Frequency of Family Forms of Multiple Sclerosis in a Center in Rio de Janeiro

Frequência da Forma Familiar de Esclerose Múltipla em um Centro no Rio de Janeiro

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ABSTRACT

Familial multiple sclerosis (fMS) is defined as multiple sclerosis cases occurring in at least two family members, and there is no data on the recurrence risk of fMS in the Brazilian population. This study estimated the multiple sclerosis recurrence risk in patient families in RJ and investigated the relationship with Caucasian and African ancestry. A study was conducted in RJ (Brazil), with 197 patients followed by a RJ specialized outpatient clinic. Recurrence risks were calculated by relative MS patient categories through Age-adjusted and Crude recurrence risks. fMS frequency (7.10%) was identified in the RJ study population. The risk of Age-adjusted recurrence (ARR) was high among grandparents, at 2.72 (95% CI 2.16 - 3.28). Concerning the parent relationship, ARR was 1.57 (95% CI 1.36 - 1.78) and increased to 1.76 (95% CI 1.41 - 2.11) in the presence of a European ancestor. Among uncles/aunts, a significant increase from 1.42 (95% CI 1.01 - 1.83) to 2.91 (95% CI 2.28 - 3.54) risk in individuals with Caucasian ancestry was observed, and to 2.65 (95% CI 2.02 - 3.27) in individuals with African ancestry. A higher risk among individuals with Caucasian ancestry was observed compared to Afro-descendant ancestry.

Keywords: Familial Multiple Sclerosis; Recurrence Risk; Brazil; Ancestry; Familial Epidemiology;
RESUMO

Esclerose múltipla familiar (EMf) é definida como casos de esclerose múltipla ocorrendo em pelo menos dois membros da família, e não há dados sobre o risco de recorrência de EMf no Brasil. Foi estimado o risco de recorrência de esclerose múltipla (EM) em famílias de pacientes no RJ e a relação com ascendência caucasiana e africana. O estudo ocorreu no RJ, com 197 pacientes acompanhados em um ambulatório especializado. Os riscos de recorrência foram calculados por categorias relativas de pacientes com EM por meio de riscos de recorrência ajustados por idade e brutos. A frequência de EMf (7,10%) foi identificada na população do estudo. O risco de recorrência ajustada por idade (ARR) foi alto entre os avós, em 2,72 (IC 95% 2,16 - 3,28). Com relação ao parentesco, o ARR foi de 1,57 (95% CI 1,36 - 1,78) e aumentou para 1,76 (95% CI 1,41 - 2,11) na presença do ancestral europeu. Entre tios/tias, foi observado um aumento de 1,42 (95% CI 1,01 - 1,83) para 2,91 (95% CI 2,28 - 3,54) o risco em indivíduos com ascendência caucasiana, e para 2,65 (95% CI 2,02 - 3,27) em indivíduos com ascendência africana. Observou-se maior risco entre os indivíduos com ascendência caucasiana em comparação com os afrodescendentes.

Palavras-chave: Esclerose Múltipla Familiar; Risco de Recorrência; Brasil; Ancestralidade; Epidemiologia Familiar

INTRODUÇÃO

Multiple sclerosis (MS) is an autoimmune disease central nervous (Chi C et al., 2019; Milo R, Kahana E 2010; Cotsapa C et al., 2018). Its prevalence tends to increase with geographical latitude (Alvarenga RMP et al., 2015), presenting higher frequencies in the North and lower frequencies in the South (Kurtzke JF, 1980; Wade BJ, 2014; Pirttisalo AL, Soilu-Hänninen M, Sipilä JOT 2019). Peculiarities in MS distribution in South America (SA) are noted (Cristiano E et al., 2016; Vizcarra ED et al., 2009; Abad P et al., 2010), namely in Buenos Aires (38.2%) and Guayaquil (0.75%). Significant variability in this disease was observed in different Brazilian regions (Gama PAB et al., 2015; Ferreira MLB et al., 2004; Finkelsztejn A et al 2014).

