

# CLINICAL FEATURES OF MULTIPLE SCLEROSIS IN THE SOUTH OF BRAZIL

## A partial analysis

*Alessandro Finkelsztejn<sup>1</sup>, Rafael do Amaral Cristovam<sup>2</sup>, Gisele Silva de Moraes<sup>2</sup>,  
Mariah Graziani de Souza Mello Lopes<sup>2</sup>, Aline Vitali da Silva<sup>2</sup>, Marcio Severo Garcia<sup>2</sup>,  
Caroline Miotto Menegat Cola<sup>2</sup>, Carlos Eduardo Bastiani<sup>2</sup>, Lísia Barros Ferreira<sup>2</sup>,  
Amanda Lucas da Costa<sup>2</sup>, Silvete Maria Brandão Schneider<sup>3</sup>, Thirzá Baptista Frison<sup>4</sup>*

**Abstract** – There are no published studies on the characteristics of multiple sclerosis (MS) patients from the south of Brazil. **Objective:** To identify the clinical features of a series of MS patients and to compare to other Brazilian series. **Method:** Retrospective study with 67 patients followed in The MS Reference Center - RS, Brazil during the year of 2008. We analyzed demographic and clinical data. **Results:** Most were women (74.6%), the general average age was 43.5 years old, and the general average EDSS score was 4.1. Of those patients, 81.8% had relapsing-remitting MS. Sexual dysfunction prevalence was 31.1% in men and 68.9% in women ( $p < 0.01$ ). We found a positive correlation (Spearman=0.444,  $p < 0.05$ ) between EDSS and depressive symptoms. **Conclusion:** This study showed a very similar sample compared to other states of Brazil. Moreover, there was found a high prevalence of sexual dysfunction and a straight relation between EDSS and depressive symptoms.

KEY WORDS: multiple sclerosis, epidemiology, depressive symptoms, sexual dysfunctions.

### Características clínicas da esclerose múltipla no sul do Brasil: uma análise parcial

**Resumo** – Não há dados publicados sobre as características clínicas da esclerose múltipla (EM) no estado do Rio Grande do Sul (RS). **Objetivo:** Identificar e comparar as características clínicas de uma série de pacientes com EM no RS com as de outras séries nacionais. **Método:** Foram coletados e avaliados dados demográficos e clínicos de 67 pacientes atendidos em nosso centro. **Resultados:** Houve predomínio de mulheres (74,6%), idade média geral foi de 43,5 anos e EDSS médio de 4,1. O tipo surto-remissão correspondeu a 81,8%. A prevalência de disfunção sexual foi de 31,1% nos homens e 68,9% nas mulheres ( $p < 0,01$ ). Encontrou-se correlação de 0,444 ( $p < 0,05$ ) entre depressão e EDSS. **Conclusão:** Este estudo demonstrou uma amostra semelhante às demais amostras brasileiras, apresentando, adicionalmente, elevada prevalência de sintomas sexuais e a estreita associação entre depressão e o grau de incapacidade.

PALAVRAS-CHAVE: esclerose múltipla, epidemiologia, sintomas depressivos, disfunção sexual.

Multiple sclerosis (MS) is an immunomediated neurological disease, affecting people in the early adulthood. It is the most common cause of acquired physical disability in many countries of North America and Europe<sup>1</sup>. In Brazil, the prevalence of MS is approximately 15 cases/100.000 habitants in the southeastern region<sup>2,3</sup>, however, since the Brazilian large territorial extension, it is considered a

country which present a low prevalence because many areas of tropical and equatorial climate display rates lower than 5 cases/100.000 habitants, such as occurs in the city Recife, with a rate of 1,36 cases/100.000 habitants<sup>4</sup>. MS affects more women than men and has four different evolution forms: relapsing-remitting, primary progressive with or without relapses, and secondary progressive form<sup>1,5</sup>. Re-

Hospital de Clínicas de Porto Alegre, Porto Alegre RS, Brazil: <sup>1</sup>Neurologist, Master in Epidemiology, Federal University of The State of Rio Grande do Sul; <sup>2</sup>Medical Student, Federal University of The State of Rio Grande do Sul; <sup>3</sup>Nurse, Hospital de Clínicas de Porto Alegre; <sup>4</sup>Psychologist, Master in Neuroscience.

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Dr. Alessandro Finkelsztejn – Rua Mostardeiro 5 / 1002 - 90430-001 Porto Alegre RS - Brasil. E-mail: afinkels@portoweb.com.br

lapsing-relapsing MS is the most common form, representing 80–85% of cases<sup>1</sup>. The geographic factor is a heavy determinant of disease distribution because colder countries display the highest prevalence rates of MS worldwide.

