Prevalence of multiple sclerosis in the L'Aquila district, central Italy

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Abstract

Objective—To estimate the prevalence of multiple sclerosis in the L'Aquila district, central Italy.

Methods—All available case sources were screened. Definite and probable cases of multiple sclerosis, classified according to the Poser criteria, were considered as prevalent cases.

Results—On the prevalence day, 31 December 1996, 158 patients (105 women and 53 men; ratio 2:1) affected by definite (n=131) or probable (n=27) multiple sclerosis were alive and resident in the L'Aquila district. Mean (SD) age was 38.4 (11.9) years (38.9 (11.7) years for women and 38.5 (12.3) years for men, $p=0.9$). The overall crude prevalence was 53.0/100 000 (95% confidence interval (95% CI)=45.4–62.0); 68.4/100 000 (95% CI=56.5–82.8) in women, and 36.7/100 000 (95% CI=28.1–48.0) in men. The prevalence was similar (55.9/100 000) when standardised to the 1996 European population. Mean (SD) age at onset of multiple sclerosis was 29.4 (9.6) years and mean (SD) duration of the disease was 9.4 (7.4) years, without any significant difference between sexes. Mean age at onset was significantly higher in patients with the primary progressive than in those with the relapsing-remitting course ($p=0.0002$, Scheffé's test).

Conclusions—The prevalence found in the L'Aquila district gives support to the consideration of Italy as an area in which multiple sclerosis has been shown to have high prevalence at least in the populations that were surveyed recently.

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Keywords: multiple sclerosis; epidemiology; prevalence; Italy

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Patients and methods

The L'Aquila district is located in central Italy between latitudes 41°41' and 42°31' N, and covers an area of 5 034.46 km² (figure). The district is divided into 108 towns and has wide availability of health services and easy access to hospitals. At the 1991 census, the total study population, 48% rural, was 297 838 (153 535 women and 144 303 men).¹³

Cases of multiple sclerosis were identified from all the available sources: clinical records of the departments of neurology; files of the neuroradiology services; records of the rehabilitation units; files of patients affiliated to the local section of the Italian Association for Multiple Sclerosis; records of the National Health Service; records of patients admitted within and out of the district; and general practitioners. To avoid the exclusion of patients with long latency between disease onset and diagnosis, all sources were continuously monitored after the prevalence day. Data on patients diagnosed with multiple sclerosis, or having clinical signs and symptoms of optic neuritis, myelopathy, and spastic paraparesis, were also reviewed. When the diagnosis was not fully supported by medical records, patients were asked to undergo further examinations. Date of onset, defined as the time of the first appearance of neurological signs and symptoms attributable to the disease, was obtained from the medical records or directly from the patient. All definite and probable cases of multiple sclerosis classified according to the Poser criteria¹⁴ were accepted as prevalent cases. Clinical course was defined as relapsing-remitting, primary progressive, or secondary progressive.¹⁵ Disability was coded by the expanded disability status scale (EDSS)¹⁶ and the European data base for multiple sclerosis (EDMUS) impairment scale (EIS).¹⁷ All data were recorded on the EDMUS data base.^{17 18}

Prevalence was computed considering all the alive patients with multiple sclerosis who were resident in the L'Aquila district on the prevalence day of 31 December 1996. Crude prevalence rates together with 95% confidence intervals (95% CIs) for single binomial proportions were calculated by the exact approach.¹⁹ Standardised prevalence rates were obtained by the direct method using 10 year age grouping of the 1996 European population as standard.²⁰ The expected number of patients missed by all the case finding sources was estimated by an extrapolation of the capture-recapture technique, using a log linear model which included all the inpatient and outpatient sources, together with their second order interaction terms.²¹ Analysis of variance was used to

In Europe, epidemiological data on multiple sclerosis showed increasing frequency at increasing latitudes.^{1 2} Variations in frequency within areas located at the same latitude were also reported.^{3 4} In Italy, previous epidemiological studies showed a low prevalence of multiple sclerosis, ranging between 4 and 21 cases per 100 000,⁵ whereas more recent studies found values between 39 and 102 cases per 100 000 in different areas.^{5–12} All these studies were performed in northern and insular Italy, whereas no relevant large scale studies were conducted in central Italy.

To obtain reliable data on the impact of multiple sclerosis, we evaluated the prevalence of the disease in the L'Aquila district.

District of L'Aquila, central Italy.

compare continuous variables among groups. Multiple comparisons among subgroups were performed by the Scheffé's test. Two sided values of $p < 0.05$ were considered to indicate significance. All the data were analysed with SPSS software.