Despite the increasing knowledge on MS epidemiology in SA over the last decades, information concerning the frequency and characteristics of familial multiple sclerosis (fMS) are scarce (Farez MF et al., 2014; Alvarenga RMP et al., 2015). fMS is defined as the occurrence of more than one MS case among individuals belonging to the same family (Ebers GC et al., 2000; Hader WJ, Yee IM, 2014). Only one study conducted in Buenos Aires estimated the risk of fMS using age-adjusted risk (ARR) (Farez MF et al., 2014). The Argentinian population consists mainly of Italian and Spanish immigrants (Cristiano E, Patrucco L, Rojas JI, 2008). It differs from Brazil, which in the 2010 census identified 47.7% whites, 43.1% brown, 7.6% black, 1.1% yellow and 0.4% indigenous people (IBGE, 2012).

Studies on fMS risk estimates indicate that the recurrence risk rate for fMS increases with increasing MS prevalence (Robertson NP et al., 1996; Nielsen NM et al., 2005; O’Gorman C et al., 2011; Westerlind H et al., 2014; Sadovnick AD, Baird PA, Ward RH, 1988). In 2018, a systematic meta-analysis review estimated an fMS prevalence in the worldwide MS population at 12.6% (Harirchian MH et al., 2018). In higher latitude countries, for example, Canada (52° N),
MS prevalence is of 110/100,000 inhabitants, and fMS prevalence, of 32.7% (Hader WJ, Yee IM, 2014; Sadovnick AD, Baird PA, Ward RH, 1988), while in Belgium (50.5° latitude), MS prevalence is of 88/100.000, and fMS prevalence of 15.4% (Carton H et al.,1997). Therefore, caution is required when using global extreme latitude results, making local data investigations recommended (O'Gorman C et al., 2013).

No studies synthesizing these recurrence risk measures concerning fMS in a Brazilian context are available. Thus, current information does not refer to Brazil, as applying data obtained in other countries is inadequate (O'Gorman C et al., 2013). Therefore, the present study aims to estimate the MS recurrence risk among patient families in Rio de Janeiro (location 22°S 42.7°W) and investigate its relationship to Caucasian and African ancestry.

METODOLOGIA

Ethical considerations

The study was submitted and approved by the Ethics Committee: Gaffrée & Guinle Teaching Hospital, the Federal University of State of Rio de Janeiro report number # 2,478,525.

Study area

The present study was conducted in the city of Rio de Janeiro (RJ).

Patient selection

Concerning a reference center of central nervous system (CNS) diseases in RJ, patients were recruited according to the following inclusion criteria: being followed at the institution, having an MS diagnosis confirmed by the neurologist based on McDonald's diagnostic criteria (Polman Het al., 2005) and living in the city of RJ. The study was designed to be random in terms of case identification and family MS history and accommodate only one index case per family adopted patient relatives, half-brothers, half aunts/uncles, and half cousins were not eligible. A total of 210 MS patients were invited to participate in the study.

We got a classification of patients according to race, according to some phenotypic characteristics: skin color characteristics (black, white or brown); lip appearance (thin or thick); hair texture (straight or curly/frizzy) and nose shape (large or small) (Pereira FDSCF et al., 2019). From that, we could classify the patient's race/skin color as white or Afro-Brazilian (black and brown). In addition, we obtained a self-reported classification (IBGE, 2010), and we estimated the agreement between those criteria through the kappa test.

The questionnaire structured by Farez et al. (2014) was applied to collect relative data information regarding number and category (parents, children, siblings, uncles/aunts, nephews/nieces and first cousins) and their total number. Subjects were asked if anyone in the
family presented an MS diagnosis. When multiple cases in a single-family were noted, the first to be treated was considered the index subject, and the others classified as relatives. If both the patient and the affected family member answered the questionnaire, the one with the earliest diagnosis was considered the index case. Additional information was obtained from patients by telephone, email, or a re-interview. Medical records were reviewed for diagnosis confirmation and additional data collection.

