Journal of Clinical Neuroscience 28 (2016) 97–101

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical Study

Disability profile of multiple sclerosis in New Zealand

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ARTICLE INFO

Article history:
Received 3 June 2015
Accepted 6 September 2015

Keywords:
Age
Disability
Disease duration
Multiple sclerosis
New Zealand
Prevalence

ABSTRACT

New Zealand is a high risk region for multiple sclerosis (MS). The aim of this study was to investigate demographic, clinical and temporal factors associated with disability status in the New Zealand National Multiple Sclerosis Prevalence Study (NZNMSPS) cohort. Data were obtained from the 2006 NZNMSPS with MS diagnosis based on the 2005 McDonald criteria. Disability was assessed using the Expanded Disability Status Scale (EDSS). Disability profiles were generated using multiple linear regression analysis. A total of 2917 persons with MS was identified, of whom disability data were available for 2422 (75% females). The overall disability was EDSS 4.4 ± standard deviation 2.6. Higher disability was associated with older age, longer disease duration, older and younger ages of onset, spinal cord syndromes with motor involvement at onset, and a progressive onset type. Lower disability was associated with sensory symptoms at onset and a relapsing onset type. Overall, the factors studied explained about one-third of the variation in disability, and of this, about two-thirds was accounted for by age, age of onset and disease duration and one-third by the nature of first symptoms and type of disease onset (progressive or relapsing). Current age, age at onset and disease duration all had independent associations with disability and their effects also interacted in contributing to higher disability levels over the course of the disease.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disorder of the central nervous system that commonly has its onset in young adults aged between 20 and 35 years of age. A relapsing-remitting onset of disease is seen in about 85% of cases, and a progressive onset occurs in about 15%. In 2006 the New Zealand National Multiple Sclerosis Prevalence Study (NZNMSPS) [1] confirmed New Zealand (NZ) as a high risk population for MS with an overall age and sex standardised prevalence rate of 73.1 per 100,000 population, although in Māori, the indigenous population of NZ, the prevalence was substantially lower at 24.2 per 100,000 population [1–3].

After prolonged follow up (typically spanning several decades), the majority of people with MS will have developed substantial and irreversible locomotor disability. However, there is a great deal of inter-individual variability in the disease course and for a significant proportion of subjects there is little or no disability for many years. At present, there are no tools that can reliably predict an individual's progression over time. Natural history and longitudinal studies [4–11] have succeeded to a certain extent in defining the course and the prognostic value of certain demographic and clinical characteristics of patients at disease onset. These studies have shown a number of demographic (for example, age, sex) and clinical factors (for example, type of MS, age at onset, symptoms at onset) associated with disability evolution [7,10,12,13]. However, most of these studies have derived disability data from northern hemisphere populations; data from the southern hemisphere are sparse with little or no countrywide data available.

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http://dx.doi.org/10.1016/j.jocn.2015.09.020
0967-5868/

Furthermore, disability levels of the MS population and factors associated with disability status have not been previously studied throughout NZ. The aim of this study is to describe the disability profile, including demographic, clinical and temporal factors associated with disability status, among persons with MS in the NZ population.

2. Methods

Data were obtained from the NZNMSPS, a cross-sectional study that identified all persons diagnosed with MS (2005 McDonald criteria) [14] resident in NZ on national census day, 7 March 2006. Patients with clinically isolated syndromes, possible MS, neuromyelitis optica and neuromyelitis optica spectrum disorders [15] were excluded. Multiple sources of case ascertainment were used including neurologists and MS society databases, hospital discharge records, public advertising, Māori health workers and NZ government health information statistics. A capture-recapture analysis of multiple sources of ascertainment estimated between 95.2% and 98.8% capture with 95% confidence. Ethical approval for the study was obtained from the NZ multi-region ethics committee. For detailed information of study methodology, see Taylor et al. [1].

The NZNMSPS used a self-administered survey questionnaire to obtain demographic data including age, sex and ethnicity. In keeping with NZ census ethnicity definitions [16], only those who self-identified Māori ethnicity on the questionnaire were included as Māori for this analysis [3]. Those who did not have a positive response for Māori ethnicity are referred to as "non-Māori". Clinical information, including age at symptom onset, disease duration, onset type (relapsing or progressive onset) and nature of symptoms at onset, were obtained from the person's medical record by their treating neurologist or by direct review by a study neurologist. Disability was assessed using the Expanded Disability Status Scale (EDSS) [17]. A majority of patients (75%) had a telephone EDSS [18] and in 25% of cases disability was obtained from a clinical EDSS [17] performed either by the patient's neurologist or study neurologists.

