Acta Neurol Scand DOI: 10.1111/j.1600-0404.2010.01411.x

ACTA NEUROLOGICA
SCANDINAVICA

Multiple sclerosis in Vest-Agder county, Norway

Vatne A., Mygland Å., Ljøstad U. Multiple sclerosis in Vest-Agder county, Norway.
Acta Neurol Scand: DOI: 10.1111/j.1600-0404.2010.01411.x.

Objective – To examine multiple sclerosis (MS) prevalence, rate of immunomodulatory treatment and frequency of *Borrelia Burgordorferi (Bb)* antibodies in Vest-Agder, Norway. *Materials and methods* – Patients in the period 1996–2006 who met the Poser criteria for definitive or probable MS were included. Clinical and demographical data, and presence of *Bb* antibodies were registered. *Results* – A total of 295 patients were identified. The crude prevalence was 180 per 100,000 population (95% CI = 160.9–218.0), age-adjusted prevalence was 186 per 100,000 population (95% CI = 166.3–225.3). The age-adjusted incidence rates were 7.5 and 8.0 for 1996–2000 and 2001–2006, respectively. Thirty-eight per cent were treated with immunomodulatory agents when compared to 28% in the rest of the country. *Bb* serum antibodies were detected in 7% of patients with MS. *Conclusions* – Vest-Agder county has the highest prevalence of MS reported in Norway, and a high treatment rate. *Bb* antibodies were not more prevalent than in healthy individuals.

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Key words: multiple sclerosis; Norway; incidence; prevalence; Borrelia antibodies; immunomodulatory treatment

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Accepted for publication June 23, 2010

Introduction

The distribution of multiple sclerosis (MS) in the world is uneven, with a higher frequency in the geographical areas far away from the equator. Norway is a high risk area of MS, with prevalence rates from 73 to 164 per 100,000 population (1–7). The prevalence in the southern part of Norway has not been reported.

Norwegian guidelines for immunomodulatory treatment in MS were established in 2000–2001, and the nationwide treatment practice was evaluated in 2007 (8). Based on a calculated average prevalence of MS of 150 per 100,000 inhabitants in each county, the treatment frequencies varied county wise from 15% to 47% with Vest-Agder on top (8). This called for an epidemiological study to find out whether MS is more common in Vest-Agder county than in other parts of Norway, and/or whether the treatment practice differs from the rest of the country. Vest-Agder is a high-endemic area for *Borrelia Burgdorferi (Bb)* infections, and we also wanted to investigate whether presence of *Bb* antibodies were more frequent among patients with MS than the rest of the population.

Material and methods

Characteristics of the area

Vest-Agder county is located in the southern part of Norway, about latitude 58 degrees north and longitude 8 degrees east. The shoreline is 709 km long, and the total area is 7281 km^2. The greatest city is Kristiansand, with 78919 inhabitants (on 1 January, 2008). The main occupations are based on industry and different types of business (trade, tourism). The climate is humid and temperate, with average temperatures around 3–8°C and 1000–2000 mm precipitation on a yearly basis (source: met.no). The population at risk was 163,702 on the prevalence day 1 January 2007. The proportion of immigrants resident in the area ranged from 3.0% to 3.8% between 1996 and 2006, with an average rate of 3.3% in the years 2003–2007 (source: ssb.no).

Case ascertainment and diagnostic criteria

Our sources of information were the files of patients at the only Department of Neurology in the county (Sorlandet Hospital, Kristiansand), and

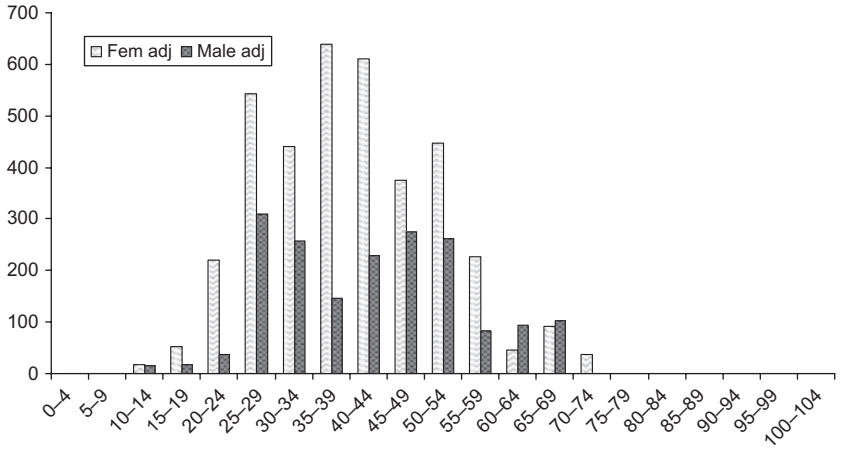

Figure 1. Age-specific prevalence rates of multiple sclerosis in Vest-Agder county by gender 1 January 2007. Horizontal axis: age (years), vertical axis: prevalence of multiple sclerosis per 100,000 population.