Data analysis

The calculation of Crude and adjusted recurrence risk (ARR) (Farez MF et al., 2014; O'Gorman C et al., 2011) was performed for all relative categories by dividing the number of relatives affected by the total number of relatives in this category. This method may underestimate the real risk of developing MS, as it does not consider the fact that many relatives have not yet reached the maximum risk age (Farez MF et al., 2014). Thus, age-adjusted risks were calculated for mother, siblings, uncles/aunts, grandparents, and cousins using the age at onset of the disease. This age adjustment method accommodates the increased risk of developing MS in family members who have not yet reached the maximum risk age (Farez MF et al., 2014).

We performed modeling data through Poisson regression models. The Poisson regression model is the most appropriate when the data of the dependent variables are countable, as is the case in our analysis. Some usual procedures for assessing the quality of the model and adjusting the Poisson regression data include residual analysis. To compare the association estimates obtained from the Poisson regression, we used the deviance measure obtained from the analysis of the model's residuals. Adjusted deviances are measures of variation of different components of the model. The adjusted deviance of the regression model quantifies the difference between the current model and the model generated from the inclusion of a new variable.

The assumptions are that the age of relatives' illness is the same as that of patients. The family recurrence pattern is predictive of future recurrence. This proposal is supported by previous studies that performed the same type of adjustment (Farez MF et al., 2014; O'Gorman C et al. 2011). This study was designed to accommodate only one index case per family.

RESULTS

Two hundred ten individuals met the eligibility criteria during the study period, and 197 agreed to participate in the study. Of these, 14 patients (7.1%) were classified as presenting familial forms of MS by reporting at least one other MS family case (father, mother, siblings, uncle, aunt, grandparents, and cousins). The sum of family members identified by the 197 patients was of 2729 relatives.
Table 1 presents the general characteristics of the studied population, discriminating the probands (first MS affected individual in the family) of fMS cases. Overall, the mean age identified among fMS cases was 44.78 years (SD = 9.37), while the probands presented a value of 43.96 years (SD = 13.11), with no statistically significant difference between both cases.

Table 1: Study participant characteristics (n = 197).

<table>
<thead>
<tr>
<th>Variable</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Probands (n=183)</td>
<td>Familial MS (n=14)</td>
<td>Total (n=197)</td>
<td>p value</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38</td>
<td>20.8</td>
<td>2</td>
<td>14.3</td>
<td>40</td>
<td>20.4</td>
</tr>
<tr>
<td>Female</td>
<td>145</td>
<td>79.2</td>
<td>12</td>
<td>85.7</td>
<td>157</td>
<td>79.6</td>
</tr>
<tr>
<td>Schooling</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elementary School</td>
<td>16</td>
<td>8.7</td>
<td>0</td>
<td>0.0</td>
<td>16</td>
<td>8.1</td>
</tr>
<tr>
<td>High school</td>
<td>73</td>
<td>39.9</td>
<td>4</td>
<td>28.6</td>
<td>77</td>
<td>39.1</td>
</tr>
<tr>
<td>University education</td>
<td>94</td>
<td>51.4</td>
<td>10</td>
<td>71.4</td>
<td>104</td>
<td>52.8</td>
</tr>
<tr>
<td>Race/Skin Color</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>101</td>
<td>55.2</td>
<td>8</td>
<td>57.1</td>
<td>109</td>
<td>55.3</td>
</tr>
<tr>
<td>Black/Brown</td>
<td>82</td>
<td>44.8</td>
<td>6</td>
<td>42.9</td>
<td>88</td>
<td>44.7</td>
</tr>
<tr>
<td>Age</td>
<td>43.96</td>
<td>13.11</td>
<td>44.78</td>
<td>9.37</td>
<td>44.02</td>
<td>12.86</td>
</tr>
<tr>
<td>Age of MS onset</td>
<td>31.06</td>
<td>11.25</td>
<td>30.28</td>
<td>9.09</td>
<td>31.01</td>
<td>11.09</td>
</tr>
</tbody>
</table>

*Multiple sclerosis

The number of women was the absolute majority in this sample. The number of fMS cases with higher education is noteworthy (71.4%). Only 8% of the participants attended elementary school only. Referring to the phenotypic classification performed by the principal researcher, the black/brown group represented 44.7% of the total MS patients.

