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ARTICLE

Prevalence of multiple sclerosis in key cities of Brazil. A study in Joinville, Southern Brazil

Prevalência de esclerose múltipla em cidades-chave do Brasil. Estudo em Joinville, Sul do Brasil

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ABSTRACT

Background: The Brazilian Committee for Treatment and Research in Multiple Sclerosis (BCTRIMS) has launched an initiative to determine the prevalence of multiple sclerosis (MS) in Brazil, based on key cities deemed representative of their regions in terms of demographic and environmental features. **Objective:** To investigate the prevalence rate of MS in Joinville. **Methods:** We reviewed the medical records of all patients who lived in Joinville and met the 2010 McDonald's diagnostic criteria revised for MS on the prevalence day (March 11, 2016). Potential MS patients included individuals treated by all practicing neurologists in the city and the ones found in patients' association and the database of the Municipal Department of Health. Advertisements about the survey were also broadcast on radio and television. Patients who were not living in Joinville on the prevalence day were excluded. All potential MS patients were invited to an in-person diagnostic review, carried out by a panel of experienced neurologists with special expertise in MS on March 11, 2016. **Results:** The MS prevalence rate was 13.5 per 100,000 inhabitants (95% confidence interval [95%CI] 12.9–14.0/100,000). A total of 51 (66.2%) participants were females, and 26 (33.7%) were males (female to male ratio=1.9:1). Out of the 77 patients, 73 (94.8%) were Caucasians, and four (5.1%) were mixed-race. **Conclusions:** Despite its latitude location and European colonization, the prevalence rate was below expectation. The intense internal migration from regions with lower MS prevalence rates to Joinville may have played a role in attenuating the increased risk of MS associated with latitude gradient and European ancestry. Prevalence studies in other cities from Southern Brazil with no significant internal migration and taking part in this broad project may clarify this issue.

Keywords: Multiple Sclerosis; Cross-Sectional Studies; Prevalence.

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Authors' contributions: MVMG: had full access to all data in the study. Additionally, he reviewed the literature search, performed the data extraction and interpretation, and drafted of the manuscript; FS: contributed to data extraction and critical revision of the manuscript for intellectual content; FDR: contributed to data extraction, organization of the study site, and critical revision of the manuscript for intellectual content; ALL: contributed to data acquisition and critical revision of the manuscript for intellectual content; CHA: contributed to data extraction and critical revision of the manuscript for intellectual content; EMC: contributed to data acquisition and critical revision of the manuscript for intellectual content; PRW: contributed to data extraction and critical revision of the manuscript for intellectual content; ACBE: had full access to all data in the study. She also contributed to data extraction and organization of the study site; RBL: contributed to data extraction, organization of the study site, and critical revision of the manuscript for intellectual content; RRM: contributed to data extraction and critical revision of the manuscript for intellectual content; Jefferson Becker contributed to data extraction, reviewed the concept and design and reviewed the manuscript; MALP: contributed to data extraction, reviewed the concept and design and reviewed the manuscript.

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RESUMO

Introdução: O Comitê Brasileiro de Tratamento e Pesquisa em Esclerose Múltipla (EM) (BCTRIMS) lançou uma iniciativa para determinar a prevalência da EM no Brasil, com base em cidades-chave, consideradas representativas de suas regiões em termos de características demográficas e ambientais. **Objetivo:** Investigar a taxa de prevalência de EM na cidade de Joinville. **Métodos:** Foram revisados os prontuários médicos dos pacientes residentes de Joinville e que atendiam aos critérios de diagnóstico McDonald's 2010 revisados para EM no dia da prevalência (11 de março de 2016). Os pacientes em potencial com EM incluíam todos os neurologistas em atividade na cidade, a associação de pacientes e o banco de dados da Secretaria Municipal de Saúde. Anúncios sobre a pesquisa também foram veiculados no rádio e na televisão. Foram excluídos os pacientes que não moravam em Joinville no dia do estudo. Todos os casos potenciais de EM foram convidados para uma revisão presencial do diagnóstico clínico realizada por um painel de neurologistas experientes em EM no dia 11 de março de 2016. **Resultados:** A prevalência da EM foi de 13,5 por 100.000 habitantes (intervalo de confiança de 95% [IC95%] 12,9–14,0/100.000). 51 pacientes (66,2%) eram do sexo feminino e 26 pacientes (33,7%) do sexo masculino (razão mulher:homem de 1,9:1). Dos 77 pacientes com EM, 73 (94,8%) eram caucasianos e 4 (5,1%) se declararam como pardos. **Conclusões:** Apesar da colonização europeia, a taxa de prevalência foi abaixo da expectativa, possivelmente devido à elevada taxa de imigração interna associada ao perfil econômico de Joinville. Estudos de prevalência em outras cidades da região sul do Brasil sem imigração interna significativa, e como parte desse amplo projeto, podem esclarecer essa questão.

