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Review

Multiple sclerosis in New Zealand

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ABSTRACT

New Zealand (NZ) is a high risk country for multiple sclerosis (MS) with an overall age and sex standardised prevalence of 73.1 per 100,000 population. The age and sex standardised prevalence within the Māori population is substantially lower at 24.2 per 100,000 population. A latitudinal gradient exists with MS prevalence increasing threefold from the North (37°S) to the South (48°S) of NZ. Over 1600 (56.8%) persons with MS experience moderate to severe disability. Despite the high prevalence of MS and the significant degree of disability experienced by people with MS, the availability and prescribing guidelines for MS disease modifying treatments are more restrictive in NZ than in other developed nations.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system with a predilection for white matter within the brain, spinal cord and optic nerves. It predominantly affects those of Northern European ancestry and is uncommon in New Zealand (NZ) Māori and Pacific peoples [1]. The disease affects females at a ratio of 3:1, and in Western countries is the most common cause of neurological disability in young adults [2]. The cause of MS remains elusive; however a substantial body of evidence suggests that it results from a complex interplay between genetic and environmental factors leading to immune-mediated tissue injury [3]. The modest effect of MS on survival, coupled with the chronic and progressive disability that typically accumulates over decades, means that MS has a major impact on the health and quality of life of sufferers and their careers. It also results in significant healthcare and socio-economic costs [4]. The purpose of this article is to review the epidemiology and socio-economic impact of MS in NZ.

2. MS prevalence in NZ

The prevalence of MS varies considerably around the world ranging from rates of over 200 per 100,000 in the Orkney and Shetland Islands of Scotland and Saskatoon, Canada, to only rare cases among African Blacks and Japanese [5–7]. Recent reviews in geographically different parts of the world suggest a steady rise in prevalence [8–10]. This probably reflects a true increase in disease incidence along with improvements in diagnosis, longer survival and better case ascertainment.

On census day 2006 the New Zealand Multiple Sclerosis Prevalence Study (NZMSPS) [1] determined the prevalence of MS in New Zealand. The study was the first MS prevalence study to include an entire country and sought to address the limitations of smaller, regional studies worldwide. It utilised multiple sources of case ascertainment. All cases were confirmed as definite MS by study neurologists using standardised diagnostic criteria (McDonald Criteria 2005) [11]. Capture-recapture analysis was used which confirmed a case ascertainment between 95.2% and 98.8%. National census data from prevalence day was used as the denominator.

The study identified 2917 persons with MS of whom 75% were women. The age-standardised prevalence rate was 73.1 per 100,000 population. In Māori, New Zealand's indigenous population who comprise 14% of the population, the age-standardised prevalence rate was 24.2 per 100,000.

Prior to 2006, five regional prevalence studies had been conducted within NZ: one in the South Island (Christchurch), [12] three [13–15] in the North Island (one in the Bay of Plenty, two in Wellington) and one [16] that compared rates in the far south (Otago-Southland) with those in the north (Waikato). Prevalence rates reported in these studies ranged between 23.6 and 62.0 per 100,000 in the North Island, and 37.0 and 69.0 per 100,000 population in the South Island (Fig. 1). Only one of the five regional studies provided age and sex standardised rates [16] and, as with many historical studies, criteria for MS diagnosis were not uniform amongst the studies and only one study [13] included MRI in the diagnosis of MS. However regardless of differences in the methodologies, MS prevalence rates in NZ appear to be increasing (Fig. 1).

