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ORIGINAL COMMUNICATION

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Prevalence of multiple sclerosis in Valladolid, northern Spain

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Abstract The aim of this study was to ascertain the prevalence of multiple sclerosis (MS) in a northern Spanish region and to compare it with that from the most recent epidemiological studies in the country. MS prevalence was studied for a period of 2 years using multiple sources of information in the province of Valladolid, with a sample comprising a total population of 92,632. Patients were classified according to the Poser criteria. The crude prevalence of definite and probable MS was 58.3 per 100,000 (95% confidence interval: 43.7–75.7). The same methods have been used in ascertaining similar prevalence rates in Vélez-Málaga, Osona, and Gijón and a slightly lower rate in Teruel. Our survey confirms Spain as a high-risk area for MS, with prevalence rates over 50 per 100,000.

Key words Multiple sclerosis · Prevalence · Spain

Introduction

Surveys on the prevalence of multiple sclerosis (MS) carried out in large populations in Spain before 1992 used various diagnostic criteria and were based almost exclusively on hospital records [1, 2, 6, 8, 14, 16, 18, 25, 28, 29]. These studies defined Spain as an area of low to medium risk for MS, according to Kurtzke [12]. Using every reasonable information source available for populations under 100,000, prevalence rates between 32 and 65 per 100,000 in northern and southern Spain have been obtained [3, 7, 17, 30]. Dean and Middleton used the same methods and reported similar figures for Sicily and Cyprus, at a latitude similar to that of Spain, [4, 15, 26].

Except for a previous survey in Salamanca and Zamora [25], there are no recent data on the frequency of MS in our region, located 200 km north of Madrid. Nevertheless, the number of followed-up patients in our health area suggested the prevalence of MS here to be similar to that recently reported for the north and south of our country.

Study population and methods

The area investigated includes six health zones, each of with its own health center and with a single outpatient clinic of specialties run by the Neurology Department of the Hospital Universitario of Valladolid. These six areas are within the city of Valladolid and comprise a total area of 197 km^2 (41°39′N–4°44′W) and a population of 92,632 (November 1996). The region has a continental climate with a mean temperature of 12.4° C. Its average altitude is 698 m above sea level (Fig. 1). Economic activity is fundamentally industrial, largely car and machinery manufacturing, and services. The population level in Valladolid is stable, having increased only slightly over the past 15 years. There is a high racial uniformity and migratory movements are rare.

The survey was carried out over a 2-year period from September 1995 to August 1997. The day of 1 March 1997 was chosen as the prevalence day since this was the date when all the patients began to be checked for the second time to confirm they were still alive and living in the area. Poser's classification of MS was used, and only those persons with probable or definite MS were included

[22]. Disability was assessed using the Expanded Disability Status Scale (EDSS) of Kurtzke [10]. A disability of 0–3 was considered mild disability, 4–6 moderate disability, and 7–9.5 severe disability. A progression index was defined as the ratio of the disability status (EDSS) to the duration of the disease in years [21]. The type of progression was defined according to the consensus criteria established by Lublin et al. [13]. The onset of MS was determined by interviewing patients and reviewing their medical records, and the classification of definite and probable signs and symptoms of MS proposed by Poser was used [19].

Multiple methods for case ascertainment were used. Records of both Valladolid hospitals (Hospital Universitario and Hospital Universitario del Río-Hortega), data from the Neurology Service of the Hospital Universitario and the records from outpatient clinics of specialties were reviewed, searching for the code number 340 (MS). Further information was obtained from 41 general practitioners in the area by periodically interviewing medical coordinators from each one of the six health zones. Other sources of information included private neurologists (4), internists (14), records of evoked potential studies in Hospital Universitario, a home hospitalization unit, welfare workers, and the local MS patient association. Information from the city's two units of magnetic resonance imaging (MRI) could not be obtained as their files were not on a data base. Searching for nonidentified patients, two symposia for relatives and patients were held and reported by the public media.

All possible MS patients were examined by two neurologists. A second examination was carried out by the same physician in all cases. MS had to be confirmed by both physicians for the diagnosis to be accepted.

Adjusted prevalence rates were calculated by the direct method [11] using 5-year groupings, with the total Spanish population (1991 census) as a standard. Confidence intervals (95%) were computed assuming the Poisson distribution [27]. The chi-square test was used to analyze the homogeneity in the distribution of patients over the six health zones [9]. The survey was reviewed by the Hospital Universitario of Valladolid Research Committee and by the Board of the ONCE Foundation for the cooperation and social integration of the disabled.

