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What is This?

Towards establishing MS prevalence in Latin America and the Caribbean

MO Melcon[1], CM Melcon[1], L Bartoloni[1], E Cristiano[2], JC Duran[3], AK Grzesiuk[4], YD Fragoso[5], JB Bidin Brooks[5], V Díaz[6], KM Romero García[7], JA Cabrera Gomez[8], P Abad[9], MA Macías Islas[10], F Gracia[11], VF Hamuy Diaz de Bedoya[12], ME Córdova Ruiz[13], JH Hackembruch[14], C Oehninger[14], CN Ketzoian[14] A Soto[15] and the 'Grupo Colaborativo Multicéntrico para el Estudio de la Esclerosis Multiple en America Latina y el Caribe' (GEEMAL)

Abstract

A very high prevalence of multiple sclerosis (MS) has been reported in some Western European and North American countries. The few surveys of MS epidemiology in South America reveal lower prevalence rates, implying that susceptibility varies between distinct ethnic groups, thus forming an important determinant of the geographic distribution of the disease. The objective of this study is to review MS prevalence estimates in different Latin American and Caribbean countries. We reviewed surveys of regional MS prevalence from 1991 to 2011. Sources included an online database, authors' reports and proceedings or specific lectures from regional conferences. We obtained a total of 30 prevalence surveys from 15 countries, showing low/medium MS prevalence rates. Both the number and the quality of prevalence surveys have greatly improved in this region over recent decades. This is the first collaborative study to map the regional frequency of MS. Establishment of standardized methods and joint epidemiological studies will advance future MS research in Latin America and the Caribbean.

Introduction

Prevalence surveys for multiple sclerosis (MS) have been conducted in different regions, providing a wide array of prevalence figures worldwide.[1,2] A relatively high prevalence of MS is found in Western Europe and North America. These continents have higher Caucasian or European populations, higher mean household incomes, and better access to high-quality medical facilities. On the contrary, the lowest prevalence of MS has been reported in the Mestizo (mixed white and Amerindian) populations living in the Tropics, in low-income countries with generally limited availability of and access to healthcare services.[3]

Many studies have examined the role of ethnicity or ancestry in MS epidemiology. For example, the rarity of MS among Amerindians indicates that different susceptibility of distinct ethnic groups may be an important determinant of the observed geographic distribution of the

[1]Foundation for Neuroepidemiology Research, Junín, Argentina.
[2]Hospital Italiano, Buenos Aires, Argentina.
[3]Department of Neurology, Hospital de Clínicas, La Paz, Bolivia.
[4]Hospital Santa Rosa, Cuiabá, Brazil.
[5]Department of Neurology, Universidade Metropolitana de Santos and Reference Center for Multiple Sclerosis for the Coastal Region of the State of São Paulo, Brazil.
[6]Hospital Clínico de la Universidad de Chile.
[7]University of Havana, Cuba.
[8]Multiple Sclerosis Clinic of the Cuban MSSociety, Havana, Cuba.
[9]Hospital Metropolitano, Universidad de las Americas, Quito, Ecuador.
[10]Department of Neurology, Universidad de Guadalajara, México.
[11]Hospital Santo Tomás, Panamá City, Panamá.
[12]Hospital I.M.T. Asunción, Paraguay.
[13]Neurology Section, Universidad Nacional Mayor de San Marcos, Lima, Perú.
[14]Institute of Neurology, Hospital de Clínicas, Montevideo, Uruguay.
[15]Hospital Domingo Luciani, Caracas, Venezuela.

Corresponding author:
Mario Melcon, Fundación para la Investigación en Neuroepidemiología (FINEP), Solana 54, B6000EKB Junín, Argentina.
Email: finep@infovia.com.ar

disease.[1] It is also widely accepted that MS has a lower prevalence in tropical areas where solar radiation has a protective role.[4]

The objective of this study was to launch a collaborative group for studying MS in Latin America and the Caribbean (LAC) and to systematically review prevalence rates in these countries. This newly-formed "Grupo Colaborativo Multicéntrico para el Estudio de la Esclerosis Multiple en America Latina y el Caribe" (GEEMAL) translates to Collaborative Multicentric Group for the Study of MS in Latin America and the Caribbean.

Methods

Data collection and inclusion criteria

Members of the collaborative group GEEMAL were asked to submit any MS prevalence studies conducted between 1991 and 2011 in their LAC countries, that included a distinct study area (survey site), authors, prevalence rate (point or time period), time reference, methods, sources of information, diagnostic criteria (Poser and/or McDonald criteria), and the MS prevalence per 100,000 inhabitants.[5,6] Only reports based on approved diagnostic criteria applied by a neurologist were included in our study.