Epidemiologic studies in many Brazilian regions have been published<sup>2-12</sup> presenting demographic and clinical characteristics of treated patients at different clinics and hospitals. Nevertheless, there are no published data on MS patients in the state of Rio Grande do Sul. There are only indirect data on MS prevalence in this region, as demonstrated in a recent thesis that estimates the number of hospital admissions for MS relapse since 2002 through 2006. This study demonstrated that the state of Rio Grande do Sul was the second one considering the absolute numbers of hospital admissions for the treatment of MS<sup>13</sup>.

The Neurology Service from Hospital de Clínicas de Porto Alegre (HCPA) has a complete medical aid for MS patients: neurologists, nurses, neuropsychologists, psychiatrists, emergency room consultation, day-hospital, and inpatient admissions. The Neurology Service from HCPA has joined to the Health Public Department of the State of Rio Grande do Sul since the year of 2006, with the objective of evaluating all prescriptions of interferon beta or glatiramer acetate from our State. Since that time, outpatient assistance of MS patients has been reorganized.

We started a new registration system for these patients, collecting clinical and demographic data in a faster way, and yet have gathered data from 50% of patients. Nevertheless, we decided to analyze the data already collected, comparing them with those of other published Brazilian series.

**METHOD**

This is a retrospective study of 67 patients attending our Center, during the year of 2007 and 2008. All patients were diagnosed by the Revised McDonald Criteria<sup>14</sup> and clinical and demographic data have been collected by the authors during consultation. The database created was analyzed for that period. The variables analyzed were age, gender, race, age of disease onset, type of evolution according to Lublin classification<sup>4</sup>, Expanded Disability Status Scale (EDSS)<sup>15</sup>, amount of years suffering the disease, treatment with interferons, glatiramer acetate or other medications and its side effects, Beck depression scale<sup>16</sup>, and urinary dysfunction symptoms through a questionnaire comprising fundamental questions regarding lower urinary tract symptoms<sup>17</sup>.

The research project has been approved by the HCPA Research Ethical Committee. As were the authors who collected the data from medical registers, they signed the informed consent, respecting privacy and anonymity of patients.

Data have been analyzed through SPSS version 11.5 software, by calculating continuous variables averages, standard deviation (SD) and also categorical variables proportions. T-test was

used when appropriate, likewise Pearson or Spearman correlation test.

**RESULTS**

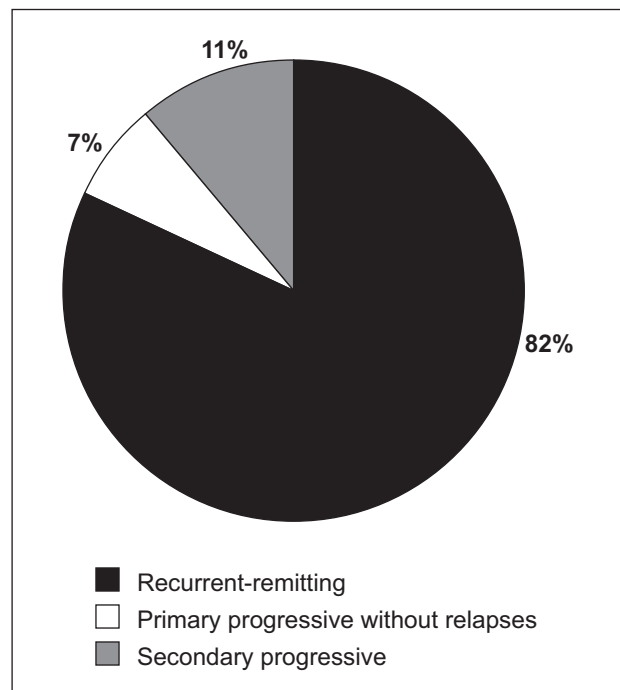
The average age of our sample was 43.5 years (SD 11.2). The average time since the first symptoms of disease was 11.5 years (SD 6.7). The average EDSS was 4.1 (SD 2.4). The proportion between women and men was 2:1 (50 women and 17 men). Demographic and clinical characteristics data are summarized in Table 1 and compared to other Brazilian series Table 2. The Fig 1 shows the distribution of MS evolutive forms in our sample.

Distribution of the different prescribed drugs is summarized in Fig 2. There are 5 main drugs of first choice for the treatment of MS: interferon beta 1A 30 micrograms, interferon beta 1A 22 micrograms, interferon beta 1A 44 micrograms, interferon beta 1B 300 micrograms and glat-

*Table 1. Clinical and demographic characteristics of MS patients in the South of Brazil.*

Sample characteristics	Mean±SD*
Age (years)	43.5±11.2
Age of symptoms beginning (years)	32±9.3
Age at diagnosis (years)	35.5±10.6
Time of disease (years)	11.5±6.7
EDSS	4.1±2.4
Beck depression scale	16.3±8.8

\*SD: standard deviation.



