J Neurol (1997) 244 : 182–185

ORIGINAL COMMUNICATION

P. J. Modrego Pardo
M. A. Pina Latorre
A. López
J. M. Errea

Prevalence of multiple sclerosis in the province of Teruel, Spain

Received: 7 May 1996
Received in revised form:
17 September 1996
Accepted: 23 September 1996

P. J. Modrego Pardo · J. M Errea
Neurology Unit,
Hospital del Insalud de Alcañiz,
E-44600 Alcañiz, Spain

M. A. Pina Latorre · A. López
Neurology Section,
Hospital del Insalud de Teruel, Spain

P. J. Modrego (✉)
c/ Juan Carlos I, 21,
E-50009 Zaragoza, Spain

Abstract There have been few reports about the frequency of multiple sclerosis (MS) in Spain. We undertook a prevalence study in the province of Teruel, which is served by two hospitals as referral centres for a population of 143,680. We found a total of 46 patients who fulfilled Poser's criteria for clinically definite or probable MS with a prevalence rate of 32/100,000 [95% confidence interval (CI): 22.8–41.3]. The prevalence rates for males and females were 23.5 (95% CI: 12.3–34.7) and 40.6 (95% CI: 25.8–55.4) respectively. We found an incidence rate of 2.2/year per 100,000 in the last 5 years. The sex ratio (females/males) was 1.7. The mean age on prevalence day was 40.6 years (range: 15–76). The clinical course was relapsing-remitting in 82% of patients, progressive in 9% and secondary progressive in the other 9%. The mean EDSS score was 3.73 (range: 1–8.5). Our results confirm the hypothesis that Spain is an area at high risk for MS.

Key words Multiple sclerosis · Prevalence · Spain

Introduction

Multiple sclerosis (MS) is one of the most frequent neurological diseases in young adults and its prevalence depends on latitude as well as on environmental and genetic factors. Northern Europe, the northern United States, southern Canada, southern Australia and New Zealand are considered to be zones with high prevalence rates (> 25/100,000). Southern Europe has been regarded as a zone of medium prevalence (5–25/100,000) [8] but this is only partly true. Previous epidemiological studies revealed that the prevalence rate of MS in southern Europe is not as low as expected. A prevalence rate from 50 to 60/100,000 was found in Sicily [2, 3, 19, 20] and 59/100,000 in the Alghero district [17]. In Ferrara it was somewhat lower (46.1/100,000) [7]. In the past, several studies of prevalence have been conducted in Spain. In the Alcoy area (southern Spain) [11] the prevalence rate was 17/100,000 with significant variations in the different subareas. In Asturias (northern Spain) [22] it was 23/100,000. In other studies the prevalence was lower (5.6–15/100,000) [4, 6, 12, 21], but these studies were only based on hospital records. Three recent studies have yielded a high prevalence of MS in Spain, similar to that obtained in some countries of northern Europe. In Gijón (northern Spain) [23] the prevalence was 45/100,000; in Vélez-Málaga (southern Spain) [5] it was 53/100,000 and in the Osona area (northern Spain) [1] 58/100,000.

The aim of this study was to determine the prevalence rate of MS in the province of Teruel, where no previous work on this matter had been conducted.

Study population and methods

The province of Teruel is located in the east of Spain (39° 51′–41° 21′N and 3° 58′–1° 53′E longitude in relation to the meridian of Madrid) in the region of Aragón (Fig. 1). The mean temperature varies from 10° C to 17° C. From an ethnic viewpoint this region is heterogeneous since was successively occupied by Celtiberians (people of celtic origin), Romans, Visigoths (Germanic-type people from Central Europe) and Arabs. This province has a popula-