In addition, we performed an online search of PubMed (http://www.pubmed.org) and EMBASE (http://www.embase.com) for any English-language publications since 1990, as well as Lilacs (http://www.bireme.br) for articles written in Spanish that matched the following keywords: multiple sclerosis, prevalence, epidemiology, Latin America, South America, environmental factors and ethnicity. Also, we searched for related lectures from the VI LACTRIMS (Latin American Committee for MS Research) conference that took place in Santiago, Chile, on August 12–14, 2010 (http://www2.kenes.com/lactrims/pages/home.aspx).

Geographical distribution

We collected information on geographical distribution and related latitudes in South America and the Caribbean, to compare to known geographical distribution of MS. Based on published prevalence figures, Northern Europe, North America, and some parts of New Zealand and Southern Australia are high-prevalence zones (over 30 MS cases per 100,000 inhabitants); *medium prevalence* (5–29 per 100,000) is found in Southern Europe and Southern USA; and the *low-prevalence zones* (<5 per 100,000) are in Asia, Africa and South America.[7,8] Rates above 100 per 100,000 are found in Scotland and its offshore islands, Northern Ireland, Scandinavia, the Italian island of Sardinia, and Canada.[1,2,9] In LAC countries, the city of San Pedro Garza Garcia, Mexico reported the highest prevalence (30 per 100,000) in a region previously considered to have low MS frequency.[10]

Ultraviolet (UV) radiation

Ultraviolet radiation (UVR) values were obtained from the national weather service of each country, in order to assess its relationship to local MS prevalence. We expressed the strength of solar UV irradiation as a Solar UV Index or Sun Index, following a system developed by the World Health Organization (WHO). UV Index predicts UV intensity levels on a scale of 1–16, with 1–3 being low and ≥ 16 as extremely high. This data may matter, because UVR plays an essential role in the production of vitamin D.[11]

Results

General prevalence and distribution analyses

Out of the 15 LAC countries covered by GEEMAL, we found 30 crude MS prevalence surveys. Table 1 shows estimates for the prevalence of MS (per 100,000 inhabitants) for each country, as published, and additional collected data. Although study methodologies varied greatly, they provided general evidence of the homogeneity of MS crude prevalence rates throughout the regions studied.

As seen in Figure 1, the distribution of MS in LAC countries can be divided into several regions: "Intertropical," which is the area bounded by the Tropic of Cancer in the north (23.5°N) and the Tropic of Capricorn in the south (23.5°S), which is subdivided here into A1, north of the Equator, and A2 south of the Equator; and B, the "Southern Cone," composed of the southernmost areas of South America, south of the Tropic of Capricorn (23.5°S to 56°S). The lowest average crude prevalence rate seen was 4 per 100,000 in the Tropics south of the Equator to the Tropic of Capricorn. Figure 2 shows our collected MS prevalence rates north and south of the Equator, as well as in the Southern Cone, as documented by several studies.

Analysis by country

North of the Equator. In Mexico, the city of San Pedro Garza García in the state of Nuevo León reported the highest MS prevalence rate for the region (30 per 100,000). This city has a population of 127,978 and is located in the northeast, along the US border with the state of Texas. The prevalence of MS in Texas is two to three times higher in Paso county and northeast Texas (49 per 100,000 and 71 per 100,000 respectively) and reaches 100 per 100,000 at latitude 29° N in southeast Texas. The population of Garza García is mainly Mestizo, but with medium to high economic status and easy access to healthcare services.[10] In contrast, a multicenter study including eight hospitals from five of the most populated

Table 1. Prevalence rates (per 100,000) of multiple sclerosis (MS) in Latin America and Caribbean (LAC) countries, obtained from published investigations citing the most recent surveys.

