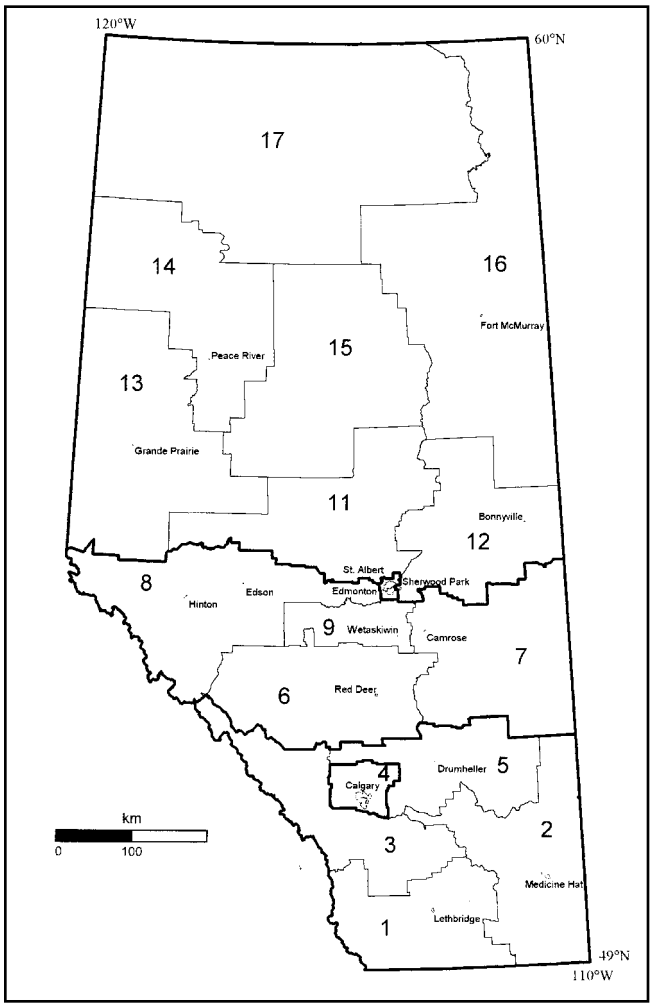

Figure 1: *Regional Health Authority Boundaries for the Province of Alberta, Canada.*

RESULTS

Period Prevalence

Between January 1, 1994 and December 31, 1995, 208 cases (125 men, 83 women) of MND were identified, based on physician claims giving a period prevalence of 7.38 (8.9 for men, 5.9 for women) per 100,000 population. Overall, a male to female ratio of 1.5 was observed. Men were found to be at a greater risk for receiving a diagnosis of MND (OR = 1.52, 95% CI 1.14, 2.02). Prevalence estimates did not differ significantly across the five geographic regions.

A neurologist, neurosurgeon, or internist provided the MND diagnosis for 76% (158) of the cases identified in this study. A total of 83% (172) of the cases included in the study were seen by a physician holding a speciality certification and 66% (136 cases) had received a MND diagnosis from a physician at one of the two neuromuscular disorder clinics operating in the province.

The mean age of 59.4 years (59 years for men, 60 years for women) did not differ between the sexes ($t_{206} = 0.43$, $p > 0.05$) nor did it differ across geographic region ($F_{4,202} = 1.52$, $p > 0.05$). 47% (43% of men, 52% of women) were over the age of 65. The risk of receiving a MND diagnosis was significantly greater for

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Table 1: Age-standardized motor neurone disease period prevalence per 100,000 population by geographic region.

Region	Sex		
	Male (n)	Female (n)	Total (n)
South	9.34 (16)	6.38 (13)	7.80 (29)
Calgary	9.93 (39)	6.04 (25)	7.89 (64)
Central	4.24 (11)	5.08 (12)	4.68 (23)
Edmonton	10.94 (40)	6.81 (26)	8.82 (66)
North	9.18 (19)	3.32 (6)	6.41 (25)
Unknown Res.	– (0)	– (1)	– (1)
Total	8.87 (125)	5.90 (83)	7.38 (208)

Table 2: Age-specific period prevalence per 100,000 population, male to female ratio and rate ratio of motor neurone disease in Alberta.