the only neurological specialist practice (Spesialistsenteret, Kristiansand). Altogether, eight neurologists and six assistant doctors work at the two institutions. No other local hospitals provide neurological services in the area. Case ascertainment was carried out by re-evaluation of the information given in the records. In most patients, we had information on CSF and MRI results. In addition, the patients answered a questionnaire about site of living when their MS was diagnosed, if they had family members with MS, and if they wanted to participate in the study of MS features and treatment. All patients with definite or probable MS according to the Poser criteria (9) who lived in Vest-Agder in the registration period 1996–2006 were included in the study of prevalence and incidence. We registered MS features and treatment in patients who gave their written consent.

The study was approved by The Regional Committee for Medical Research Ethics in Southern Norway and the Norwegian Data Inspectorate.

Statistical methods

The crude prevalence was calculated as the number of patients with MS living in Vest-Agder county per 100,000 population on prevalence day 1 January 2007. The annual incidence rates were based on the number of patients with onset of MS in the periods 1996–2000 and 2001–2006. For calculation of age-adjusted prevalence and incidence rates, we used the European standard population (10). SPSS16 was used for the analysis, and we calculated 95% confidence intervals (CI) and age-adjusted rates manually. To compensate for the short observation period and the small number of patients, we used the Fay's statistical method (11). The difference in the incidence rates in the two periods 1996–2000 and 2001–2006 was statistically tested by calculating their relative size according to Fay. The 95% CI of the relative size was calculated using the statistical program R.

Results

We identified a total of 324 patients with MS in the hospital files and in the files from the specialist practice. Eleven patients were excluded because they did not fill the diagnostic criteria and one lived outside Vest-Agder. Eighteen patients had died. We included 295 patients with probable or definite MS living in Vest-Agder. This makes a crude total prevalence of 180 per 100,000 population (95% CI = 161–202). The crude prevalence was 119/100,000 (95% CI = 98–146) for men and 240/100,000 (95% CI = 209–276) for women. The calculated total age-adjusted prevalence was 186 per 100,000 population (95% CI = 166–209), for men 120/100,000 (95% CI = 99–147) and for women 255/100,000 (95% CI = 221–293). Age-specific prevalence rates are shown in Fig. 1. The observation time regarding incidence was split into two periods: 1996–2000 and 2001–2006. The incidence figures based on the year of onset of MS symptoms are shown in Table 1. The difference in age-adjusted incidences for 1996–2000 and 2001–

Table 1 Incidence and age-adjusted incidence of multiple sclerosis in women and men in the periods 1996–2000, and 2001–2006

	Incidence per 100,000 population			Age-adjusted incidence per 100,000 population (95% CI)		
Years	Women	Men	Total	Women	Men	Total
1996–2000	8.8	5.3	7.2	9.3 (4.4–9.7)	5.6 (2.1–14.9)	7.5 (4.2–13.5)
2001–2006	9.6	5.1	7.5	10.3 (5.1–20.6)	5.6 (2.1–14.9)	8.0 (4.6–14.2)

2006, respectively, was tested statistically according to Fay (11). The comparative size was 7.49/7.51 = 0.99 (95% CI = 0.68–1.43). As the 95% CI contains one, we conclude that there was no significant change in the age-adjusted incidences of MS in the two periods compared.

A total of 271 patients gave their consent to participate in the study of clinical features and treatment. The results regarding clinical features are shown in Table 2. Information on ongoing treatment at prevalence day was available in 270 patients, and on previous treatment in 261. On prevalence day, 92 patients (34%) received treatment with interferons or glatirameracetate, 12 (4%) received mitoxantrone, and 166 (62%) did not receive immunomodulatory treatment. Forty-two patients (16%) had changed therapy during the disease (33 of them were on interferons or glatirameracetate and 9 on mitoxantrone at prevalence day). Forty-four patients (17%) had withdrawn from immunomodulatory treatment (30 from interferons or glatirameracetate, 9 from interferons or glatirameracetate and mitoxantrone, three from mitoxantrone alone, one from azathioprine, and one unknown). The overall reasons for withdrawal or change were as follows: no effect of treatment (21/86), unacceptable side effects (35/86), MS progressing from RRMS to SPMS without fluctuations (8/86), full dose of mitoxantrone (12/86), planning pregnancy (4/86) and a combination of the reasons listed earlier (6/86). One hundred and eighteen patients (45%) had never received any immunomodulatory treatment (52 with RRMS, and 66 with SPMS, PPMS or not classified MS).

