Incidence of multiple sclerosis in Buenos Aires: a 16-year health maintenance organization–based study

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Objective: The present study was undertaken to determine the incidence of MS in a health maintenance organization from Buenos Aires, the largest populated area in Argentina.

Methods: Population was all members of a hospital-based health maintenance organization who were affiliated since January 1992 up to December 2007. Each person was followed contributing time at risk since January 1992 or enrollment date to the final date. Patients with definite diagnosis according to Poser’s criteria were included. Incidence density was calculated with 95% confidence intervals.

Results: A total of 145,000 patients were followed for a total of 1,021,515 person-years, of whom 18 developed the disease. Incidence density (ID): 1.76 /100,000 person-years (95% CI: 1.1–2.8/100,000 person-years).

Conclusion: The incidence density of 1.76 per 100,000 suggests a low-median risk area for MS. This study constitutes the first of its kind to cover data of MS incidence in Argentina.

Introduction

Multiple sclerosis (MS) is a complex demyelinating disease of the CNS in which several environmental factors act together in a genetically susceptible individual to cause disease [1].

Kurtzke [2] classified regions of the world according to prevalence: a low prevalence was considered less than five cases per 100,000 persons; an intermediate prevalence 5–30 per 100,000 persons; and a high prevalence more than 30 per 100,000 persons.

Over the past years, several studies on MS epidemiology have been published as part of an attempt to better define the distribution of the disease and thus clarify its occurrence around the world [3–12]. The prevalence reported by these studies demonstrated a higher frequency of MS cases in northern Europe, southern Australia, the central region of North America [13] and lower frequencies of MS cases in tropical areas like South America [14].

Despite this wealth of data, current knowledge of MS epidemiology is based mostly on North American or European studies whilst scarce data have been published from South America [3,4,15–19]. In Argentina, the southernmost country of South America, there are few studies reporting MS prevalence [17,20], and there are none concerning MS incidence.

As epidemiological and clinical characteristics of MS may vary according to environmental, racial, climatic and genetic factors, epidemiological characteristics of MS in South America should contribute to elucidate the disease pattern in this population. This step would allow us to better understand associated environmental factors of the disease, such as viral infections, population movements, exposure to UV radiation and geographic location (latitude and socioeconomic conditions) [3–7,21].

Thus, considering the relevance of epidemiological data, the present study was undertaken to determine the incidence of MS in a health care organization from Buenos Aires, the largest populated area in Argentina.

Methods

Setting

The population studied was the membership of the Italian Hospital Medical Care Program (IHMCP), a prepaid health maintenance organization. IHMCP provides comprehensive medical and health services through two main hospitals and 24 medical office
buildings to over 145,000 members primarily located in the urban areas around the Autonomous City of Buenos Aires, Argentina. The Autonomous City of Buenos Aires straddles the tropic of Capricorn at latitude 34°S and longitude 58°W. The city covers an area of 202 km² and has a subtropical climate. It is located on the western bank of the Rio de la Plata and has a population of 2,965,403 inhabitants. Ninety-seven percent of the population is white and of European descent and the remaining 3% is a mixture of native Indians and other ethnicities.

Argentina has an extremely segmented health system consisting of three large sectors: public, private and social security (the last two covering a population of nearly 18.3 million people, distributed amongst close to 300 entities of varying scope and size). Beneficiaries of the private system can freely choose their health maintenance organization (HMO). The IHMCP is a private health system insurance, selected by many metropolitan inhabitants because of the excellence and responsibility of the services provided as well as the affordability of the insurance. Approximately 5–7% of the population in these geographic areas are affiliated to the IHMCP. The IHMCP population characteristics are highly representative of the metropolitan population of the Autonomous City of Buenos Aires, as demonstrated by 2001 census data [22] (Table 1 and 2) covering a number of demographic and socioeconomic categories.

The present study was conducted with approval by the Institutional Review Board of the Italian Hospital of Buenos Aires.

Case definition

In order to assess the incidence, the medical records obtained during a 16-year period (1 January 1992 to 31 December 2007) at IHMCP were retrospectively examined. Those satisfying the Poser’s criteria [23] for clinically or laboratory definite MS were accepted as incidence cases. The incidental year for each patient was considered when the Poser’s criteria [23] were fulfilled.

To be considered an incident case, the person must have been affiliated to the IHMCP for at least 12 months before the diagnosis of MS was made. Patients with clinically isolated syndromes (CIS) diagnosed during the 16-year period were excluded from the analysis if they did not convert to MS during the study period.

Case ascertainment

Multiple methods for case finding were used to ensure complete ascertainment: a) patients included in neurologist databases; b) patients with the ICPS (International Classification of Primary Care) code N86 in the HMO computer-based patient record system; c) patients with ICD 9 (International Classification of Diseases) codes 340/341 on admission to hospital; and d) patients receiving interferon beta or glatiramer acetate (Anatomical Therapeutic Chemical codes L03AB07, L03AB08, L03AX13). All neurologists in IHMCP were notified of the study and were asked to refer newly diagnosed or suspected MS patients.

A list of cases was obtained from sources outlined earlier. Confirmation of residence and affiliation status was obtained from the HMO registers. Each potentially eligible subject underwent a standard process to confirm the diagnosis by two MS experts (EC and LP) who subsequently determined whether patients fulfilled Poser’s definite MS criteria [23].