Results

A total of 158 patients with multiple sclerosis were alive and resident in the L'Aquila district on 31 December 1996. The provisional registry included 244 patients. Eighty six patients were excluded from the registry because of residency out of the district ($n=75$), diagnosis other than multiple sclerosis ($n=7$), or death occurring before the prevalence day ($n=4$). Seven patients (4.4%), who were diagnosed as having multiple sclerosis after the

prevalence day, were also included into the study because the onset of the disease, after meticulous ascertainment, was found to have occurred previously (median 7 months). One hundred and twenty four patients (78.5%) were identified from the neuroradiology services, 114 (72.1%) from the departments of neurology, 87 (55.1%) from the general practitioners, 39 (24.7%) from the rehabilitation units, 25 (15.8%) from the local section of the Italian Association for Multiple Sclerosis, 22 (13.9%) from neurological departments out of the district, and 12 (7.6%) from the Social Insurance Service (Istituto Nazionale della Previdenza Sociale). One hundred and twenty five patients (79.1%) were identified by more than one source. Four patients (2.5%) were estimated to be missed by the capture-recapture technique.

The overall crude prevalence was 53.0/100 000 (95% CI 45.4–62.0); 68.4/100 000 (95% CI 56.5–82.8) in women and 36.7/100 000 (95% CI 28.1–48.0) in men. Age and sex specific prevalence are reported in table 1. Prevalence was similar (55.9/100 000), when standardised for age and sex to the European population.

One hundred and five patients were women and 53 were men (ratio 2:1). Mean (SD) age was 38.4 (11.9) years (range, 12 to 73 years), without any significant difference ($p=0.9$) between women (38.9 (11.7) years) and men (38.5 (12.3) years). Mean (SD) age at onset of multiple sclerosis was 29.4 (9.6) years (range 7 to 57 years), again without any significant difference ($p=0.7$) between sexes (29.6 (10.1) years in women and 29.1 (8.9) years in men). The overall mean (SD) duration of the disease was 9.4 (7.4) years (range 0 to 33 years), 9.1 (7.1) years in women and 9.8 (8.2) years in men.

One hundred and thirty one patients (83%) were affected by definite multiple sclerosis and 27 (17.0%) by probable multiple sclerosis. The clinical course of the disease was relapsing-remitting in 118 patients (74.7%), secondary progressive in 29 (18.3%), and primary progressive in 11 (7.0%). Mean (SD) age at onset was 27.7 (8.3) years in patients with the relapsing-remitting course, 32.8 (10.3) years in patients with the secondary progressive course, and 38.2 (14.3) years in patients with the primary progressive course. Mean age at onset was significantly higher in patients with the primary progressive than in those with the relapsing-remitting course ($p=0.0002$, Scheffé's test). Symptoms at onset of the disease were fully

Table 1 Age and sex specific prevalence rates of multiple sclerosis in the L'Aquila district on the prevalence day (31 December 1996)

Age (y)	Men			Women			Total		
	No	Rate/10 ⁵	95% CI	No	Rate/10 ⁵	95% CI	No	Rate/10 ⁵	95% CI
0–14	1	4.0	0.7–22.9	1	4.2	0.7–23.9	2	4.1	1.1–15.1
15–24	7	33.1	16.0–68.3	7	33.9	16.4–69.9	14	33.5	19.9–56.2
25–34	15	68.2	41.3–112.5	38	173.7	126.6–238.3	53	120.8	92.4–158.0
35–44	11	53.0	29.6–94.8	33	164.8	117.4–231.4	44	107.9	80.4–144.8
45–54	15	94.4	57.2–155.6	14	87.3	52.0–146.5	29	90.8	63.2–130.4
55–64	2	12.0	3.3–43.8	10	51.8	28.1–95.3	12	33.4	19.1–58.3
65+	2	8.7	2.4–31.6	2	6.2	1.7–22.8	4	7.3	2.8–18.7
Total	53	36.7	28.1–48.0	105	68.4	56.5–82.8	158	53.0	45.4–62.0