Results

After an intensive search, 54 definite or probable MS patients were ascertained, all alive and living in the area on 1 March 1997 (18 men and 36 women). Fifty-one patients had definite MS (18 men and 33 women), including 4 with laboratory-confirmed MS. Three women had clinically probable MS. The crude prevalence rate found in the area was 58.3 per 100,000 (95% CI: 43.7–75.7). The prevalence for clinically definite MS alone was 55.1 per 100,000. Age- and sex-specific prevalence rates are shown in Table 1. The distribution of cases within the study area, analyzed according to the six health zones, was uniform (chi-square = 7.2; d.f. = 5; $P = 0.2$). Crude prevalences and age- and sex-adjusted prevalence rates of the 1991 Spanish population in the most recent epidemiological studies carried out in Spain are shown in Table 2.

Forty-five patients were visited or admitted to hospital during the study. Five patients were identified by hospital records. One patient was being visited by a private neurologist and another patient by an internist. The collabora-

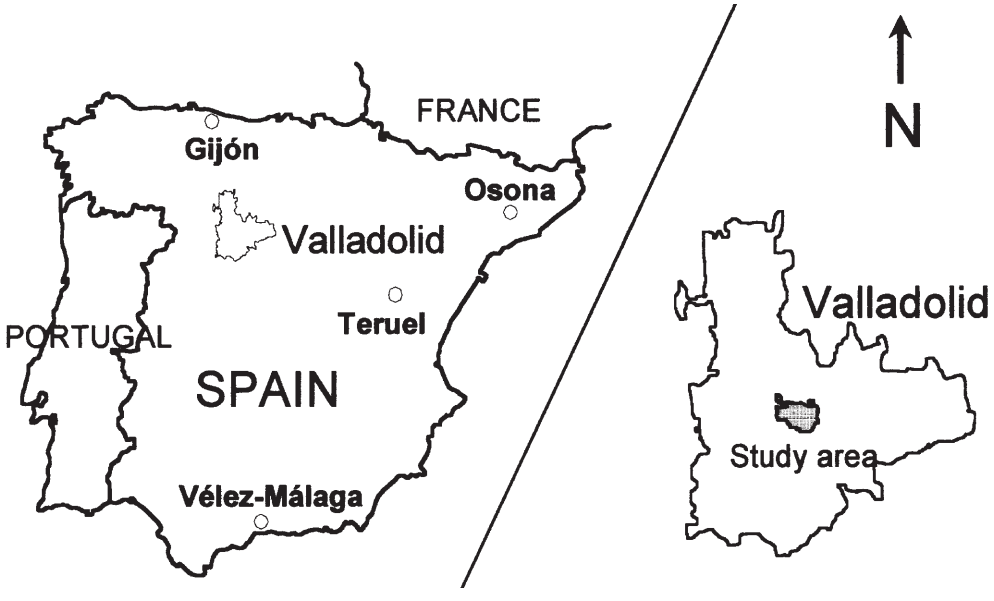

Fig. 1 Map of Spain, with the province of Valladolid (*left*) and the study area (*right*). The areas of Gijón, Osona, Teruel, and Vélez-Málaga are also shown

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	Total	M	W	Total
≤ 19	9,044	8,822	17,866	2	2	4	22.1	22.7	22.4
20–29	9,412	9,579	18,991	6	12	18	63.7	125.3	94.8
30–39	6,067	6,580	12,647	2	12	14	33	182.4	110.7
40–49	6,014	6,844	12,858	3	5	8	49.9	73.1	62.2
50–59	5,794	5,899	11,693	5	4	9	86.3	67.8	77
≥ 60	7,921	10,656	18,577	–	1	1	–	9.4	5.4
All	44,252	48,380	92,632	18	36	54	40.7	74.4	58.3

Table 2 Comparison of the most recent prevalence studies in Spain (*MS* multiple sclerosis, *CI* confidence interval)

	Population	MS patients	Crude prevalence [CI 95%][a]	Age- and sex-adjusted prevalence[b]
Vélez-Málaga [7]	36,014	19	52 [31.7–82.2]	61
Osona [3]	71,985	42	58 [42.0–78.7]	60
Gijón [30]	33,775	22	65 [40.8–98.3]	59
Teruel [17]	143,680	46	32 [22.8–41.3]	35
Valladolid	92,632	54	58 [43.7–75.7]	53

[a] Crude prevalence per 100,000 population
[b] Age- and sex-adjusted prevalence per 100,000 in the 1991 Spanish population

tion of the local MS patient association allowed us to find one patient not identified by other methods. A general practitioner reported the case of a woman suffering from MS for 24 years who had not been visited by a neurologist for the past 10 years. The remaining methods for case ascertainment detected no patient not already known by the local neurologists.