### Table 1: Demographic data of the Autonomous City of Buenos Aires and IHMCP based on 2001 Argentinean census

<table>
<thead>
<tr>
<th>Age group</th>
<th>City of Buenos Aires</th>
<th>IHMCP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–14 years</td>
<td>468 961 (17)</td>
<td>26 100 (18)</td>
</tr>
<tr>
<td>15–24 years</td>
<td>414 621 (14.8)</td>
<td>18 995 (13.1)</td>
</tr>
<tr>
<td>25–34 years</td>
<td>435 963 (15.7)</td>
<td>20 735 (14.3)</td>
</tr>
<tr>
<td>35–44 years</td>
<td>356 261 (12.8)</td>
<td>17 400 (12)</td>
</tr>
<tr>
<td>45–54 years</td>
<td>350 165 (12.2)</td>
<td>16 385 (11.8)</td>
</tr>
<tr>
<td>55–64 years</td>
<td>281 722 (10.1)</td>
<td>17 110 (11.8)</td>
</tr>
<tr>
<td>≥ 65 years</td>
<td>488 505 (17.3)</td>
<td>28 275 (19.5)</td>
</tr>
<tr>
<td>Total</td>
<td>2 965 403</td>
<td>145 000</td>
</tr>
</tbody>
</table>

IHMCP, Italian Hospital Medical Care Program.

### Table 2: Socioeconomic level and ethnic origin of Autonomous City of Buenos Aires inhabitants and IHMCP affiliates, based on 2001 Argentinean census

<table>
<thead>
<tr>
<th>Socioeconomic class</th>
<th>City of Buenos Aires (%)</th>
<th>IHMCP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper class</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Upper middle class</td>
<td>16</td>
<td>19.4</td>
</tr>
<tr>
<td>Middle class</td>
<td>30</td>
<td>37.5</td>
</tr>
<tr>
<td>Lower middle class</td>
<td>21</td>
<td>25.6</td>
</tr>
<tr>
<td>Lower class</td>
<td>17</td>
<td>12.5</td>
</tr>
<tr>
<td>Poor</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ethnic origin</th>
<th>City of Buenos Aires (%)</th>
<th>IHMCP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>92</td>
<td>95.5</td>
</tr>
<tr>
<td>Asian</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>African American</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Mestizo*</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

IHMCP, Italian Hospital Medical Care Program; *Mestizo (Spanish term used to designate people of mixed European and Amerindian ancestry living in the region of Latin America).
Data collection
Data regarding demographic characteristics (age at onset, age at diagnosis and follow-up status) were obtained from medical records of each patient. Each person was followed during the study period until voluntary disenrollment, death or finalization of the study (31 December 2007).

Because of fluctuations in enrollment and disenrollment in the health plan, person-years were calculated from monthly membership records and used as the denominator in all calculations.

Statistical analysis
Analysis was performed using Stata 9.1 version [24]. Incidence density (ID) for MS were calculated per 100 000 person-years. Rates were adjusted using direct standardization with the age and gender distribution of the 2000 world population and the 2001 Argentinean population [22,25–27].

Results
During the 16-year study period, 145 000 patients were followed for a total of 1 021 515 person-years, of whom 18 developed MS (11 women). The mean age at diagnosis was 35.7 years (range 21–48). The ID was 1.76 per 100 000 person-years (95% CI 1.1–2.8/100 000 person-years); 1.86 for women (95% CI 1.03–2.36/100 000 person-years) and 1.62 for men (95% CI 0.77–3.39/100 000 person-years). The female-to-male ratio was 1.14. The overall ID was 2.7 per 100 000 (95% CI 2.4–3.1 per 100 000) when adjusted to the world standard population and 2.5 per 100 000 (95% CI 2.1–2.8 per 100 000) when adjusted to the 2001 Argentinean population.

Regarding the annual ID, we observed a stable disease frequency through the study period, ranging from 1.1 to 2.6 per 100 000 person-years. Eight patients with CIS were excluded from the analysis because they did not convert to clinically definite multiple sclerosis during the study period.

Discussion
Valuable information can be obtained from South America, where scarce publications exist about MS epidemiology. This study constitutes the first of its kind to cover MS incidence in a well-defined area of South America.

The incidence density of 1.76 per 100 000 found, shows a low-median risk area for MS. Significant differences exist between our findings and incidence from European and North American countries [2].

We adjusted our findings to the 2000 world standard population and the 2001 Argentinean population to increase the accuracy of the data [22,25,26]. After adjustment, ID values did not significantly change our initial findings.

When we analyzed the annual ID, we did not detect any significant temporal trend over the study period. It is important to remark that issue in order to discard information bias. The sex ratio found in our study was intriguingly low (female-to-male 1.14:1), in accordance with countries from eastern Europe [28,29] and with significant differences with North American and western European countries [30], where an increase in female to male sex ratio has been reported over the last years. The reason for the low ratio is still unknown, but it may be because of the low number of ascertained cases found during the study period.

This study supports that the MS incidence for the area of Autonomous City of Buenos Aires in which the study was carried out, is in accordance with its prevalence [31]. We believe that the study’s most important contribution is that it expands knowledge on the pattern of geographic differences in MS distribution around the world.

We are well aware that the low incidence rate could be because of the under-ascertainment of MS cases in the study, a potentially confounding factor. However, the manner in which the cases were ascertained makes this highly improbable (neurologist databases, HMO computer-based patient record system, admission to hospital registries, etc.). Of course, another limitation of these results could be that they are drawn from an HMO and therefore contain a selection bias; nonetheless, comparison of this HMO population with the Autonomous City of Buenos Aires census data demonstrates that it is representative of the general population in demographic, ethnic and socioeconomic characteristics. It is also worth to mention that the HMO covers a wide area from the Autonomous City of Buenos Aires. For that reason, results obtained could be cautiously generalized to the Autonomous City of Buenos. Further studies will help us to confirm our initial findings.

References