Table 2 Prevalence of multiple sclerosis in Italy

Area	Year	Rate per 100000	95% CI	Diagnostic criteria
Valle d'Aosta ⁸	1985	38.4	28–51	a
Pordenone ²²	1987	51.5	34–75	b
Reggio Emilia and Modena ⁹	1990	39.4	34–46	c
Ferrara ⁶	1981	46.1	40–53	b
Ferrara ¹¹	1993	68.3	60–77	a
San Marino ²³	1982	51.6	26–92	b
Macerata ²⁴	1988	37.5	31–45	a
Ascoli Piceno ²⁴	1988	42.8	36–50	a
Pescara ²⁵	1990	21.5	15–26	a
Chieti ²⁵	1990	22.0	17–27	a
Northwestern Sardinia ¹⁰	1991	102.6	92–115	a
Caltanissetta ⁷	1986	51.1	35–72	a
Monreale ¹²	1991	72.4	43–113	a
Present study	1996	53.0	45–62	a

a=Poser *et al.*¹⁴ b=Allison and Millar,²⁶ c=McAlpine *et al.*²⁷

recalled and reported by 146 patients (92.4%). Motor symptoms were present in 63 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (51%) more than one symptom was reported. Median disability scores were 3.5 at the EDSS and 3.0 at the EIS; mean values were 3.9 at the EDSS and 3.7 at EIS.

Discussion

Our prevalence (53.3/100 000) was among the highest found in continental Italy (table 2) and was higher than that reported in studies conducted in the 1980s using different diagnostic criteria.^{6 7 9 22 23 28} Surveys using comparable methods of case ascertainment reported lower prevalence in the Valle d'Aosta region,⁸ Marche region,²⁴ and in the neighbouring districts of Pescara and Chieti.²⁵ A higher prevalence was found only in the repeated prevalence surveys conducted in Ferrara¹¹ and Monreale.¹²

Recent studies reported a higher prevalence in surveys performed in the past, supporting the consideration of an increase in prevalence of multiple sclerosis in the past decades. It is very difficult to decide if this increased prevalence represents a true change or only reflects improved case identification and ascertainment, considering differences in methodology among the surveys. Further studies may help to map the prevalence of multiple sclerosis in Italy and might disclose future changes in prevalence, but are unlikely to resolve the question of whether or not estimates obtained before the introduction of new improved diagnostic methods were lower because of lower levels of detection or also because of lower prevalence of multiple sclerosis at that time.

The wide range of the latency between onset of symptoms and diagnosis might have limited the inclusion of patients who were still undiagnosed on the prevalence day. The continuous monitoring of all the available sources thereafter, helped to reduce this bias. Nevertheless, despite measures that should have contributed to minimise this occurrence, a minority of our patients (4.4%) were diagnosed and included into the study after the prevalence day.

To avoid the exclusion of patients with multiple sclerosis who might have received medical care out of the district, we continuously monitored neighbouring hospitals. This additional

measure allowed the identification and inclusion of 13.9% of our patients. Consequently, the proportion of cases (2.5%) estimated to be missed by the capture-recapture technique was very low. Continuous clinical follow up and MRI contributed to the exclusion of patients with misdiagnosed disease who might have been included into the study. Finally, to avoid any related bias, we included only patients with definite and probable multiple sclerosis. Accordingly, the proportion of patients with probable multiple sclerosis (17%) was within the range reported by other surveys (10.8 to 37.4%).^{11 29–32}

Our women to men ratio of 2:1 confirmed the well known higher occurrence of the disease in women.^{6 11 29–32} As suggested by previous studies, mean age on the prevalence day, mean age at onset, and duration of the disease did not differ between sexes.^{6 11 12 21 32} Mean age on the prevalence day (38.4 years) and mean duration of the disease (9.4 years) in our patients were in agreement with data reported in some studies^{7 21 33} and lower than in others.^{9 11 12 29 31 32} This difference might have depended on the exclusion of some patients with a remote occurrence of symptoms of multiple sclerosis. In fact, before the introduction of MRI to screen patients with multiple sclerosis, the possibility of diagnosing the disease in the presence of a very benign course was unlikely. It is also recognised that patients with a benign course did not often seek medical advice. Moreover, mean age on the prevalence day and duration of the disease is reported to increase when surveys were replicated in the same area.^{6 7 11 12}

We confirmed the significantly higher mean age at onset in patients with the primary progressive than in those with the relapsing-remitting course^{11 15 34} in the presence of widely reported differences.^{34–36} Whether these differences were so important to suggest different diseases or represented different aspects of the same disease remains to be clarified.³⁶ Among our patients there was a predominance of motor and sensory disturbances with respect to optic neuritis and brainstem symptoms at onset, as already reported by others.^{15 29}

Our findings support the consideration of Italy as an area in which multiple sclerosis has a high prevalence, in agreement with the geographical zonal division in high, medium, and low frequency.² However, it is worth mentioning that recently reported estimates from North America and Europe >100/100 000 might alternatively suggest considering Italy as a medium prevalence zone.³⁷

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