Location of survey	Latitude	Time reference	Case-finding methods Crude	PR[a]/ 100,000	Ref.
Mexico, San Pedro G. García, Nuevo León, Monterrey	25° N 100°W	31/12/2003	Hospitals, out-patients, neurologists, MS Society, MRI, healthcare systems,	30	10
Mexico, Monterrey, Sinaloa, Guadalajara, DF, Puebla	25° N 17°N 96° W 106°W	01/02 – /02	Hospitals, survey by neurologists	7.5 1.5–13	12
Mexico, Chihuahua, Aguas-calientes, Potosí, Jalisco, DF	28° N 19° N 98° W 106°W	01/07/2007	MS Society, neurologists (postal survey) healthcare systems, MRI, suppliers of drugs	7	13
Cuba, Cienfuegos	21° N 80° W	2008	National Reference Center for MS	10/25.5	14
French West Indies, Martinique and Guadalupe	14° N 61° W 16° N	01/1/1998 – 31/12/2004	Prospective population study- follow up	14.8	15
Costa Rica	10° N 84° W	2010	Capture-recapture method	6	16
Venezuela, Isla Margarita	10° N 67° W	15/12/2009	Descriptive study. Multiple sources	5.26	17
Panama	8° N 25° W	2000–2005	Cross-sectional. Neurologists, epidemiologists, immunologists, National MS Registry	5.24	18
Colombia, Antioquia, Caldas, Santander, Risaralda y Bolívar	4° N 10° N 72°W 77°W	01/07/1995– 01/06/2000	Capture-recapture method	3.2 1.48–4.98	19
Colombia, Bogota	4° N 74° W	31/12/2002	Hospitals, health care center, neurologists	4.41	20
Ecuador, Quito	0.15°S 78°W	5/2– 6/30/06	Capture-recapture method	5	21
Ecuador, Guayaquil, on coast	2.15°S 79°W	5/2-–6/30/06	Hospital, Ecuadorian Foundation of MS	2.2	21
Ecuador, Cuenca, in the south	2.53°S 79°W	5/2– 6/30/06	Hospital, Ecuadorian Foundation of MS	0.75	21
Peru, Lima	12° S 77° W	01/08/2007	Capture-recapture method Hospitals, MS organization	7.6	22
Peru, Lima	12° S 77° W	2006–2009	Hospitals, MS Society, multiple sources	7.4	23
Brazil, Cuiabá, Mato Grosso	15° S 56° W	01/07/2007	Neurologists, pediatric neurologists, neurosurgeons, pharmacy	4.41	24
Bolivia, Cochabamba	17° S 66° W	01/01/2007	Hospital, neurologists, healthcare systems	1.5	25
Paraguay, Asunción	23° S 58° W	2000–2005	Multiple sources of information	5.7	26
Brazil, São Paulo	23° S 53° W	01/07/1997	MRI services, Universities, other sources	15	27
Brazil, Santos, SP	23° S 46° W	30/06/2005	MS Association, Reference Center for MS of the coastal region of SP	15.5	30
Chile, whole country	17° S 56° S	2001–2006	National registry of hospitalizations	5.69	39
Uruguay, Montevideo	34° S 56° W	01/09/1997	Capture-recapture method Multiple sources of information	20.5	33
Argentina, Buenos Aires	34° S 58° W	01/07/1996	Medical records linkage systems and centralized diagnostic index	25.6	34
Argentina, Buenos Aires	34° S 58° W	01/07/1996	Capture-recapture method	18.5	35
Argentina, Junín	34° S 60° W	01/01/1991	Multiple Sources of information	12	36
Chile, Punta Arenas Magallanes region 48°S-56°S	53° S 70° W	1998-–2005	Hospital, neurologists, Capture-recapture method	13–14	38
Argentina, Neuquén	39° S 68° W	01/03/2002	Multiple sources of information	17.7	37
Argentina, Trelew	43° S 65° W	01/03/2002	Multiple sources of information	13.4	37
Argentina, Rio Gallegos	51° S 69° W	01/03/2002	Multiple sources of information	21.5	37
Argentina, Ushuaia	55° S 68° W	01/03/2002	Multiple sources of information	15.3	37
Argentina, 4 Patagonian cities	55° S 36° W	01/03/2002	Multiple sources of information: Neurologists, MS clinic, MS Society, media announcements, lay referrals	17.2	37
Antarctic - South Pole	**60° S**				

[a]Crude prevalence ratio: The total number of cases of a disease in a given population at a specific time
MRI: Magnetic resonance imaging

regions in Mexico (covering North, Central and South Mexico), provides an average MS prevalence of 7.5 per 100,000.[12] Another study, based on a questionnaire from the International Federation of MS Societies and the WHO, included the states of Aguascalientes, Chihuahua, Mexico City, Jalisco and Potosí, covering 20% of the total Mexican population, which provides a prevalence of 7 per 100,000 and an incidence of only one new case each year, per 100,000.[13]

During the past two decades, the number and quality of MS-related studies in LAC has greatly improved. Reliable new data were reported from Cuba and Martinique. The first case of MS in Cuba was published in 1965. After 1990, the prevalence of clinically–definite MS in the different