Twelve out of 179 (7%) patients with available data had *Bb* antibodies in serum. None of 120 patients examined had intrathecal *Bb* antibody production.

Table 2 Clinical and demographical data on the prevalence day 01.01.07

	Women *n* = 177	Men *n* = 94	Total *n* = 271
Diagnostic classification *n* (%)			
Definite	160 (90)	79 (84)	239 (88)
Probable	17 (10)	15 (16)	32 (12)
Type of multiple sclerosis (MS) *n* (%)			
RRMS	105 (59)	51 (54)	156 (57)
SPMS	45 (25)	25 (27)	70 (26)
PPMS	19 (11)	15 (16)	34 (13)
Not classified	8 (5)	3 (2)	11 (4)
Number of patients with firstdegree relatives ill with MS *n* (%)	15 (9)	10 (11)	25 (9)
Mean age (years) at onset (SD)	35.7 (9.6)	37.7 (11.4)	36.4 (11.0)
Mean duration (years) of disease (SD)	10.0 (2.2)	12.1 (0.4)	9.3 (1.3)
Mean time delay (years) from onset to diagnosis (SD)	4.9 (1.3)	3.5 (0.4)	4.1 (1.4)

Table 3 Prevalence per 100,000 population in different regions of Norway

Counties	Prevalence year	Crude prevalence per 100,000 population
Troms and Finnmark (5)	1993	73.0
More and Romsdal (7)	1985	74.5
Vestfold (4)	1983	86.4
Nordland (1)	1999	105.6
City of Oslo (2)	1995	136.0
Hordaland (6)	2003	150.8
Nord-Trondelag (3)	2000	163.5
Vest-Agder (present study)	2007	180.2

Discussion

The highest crude prevalence rates of MS in Norway are the ones most recently reported (3,6). Maybe the result reflects an increasing use of MRI for diagnosing MS along with a greater tendency to include mild MS cases. A crude prevalence of 180 per 100,000 population is the highest reported in Norway (1–7) (Table 3). The reason why MS seems to be more common in Vest-Agder county than in other parts of the country is unknown. On the other hand, the period of time and number of patients are limited, and the results must be interpreted with caution.

If we, on the other hand, regard the prevalence of MS in Vest-Agder as higher than in the rest of Norway, it is interesting to look for environmental conditions in Vest-Agder county disposing for MS. Several infectious and non-infectious causes of MS have been suggested (12–15). As Vest-Agder county is a high-endemic area for Lyme borreliosis (16), we wanted to chart a possible association between former borrelia infection and MS. The frequency of detected *Bb* antibodies in serum among our patients was however lower (7%) than among blood donors in the county (18%) (17). This finding is in accordance with some earlier studies (18), but in contrast to others (19). This may imply that patients with MS are less engaged in outdoor activities than the healthy population and does not support the theory of borrelia infection as a disposing factor for MS. Other explanatory factors for a high prevalence of MS could not be found among the registered features of this study either. Results regarding mean age of onset, distribution of MS subgroups, number of first degree relatives with MS and diagnostic delay were comparable to what has been found in other places in Norway (3,6).

The proportion (38%) of patients with ongoing immunomodulatory treatment in Vest-Agder county seems to be smaller than formerly presumed (8), but still this number is higher compared to the treatment frequency (28%) for the whole country

(8). It is noteworthy that another 17% (44/261) of the patients had cessated immunomodulatory treatment, mainly because of side effects or lack of effect. This may reflect a more liberal treatment practice in Vest-Agder.

Conclusion

This study shows that Vest-Agder county in Norway is a high-endemic area for MS, with the highest prevalence rate of disease reported in Norway up till now. The treatment frequency also seems to be among the highest in the country. We did not detect a higher frequency of *Bb* antibodies in serum from patients with MS than in healthy controls.

Acknowledgements

The authors thank Dr Per Monstad, Spesialistsenteret, Kristiansand for data collection. We also thank the statisticians Are Hugo Pripp and Tore Wenzel-Larsen at The Department of Research support, Rikshospitalet, Oslo, Norway, for advice and support in the statistical calculations.

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