Palavras-chave: Esclerose Múltipla; Estudos Transversais; Prevalência.

INTRODUCTION

Multiple sclerosis (MS) is the most prevalent chronic inflammatory autoimmune disease of the central nervous system (CNS)[1,2]. It is linked to a variety of risk factors[3], including smoking[4], lack of vitamin D[5], obesity[6], and previous contact with the Epstein-Barr virus[7,8]. Most frequently, MS affects young adults between 20 and 40 years and is three times more prevalent in women than in men[9].

Two systematic reviews identified 19 studies from different Brazilian cities reporting prevalence rates ranging from 1.36 to 27.2/100,000 population[10,11]. However, given the marked heterogeneity of methods employed across studies, a nationwide distribution of MS prevalence in the country and an accurate comparison between the prevalence rates in different regions of Brazil are not yet available.

In this context, the Brazilian Committee for Treatment and Research in MS (BCTRIMS) has launched an initiative to determine the prevalence of MS in Brazil, based on key cities deemed representative of their regions in terms of demographic and environmental features. We herein report the point prevalence of MS in the city of Joinville, Southern Brazil, on March 11, 2016.

METHODS

This is a point-prevalence study conducted in the city of Joinville, Santa Catarina State, Southern Brazil. This study was approved by the Research Ethics Committee of the Universidade Federal de Minas Gerais.

Joinville demographic data and socioeconomic aspects were obtained from the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística — IBGE)[12]. Of note, the latest official survey on healthcare resources was performed in 2016, and the latest set of comprehensive demographic data, including age, sex, and ethnicity of the population, was derived from the 2010 census.

We aimed to identify all MS patients living in Joinville on the prevalence day — March 11, 2016. Between August and December 2016, we identified and reviewed the medical records of all patients who lived in Joinville and met the revised 2010 McDonald's diagnostic criteria for MS[13] on the prevalence day. In addition to medical records from all practicing neurologists in Joinville at the time of the study, we consulted the database of the Municipal Department of Health, which is responsible for providing disease-modifying therapy (DMT) for nearly all MS patients living in the city, as well as the membership list of the local MS patient association. Advertisements were broadcast on radio and television to make the community aware of our efforts to identify all eligible MS patients.

Patients who were not living in Joinville on the prevalence day were excluded. All potential MS patients were invited to an in-person diagnostic review, carried out by a panel of experienced neurologists with special expertise in MS on March 11, 2016.

Patient assessment included demographic information, history of MS-related events, physical examination, and results of paraclinical tests (especially magnetic resonance imaging and, when available, cerebrospinal fluid analysis). We used the modified McDonald criteria (2010)[13] to confirm the diagnosis of MS and the Expanded Disability Status Scale (EDSS)[14] to evaluate the severity of disability. Cases in which the diagnosis of MS could not be confirmed by the panel of neurologists were discarded.

The point prevalence rate on March 11, 2016, was calculated using the official 2016 population estimate, and 95% confidence intervals (95%CIs) were estimated using the method proposed by Schoenberg[15].

We adopted the Standards of Reporting of Neurological Disorders (STROND) checklist — Application to MS, aimed to aid high-quality reporting of incidence and prevalence studies of MS[16].

RESULTS

Area and population

Joinville is located at 26º18' South latitude and 48º 50' West longitude (Figure 1)[15]. The total area of 114,687 square kilometers comprises both urban and rural environments[16].

According to the official estimate, the total population of Joinville on March 11, 2016, was 569,645[12]. As reported by the latest official census in 2010, 98% of its inhabitants lived in the urban area, and the vast majority had Caucasian ethnicity (87%)[12]. The Municipal Human Development Index (MHDI), also from 2010, was 0.809 (classified as high)[12].

After excluding duplicates and patients who did not live in Joinville on the prevalence day, 86 potential MS cases were identified. Nine additional patients were discarded (five with clinically isolated syndromes and four whose clinical symptoms and imaging signs were better explained by conditions other than MS). The remaining 77 patients were alive on the date of the study, and their diagnoses were confirmed by the study team.

Prevalence

The crude point-prevalence rate for MS in Joinville on March 11, 2016, was 13.5 per 100,000 inhabitants (95%CI 12.9–14.0 /100,000).