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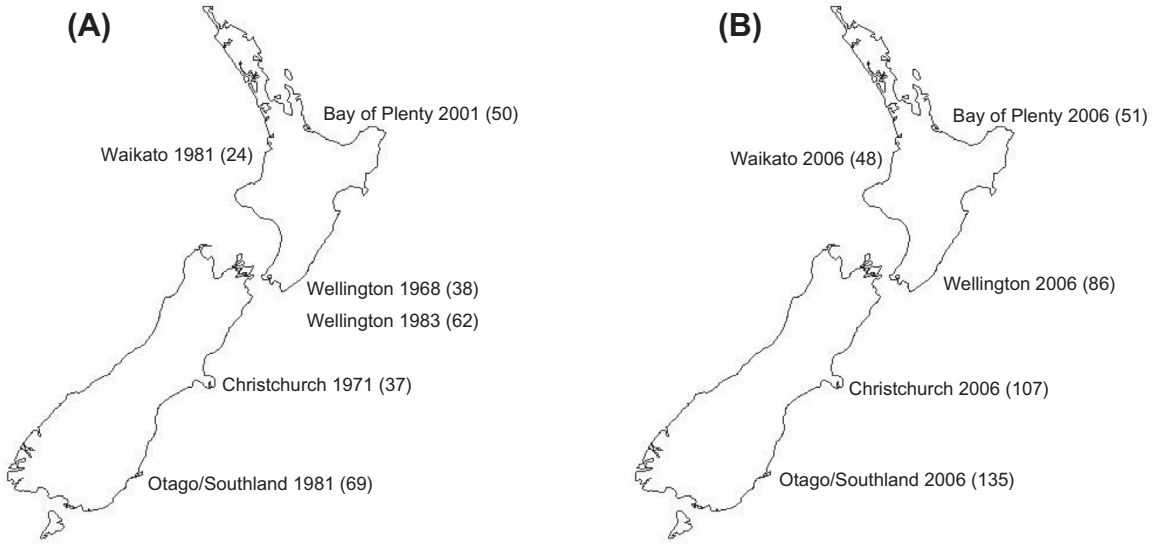

Fig. 1. Comparison of prevalence rates of multiple sclerosis (MS) per 100,000 population between (A) regional studies from 1968–2001 to (B) the New Zealand National Multiple Sclerosis Prevalence study in 2006 [1].

3. Prevalence of MS in Māori and Pacific peoples

Data from the NZMSPS found the prevalence of MS in Māori to be three times lower than the national rate (24.2 *versus* 73.1 per 100,000) and whilst it is well recognised that under-reporting is a factor in low disease prevalence in indigenous populations, differences in genetic factors, such as a low frequency of HLA-DRB1∗15:01 [15,17] and differing susceptibility to environmental factors [18] are also likely to play a role. As with the national prevalence rate, the prevalence in Māori also appears to have increased. Three [12,14,16] of the five previous regional studies (1968–1981) did not identify any Māori persons as cases, whilst two [13,15] (1983, 2001) noted a very small number of Māori cases (one patient and three patients, respectively). The 2006 national prevalence study [1] identified 90 Māori as cases based on self-reported ethnicity and grandparent ancestry. The study identified only one person of Pacific Island descent confirming that MS remains rare within Polynesian ethnic groups in NZ.

4. Incidence of MS in NZ

To our knowledge, no national incidence study of MS has been undertaken in NZ. Only two previous studies reported the incidence of MS in NZ; both were regional studies and were conducted between two and four decades ago (1957–1981) [14,16]. These studies reported an incidence of 1.2 and 1.8 per 100,000 in the North Island (Wellington and Waikato) and 4.8 in the South Island (Otago-Southland). The lack of recent national incidence figures is a notable knowledge gap since incidence data provides the best measure of disease risk within a population and its change over time. Up-to-date incidence data would allow for more accurate prediction of healthcare and socio-economic costs and appropriate allocation of resources. For this reason a national incidence study was begun in 2013.

5. Environmental factors

One of the most enigmatic environmental risk factors for MS is that of latitude with those living furtherest from the equator in both hemispheres having the greatest risk.

