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Multiple sclerosis in Brazil: A systematic review

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ABSTRACT

Background: The natural history of multiple sclerosis (MS) in Brazil has been available in different regions of country. There is no nationwide population-based studies that express general data in Brazil.
Objective: To review and synthesize available data about MS in Brazil.
Material and methods: Systematic review was performed through a search of medical literature databases to identify Brazilian studies published during 1990–2012.
Data sources: PubMed, SciELO, and Lilacs.
Keywords: "Brazil" or "Brazilian" combined with the following terms: "multiple sclerosis", "clinical profile", "demographic profile", "natural history", "clinical course", "pediatric", or "familial form".
Results: In total of 45 pediatric and 1922 adult patients, the median age at onset was 10 years in pediatric patients and 32 years in adult patients. Women were more affected. Motor-control complaints and relapsing-remitting phenotype at onset were the most common. Predictors to disability and progression were number of relapses during the first year of disease, older age, male gender and African ancestry.
Conclusions: The profile of the MS in Brazilian seems to correspond to that observed in high-MS-prevalence areas. African ancestry is a risk factor to disability and progression early. In Brazil, factors that limit MS incidence do not interfere with the clinical pattern and outcomes.

Contents

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1. Introduction

Multiple sclerosis (MS) is a disease that affects young adults, causing inflammation of the white and gray matter of the central nervous system (CNS) by means of an autoimmune reaction triggered by the interaction of genetic and environmental factors. Although MS is considered polygenic disease [1], the human leukocyte antigen class II genes, the DR2 haplotype alleles in particular, are the ones most frequently associated with greater susceptibility to the disease [2]. Among the environmental factors, the most frequent identified as trigger of MS were: the influence of smoking, stress, hygienic conditions, immunizations, and viral infections; additionally poor exposure to the sun in the world's northernmost and southernmost latitudes and consequent vitamin D deficiency has been investigated. However, to date, the causal relationship between those factors and the disease could not be fully confirmed [3].

The prevalence of MS increases as latitude increases, and it exhibits a particular racial and geographic distribution, occurring more frequently among Caucasians and in the Western countries of the northern hemisphere [4]. MS is not frequent in Brazil, which has a racially mixed population and tropical climate, which are the opposite of the typical conditions of the places with the highest prevalence of MS [5].

The earliest data on MS in Brazil were reported in 1939, when 22 cases were described, two of which were confirmed in anatomical pathological examination [6] The first Brazilian multicenter study known as the South Atlantic Project (Projeto Atlântico Sul – PAS) [5], whose main aim was to present and describe the clinical and demographic profile of MS in Brazil was conducted from 1995 to 1998. PAS included 22 reference centers across the five Brazilian regions and a total of 602 patients. The results show that 30% of patients had African ancestry, and the clinical, laboratory, and genetic profile of MS in Brazil corresponds to the "*Western MS type*" [5].

Twenty-one years have passed since PAS and new data on the natural history of MS in Brazil have been available in different regions of country. However, there is no nationwide population-based studies that express general data in Brazil. For this reason, we performed a systematic review of epidemiological studies conducted in different regions of Brazil with in order to observe different aspects of those already obtained by individual studies that analyzed a limited number of patients.

2. Material and methods

2.1. Study design: systemic review of case series

2.1.1. Setting

A comprehensive search using as keywords "Brazil" or "Brazilian" combined with the terms "multiple sclerosis"; "clinical profile"; "demographic profile"; "natural history"; "clinical course"; "pediatric"; and "familial form" was performed in the medical literature databases: National Library OF Medicine and The National Institutes Of Health (Medline/PubMed) Literature Latino-Americana e do Caribe em Ciências da Saúde (LILACS) and Scientific Electronic Library Online (SciELO); to identify relevant Brazilian studies published during 1990–2012.

2.1.2. Selection strategy

Titles and abstracts in English, Spanish, and Portuguese identified by electronic searches were examined independently by two researchers (CCFV and BCR) to select potentially relevant studies containing demographic (ethnicity and gender), clinical (age and clinical phenotype at onset), and outcome (benign course, time to disability, and progression phase) information of MS in Brazilian patients. Articles on prevalence that did not contain demographic and clinical data were excluded.

From the 81 articles found, 22 studies were selected full reading. To avoid that patients were counted multiple times, three non-longitudinal observational studies were excluded after full reading because of the risk of contain patients and data already presented in a more complete study of the same service or group [7–9]. Then, 19 studies were included after full reading, being two about case series of pediatric MS [10,11]. Fourteen non observational studies conducted with adults contained information on demographic (gender and ethnicity) and clinical variables (age at onset, clinical presentation, and clinical phenotypes) [7–9,12–22], and three longitudinal observational studies conducted with adults too (analysis of prognosis: time to reach to progression and disability milestones) [23–25]. No article mentioned the familial form of MS. Among 14 non-longitudinal observational studies selected, 11 included patients with all three clinical forms of MS (relapsing-remitting, RR; secondary progressive, SP; and primary progressive, PP) [12–14–16,7–9,18–20], two only included patients with RRMS [17,21], and one included patients with PPMS [22]. Among the three longitudinal observational studies, two included cases of RRMS only [23,24], and one included cases of PPMS only [25] (Fig. 1).

The data were subjected to three separate analyses: **analysis 1,** on the pediatric cases described in two non-longitudinal studies (younger than 18 years old); **analysis 2**, on the adult population in non-longitudinal studies (14 studies); and **analysis 3**, on the adult population in longitudinal studies (3 studies).

The data from the longitudinal studies included in analysis 3 were not included in analysis 2 because there could be an overlap with the cases of the non-longitudinal studies, in addition to the fact that they examined different clinical forms of MS.

The authors adhere to the reporting guidelines by MOOSE (Meta-analysis of Observational Studies in Epidemiology) statement.

2.1.3. Statistical analysis

The categorical variables were expressed as percentages, the mean and median values were calculated in the case of continuous variables, and the variables gender and ethnicity were expressed as ratios. All analyses were performed relative to the total population

Table 1
Demographic and clinical characteristics of pediatric MS published in Brazil.

	Guilhoto et al., 1995* (n = 14)	Ferreira et al., 2008# (n = 31)	Total (n = 45)
Gender	8	20	28
Female (n)	6	11	17
Male (n) rate	1.3:1	1.8:1	1.6:1
Age at onset			
Mean (years)	8.6	11.7	10
Median (years)	NA	NA	107 (15.5)
Until 5 years old (%)	4 (28.5)	3 (9.7)	
from 6 to 10 years old(%)	3 (21.4)	9 (29)	12 (26.6)
from 11 to 17 years (%)	7 (50)	19 (61.3)	26 (57.7)
Initial symptoms (%)			
Motor	64.0	38.7	46.6
Sensory	21.4	19.4	20.0
Visual	28.5	19.4	22.2
Cerebellar/Brain stem	35.7	22.5	26.6
Clinical patterns at onset (n)			
CIS	0	1	1
RR	14	29	43
PP	0	1	1

CIS-clinical isolated syndrome; RR-relapse-remitting; PP-primary progressive; * Poser et al. Criteria (1983) applied; #McDonald Criteria (2001 and/or 2005) applied.