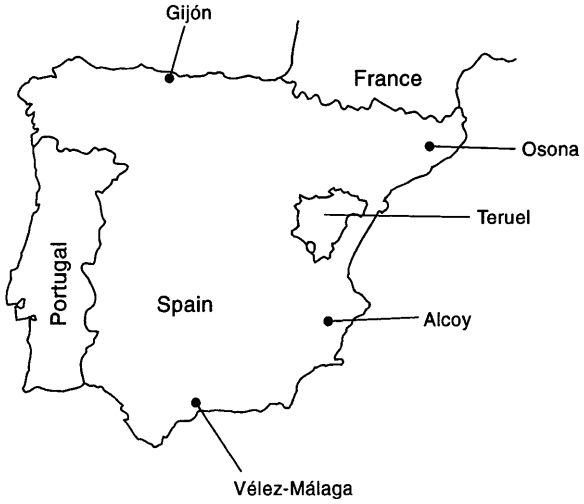

Fig. 1 This map shows the province of Teruel and the points where previous surveys have been conducted in Spain

tion of 143,680 (72,251 men and 71,429 women). This population may be defined as old according to the ageing index (AI = population > 65/total population × 100), that is 19.6. These data were obtained from an official published source (National Institute of Statistics 1991). In the last 10 years a very low migration rate has been observed. Most of the population is rural; only two towns have a population over 10,000. There is not much industry in the area. Farming, including cattle farming, is the most frequent occupation.

We have only two hospitals in the province (in Alcañiz and in Teruel) that serve this defined community almost as its only resources for secondary and tertiary health care. They operate a retrieval system, consisting essentially of personal trawl of records, that allows the collection and ascertainment of complete and accurate data. There are four neurologists in the province. Techniques of diagnosis, such as evoked potentials, computed tomography and magnetic resonance imaging (MRI), are available.

Given these conditions, we decided to undertake a prevalence study [10] in the two hospitals. The study was carried out from September 1994 to 1 March 1996. The latter date was chosen as the prevalence data. An intensive search was begun for all cases of patients with known or suspected MS. All records of patients with a diagnosis of MS, demyelinating disease, optic neuritis, encephalomyelitis and myelopathy were reviewed. The patients were examined by two independent neurologists. In almost all of them MRI was carried out. We included patients with definite or probable MS in accordance with the criteria of Poser et al. [16]

Besides our own registry, we consulted private neurologists, internists, physiotherapists, ophthalmologists and all health centres where family physicians are involved in detecting patients who might be suffering from MS.

We also examined the records of the biggest hospital of the Aragon region (Hospital Miguel Servet, Zaragoza) to detect possible cases among recently migrated patients and the records of the Spanish Multiple Sclerosis Society (AEDEM).

Once collection of data was completed, we calculated the point of prevalence on prevalence day, considering the surviving subjects with either definite or probable MS, and 95% confidence interval (CI) according to their Poisson distribution [10]. The age- and sex-specific prevalence rates were also calculated. Several days or weeks before the prevalence day all patients were ascertained to be alive either in our consultation or by telephone interview.

The incidence rate of MS was calculated in retrospective fashion by averaging the annual incidence rates of the last 5 years.

We used the EDSS [9] for assessing the degree of disability of the patients. The results are reported as mean, range, standard deviation and 95% CI.

Results

On prevalence day we found 43 patients with clinically definite MS and 3 with clinically probable MS. The crude prevalence of MS was 32/100,000 (95% CI: 22.8–41.3). Of these patients 17 were men and 29 women (females/males sex ratio: 1.7); the prevalence rate for men was 23.5 (95% CI: 12.3–34.7) and 40.6 (95% CI: 25.8–55.4) for women. In Table 1 the age- and sex-specific prevalence rates are shown. The approximate incidence rate was 2.2/year per 100,000 in the last 5 years.

The sources of detection of the patients were as follows: 38 patients were detected in our hospitals, 2 in the registry of the AEDEM, 1 in the records of another Aragon hospital and 5 were detected in collaboration with

Table 1 Age and sex-specific prevalence rates (*MS* multiple sclerosis, *M* men, *W* women)