The existence of a latitudinal gradient in MS prevalence within the southern hemisphere has been known since the 1960s. Dean (1960) [19], Acheson (1961) [20] and Sutherland et al. (1962) [21] were the first to report the existence of a latitudinal gradient in MS prevalence within the southern hemisphere. NZ, with a latitude extending over 13 degrees (35–48 degrees south), provided an ideal location for demonstrating the presence of a latitudinal gradient and for examining changes over time. In 1981 Skegg et al. found prevalence and incidence rates to be almost three times higher within the southern provinces of NZ (Otago and Southland) compared with a northern region (Waikato) [16]. Twenty-five years later the NZMSPS demonstrated a similar threefold difference in age standardised prevalence rates between the North (50.8 per 100,000) and the South Islands (134.6 per 100,000) [1]. It is interesting to note that whilst the overall prevalence of MS appears to be increasing, the latitudinal gradient appears relatively stable. In Māori, a statistically insignificant gradient (due to a small sample size) was observed in the South Island with no gradient observed in the North Island. Cases with relapsing-remitting and secondary-progressive phenotypes were found to have a latitudinal gradient 7.2 times greater than those with primary-progressive MS, confirming a lesser effect of latitude on the primary progressive phenotype [1].

Both genetic and environmental explanations have been proposed for the latitudinal gradient and the relative importance of each have been extensively debated [18]. The major contributors are thought to be environmental, based on the presence of a latitude gradient within genetically homogenous populations of Northern European origin and migration studies which show that those who migrate before adolescence assume the risk of their new country, whereas those who migrate after adolescence retain the risk of their home country [19].

Proposed environmental factors include prior infection with Epstein-Barr virus and the presence of Vitamin D insufficiency at higher latitudes due to decreased ambient winter ultraviolet radiation exposure. A number of recent studies have confirmed that low Vitamin D levels increase the risk of MS [22,23]. Emerging evidence from a number of epidemiological studies have shown that the risk of a number of medical conditions is lowest in people with Vitamin D levels above 80 nmol/L [24–26]. In the NZ population over 15 years, the mean 25-hydroxyvitamin D level of 50 nmol/L

was significantly less than both adult US populations and those of similar latitudes in the UK [27].

6. Genetic factors

Variation in the proportion of genetically susceptible individuals between Northern and Southern regions is another explanation that has been proposed to explain the latitudinal gradient seen in MS prevalence and incidence in NZ. The lower prevalence in the North Island has been variously attributed to a dilution effect by immigration and the presence of a higher proportion of people of Māori ancestry, hence greater genetic admixture in the North Island. The higher prevalence in Southern regions is attributed to greater numbers of people of Scottish ancestry [18,28].

The association between major histocompatibility complex (MHC) genes and MS risk was first established in the early 1970s with the largest effect located in the human leukocyte antigen (HLA) Class II region [29,30]. Whilst no single gene has been found to be either sufficient or necessary for the development of MS, improvements in genotyping and increasing sophistication of the nomenclature of alleles have confirmed the association between MS and HLA Class II haplotype DRB1*15:01, formerly serological allele HLA-DR2. This haplotype, carried by 28–33% of Caucasian people with MS compared with 9–15% of controls is the strongest susceptibility locus in MS [15,29,31].

In 1986, Miller et al. were the first to conduct HLA genotyping as part of their MS prevalence survey in the Wellington region [15]. This study included 192 persons with MS, 185 European controls, and 79 Māori controls. The results showed a higher frequency of HLA-DR2 distribution in persons with MS (63%) compared with European (30%) and Māori controls (7%). In addition the frequency of HLA-A3 and HLA-B7, other MS risk genes, in Māori controls was about a fifth of that of European controls. It seems plausible therefore that the low prevalence of MS in Māori may be related to a low frequency of HLA-DR2 in Māori. This is the suggested mechanism in indigenous Sami who also have a low frequency of the HLA-DRB1*15:01 haplotype (DR2) and a low prevalence of MS [17].