Comparing the groups of cases and probands, the age of disease onset (the date of the first outbreak) remained stable, with an average of 31.01 (SD = 11.09).

Table 2 presents the description of the case series (n = 14) with fMS. The age of the patients at the time of the research ranged from 27 to 60 years. The variability in the age of disease onset comprised a minimum age of 13 and a maximum of 47 years old. Among nine fMS index cases, EUR, AFR or AMR ancestry were mentioned in the following frequencies: 44.4% EUR, 33.3% AFR and AMR 22.2%. The Kappa coefficient was applied to measure the degree of
agreement for the interobserver classification (interviewer and patient), calculated at $k = 0.79$
(95% CI 0.76 - 0.81).

Crude recurrence risks and ARR and those specific to African and European ancestry are
presented for the 197 proband family members in Table 3. All adjustments are presented at 95%
confidence intervals. Based on Argentina's reference population (Farez MF et al., 2014), a high
ARR was found among grandparents 2.72 (95% CI 2.16 - 3.28). We found the lowest association
among cousins (AAR=1.13, 95% CI 0.98 – 1.28). This non-significant association possibly is due
to misclassification, considering the bias from the occurrence of consanguineous kinship or not.

The adjusted model for race allows us to observe how much race can interfere in the
strength of association. Systematically the white race seems to be more associated with familial
multiple sclerosis. When we analyze the effect of the black race, there is a loss in the strength of
association. Although all of them are statistically significant (even among blacks), there is a
reduction in the association by up to 13%, for example, in the association with mothers and
siblings.
Table 2: Description of the 14 cases of familial MS in the study sample

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Literacy</th>
<th>Race</th>
<th>Age of MS</th>
<th>African ancestry</th>
<th>Caucasian ancestry</th>
<th>Indigenous ancestry</th>
<th>Familial case</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>45</td>
<td>Female</td>
<td>University education</td>
<td>White</td>
<td>26</td>
<td>No</td>
<td>Yes</td>
<td>Grandmother</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>51</td>
<td>Female</td>
<td>University education</td>
<td>White</td>
<td>33</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Sister</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>Female</td>
<td>High school</td>
<td>Afro-Brazilian</td>
<td>39</td>
<td>Yes</td>
<td>Father</td>
<td>Grandmother</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>36</td>
<td>Female</td>
<td>University education</td>
<td>Afro-Brazilian</td>
<td>19</td>
<td>Sim</td>
<td>Grandmother</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>Female</td>
<td>High school</td>
<td>White</td>
<td>24</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Mother</td>
</tr>
<tr>
<td>6</td>
<td>37</td>
<td>Male</td>
<td>High school</td>
<td>White</td>
<td>33</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Cousin</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>Female</td>
<td>University education</td>
<td>White</td>
<td>36</td>
<td>No</td>
<td>No</td>
<td>Grandfather</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>55</td>
<td>Female</td>
<td>University education</td>
<td>White</td>
<td>31</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Mother</td>
</tr>
<tr>
<td>9</td>
<td>37</td>
<td>Female</td>
<td>University education</td>
<td>Afro-Brazilian</td>
<td>13</td>
<td>No</td>
<td>Yes</td>
<td>Grandfather</td>
<td>Yes</td>
</tr>
<tr>
<td>10</td>
<td>27</td>
<td>Female</td>
<td>University education</td>
<td>White</td>
<td>24</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Aunt</td>
</tr>
<tr>
<td>11</td>
<td>54</td>
<td>Female</td>
<td>University education</td>
<td>Brown</td>
<td>47</td>
<td>No</td>
<td>Yes</td>
<td>Father</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>55</td>
<td>Female</td>
<td>University education</td>
<td>White</td>
<td>36</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Brother</td>
</tr>
<tr>
<td>13</td>
<td>37</td>
<td>Male</td>
<td>University education</td>
<td>White</td>
<td>24</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Mother</td>
</tr>
<tr>
<td>14</td>
<td>43</td>
<td>Female</td>
<td>High school</td>
<td>Afro-Brazilian</td>
<td>39</td>
<td>Yes</td>
<td>Grandmother</td>
<td>Yes</td>
<td>Grandfather</td>
</tr>
</tbody>
</table>