*Fig 1. MS Evolution forms in a sample from the south of Brazil.*

Table 2. Results of epidemiologic studies about MS in Brazil.

Authors	n	F:M	Race (%)	Clinical form	Initial mean Age±SD
Callegaro <sup>20</sup> (1989)	120	1.6:1	79.2 W 10.0 M 10.0 Bl 0.8 As	85% RR 10.2% PP 4.2% SP	27.9±8.9
Leite et al. <sup>21</sup> (1990)	51	2.1:1	62.7 W 37.4 no W	47% RR 19.7% PP 33.3% other forms	34.5±13.9
Lana-Peixoto <sup>22</sup> (1992)	67	2.3:1	76.0 W 19.4 M 4.5 Bl	–	28.9±10.4
Tilbery et al. <sup>23</sup> (1995)	214	2.9:1	96.0 W 4.2 Bl 0.5 As	82% RR 18% PP	28.0
Papaiz-Alvarenga et al. <sup>12</sup> (1995)	88	3:1	68.2 W 31.8 Bl	88.6% RR 4.5% PP 6.8% SP	27.9±11.3
Oliveira et al. <sup>11</sup> (1999)	50	2:1	64.0 W 34.0 M+W 2.0 As	60% RR 30% PP 10% SP	32.5±9.6
Moreira et al. <sup>10</sup> (2000)	302	3.5:1	94.0 W 5.0 Bl 1.0 As	72.8% RR 13.6% PP 13.6% SP 19.8% benign form	28.7
Arruda et al. <sup>9</sup> (2001)	200	1.8:1	98.5 W 1.5 Bl	91% RR 8% PP 1% SP	32±9.9
Brito Ferreira et al. <sup>4</sup> (2004)	118	4.1:1	5.9 W 0.8 Bl 93.2 Ds	70.4% RR 5.9% PP 23.7% SP	33.2±11.5
Fragoso, Fiore <sup>3</sup> (2005)	81	3.3:1	94 W 2.4 M 2.4 Bl 1.2 As	82.7% RR	32
Cardoso et al. <sup>6</sup> (2006)	121	4:1	20 W 19.7 M 20 Bl	91.3% RR 6.1% PP 1.7 SP	31.1±11.02
Grzesiuk <sup>7</sup> (2006)	20	3:1	80 W 20 Bl	75% RR 5% PP 20% SP	33.8
Santos et al. <sup>8</sup> (2006)	283	3.7:1	–	100% RR	29.7±10.2
Current series (2008)	67	2.9:1	96 W 4 Bl	81.8 RR 10.9 SP 7.3 PP	32±9.3

n: sample; F:M: female/male ratio; W: white; Bl: black; M: mulatto; As: Asian; Ds: dark skin; RR: relapsing-remitting; PP: primary progressive; SP: secondary progressive; SD: standard deviation.

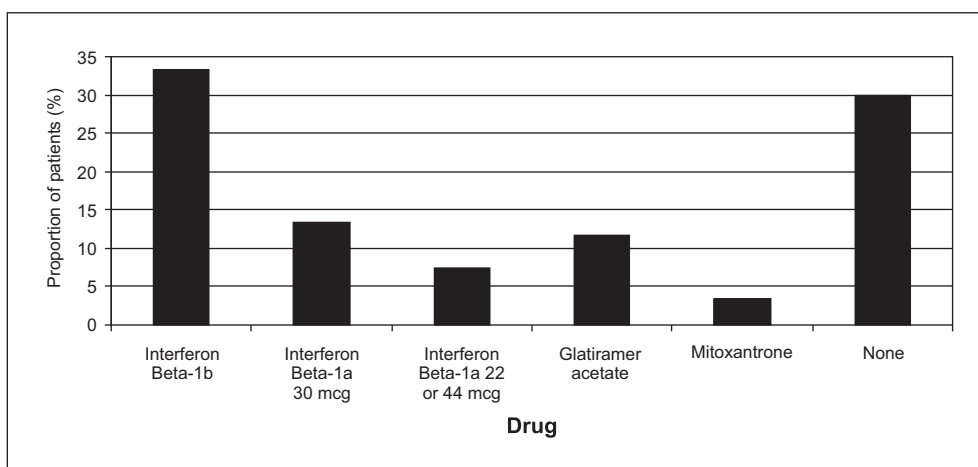


Fig 2. Distribution of use of modifying disease drugs among patients with MS in the south of Brazil.

iramer acetate 20 mg. In cases of treatment for secondary progressive MS, Mitoxantrone was used. In our sample, there were 2 patients treated with this drug, since they met the criteria for this evolution form.