7. Disability and socio-economic impact of MS in NZ

It is widely acknowledged that MS has a profound effect on the socio-economic and work status of people living with the disease. Despite the fact that over 90% of people with MS have a work history [32,33], unemployment rates as high as 80% have been reported worldwide [34–36]. Burden of illness studies have identified that loss of employment may cost an individual as much as 40% of their lifetime earnings [37,38]. Prior to 2006, two regional surveys on employment status of persons with MS in NZ had been conducted, one in Manawatu-Wanganui [39] and the other in the Canterbury/Westland region [40]. Approximately 50% of persons diagnosed with MS in these regions were not in paid employment. The majority attributed this to fatigue, lack of mobility and lack of concentration associated with MS [39,40]. The average cost of MS per person for the year 1999 in the Canterbury/Westland region [40] was $NZD 19,857. The excess costs encountered by people with MS were potential income loss costs (49%), resource costs (33%) and other costs (18%) including medical-related costs.

The NZMSP study comprehensively examined the income and socio-economic status of the working age (25–64 years) population living with MS and found that MS continues to profoundly influence the employment status of those with the disease [1]. Approximately 54.6% of the working age MS population were not working despite over 90% having a work history. This was in contrast to the general NZ population of whom 22% were not working. The major drivers of loss of work status in people with MS were increasing age, female sex, progressive forms of disease, higher levels of disability and longer disease duration. In addition however, loss of work status was found to occur early in the disease course, affecting 55% of working age people in the first 4 years after diagnosis when disability levels remained modest. Fatigue, reduced lower body motor function, altered cognitive function and multifactorial causes were the most frequent self-reported reasons for loss of employment status. The study also found that at least 67% of the working age MS population had, at some stage, changed their employment status due to the effects of MS. Both men and women experienced a decrease in socio-economic status; however, the effect was significantly greater for females. The median annual personal income for the working age MS population on prevalence day was $NZD 20,000 compared with $NZD 34,750 for the general NZ population. Income sources also showed that over 30% were receiving an invalid's benefit compared with 3% of the NZ population.

In addition to the socio-economic costs a significant level of disability, as measured by the Expanded Disability Status Scale (EDSS) was also found within the MS community. In the NZMSPS a third of patients experienced only mild disability, 50% experienced moderate disability or required aids to walk and 16% were "severely disabled" and were restricted to bed or chair. Not unexpectedly those with relapsing-remitting disease were found to have a lower disability score than those with secondary progressive or primary progressive disease.

The loss of this productive group from the working population is enormous and there can be little doubt that the burden of illness from disability to people with MS and to NZ as a whole is significant.

8. Treatment in NZ

In the last 10 years there has been an exponential rise in effective disease modifying treatments for relapsing remitting MS [41]. Many of the newer agents have been shown not only to reduce disease activity (relapses and inflammatory brain lesions) but to also decrease disability [42–44]. Emerging data suggest that there are also longer term benefits in terms of slower accumulation of disability [45] and reduced mortality [46]. All these treatments have been shown to be most effective early in the disease course and most have little or no impact once a progressive form of MS becomes established.

NZ has three funded first line disease-modifying drugs: interferon beta 1-a, interferon beta 1-b and glatiramer acetate. However, the strict funding criteria for these medications means that less than 20% of patients are eligible for funded treatment, in stark contrast to Australia where between 42% and 55% (data from Australian state MS societies) of patients receive treatment. In addition the requirement for established disability (EDSS 2.0–5.5) prior to the initiation of treatment in NZ raises the possibility that treatments are initiated too late to impart significant benefit. In most other Western countries those with severe disease and those who "fail" first line treatments are switched to newer and more potent therapies. The availability of newer treatments in NZ is restricted to a single agent, natalizumab, which receives limited funding in some but not all district health boards. Similarly effective oral treatments that are funded in Australia are not available in NZ.

9. Conclusion

MS remains an uncommon disease in NZ. However the high prevalence among young working-age people and limited access to effective medications mean that the disease results in a large

burden of illness and results in a significant socio-economic and healthcare cost to society.

Conflicts of interest/disclosures

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

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