*Multiple sclerosis
Table 3: Age-adjusted Crude Risk for Kinship (n = 197)

<table>
<thead>
<tr>
<th>Relative</th>
<th>Total</th>
<th>Crude risk (%)</th>
<th>ARR (95% CI)</th>
<th>Crude</th>
<th>Race-Adjusted</th>
<th>P value&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother</td>
<td>3/179</td>
<td>1.67</td>
<td>1.57 (1.36 – 1.78)</td>
<td>1.76 (1.41 – 2.11)</td>
<td>1.54 (1.19 – 1.89)</td>
<td>0.028</td>
</tr>
<tr>
<td>Father</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Siblings</td>
<td>8/446</td>
<td>1.79</td>
<td>1.41 (1.22 – 2.08)</td>
<td>1.96 (1.51 – 2.41)</td>
<td>1.71 (1.26 – 2.16)</td>
<td>0.019</td>
</tr>
<tr>
<td>Grandfather/Grandmother</td>
<td>1/347</td>
<td>0.29</td>
<td>2.72 (2.16 – 3.28)</td>
<td>1.54 (1.29 – 1.78)</td>
<td>1.36 (1.11 – 1.61)</td>
<td>0.036</td>
</tr>
<tr>
<td>Uncles/Aunts</td>
<td>3/873</td>
<td>0.45</td>
<td>1.42 (1.01 – 1.83)</td>
<td>2.91 (2.28 – 3.54)</td>
<td>2.65 (2.02 – 3.27)</td>
<td>0.039</td>
</tr>
<tr>
<td>Cousin</td>
<td>4/884</td>
<td>0.34</td>
<td>1.13 (0.98 – 1.28)</td>
<td>1.21 (0.96 – 2.00)</td>
<td>1.09 (0.89 – 1.93)</td>
<td>0.067</td>
</tr>
</tbody>
</table>

<sup>a</sup>Prevalence estimate ($\lambda$s) based on a similar risk study published (Farez MF et al., 2014)
<sup>b</sup>We joined Afro-Brazilian black and brown into the same categories.
<sup>c</sup>Obtained by deviance analysis

**DISCUSSION**

fMS recurrence risk was estimated here in a city located in Southeastern Brazil, presenting a tropical climate, where 50.7% of the population is black or brown (IBGE, 2012). The prevalence of MS has been estimated at 18/100,000 inhabitants (Gama PAB et al., 2015).

The only fMS risk study publication to date in Latin America was published by a group of researchers in Buenos Aires, Argentina (latitude 34°S) (Farez MF et al., 2014). The applied method was the basis for the design of the research reported herein. The size of the samples collected by both Brazil and Argentina allows for the identification of disease risk variability in South America. Both countries are located in a low MS prevalence region. However, Argentines are mostly self-referred to as white individuals and the descendants of Italian, Spanish and Amerindian immigrants (Cristiano E, Patrucco L, Rojas JI, 2008). At the same time, Brazil is made up of 52.3% of mostly non-white individuals.
fMS frequency among the 197 patients living in Rio de Janeiro was 7.10%, like that previously described by Papais Alvarenga et al. (2015), also in RJ, of 6.14%. However, the current estimate remains lower than the rates described in Buenos Aires, of 10.5% (Farez MF et al., 2014).