Age Group	Prevalence per 100,000			M:F Rate Ratio
	Male (n)	Female (n)	Total (n)	
<25	0.19 (1)	0.81 (4)	0.49 (5)	0.23
25-34	3.54 (8)	2.14 (5)	2.83 (13)	1.65
35-54	10.37 (40)	5.05 (19)	7.74 (59)	2.05
55-64	22.45 (22)	12.34 (12)	17.42 (34)	1.82
65-74	45.40 (33)	30.41 (25)	37.44 (58)	1.49
75+	49.78 (21)	27.41 (18)	36.16 (39)	1.82
Total	8.87 (125)	5.90 (83)	7.38 (208)	1.50

those age 65 and older (OR = 9.05, 95% CI 6.83, 11.99) and there was an increase in MND associated with increasing age (χ^2_{trend} = 371.7, p < 0.001).

Point Prevalence

As at July 1, 1995, there were 171 living cases (103 males; 68 females) identified as having MND giving a provincial point prevalence of 6.07 (7.31 for males; 4.84 for females) per 100,000 population with a 1.51:1 male to female ratio. Males were at a higher risk of receiving a diagnosis for MND (OR = 1.52, 95% CI 1.11, 2.09). Similar to the period prevalence, no statistically significant difference across geographic region was noted.

The mean age of 59.2 (58.5 for males; 60.3 for females) did not differ (t_{169} = 0.71, p > .05) between the sexes nor across the five regions ($F_{4,165}$ = 1.22, p > .05). The age of the cases ranged from 19 to 90 years. Figure 2 displays the age- and sex-specific rates of MND. MND prevalence increased with age (χ^2_{trend} = 281, p < .0001) with 48% (45% of males; 53% of females) being

Table 3: Age-standardized motor neurone disease point prevalence per 100,000 population by geographic region.

Region	Sex		
	Male (n)	Female (n)	Total (n)
South	8.15 (14)	5.32 (11)	6.69 (25)
Calgary	7.91 (31)	5.58 (23)	6.68 (54)
Central	3.85 (10)	3.32 (8)	3.62 (18)
Edmonton	8.76 (32)	5.53 (21)	7.11 (53)
North	7.76 (16)	2.17 (4)	5.13 (20)
Unknown Address	– (0)	– (1)	– (1)
Total	7.31 (103)	4.83 (68)	6.07 (171)

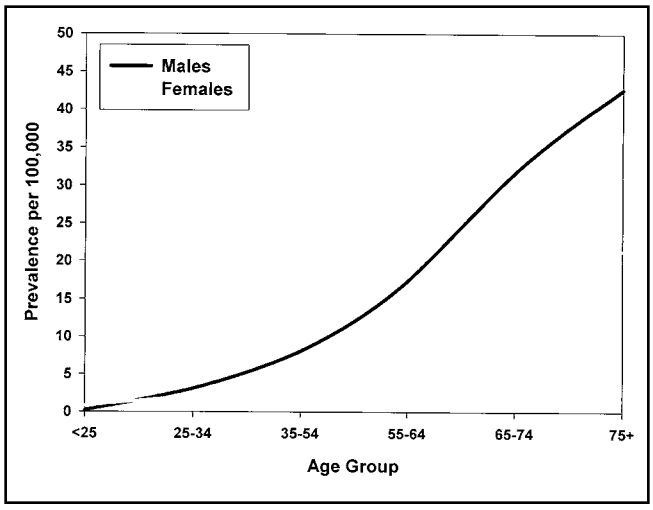

Figure 2: Age-specific Point Prevalence Estimates of Motor Neurone Disease.

65 years of age or older. With the exception of the youngest age groups, males had higher age-specific rates.

Mortality

By the end of the study period, 28% (30% of men, 25% of women) of cases had died. The mean age of those who had died was 66.2 years (64.6 for men, 69.2 for women) and ranged from 30 years of age to 89. Although males were slightly more likely to have died over the study period, the difference was not statistically significant (OR = 1.29, 95% CI 0.66, 2.53).