Age (years)	Population			MS patients		Prevalence/100,000		
	M	W	Total	M	W	M	W	Total
< 15	11958	11280	23238	–	–	–	–	–
15–19	5079	4258	9337	–	1	–	23.4	10.7
20–24	4366	4455	8821	1	1	22.9	22.4	22.6
25–29	5239	4932	10168	2	5	38.1	101.3	68.8
30–34	5086	4301	9387	4	3	78.6	69.1	74.5
35–39	4543	4040	8583	1	5	22	123.7	69.9
40–44	4015	3570	7585	2	4	49.8	112	79.1
45–49	3644	3195	6839	2	4	54.8	125	87.7
50–54	3358	3682	7040	3	1	89.3	27.1	56.8
55–59	5056	4865	9921	–	–	–	–	–
60–64	5245	5182	10427	1	4	19	77.1	47.9
> 64	14662	17669	32331	1	1	6.8	5.6	6.1

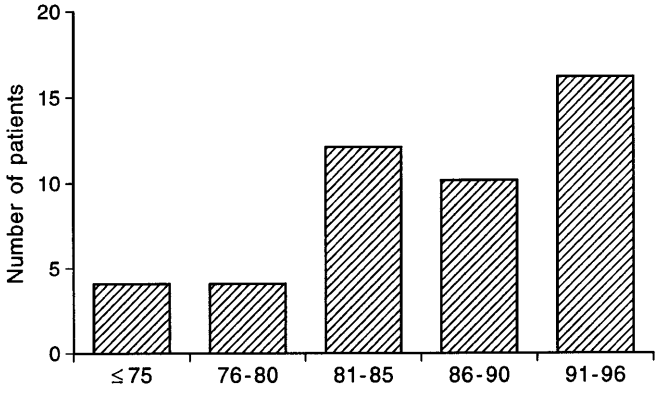

Fig. 2 Distribution per onset-year

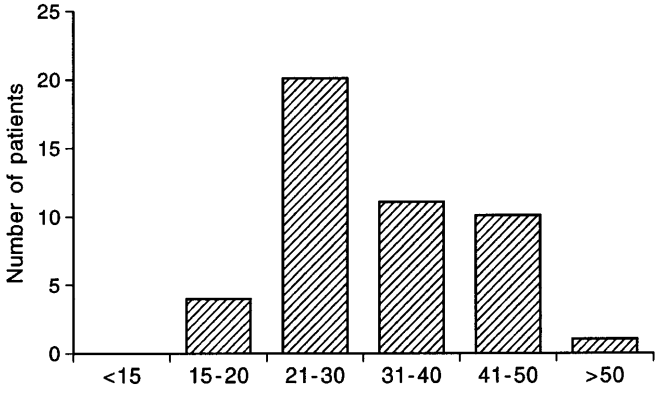

Fig. 3 Distribution by age at onset

general practitioners (3 patients diagnosed elsewhere and 2 patients previously not diagnosed).

The mean age of the patients on prevalence day was 40.6 years (range: 15–76) and the mean age of onset of the disease was 30.5 years (range: 15–55). Figure 2 shows the distribution per year of first symptoms, considering those patients alive on the prevalence day. Figure 3 shows the distribution of ages at onset of disease and a unimodal distribution with the highest peak between 21 and 30 years. The mean time interval between the first symptom and diagnosis was 3.6 years (range: <1–16).

The clinical course of 38 cases (82%) was relapsing-remitting, of 4 (9%) relapsing-progressive and of 4 (9%) chronic progressive since the onset. The most frequent symptoms at onset were weakness in one limb or more (motor pyramidal dysfunction) in 21 patients, diplopia (brain stem dysfunction) in 9 patients, sensory symptoms such as paraesthesia or pain in 8, optic neuritis in 4, vertigo in 3 and ataxia in 1. The mean degree of disability on the EDSS was 3.73 points (range: 1–8.5; SD: 2.5; 95% CI: 2.68–4.78). The mean EDSS for men was 3.9 (range: 1–8; SD: 2.88) and for women 3.5 (range: 1–8; SD: 2.48). According to this scale, 18% of patients were severely disabled, 22% moderately disabled and 60% slightly or not disabled). The highest degrees of disability were observed in patients with progressive forms and in the oldest patients. The major cause of disability was spastic paraparesis.

MRI was carried out in all patients but one and revealed multiple white matter plaques in all of them.

No familial occurrence was found in our survey.