The highest ARR estimate in our study was among grandparents, calculated at 2.72. This result needs to be interpreted carefully because the diagnosis of MS before using magnetic resonance imaging (MR) was established only by clinical criteria. It is essential to highlight that the inclusion of the maternal and paternal grandparents/grandparents category in the recurrence risk measure is not standard in the fMS studies Prokopenko et al., (2003) pointed out that grandparents were excluded from an Italian sample due to poor quality of life data and clinical diagnosis. Still, researchers selected a total of 28,396 patients through the Swedish Multiple Sclerosis Registry and National Hospital Registry, stratifying ARR in grandparents (0.31), and underestimated the risk of other relative categories compared with European data (Westerlind H et al., 2014). It is important to note that Brazil does not have a single unified MS registry.

The risk of 1.57 among mothers is like the Buenos Aires study (ARR = 1.51; 95% CI 1.3 –1.7). The impact of MS on women's lives is an important aspect to note when considering the higher prevalence of this disease in Latin America (Alvarenga RMP et al., 2015) and worldwide (Wade BJ, 2014). In this sex, acute demyelinating MS activities can be of concern during pregnancy and the puerperium. However, the number of outbreaks generally decreases during pregnancy (Fragoso YD et al., 2018).

Also, in the nuclear family, sibling ARR was calculated at 1.41 (95% CI 1.22-2.08), and Caucasian ancestry conferred a 1.96-fold higher risk than the reference group. These results may aid in clinical guidance in Brazilian regions with similar genetic structures. It is worth noting, however, that these data are low when compared to those of European descent among Vancouver Canadians (ARR = 3.91) (Westerlind H et al., 2014) and French individuals from Paris (ARR = 2.50) (Sazdovitch V et al., 2000).

The risk estimate for uncles increased markedly when an adjustment for ancestry, mainly Caucasian, was performed (ARR = 2.91, 95% CI 2.28-3.54). The high estimate is not fully explained, but the reported amount of second-and third-degree kinships may be overestimated. Thus, they are less likely to share the same environmental exposure as that of first-degree relatives (Robertson NP et al., 1996). Distance from the nuclear family and the family size of each Brazilian proband corroborate the ignorance of the most distant parental relationships. No statistical difference between the age of disease onset between cases and probands was observed herein. No agreement on the clinical MS course within families is observed so far (Guaschino C et al., 2014). To date, no validated genetic risk factors that strongly influence the clinical course of the disease are known (Reich DS, Lucchinetti CF, Calabresi PA, 2018). Neurologist decision-making may be aided by this evidence. Importantly, having relatives
presenting MS can increase symptom awareness and lead to the investigation of early events (Rojas JI et al., 2016).

The present study presents certain limitations, such as patient selection only from a single center in Rio de Janeiro, which has a relative demographic complexity, making result extrapolation to other regions, particularly for the Brazilian South and Northeast, inappropriate. The recurrence risks identified herein are mainly different from those previously reported in the SH since Brazilian miscegenation characteristics are very peculiar compared to other South American countries. On the other hand, this is the first study on fMS recurrence risks that provides Brazilian data and the third in all the SH. Additionally, one of MS characteristics is the variable onset age. The data presented in the study take into account the age of disease onset (the first outbreak) (O’Gorman C et al., 2011; Westerlind H et al., 2014; Prokopenko et al., 2003).

Our study has many limitations. The most important of these were that this used reported ancestry. The gold standard would be to differentiate the ethnic background according with the molecular analysis. It would be recommended to consider the Brazil as miscegenated population. However, since 1998, Brazilian health information systems have necessarily included the variable "race/skin colour", according to the five categories described by the Brazilian Institute of Geography and Statistics (IBGE, 2010).

CONCLUSIONS

The genetic contribution to MS risk in Rio de Janeiro is different from that observed in the northern hemisphere, with significant SH variations. Among uncles/aunts, a significant increase from 1.42 to 2.91 risk in individuals with Caucasian ancestry was observed. ARR among siblings with Caucasian ancestry conferred a 1.96-fold higher risk than observed for the reference group. African ancestry imputed a lower probability of fMS in all relative categories, and Caucasian ancestry led to the lowest ARR of 1.54 (95% CI 1.29 - 1.78). The patients remain in follow-up at the reference center of MS, including for future genetic mapping to assess ancestry.

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