The New Zealand MS Incidence Study Update

The New Zealand Multiple Sclerosis Incidence Study began recruitment in 2012. The aim of the study was to identify all persons throughout NZ who were either diagnosed with MS or experienced their first symptoms of demyelination between June 1st 2012 and May 31st 2014. During the study period, we identified and recruited 463 into the study, 275 of whom had received a diagnosis of MS and 188 of whom experienced their first episode of inflammation. We also received 317 notifications of persons who didn't meet the study criteria for reasons such as the symptoms were found not to be due to MS (n=280), a number received an alternate diagnosis (n=11) or were diagnosed with MS outside the study period (n=26).

The number of people diagnosed with MS identified in each region is presented below.

Region	Number identified*	Percent
Auckland	63	22.9
Bay of Plenty	6	2.2
Canterbury	57	20.7
Hawkes Bay	6	2.2
Manawatu-Wanganui	8	2.9
Nelson - Marlborough	14	5.1
Northland	8	2.9
Otago- Southland	48	17.4
Rotorua	1	0.4
Taranaki	9	3.3
Waikato	17	6.2
Wellington	36	13.1
West Coast	2	0.7
Total	**275**	**100.0**

* These numbers represent only those diagnosed with MS during the 2 year study period.

We gathered information on all patients at entry into the study. This information included the nature of their first symptoms (for example optic neuritis, weakness or sensory symptoms), the date at which they received the diagnosis, the number of attacks or relapses they had experienced, type of MS (relapsing-remitting or primary progressive) and the level of impairment the person experienced. We have also gathered information from tests that were done such as the number of lesions on MRI.

The primary aim of this study was to determine the incidence (frequency of new cases per year) of MS throughout the country between June 1st 2012 and May 31st 2014. The preliminary findings of the study were presented at the joint American and European Committee for the Treatment and Research in Multiple Sclerosis in Boston, USA, September 2014. Preliminary results indicate that NZ continues to be a high risk country for MS with more than 3 cases being diagnosed every year per 100,000 population. The majority of those identified are NZ European origin (84%) however Māori compromise 6.3%, and Asian 2.0 % whereas MS in Pacific peoples appears to be rare (<1%). In 88% of people disease onset was relapsing-remitting in nature whereas primary progressive MS was diagnosed in 12%. The mean age at which people developed their first symptoms was 37.8 ±11.8 years. We found a 3.5 times higher incidence in the south than the north of NZ. This rate is higher than was found in the 2006 prevalence study. This is likely to be because incidence studies generally are a more accurate way of assessing risk factors such as the influence of latitude. These findings will help form the basis of future work trying to identify specific risk factors both genetic and environmental and how they differ between the Northern and Southern regions of New Zealand. The final results of this part of the study are expected to be published in early 2016.

In addition to the incidence data, the study planned to gather information via 6 monthly telephone calls and, where available from clinic visits for all study participants for a further 2 years. Due to an overwhelming response rate (just over 95%) from study participants and their generous support, we have extended the study follow-up out to five years. We are particularly interested in assessing the uptake and benefits of the medications that became available to people with relapsing remitting MS in November 2014. To date we have completed the 6 month follow-up assessments in 90% of participants, 12 months in 80%, 24 months in 50%, 30 months in 35% and 36 months in 15% of patients. Once all patients have completed 2 years of follow-up we will be able to provide more information about MS and its course in New Zealand. We have also had excellent response rates to the questionnaires we have sent to participants with over 80% returning their completed forms. These will provide information on how MS affects socioeconomic status including employment and income, and also how it affects each person's quality of life as well as providing information about risk factors for disease progression such as smoking.

We are once again very fortunate to have Professor David Miller, University College London, join us for 3 weeks in May 2015. He gave talks to both researchers and doctors at the University of Otago and Christchurch hospital and to the members of the MS Society and public on World MS day (27 May) in Christchurch. Prof Miller's visit was kindly sponsored by the New Zealand Brain Research Institute and the Canterbury Medical Research Foundation. We also invited Tomas Kalincik who works as a MS and Neuroimmunology Fellow at the Royal Melbourne Hospital and the University of Melbourne. He is part of the scientific leadership group of MS Base, a worldwide MS registry. His talk was entitled "Observational data can inform evidence-based treatment decisions in MS".

The MS group has been highly productive with a number of presentations and publications over the last year. We have 3 articles accepted for publication in international journals and 4 abstracts accepted for presentation at the European Committee for the Treatment and Research in Multiple Sclerosis, Barcelona, 2015. The details of these publications and presentations will be available on MS Society's website soon. Once again we would like to thank MS Society of New Zealand for their generous support without which none of these projects would be possible. The support of PwMS for this study has been incredible and the information we have collected is beginning to draw international attention with several requests lately for papers we have published. We believe this will lead to increasing collaborations that will continue to extend the research work we are doing in New Zealand.

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The incidence of multiple sclerosis in New Zealand: A prospective, nationwide population-based study

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BACKGROUND

Incidence studies are a well validated tool to better elucidate the cause and risk factors of a disease and plan effective preventive and management strategies. New Zealand (NZ) is ideally suited to such an observational study as it has a geographically well-defined population of manageable size (4,242,048) with a latitude extending from 35^{0}S to 48^{0}S and a uniformly accessible health care system.

Worldwide, the incidence of multiple sclerosis (MS) appears to be increasing. Currently there are no national estimates of the incidence of MS in NZ. Only two studies[1,2] have been undertaken to measure the incidence of MS in NZ, both are regional, and were conducted between two and four decades ago. It is likely that changes in diagnostic criteria, improved case ascertainment and a possible increase in incidence mean that these lack current validity. The 2006 NZ national MS prevalence study[3] reported a high prevalence of MS in NZ (73.1 per 100000 population) as well as a 3 fold increase in prevalence between northern (35^{0}S) and southern regions (48^{0}S). The current study was designed to survey the incidence of MS in NZ, examine its relationship with latitude, ascertain changes in incidence over time and investigate possible environmental risk factors.