Among patients using interferon or glatiramer acetate, 38% related some adverse events (AE). Among men, 33% had headache and 17% had transitory elevation of liver enzymes. Among women, the AE were 15.8% for flu symptoms, 15.8% for pain at site of injection, 10.5% for headache, 10.5% for fever, and 5.3% for generalized body pain.

The general prevalence of urinary dysfunction in our sample was 79% but not significantly different between men and women (50% versus 80%,  $p=0.09$ , NS). In our center is routine to ask patients whether they have any urinary symptom. We considered that patients had urinary dysfunction when complained urgency, frequency, dysuria, retention, incontinence, whether they used any form of continence protection and, if they did, the reason: (1) as a precaution; (2) the presence of urine leakage regularly between urinations.

Sexual dysfunction was significantly higher in women than in men (68.9% versus 31.1%,  $p<0.05$ ). We found a positive correlation (Spearman coefficient=0.444,  $p<0.05$ ) between Beck depression score and EDSS score, which didn't occur with other clinical variables. When testing this correlation independently by gender we didn't find a significant difference.

## DISCUSSION

The results presented in this paper were calculated by analyzing demographic and clinical data from a Brazilian south case series. We chose to analyze traditional data such as age, gender and evolutive patterns of MS relating them to the presence of depressive symptoms, sexual dysfunction, urinary disorders and adverse reactions from immunomodulators. We decided to analyze all of those

together in order to best study our sample. This study is innovative, as it is the first national one studying all this data together, and as it is the first to be carried out in the state of Rio Grande do Sul.

The average age of the onset of disease was 32 years ( $\pm 9.3$ ). The distribution of the clinical evolution forms were calculated: relapsing/remitting 81.8%, secondary progressive 10.9% and primary progressive without any relapse 7.3%. These results are similar to other national data. The F:M (women to men ratio) was 2.9:1, like the southern and southeastern Brazilian regions.

The average EDSS score was 4.1 (SD 2.4) which means that our sample has a large physical disability. The average disease duration time was 11.5 years (SD 6.7).

High Beck scores (average of 16.3, SD 8.8) means that our sample has moderate depressive symptoms, when compared to the population reference values<sup>18</sup>. This rate should alert physicians to ask for depression symptoms and to refer to a psychiatric evaluation, whenever needed. This diagnosis deserves much attention because the improvement of this condition contributes to a better quality of life.

The high proportion of patients with urinary dysfunction shows that we cannot underestimate such symptoms. We concluded that it is of extreme importance an anamnesis directed to the search of urinary dysfunction symptoms, and if those are positive, urological evaluation from a specialist is suggested. According to literature, the prevalence of neurogenic bladder is high in those patients and the treatment of this complication has the possibility of favorable results, and several options of therapy are available<sup>19</sup>. However, in our study, we didn't use a validated questionnaire for the Brazilian population. There are some questionnaires for the detection of lower urinary tract symptoms, but most are complex and difficult to apply. It is necessary that short validated questionnaires

in Portuguese be constructed to study MS patients in a more effective way. On the other hand, when considering sexual dysfunction, it is well-known that answers might depend on several variables and it could be necessary a skilled team to deal with these symptoms. Our approach should be considered as a simple screening, not excusing patients from a complete urologic or gynecologic consultation. And besides, since we know that there can be some important differences between men and women, we didn't perform a complete analysis in this way since our sample was a partial one, and a complete analysis will begin soon.

There were important limitations when carrying out this study, since data were not prospectively collected and not aimed for the ends of this study. These limitations are inherent to any retrospective study. However after collecting and analyzing data from all patients assisted at our hospital, we plan to carry out a prospective and longitudinal study in order to follow a real cohort.

It is important to point out that other important limitations are when comparing our sample to other Brazilian ones. For instance, there were differences in the data collected and in the methodology applied for gathering them in those series. The comparisons performed in our study aim to stimulate the Brazilian researchers in the MS field to gather new data using a more unified way. This will serve to enhance our knowledge on MS in our country.

In conclusion, our study analyzed demographic and clinical data, in order to have a better knowledge of MS patients in the state of Rio Grande do Sul, providing more comparable data to other national samples. It also presented important data on urinary and sexual symptoms which are not routinely asked in many centers. Our study demonstrated a significant level of physical disability and depressive symptoms. It does not aim to be a study of broad external validity as long as data were collected from a convenience sample and in a retrospective basis. Larger studies should be done to better understand those symptoms in Brazilian MS patients, as well as unified ones in a national basis.

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