Discussion

A number of limitations when using administrative data to estimate prevalence are acknowledged. Firstly, data are dependent on an individual with MND receiving a medical service and having the disorder correctly identified as MND on the physician submitted claim. The effect of such a bias would be to underestimate prevalence resulting in conservative estimates. However, given the rapid progression associated with MND, it does not seem unreasonable to assume that all cases would have had at least one contact with the health care system over a two year period.

Secondly, it was not possible for us to confirm the diagnoses for each case in this retrospective review. However, 76% (158 of 208 cases) of the cases included had been seen by either a neurologist, neurosurgeon or an internist and 66% (136 of 208 cases)

Table 4: Age-specific point prevalence per 100,000 population, male to female ratio and rate ratio of motor neurone disease in Alberta.

Age Group	Prevalence per 100,000			M:F Rate Ratio
	Male (n)	Female (n)	Total (n)	
<25	0.19 (1)	0.61 (3)	0.40 (4)	0.32
25-34	3.54 (8)	2.14 (5)	2.83 (13)	1.65
35-54	8.29 (32)	3.99 (15)	6.17 (47)	2.08
55-64	16.32 (16)	9.26 (9)	12.81 (25)	1.76
65-74	38.52 (28)	24.33 (20)	30.99 (48)	1.58
75+	42.67 (18)	24.36 (16)	31.52 (34)	1.75
Total	7.31 (103)	4.84 (68)	6.07 (171)	1.5:1

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received their diagnosis at one of the two neuromuscular disorder clinics in the province. For cases included in the point prevalence estimate, 143 (84%) were diagnosed by a neurologist, neurosurgeon, or internist. Roos et al.[22] have demonstrated that the accuracy of diagnostic information found within administrative data sets is improved when the diagnosis is made by a specialist or when the disorder is well-defined. Both of these criteria have been met in this study.

Despite the limitations identified above, a number of advantages to this approach are evident. The identification of cases was non-intrusive and cost-effective. It was not necessary to contact individuals, clinics, hospitals, or health care providers directly. The estimates are population-based and individuals were assigned to a region of residence, regardless of where they obtained their medical services, thereby reducing selection bias. Given the publicly funded universal nature of the health care system in the Province of Alberta, there are no disincentives for obtaining medical care, thus improving the likelihood of capturing cases.

Consistent with other studies, an increasing risk of MND was associated with increasing age, particularly for those over the age of 65[4,15,23] where there is an eight-fold risk compared to those under age 65. The age-specific incidence reported by Chancellor and colleagues[4] for Scotland closely resembles the age-specific prevalence described in this analysis. A male preponderance towards MND reported in the present study is also consistent with the findings in other locations.[12-14,16,17] Also similar to other studies,[4,23] the sex ratio of cases decreased with age. A ratio of 1.1:1 (M:F) was noted for cases over the age of 75 years, down from the overall ratio of 1.5:1. This ratio, however, does not take into account the differences in population size between the sexes in the older age groups. The ratio of the prevalence estimates continues to show a greater risk for males and is the better measure given the greater life expectancy of women.

Unlike the findings of Hudson et al.,[11] no apparent urban-rural difference was found. This may be related to the small number of cases or to patients with MND moving to urban locations where more comprehensive services are available. Unfortunately, the current data do not provide a complete residence history. Current residence location may have minimal association with exposure to potential risk factors. A case-control study would need to be performed to obtain this information as well as more detailed information on potential risk factors.

The prevalence of MND reported in the present study is the highest reported in Canada to date. It is also among the higher reported estimates in the world literature. The prevalence estimates reported here are comparable to those of the Sweden (8.5/100,000)[9,13] and Finland (6.4/100,000).[13] These countries also have universal publicly run health insurance programs similar socio-economic characteristics and a similar climate.

The high number of cases identified, relative to other studies, would make the province of Alberta an ideal location for further research examining potential risk factors. There is a need to confirm these high rates with a well-designed community-based validation study. The consistency of these findings with other studies support the use of administrative databases as an efficient and cost-effective way to estimate the prevalence of MND at a population level and provide ongoing surveillance.

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