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

Rocco Totaro, Carmine Marini, Agostino Cialfi, Mario Giunta, Antonio Carolei

Abstract
Objective—To estimate the prevalence of multiple sclerosis in the L’Aquila district, central Italy.
Methods—All available case sources were screened. Defined 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 course (p=0.0002, Scheffe’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.

Key words: multiple sclerosis; epidemiology; prevalence; Italy

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 (153 335 women and 144 303 men).

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 criteria were accepted as prevalent cases. Clinical course was defined as relapsing-remitting, primary progressive, or secondary progressive. Disability was coded by the expanded disability status scale (EDSS) and the European data base for multiple sclerosis (EDMUS) impairment scale (EIS). All data were recorded on the EDMUS data base.

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. Standardised prevalence rates were obtained by the direct method using 10 year age grouping of the 1996 European population as standard. 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. Analysis of variance was used to...
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>
<thead>
<tr>
<th>Age (y)</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–14</td>
<td>1</td>
<td>0.0</td>
<td>2</td>
</tr>
<tr>
<td>15–24</td>
<td>7</td>
<td>0.0</td>
<td>14</td>
</tr>
<tr>
<td>25–34</td>
<td>15</td>
<td>0.0</td>
<td>30</td>
</tr>
<tr>
<td>35–44</td>
<td>11</td>
<td>0.0</td>
<td>22</td>
</tr>
<tr>
<td>45–54</td>
<td>15</td>
<td>0.0</td>
<td>30</td>
</tr>
<tr>
<td>55–64</td>
<td>2</td>
<td>0.0</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>53</td>
<td>36.7</td>
<td>158</td>
</tr>
</tbody>
</table>

Table 1 Age and sex specific prevalence rates of multiple sclerosis in the L’Aquila district on the prevalence day (31 December 1996)
Table 2 Prevalence of multiple sclerosis in Italy

<table>
<thead>
<tr>
<th>Area</th>
<th>Year</th>
<th>Rate per 100000</th>
<th>95% CI</th>
<th>Diagnostic criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valle d’Aosta</td>
<td>1985</td>
<td>38.4</td>
<td>28–51</td>
<td>a</td>
</tr>
<tr>
<td>Pordenone</td>
<td>1987</td>
<td>51.5</td>
<td>34–75</td>
<td>b</td>
</tr>
<tr>
<td>Reggio Emilia and Modena</td>
<td>1990</td>
<td>39.4</td>
<td>34–45</td>
<td>c</td>
</tr>
<tr>
<td>Ferrara</td>
<td>1991</td>
<td>46.1</td>
<td>40–53</td>
<td>b</td>
</tr>
<tr>
<td>Ferrara</td>
<td>1993</td>
<td>68.3</td>
<td>60–77</td>
<td>a</td>
</tr>
<tr>
<td>San Marino</td>
<td>1982</td>
<td>51.6</td>
<td>26–92</td>
<td>b</td>
</tr>
<tr>
<td>Macerata</td>
<td>1988</td>
<td>37.5</td>
<td>31–45</td>
<td>a</td>
</tr>
<tr>
<td>Ascoli Piceno</td>
<td>1988</td>
<td>42.8</td>
<td>36–50</td>
<td>a</td>
</tr>
<tr>
<td>Pescara</td>
<td>1990</td>
<td>21.5</td>
<td>15–26</td>
<td>a</td>
</tr>
<tr>
<td>Chieti</td>
<td>1990</td>
<td>22.0</td>
<td>17–27</td>
<td>a</td>
</tr>
<tr>
<td>Northwestern Sardinia</td>
<td>1991</td>
<td>102.6</td>
<td>92–115</td>
<td>a</td>
</tr>
<tr>
<td>Caltanissetta</td>
<td>1986</td>
<td>51.1</td>
<td>35–72</td>
<td>a</td>
</tr>
<tr>
<td>Monreale</td>
<td>1991</td>
<td>72.4</td>
<td>43–113</td>
<td>a</td>
</tr>
<tr>
<td>Present study</td>
<td>1996</td>
<td>53.0</td>
<td>45–62</td>
<td>a</td>
</tr>
</tbody>
</table>

We confirmed the significantly higher mean age at onset in patients with the primary progressive type compared to those with the relapsing-remitting type. In the presence of widely reported differences in sex ratios, whether these differences were so important to suggest different diseases or represented different aspects of the same disease remains to be clarified. 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. 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. 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. This study was supported in part by a grant from the Istituto Superiore di Sanità—Secondo progetto di ricerca sulla Sclerosi Multipla (96/J/T42). We thank Professor Christian Confavreux for his helpful comments and Professor Domenico Gambi and Doctor Carlo Pozzilli for their contribution to the identification of patients.


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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 (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%). In 81 patients (43.1%), sensory in 62 (42.4%), brainstem in 36 (24.6%), and optic in 28 (19.2%).
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