LOCATION OF SURVEY	LATITUDE	PREV./ 100,000
MEXICO, SAN PEDRO GARCÍA GARZA	25 º N	30
MEXICO, CHIHUAHUA, DF, JALISCO, POTOSÍ	22º N 28º N	7
MEXICO, MONTERREY, SINAOLA,	25º N 17º N	7.5
CUBA, CIENFUEGOS	21 º N	10-25.5
FRENCH WEST INDIES	14 º N	14.8
COSTA RICA, CENTRAL AMERICA	10 º N	6
VENEZUELA, ISLA MARGARITA	10 º N	5.26
PANAMA, CENTRAL AMERICA	8 º N	5.24
COLOMBIA, BOGOTA	4 º N	4.41
ECUADOR, QUITO	0 º N – S	5.05
PERÚ, LIMA	12 º S	7.6
BRAZIL, CUIABA, M. GROSSO	15 º S	4.41
BOLIVIA, COCHABAMBA	17 º S	1.5
PARAGUAY, ASUNCION	23 º S	5.7
BRAZIL, SANTOS, SP	23 º S	15.5
CHILE, ALL COUNTRY	17 º S 56 º S	5.69
URUGUAY, MONTEVIDEO	34 º S	20.5
ARGENTINA, BUENOS AIRES	34 º S	25.6
ARGENTINA, JUNÍN	34 º S	12
CHILE, PUNTA ARENAS	53 º S	13-14
ARGENTINA, PATAGONIA	36 º - 55 º S	17.2
ANTARTIC	60 º S	

Figure 1. The map of the study area with the prevalence numbers (per 100,000 individuals) shows the distribution of multiple sclerosis (MS) in Latin American and Caribbean (LAC) countries, which are divided in two regions: the intertropical zone (both side of Equator) and the temperate southern cone (below the Tropic of Capricorn).

Cuban provinces was around 10 per 100,000. The latest study, in Cienfuegos province, provides a prevalence of 25.5 per 100,000.[14] In the French West Indies, comprised mainly of an Afro-Caribbean population (>90%) with some interbreeding with the Caucasian population (estimated to be <30%), a crude MS prevalence of 14.8 per 100,000 was reported. Martinique has a higher prevalence of MS (21.0 per 100,000 vs. 8.5 per 100,000) and higher incidence (2.0 per 100,000 vs. 0.7 per 100,000) than Guadeloupe.[15] In other Caribbean countries, epidemiological data are scarce: the findings from several regional studies do not fulfill the diagnostic criteria for our study.

In Costa Rica, a total of 91 cases were identified from neurology practices and hospital records, for a prevalence rate reported as 6 per 100,000.[16] A descriptive study conducted in the Venezuelan island State of Nueva Esparta (population 436,944) shows a prevalence rate of 5.2 per 100,000.[17]

Between 2000 and 2005, a cross-sectional MS study conducted in Panama shows a prevalence rate of 5.2 per 100,000, and this disease is predominantly among women (8:1). Panama has a greater number of Mestizos, at 50%, followed by Mulattos (mixed white and black ancestry) at 22%, whites at 10%, and African Americans at 8%. Approximately 6% of the population of Panama is Native American.[18]

Between July 1995 and June 2000, the prevalence of MS was determined for five Colombian provinces: Antioquia, Caldas, Santander, Risaralda, and Bolívar. Covering about 25% of the total Colombian population, adjusted prevalence varied between 1.48 and 4.98 per 100,000.[19] Another study reviewed the clinical records of patients diagnosed with MS in most hospitals in the city of Bogota (population 6,574,460): In December 2002, there were 296 patients with MS, yielding a crude prevalence of 4.41 per 100,000. Bogota, located on a plateau in the tropical Andes, consists mainly of Afro-descendant (66.3%) and Amerindian populations (30%).[20]

South of the Equator. In Ecuador, a country located at latitude zero, new 2010 data identified a total of 159 MS patients in the main public and private hospitals and MS
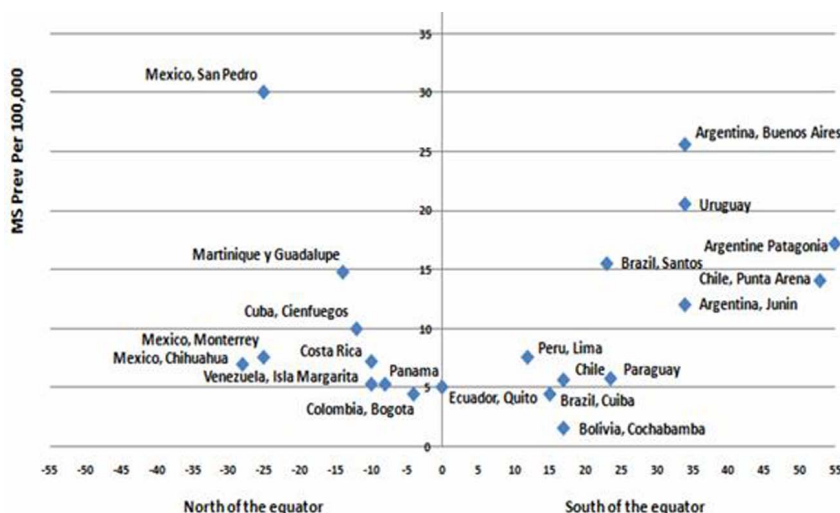
Figure 2. Multiple sclerosis (MS) prevalence levels on a graph showing the latitude of the surveys conducted from 1991–2011, north and south of the Equator, as well as in the Southern Cone (see more details in Figure 1 and Table 1).

