Multiple Sclerosis and Related Disorders (2014) 3, 375–383

Available online at www.sciencedirect.com

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

Multiple sclerosis in Iceland from 1900 to 2000: A total population study

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Received 2 September 2013; received in revised form 10 December 2013; accepted 13 December 2013

KEYWORDS
Multiple sclerosis;
Prevalence;
Incidence;
Iceland;
Scandinavia

Abstract
The epidemiology of multiple sclerosis (MS) in Iceland in1900–2000 is presented. The incidence increased significantly from 2.58×10^5 in 1950 to 5.06×10^5 in 2000 (from 2.71 to 7.03×10^5 for women and from 2.55 to 3.10×10^5 for men) with a yearly increase by a factor of 1.0816 per year for women and 1.01207 per year for men (Poisson regression analysis). Prevalence standardized to the European standard population rose from 29.9×10^5 in 1950 to 131.7×10^5 in 2000. The standardized prevalence was constantly higher amongst women ($42.8\text{-}181.6 \times 10^5$ vs. $16.7\text{-}81.5 \times 10^5$ for men) with a female to male ratio of 2.6 in 1950 and in 2000. Mean age at onset for all patients increased from 27.8 years in 1950 to 30.7 years in 2000 (from 27.0 to 30.1 years for women and from 28.6 to 32.2 years for men). Children and adolescents (<18 years) were 9.6% of all, of whom 60% were diagnosed after 1970. Mean age of onset for children and adolescents was 14.7 years (9–17 years, 95% CI 4.2 years).
The rise in incidence and prevalence can have multiple explanations, including diagnosis of milder forms of MS, increased awareness of MS in the older population, better diagnostic measures and longer survival but the authors find it likely that there has been a true rise in the MS incidence.

1. Introduction

Multiple sclerosis (MS) is a common and severe CNS disorder that is characterized by myelin loss, chronic inflammation, axonal and oligodendrocyte pathology and progressive neurological dysfunction. It is the leading cause of disability in young and middle-aged people in the developed world. The most striking epidemiological characteristics are the apparent uneven distribution of the disease across the world and that women are more often affected than men. The traditional view is that MS is particularly prevalent where Caucasians of Nordic origin live, in temperate zones and in high-income countries. A recent meta-analysis by Koch-Henriksen and Sorensen shows some evidence of a general

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http://dx.doi.org/10.1016/j.msard.2013.12.002

increase in the prevalence of MS across countries and continents (Koch-Henriksen and Sorensen, 2010).

Iceland is one of the northern latitude countries where epidemiological studies have shown high and increasing risk for multiple sclerosis. There is some evidence of MS in the Icelandic population centuries ago. The following description from around the year 1200 (Thorlakur´s Saga, ca 1200) is probably the first Icelandic description of an MS attack:

"A woman named Halla took a severe illness on Saturday infra octavas betae Virginis (*i.e. before the eight day of the blessed virgin*, *Mariamass in the autumn was held on Sept. 8th*) so that she lost her sight in both eyes, while the following day she lost her speech. She called on the mighty God for her health, despite some scepticism from those who were present, and on the holy bishop Thorlakur that she would walk to Skalholt (*the Icelandic bishops residency and a school*) and fast on water until Thorlaksmass and still with some prayers. On the third day, a wick was put around her head following which some sight returned to one eye, but she could open up both. On the Sunday, she got her speech back but on Michelmass (*Sept. 29th*) during mass she recovered the vision in the eye that had been blind".

The saga includes two other descriptions of similar incidences where a miraculous cure was attributed to prayers and calling on holy Thorlakur, a local Icelandic saint, for cure.