Demographic and clinical features

Among the 77 MS participants, 51 (66.2%) were females, and 26 (33.7%) were males (sex ratio 1.9:1). The median age on the prevalence day was 38 years (range, 21–73 years), and the median age at MS onset was 27 years (range, 18–45 years). Out of the 77 patients, 73 (94.8%) were Caucasians, and 4 (5.1%) were mixed-race.

The distribution of patients according to the clinical forms of MS was as follows: 69 (89.6%) — relapsing-remitting MS; 3 (3.8%) — primary progressive MS; 5 (6.4%) — secondary progressive MS. Of note, 3 (3.8%) patients had disease onset before the age of 18 years. The median EDSS score was 2.5 (range, 0–9.5).

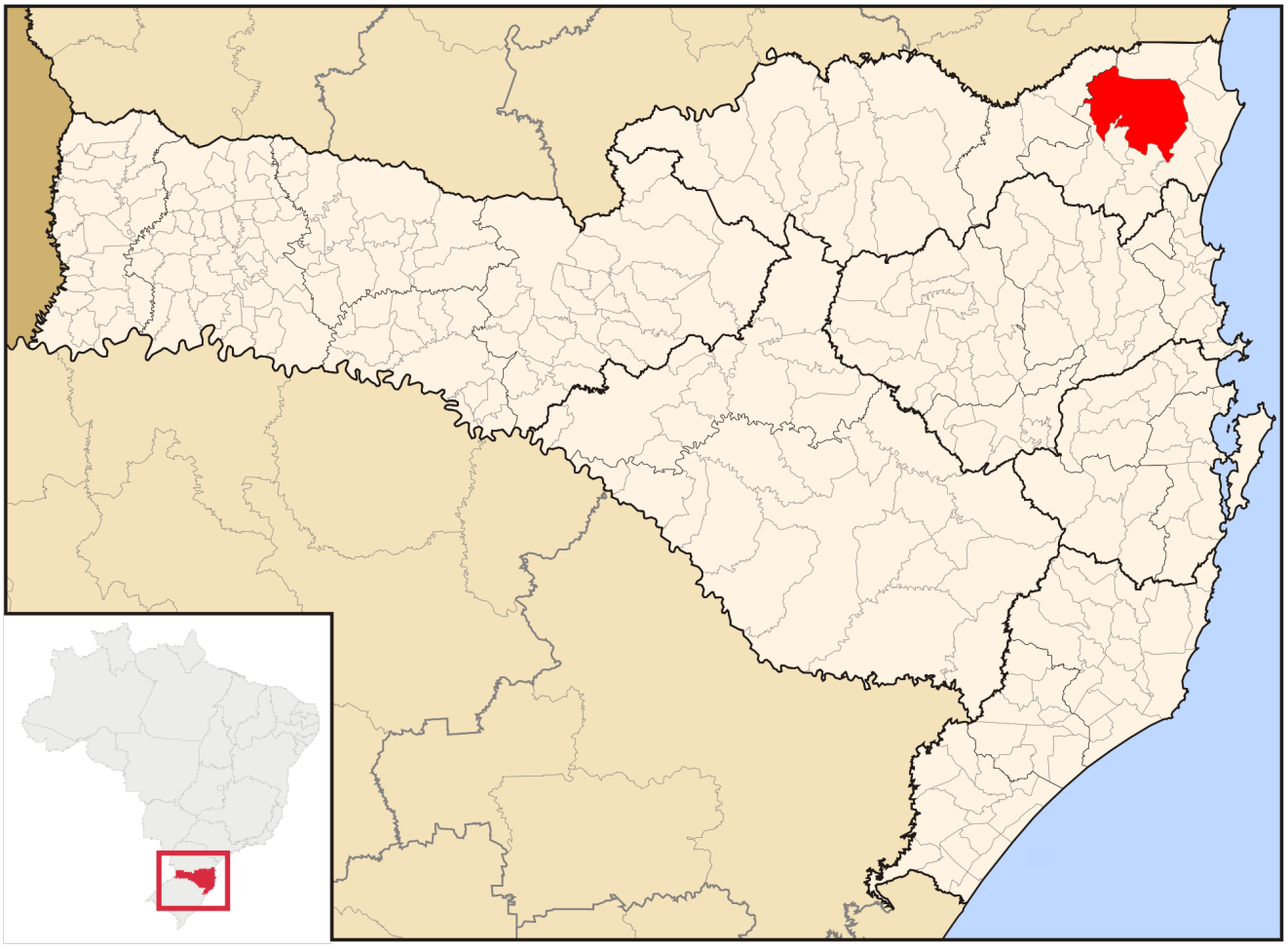

Figure 1. Location of Joinville, in Santa Catarina State, Southern Brazil.