AIM: To survey the national incidence of MS and examine its relationship with latitude in New Zealand.

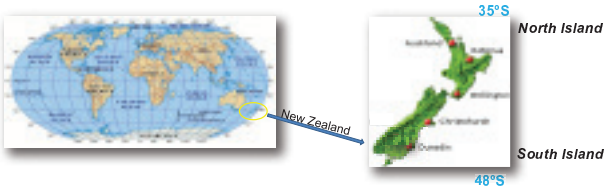

Figure 1. World Map with New Zealand's Latitudinal Extent

METHODS

The NZ National MS Incidence Study is a prospective, nationwide, population-based observational study that surveyed the incidence of MS in NZ over a period of 2 years between June 1st 2012 and May 31st 2014. All cases diagnosed with MS (revised McDonald criteria (2011))[4] during the study period, and resident in NZ at the time of diagnosis were included. Patients with clinically isolated syndromes, possible MS and neuromyelitis optica were excluded.[5] The incident cases were recruited through multiple sources including hospital and private neurology clinics, MS Societies, specialist neuro-ophthalmology clinics and neuroimaging centres. In regions with no designated neurologist, general physicians notified incident cases. The study was approved by the Multi-region ethics committee and all participants completed a written consent.

All participants were sent a self-administered questionnaire that included demographic and personal information including place of residence, education and employment history, smoking habits and quality of life. Clinical information including the date and nature of first symptoms, MS phenotype, date of diagnosis, relapse history, para-clinical tests (CSF, visual evoked potentials), MRI reports and disability assessments were provided by the notifying neurologist or physician. Disability at the time of diagnosis was assessed by a neurologist/physician using the Expanded Disability Status Scale (EDSS).[6] The population demographics were obtained from the 2013 NZ census and incidence was age standardised to the European standard population.

For analysis of incidence by latitude, the country was divided into six broad latitudinal regions from North to South. For each region, a population weighted centroid (PWC) was calculated and this centroid was taken as the latitudinal reference point for that region. The age standardised incidence (ASI) with 95% confidence intervals (CI) were calculated for each region. The latitude gradient was estimated using a simple linear regression model on the population weighted centroid latitudes south of Auckland (37^{0}S). The current incidence was compared with earlier regional incidence data using incidence rate ratios with Poisson confidence intervals.

RESULTS

A total of 245 incident cases were identified during the study period. The annual ASI of MS in NZ was 3.0 per 100,000 population (CI 2.4 - 3.5). The incidence was 1.4 (CI 1.0 - 2.0) for males and 4.4 (CI 3.5 - 5.3) for females. The female to male sex ratio was 3.3:1.

MS onset was relapsing-remitting in 90% and progressive in 10% of cases. The mean age at the onset of symptoms was 37.6 ± 12.0 years (range: 13.7 - 71.7 years) and the mean age at diagnosis was 42.4 ± 13.0 years. In 25.5%, the first symptoms occurred over the age of 40 years and in 18%, the first symptoms occurred over the age of 50 years. The mean disability at the time of diagnosis was 2.3 ± 1.6 as measured by EDSS.

A latitudinal gradient was seen with ASI increasing 3.8 times from North (37 ^{0}S) to South (48^{0}S) (p<0.001). The earlier regional study conducted in 1981[2] showed a 2.7 times increase in incidence between the northern region of NZ (Waikato, 37.9^{0}S) and the southern region (Otago-Southland, 45.8^{0}S). The present study shows a significantly higher gradient (4.5 times, p = 0.03) in incidence between the corresponding northern and southern regions.

DISCUSSION

This is the first prospective, nationwide, population-based MS incidence study worldwide. The study confirms that NZ is a high risk country for MS with a striking north to south latitudinal gradient in incidence. Unlike a number of northern hemisphere studies[7,8] which have shown a decrease in latitudinal gradient over time our study shows no attenuation of the latitude gradient, in fact there has been a 1.8 times increase in incidence gradient over the last three decades. The 3.8 times increase in the incidence of MS from the north to the south mimics the latitudinal gradient seen in MS prevalence in NZ.

Whether these increases reflect changes in environmental or genetic factors or a combination of both remains unknown. Similarly why it differs from that seen in the Northern hemisphere remains unclear.

The mean age at onset in our cohort of 37.6 years (SD 12.0) is higher than previously reported. This may in part be due to increased certainty in diagnosis in the older population due to an increased availability of MRI and improved diagnostic criteria. Interestingly, this finding is similar ((37.6 ± 7.9) to that found in an Australian study[9] which examined the role of environmental factors in first demyelinating cases (n = 216). The reasons reported for this apparent increase, which would seem to be confirmed by our cohort, are that - southern latitudes may influence disease differently than the northern latitudes, and the mean age reported may more realistically reflect the true mean age of onset of MS in the overall population.

CONCLUSIONS

We report the results of the first prospective, population-based MS incidence study to include an entire country. The incidence of MS is high in NZ with a striking latitude gradient which appears to have increased over the three decades. The age at onset of symptoms is higher than that reported in the northern hemisphere.

Funding

- The first author's research position is funded by the National MS Society of NZ and the New Zealand Brain Research Institute, Christchurch
- Travel grants were provided by the School of Medicine and Health Sciences, University of Otago, Christchurch, New Zealand AND the joint ACTRIMS-ECTRIMS meeting committee.

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