Disability was modelled by linear regression of EDSS on demographic (sex, ethnicity), clinical (type of onset, nature of first symptoms at onset) and temporal (age, age at onset, disease duration) variables. To disentangle the effects of age on age at onset and disease duration, the analysis was conducted in two pairs, that is age and age at onset or age and disease duration as in Johnson and Melzer [19]. Analysis of variance showed significant two-way interaction between age and disease type at onset ($p < 0.001$), age and age at symptom onset ($p < 0.001$), age and disease duration ($p < 0.001$), thus these interactions were added in models. The disability profiles (Fig. 1) were generated by calculating the predicted disability from the regression model at medians for age, age at onset and disease duration and the curves were further smoothed using the locally weighted scatterplot smoothing LOESS procedure [20]. Model assumptions were assessed graphically with no evidence of lack of fit. Correlation coefficients are Pearson product moment correlations. All statistical tests were two-sided with type 1 error rate of 5%, analysis carried out in R version 3.2.0 (Vienna, Austria).

3. Results

A total of 2917 persons with definite MS were identified on census day in 2006. Of these, disability data were available for 2422 (1,824 females, 598 males) including 58 Māori. The demographic and clinical characteristics of the cohort are presented in Table 1. The majority (2023 patients, 83.5%) had relapsing onset MS and 399 (16.5%) progressive onset MS (primary progressive MS). The relapsing onset cases consisted of 1200 (49.5%) patients with relapsing remitting MS and 823 (34%) with secondary progressive MS on census day.

As expected, persons with progressive onset symptoms had higher disability levels compared with relapsing onset cases. Disability levels (EDSS) stratified by type of onset are presented for sex, ethnicity and nature of onset symptoms in Table 2.

Linear modelling showed that temporal variables (age, age at onset of symptoms, and their interactions) (Table 3) or age, disease duration and their interactions (Table 4) explained 22–23% of the variation in EDSS, while onset type (relapsing or progressive) and onset symptoms, explained 10–11%, with no significant contribution from sex or ethnicity. The models also demonstrated that age has a significant effect on disability independent of age at onset of symptoms and disease duration ($p < 0.001$). Overall, the results indicated that disability increased with increasing age ($p < 0.001$) and disease duration ($p < 0.001$), and decreased with intermediate ages of onset ($p < 0.001$). Those with sensory only symptoms at the onset had milder disability compared with those with spinal motor symptoms at onset ($p < 0.05$).

The profiles of disability by age, age at onset and disease duration are presented for relapsing and progressive onset MS in Figure 1. The profiles show average disability generally increasing with increasing age and disease duration for typical combinations of age, disease duration and age of onset. The profile of average disability by age of onset appears more complex, being higher at younger and older ages of onset.

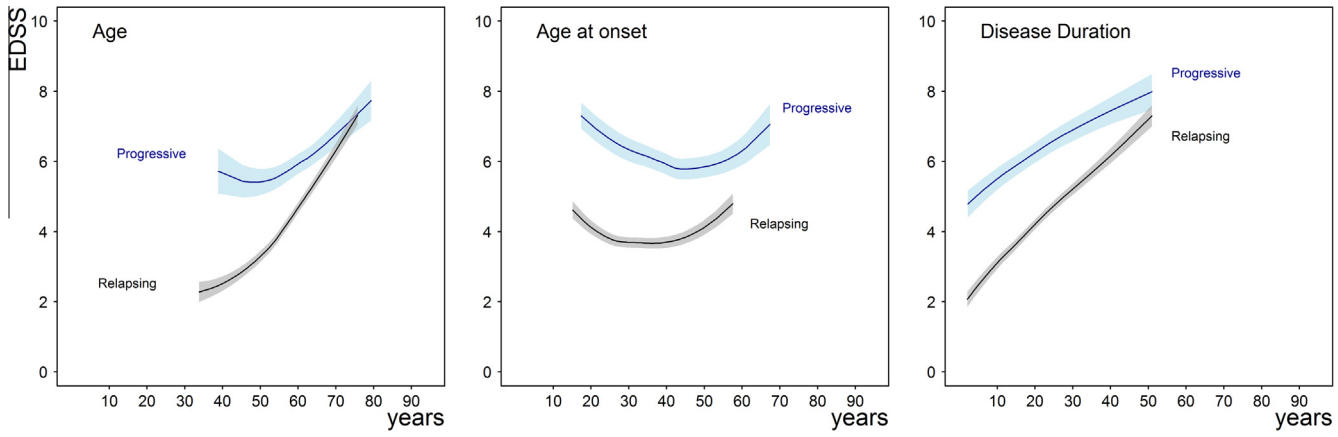

Fig. 1. Profiles of disability by (left) age, (centre) age at onset and (right) disease duration are presented for relapsing and progressive onset multiple sclerosis. EDSS = Expanded Disability Status Scale.