Four total population MS studies have been carried out in Iceland. The first one was a retrospective study in the 1950s (Gudmundsson and Gudmundsson, 1962). In 1971 Gudmundsson published a follow up study with some reappraisal of the earlier study (Gudmundsson, 1971). New cases were subsequently collected until the year 2000. Between 1978 and 2000, a formal registration of all MS cases with a long term follow up was carried out by one of the authors (J.E.G.B.). Some data from these studies have previously been published (Benedikz et al., 1991; 1994, 1994, 2001). Two more recent studies have since been reported; an incidence study in 2001–2007 (Eliasdottir et al., 2011) and a combined incidence and prevalence study in 2009, the preliminary results of which were published in the Icelandic MS journal for patients (Bergmann, 2012).

This report gives an overview of the epidemiology of MS in Iceland in 1900–2000. We realise that data before 1950 i.e. before neurology became a medical subspeciality in Iceland, are less reliable.

2. Population and methods

Iceland is an island in the North-Atlantic ocean covering 103,000 square kilometres and lies at a latitude of 63–67 °N. The population which is Caucasians of mixed Gaelic and Nordic origin steadily increased over the last century from 84,528 in 1910 to 279,049 in 2000. The population has been relatively free from immigration until ∼1990 and immigrants were 2.5% of the total population in the year 2000 (Statistics Iceland – http://www.statice.is/pages/1184). Life expectancy at birth was 79.7 years for men and 83.7 years for women in the year 2000 as stated by Statistics Iceland (http://wwwstatice.is/Statistics/Population/Births-and-deaths). The country has a comprehensive and socialised medical service and good medical records have been kept since early 1900s. In 1970, the population was served by four clinical neurologists and this number had increased to 18 in the year 2000. MRI has been available since 1990, initially at Landspitali University Hospital in the capital, Reykjavik, where the only neurology department is based, but in the year 2000 five MRI scanners were operating in the country.

The Study Cohort consists of all Icelandic patients diagnosed with MS in the period 1900–2000. Case ascertainment falls into two categories: (1) A retrospective pre-1955 MS survey (Gudmundsson and Gudmundsson, 1962; Gudmundsson, 1971), when records from all medical institutions in Iceland were searched for patients with neurological diseases with onset after 1900. Medical practitioners in the country were contacted and information about neurological patients was obtained. Death certificates were studied. All suspected patients were clinically examined and the relatives of deceased patients were interviewed. (2) The prospective post-1955 MS study and registration. Patients from the retrospective study having definite, probable and possible MS were assessed at regular intervals and newly diagnosed patients were entered into the study cohort through regular contact with medical institutions and medical practitioners in the country. The Icelandic MS society has collaborated with the search for patients since 1978. All suspected and definite MS patients were attended by a neurologist and all have been examined by at least one of the authors. The diagnostic criteria of Poser et al. (1983) were employed retrospectively for patients diagnosed before 1984 and prospectively from 1984 to 2000.

3. Statistical methods

Prevalence was calculated separately for men and women and reported in 10 years intervals. The number of definite and probable cases on the first day of the year was divided by the number of the residents of Iceland on that day as stated by the centre for the official statistics in Iceland. Patients were counted from the year of the diagnosis. For onset adjusted prevalence patients were counted as from the onset of symptoms i.e. before the diagnosis was made. This method of calculating prevalence eliminate the influence of lag time between onset of symptoms and diagnosis (Poser et al., 1992). Prevalence was given per 10^5 of population. Prevalence was standardized to the European standard population as described by the European union public health information system at http://www.euphix.org. Incidence rates were calculated at 10 years intervals, counting the number of new cases of MS in the interval divided by person years of the interval. Person years were estimated using the midpoint population multiplied by the length in years of the observation period. It was assumed that the number of new cases per year would follow the Poisson distribution and the confidence interval of the incidence rate was calculated using method suggested by Ulm (Ulm, 1990). Change of incidence with time was estimated separately for women and men using Poisson regression analysis. The model used was $X = \exp(b0 + b1 * y)$ where X is the estimated incidence and y is the year of onset of multiple sclerosis. Overdispersion was checked by dividing the deviance by degree of freedom. In order to see if the model was appropriate, residuals were plotted against predicted outcome and checked if the residuals showed