Mean age at onset was 27.3 years (men 28.7, women 26.6) and mean age on the prevalence day was 36.1 years (men 37.6, women 35.3). The mean period between the first symptom and the prevalence day was 8.7 years (men 8.8; women 8.6). The mean diagnostic delay was 3 years (range 0–23). Sensory symptoms were the most common at onset (55%), followed by pyramidal tract symptoms (49%), brainstem symptoms (31%), cerebellar symptoms (24%), and optic neuritis (14%).

Cranial MRI was performed in all patients except three, with abnormal results in 98%. In addition, the results of 32% of spinal MRI studies were also abnormal.

The median and interquartile EDSS range in clinically definite patients was 3.0 [1.5–5.0; men 3.5 (1.5–5.6), women 2.5 (1.0–4.3)]. The mean EDSS score was 3.4. The mean progression index was 0.4. Among these patients 58% were only slightly or not disabled (EDSS ≤ 3.0), and 13% were severely disabled (EDSS ≥ 7.0). Nine patients were alive after 15 years of the disease; one had low disability, four moderate, and four severe.

The clinical course was relapsing-remitting in 37 patients (68%; 11 men, 26 women), primary-progressive in 11 (20%; 4 men, 7 women), and 6 patients with an initial relapsing-remitting evolution had developed a secondary progressive clinical course (3 men, 3 women).

Thirty-four patients were born in Valladolid (63%), ten in adjacent provinces (18%), and the rest in other places in Spain, except two patients born in France and Switzerland, respectively. A family history of MS were found in two women.

Nine patients were excluded from the survey because they had been misdiagnosed. Two of these had a cervical spondylotic myelopathy; one had an Arnold-Chiari malformation; three had hyperintense lesions on cranial MRI that according to their vascular risk factors, clinical course, and age was of ischemic origin; one was diagnosed as having Childer disease, though not confirmed by necropsy; one showed typical hyperintense lesions on cranial MRI although his symptoms were considered secondary to a large cervical disk herniation; and one suffered from hysteria.

Discussion

The results of our study, together with those obtained in other Spanish regions using a similar methodology [3, 7, 17, 30], confirm our country as a high risk area for MS, with prevalence rates between 50 and 60 per 100,000. We believe that only a single further study in southern Spain is needed to confirm the survey findings of Fernández et al. [6, 7] in Málaga.

Comparison of adjusted prevalence rates to Spanish populations, except for the results of Modrego-Pardo et al. in Teruel [17], show few differences among the recent surveys carried out in Spain. The size of the study area, with a total population of 143,000 inhabitants, health-care dispersion, duration of the survey, and a high emigration rate can explain the prevalence rate in Teruel.

A number of features lend additional credence to the figures from our study. The study population has a high demographic stability and racial uniformity. The area has a good sanitary infrastructure, with well-developed health

services, and neurological care is focused in a single neurology department. Computerization of both hospital records and neurology service data made case ascertainment easier. Multiple sources of information as by Fernández et al. were used [5], allowing us to identify nine patients (16%) who were not being visited by local neurologists. If we had not used all these information sources, the prevalence figures would have been 48.6 instead of 58.3 per 100,000. Finally, the patient distribution in the studied area was homogeneous, showing easy and uniform access to neurological services.

It has been proposed as a measurement of the reliability of MS prevalence studies that the ratio of patients having a low degree of disability (EDSS ≤ 3.0) must be close to 70% [24]. This estimation has been carried out according to the concept of onset-adjusted prevalence rate proposed by Poser, after his experience on a survey in Iceland [23]. This measures the number of symptomatic MS patients (diagnosed or not) in an ethnically homogeneous population who live to the age of puberty in the same naturally defined geographical area [20]. This measurement requires case ascertainment to be extended at least 2 years after the prevalence date to increase the probability of diagnosing all the patients in the area. In our study, using the traditional concept of prevalence, the ratio of patients with low disability was 58%. This lower percentage suggests that there may be patients who have not consulted health services for their symptoms yet.

The mean age on the prevalence day (36.1 years), the mean duration of the disease (8.7 years), the reduced percentage of patients with a secondary progressive course, and the low number of patients older than 60 years suggest that there are some patients in the area who were not identified in this study. Our accumulated experience could clarify this point in a future survey.

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