Discussion

Multiple sclerosis has an unequal geographical distribution; the higher the degree of latitude, the higher the prevalence. However, genetic and environmental factors also play an important role in the aetiology and this is confirmed by the examples of Japan and Malta. Britain and Japan are located at similar degrees of latitude but their prevalence rates are extreme (the mean prevalence in Japan [15] is 2.1/100,000 in comparison with 144 in Aberdeen [14] and 112 in Cambridge [13]. The same phenomenon occurs in Sicily and Malta [24] with prevalence rates of 50–60 and 4.2 per 100,000 respectively, only 100 km away from each other.

The prevalence rate obtained in our province is not as high as those found in Gijon, Vélez-Málaga and Osona, but if we compare the CI of prevalence, the differences are not as large. The CI in these studies were 25–74 in Gijon [23], 32–83 in Velez-Malaga [5] and 40–75 in Osona [1]. Furthermore, the confidence limits of the prevalence rates were larger than those obtained in our study (22–41), essentially because of the smaller populations of the respective studies. The same occurs when we compare our prevalence rate with those obtained in Sicily: 32 (18–47) in Agrigento [3], 51 (35–72) in Caltanissetta [20] and 59 (43–78) in Alghero [17]. Our population is one of the oldest populations in Spain and this may influence the frequency of the disease, but the specific prevalence of MS in young people is also lower than in Osona or Vélez-Málaga. However, the present survey supports the hypothesis that Spain is a country with a high prevalence of MS, and not a medium prevalence as had previously been reported.

Some authors, such as Fernández et al. [23], believe that the ideal population size for conducting a prevalence study varies between 30,000 and 60,000. In this instance, the search for and detection of patients is less difficult than in larger populations and the chance of missing patients is lower, but then we face the errors resulting from the small numbers and the measured rates may be imprecise [1] and the generalization from the data must be considered with caution.

Since the ethnic composition has changed very little in the last two centuries, many other factors may have contributed to the increase in the prevalence rate of MS in southern Europe: the longer survival of patients, incorporation of high-quality diagnostic techniques, better registries,

intensive searches, health care access for the whole population by means of social security, implementation of funding for investigation and scientific level improvement.

We acknowledge the possible shortcomings of our study as there may be patients who have a benign course and therefore may never have consulted a physician. An additional and unresolved problem in the epidemiology of MS is the existence of a variable number of patients with possible MS or isolated optic neuritis who do not fulfil the criteria of the disease. As long as we do not have specific and sensitive enough diagnostic criteria for MS, we shall not be able to include these patients as prevalent or incident cases. Such limitations may result in underestimated rates, so the information provided by the CI is essential. On the other hand, the inclusion of patients with possible MS may result in overestimated rates. The demographic characteristics of our patients, such as mean age on prevalence day, sex ratio, age at onset and disease duration, do not differ very much from those found in the other Spanish surveys or in European surveys. The phenotype of our patients does not seem to be different from that found in previous reports; the mean score of EDSS was 3.73 in comparison to 4 in Osona and 3.7 in Vélez-Málaga. The survey of Ferrara [7] did not report details in EDSS scores but stated that 34.7% of the patients required partial or complete assistance. A recently published survey in Sardinia [23] revealed a similar distribution of disability with 18% of patients needing partial or complete assistance. A large number of surveys do not include the EDSS data in the results.

On the basis of the available data, we cannot yet support the hypothesis that there is a latitudinal gradient of MS in Spain. Nevertheless, we cannot rule out this suggestion until new comprehensive surveys are conducted. A multicentre comparative assessment would be very interesting.

Acknowledgements We thank the patients and general practitioners for their collaboration in the study. We are also grateful to AEDEM for allowing us access to its registry.