Sixty-two (80.5%) patients were on DMT for MS, whereas 15 (19.5%) were out of treatment. In the treated group, 20 (25.9%) patients were on fingolimod, 18 (23.3%) on interferons, 9 on glatiramer acetate, and 15 (19.4%) on other drugs.

DISCUSSION

To our knowledge, this is the first prevalence study of MS in the state of Santa Catarina, Southern Brazil. The results show that the MS prevalence rate in the city of Joinville is 13.5 per 100,000 inhabitants.

Joinville was selected as one of the target cities in the broad project to determine MS prevalence rates in key cities of different regions of Brazil for harboring some particular features. First, it is a medium-sized city, the largest in the state, and has a well-organized MS Center, which provides MS care to almost all patients living in the city and its surroundings. As a highly industrialized center in the South Region[17], the city has attracted workers from different regions of the country, making its population different from those of other cities in Southern Brazil that maintain a high gradient of original European immigration, such as the city of Santa Maria, which is situated at 29°41' S latitude and has an MS prevalence rate of 27.2 per 100,000 inhabitants[10]. This fact makes the present prevalence study particularly interesting as it may serve as a parameter to evaluate the influence of internal migration against genetic background and latitude gradient on the MS prevalence in Brazil. Flows of internal migration to some cities in Santa Catarina State, such as Joinville, Brusque, Criciúma, Chapecó, and Itajaí, in the 20th and 21st centuries have been well documented[18,19]. At the end of the 20th century, 47% of Joinville residents had not been born in the city[18,19]. In South America, as in other regions of the world, MS prevalence rates vary according to latitude. Whereas the MS prevalence in Buenos Aires was recently estimated to be 38.2 per 100,000 inhabitants, in Guayaquil, Ecuador, it is as low as 0.75 per 100,000 individuals[20]. However, it is unlikely that the latitude gradient would suffice to account for the different rates found in Santa Maria and Joinville. As both cities share similar European ancestry and are located only about 3° apart in South latitude, the lower prevalence rate in Joinville may be ascribed to internal migration.

Surprisingly, despite the latitude gradient and the strong ethnic and cultural influence of European colonization on the population of Santa Catarina, the MS prevalence rate in Joinville is lower than those reported in some cities of the Southeast Region of Brazil, such as Santos (15.5/100,000)[21], São Paulo (15/100,000)[22], and Belo Horizonte (18.1/100,000)[23], which are located at a lower southern latitude. This unexpectedly lower prevalence rate may result from attenuation of the European ancestry influence by the internal migration from other regions of Brazil with lower MS prevalence rates and with heterogeneous ethnic-cultural background, which is typical of the Brazilian population[12]. Comparative prevalence studies involving other cities of Santa Catarina that do not exhibit a prominent rate of internal migration are warranted.

This study also showed a female to male (F:M) ratio of 1.9:1 and a median age of 27 years at MS onset, similar to findings reported in other countries[24]. The Atlas of MS published by the Multiple Sclerosis International Federation in 2013[24] shows that MS is twice as common among women than men. The MS F:M ratio varies and is considerably higher in some continents, such as in East Asia (F:M=3.0) and America (F:M=2.6)[20,25]. The reason for the higher prevalence of MS in women compared to men in these populations is not fully understood, but the interaction of social and environmental factors may play a role.

The present study shows that the prevalence rate of relapsing-remitting MS and the patients' mean EDSS score in Joinville were similar to those reported in other studies in Brazil[11,21,23] and some countries in the Caribbean, Central and South America[20,26].

Regarding MS treatment, we found that over a quarter of the patients in Joinville were on fingolimod at the time of the study. This frequency of use of fingolimod among DMTs coincides with the introduction of more effective oral therapy for MS treatment in Brazil and cannot be compared with previous prevalence studies conducted in the country. However, it is similar to that reported in Canada and Japan[27,28].

Some study limitations should be mentioned. First, the recruitment may not have been thorough as some MS patients may attend MS centers in Florianópolis (capital of the state of Santa Catarina) and Curitiba, two large cities close to Joinville. Another limitation is the lack of information regarding patient ancestry. This latter feature would allow comparative analysis of MS prevalence according to ethnic background.

The MS prevalence rate in Joinville, Southern Brazil, is 13.5 per 100,000 inhabitants. This finding was below expectation as the city is located at a higher southern latitude and has a population with strong European ancestry. This lower-than-expected prevalence rate in Joinville may be associated with the intense internal migration from other regions of Brazil with lower MS prevalence rates. Internal migration might have attenuated the risk of MS associated with latitude gradient and European ancestry. Prevalence studies in other cities from the South Region of Brazil that have not experienced internal migration flows and compose this broad national project may clarify this issue.

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