Multiple sclerosis in the province of Ferrara, Italy, in 2004-13: the Emilia Romagna Multiple Sclerosis Registry (ERMes)

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Introduction and Objectives

Epidemiological studies on MS are important in explaining clinical course and to going insight to disease’s pathogenesis. The epidemiological studies of the last 40 years indicate that the multiple sclerosis (MS) distribution in Mediterranean countries, and in Italy in particular, is complex, particularly for incidence, and the Kurtke’s latitude-related model is not widely accepted [1-7]. Recent reports confirmed that MS incidence rate in southern Europe seems uneven, also within countries and in time [1-10]. An apparent increasing trend appears stable in the last two decades in several reports and in long surveys conducted in the same areas, both in Italy and other Mediterranean countries [1-4, 8, 13]. The province of Ferrara, Region of Emilia Romagna, northern Italy, is a high risk area for MS, with increasing temporal trends (1.4).

However, due to large differences in the methods and diagnostic criteria used in past MS epidemiological studies it is hard to make comparisons across studies and it directly supports the relevance of an apparently increasing temporal trend reported from the same areas [5-9]. Some authors have related this trend to only an increase in the number of diagnoses of MS in the absence of biological evidences. Therefore it is not clear whether the increase indicates a change in incidence and prevalence, or reflects improved case identification and ascertainment [9,10].

We sought to update incidence of MS in this province [1-4].

Materials and Methods

We conducted a community-based intensive incidence study, by adopting a complete enumeration approach. Incidence patients were drawn from a community-based prospective multi-source registry implemented by the MS Centre of Ferrara. The Province of Ferrara, situated in northeastern Italy between 44°32’ and 44°58’ north and between 10°13’ and 11°14’ east, has a temperate climate. The area is known to have been inhabited since the Paleolithic period. According with HLA gene frequencies, the Ferrarese people are typically of Caucasian phlegmatic root. The standards of living and medical care are high. We included MS patients diagnosed according to the McDonald’s diagnostic criteria, with disease onset in the study area, between 2004 and 2013 [15]. The mean study population for the incidence period was 355,905 (170,279 men and 185,626 women), 349,777 in 2004 and 355,334 in 2013 and served as denominator for the incidence estimation. Crude mean annual incidence rates (per 100,000) were computed based on the number of new MS cases by each clinical onset as numerator. These rates were standardized to the 2009 European Population by direct method. 95% confidence interval (95% CI) was calculated assuming a Poisson distribution [14].

Table 1. Age- and sex-specific incidence rates of MS (per 100,000) in the province of Ferrara, Italy, 2004-13.

<table>
<thead>
<tr>
<th>Age</th>
<th>0-19</th>
<th>20-24</th>
<th>25-29</th>
<th>30-34</th>
<th>35-39</th>
<th>40-44</th>
<th>45-49</th>
<th>50-54</th>
<th>55-59</th>
<th>60-64</th>
<th>65-69</th>
<th>70-74</th>
<th>75+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>6.22</td>
<td>12.98</td>
<td>21.08</td>
<td>38.71</td>
<td>29.33</td>
<td>19.66</td>
<td>13.73</td>
<td>10.11</td>
<td>8.57</td>
<td>7.58</td>
<td>6.54</td>
<td>4.09</td>
<td>0.17</td>
</tr>
<tr>
<td>Women</td>
<td>10.50</td>
<td>22.64</td>
<td>30.35</td>
<td>56.34</td>
<td>46.90</td>
<td>28.78</td>
<td>19.12</td>
<td>15.40</td>
<td>14.82</td>
<td>12.71</td>
<td>10.49</td>
<td>6.29</td>
<td>0.43</td>
</tr>
</tbody>
</table>

The increasing incidence documented in the last decades in Italy and other European areas, highlights the importance of environmental factors related to lifestyle [7]. We confirmed, with respect to the previous study, the mean age at onset. Like our survey, the majority of the incidence studies on MS in Caucasian populations indicate that the distribution of incidence of the disease according to age peaks in the age groups between 25 and 40 years [8, 11]. The mean lag time in the decade between 1965 through 1974 was 6.1 years, falling to 4.6 years between 1975 to 1984, 1.9 years between 1985 and 1994 and finally 7 months between 1994 to 2004. In others surveys the lag time between onset and diagnosis was longer [12]. In our last reports the average lag time between symptomatic onset and diagnosis resulted of 9.9 +/- 16.2 months for relapsing-remitting forms and of 11.6 +/- 17.8, including months for progressive forms too.

Discussion and Conclusions

We adopted a complete enumeration approach on a well-defined population with suitable size to ensure accuracy (over 350,000 pop.). To minimize possible biases we adopted an intensive case collection approach and were supported by adequate expertise in epidemiological surveys [1-4, 7, 16].

Among our MS incident populations 202 patients underwent to cerebrospinal fluid (CSF) analysis with isoelectric focusing, as previously described and generally accepted [17]. Among these 167 (82.2%) were positive for IgG oligoclonal bands (OCB), performed with a standardized methodology [17].

Acknowledgements

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As just suggested by other authors, to study valid time trends of MS incidence there is necessity to conduct long-term surveys and repeated surveillances. Therefore, it would be important to obtain a reinforcement of national and/or international registers and to create an implementation of strategies for the creation of clinical registers in countries where they do not have any. These would make it possible to obtain pictures of the epidemiological course of MS even over the next decades and they would provide the bases for the development of case-control studies [18].

References

[1-18] The references provide relevant details on the methodology and results of the study. The full list is too extensive to be included in this summary. For more information, please refer to the original document.