References

1. Bufill E, Blesa R, Galán I, Dean G (1995) Prevalence of multiple sclerosis in the region of Osona, Catalonia, northern Spain. J Neurol Neurosurg Psychiatry 58:577–581
2. Dean G, Grimaldi G, Kelly R, Karhausen L (1979) Multiple sclerosis in southern Europe I: prevalence in Sicily in 1975. J Epidemiol Community Health 33:107–110
3. Dean G, Savettieri G, Giordano D, et al (1981) The prevalence of multiple sclerosis in Sicily. II. Agrigento City. J Epidemiol Community Health 35: 118–122
4. Fernández O, Izquierdo G, Campos VM, Pastor M (1986) Epidemiología de la esclerosis múltiple en la provincia de Málaga (España). Un estudio de prevalencia. Neurología 1:3–11
5. Fernández O, Luque G, Bravo M, San Roman C, Bravo M, Dean G (1994) The prevalence of multiple sclerosis in the sanitary district of Vélez-Málaga, southern Spain. Neurology 44:425–429
6. García JR, Rodriguez S, Sosa Henriquez M, et al (1989) Prevalence of multiple sclerosis in Lanzarote (Canary Islands). Neurology 39:265–267
7. Granieri E, Tola R, Paolino E, Rosati G, Carreras M, Monetti C (1985) The frequency of multiple sclerosis in Italy: a descriptive study in Ferrara. Ann Neurol 17:80–84
8. Kurtzke JF (1980) Epidemiologic contributions to multiple sclerosis. An overview. Neurology 30:61–79
9. Kurtzke JF (1983) Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 33:1444–1452
10. Kurtzke JF (1984) Neuroepidemiology. Ann Neurol 16:265–277
11. Matias Guiu J, Bolumar F, Martin R, et al (1990) Multiple sclerosis in Spain: an epidemiological study of the Alcoy health region, Valencia. Acta Neurol Scand 8:479–483
12. Miro J, Rebollo M, Combarros O, Polo JM, Leno C, Berciano J (1984) Esclerosis múltiple en Cantabria. Estudio retrospectivo de 30 casos. Rev Clin Esp 175:153–156
13. Mumford CJ, Fraser MB, Wood NW, Compston DAS (1992) Multiple sclerosis in the Cambridge health district of East Anglia. J Neurol Neurosurg Psychiatry 55:877–882
14. Phadke JG, Downie AW (1987) Epidemiology of multiple sclerosis in the north-east of Scotland, an update. J Epidemiol Community Health 41:5–13
15. Poser CM (1994) The epidemiology of multiple sclerosis: a general overview. Ann Neurol 36 (s2):180–193
16. Poser CM, Paty DW, Scheinberg L, et al (1983) New diagnostic criteria for multiple sclerosis: guidelines for research protocols. Ann Neurol 13:227–231
17. Rosati G, Aiello I, Pirastru MI, et al (1987) Sardinia, a high risk area for multiple sclerosis: a prevalence and incidence study in the district of Alghero. Ann Neurol 21:190–194
18. Rosati G, Aiello I, Pirastru MI, et al (1996) Epidemiology of multiple sclerosis in northwestern Sardinia: further evidence for higher frequency in Sardinians compared to other Italians. Neuroepidemiology 15:10–19
19. Savettieri G, Daricello B, Giordano D, Karhausen L, Dean G (1981) The prevalence of multiple sclerosis in Sicily. I. Monreale City. J Epidemiol Community Health 35:114–117
20. Savettieri G, Elian M, Giordano D, Grimaldi G, Ventura A, Dean G (1986) A further study on the prevalence of multiple sclerosis in Sicily. Caltanissetta City. Acta Neurol Scand 73:71–75
21. Sosa M, Betancor P, Rosas C, Navarro MC (1983) La esclerosis múltiple en la provincia de Las Palmas. Arch Neurobiol (Madrid) 46:161–166
22. Uría DF, Virgala P, Alonso P, Crespo JR, Calatayud T, Arribas JM (1991) Epidemiología de la esclerosis múltiple en Asturias. Neurología 6:41–45
23. Uria DF, Abad P, Virgala P, Calatayud MT (1994) Prevalence and incidence of multiple sclerosis in Gijón, northern Spain. In: Firnhaber W, Lauer K (eds) Multiple sclerosis in Europe: an epidemiological update. Leuchtturm/LTV Press, Darmstadt pp 179–183
24. Vassallo L, Elian M, Dean G (1979) Multiple sclerosis in southern Europe. II. Prevalence in Malta in 1978. J Epidemiol Community Health 32(2):111–113