foundations from its three largest cities, resulting in a MS prevalence of 5.05 per 100,000 in Quito, 2.26 per 100,000 in Guayaquil, and 0.75 per 100,000 in Cuenca.[21]

The Peruvian MS Committee presented MS cases identified from hospital records from different hospitals, including a total of 600 patients.[22] Similar prevalence rates were found in a second MS prevalence study performed in 2007 in the city of Lima, which provided a prevalence of 7.64 per 100,000.[23]

A study of patients from all public and private health services in Cuiabá, in Mato Grosso (population 520,686), a city located in mid-West Brazil, reveals a prevalence of 4.41 per 100,000 individuals for July 2007, with a higher incidence of MS mainly in patients of African-descendant origin, including Pardos and Mulattos.[24]

Bolivia, a country with limited healthcare coverage, has an 80% Indigenous and Mestizo population, with a life expectancy of 67 years (Pan-American Health Organization, 2010 (PAHO)). Less than 25% of the population is covered by the National Health Security System (Sistema Nacional de Seguros de Salud: SNSS), and only 2.5% are covered by private health insurance. In the area of Cochabamba, a group of professionals identified a total of 15 MS cases from the public and private systems, during the past 10 years, giving a prevalence rate of 1.5 per 100,000 (notably, no cases among the indigenous group). Many factors contribute to such a distribution, including the origin of the population, altitude and the limited access to health services, among others.[25]

In Paraguay, MS specialists and magnetic resonance imaging (MRI) were introduced in 1985. In 2000, the first epidemiological study using multiple sources of information identified 318 MS patients (91% Caucasians and 9% Mestizos) revealing a prevalence rate of 5.7 per 100,000.[26]

The Southern Cone. The prevalence of MS in Caucasian Brazilians was 15 per 100,000 in the city of São Paulo in 1997;[27] and 18.1 per 100,000 in Belo Horizonte,[28] 17 per 100,000 in Botucatu[29] and 15.5 per 100,000 in Santos in 2005.[30] Yet among patients of Afro-Brazilian origin in 1999, the rates were 5 and 1.36 per 100,000, respectively, in Rio de Janeiro[31] and in Recife.[32]

In Uruguay, where the majority of the population is of European origin (Caucasian), a national MS survey conducted in 1996 estimated an overall prevalence of 20.5 per 100,000.[33] In Buenos Aires, Argentina, where a high proportion of the population is also of European origin (mainly Spanish and Italian), the prevalence rate was 18.5 per 100,000 in 1996.[34–36] A more recent study on 417,666 inhabitants of four cities located at different latitudes in the Argentinean Patagonia, showed a point prevalence rate of 17.2 per 100,000.[37]

The first MS survey in Chile showed a crude prevalence of 13 to 14 per 100,000 in the Magallanes region, the southernmost part of the country having a mainly European (mostly Croatian) and Chilotean origin (Gallego Spaniard, Mestizo and Indigenous) population of 157,032 inhabitants. The capital city of Punta Arenas (population 123,932) is located 37 meters above sea level. The average temperature during June, the coldest month of the year, is 1.3 °C (lowest temperature is –7.5°C), and during February, the warmest month of the year, the average temperature is 12.6° C. Sun exposure is very low in this region.[38] Another study across all

the geographical regions in Chile found no correlation between MS rates and latitude nor UV exposure: It showed a cumulative prevalence rate at 5.69 per 100,000 and an annual incidence rate of 0.90 for the period between 2002 and 2006 (V. Diaz, personal communication, February 6, 2011).[39]

Discussion

The last two decades have seen great improvements in the quality of MS research in Latin America. This first international collaborative study included a wide variety of regional epidemiology studies that were conducted on subjects of different socioeconomic and cultural background.[1,2]

The systematic literature review yielded few articles providing information on the incidence and prevalence rates of MS in Latin America.[40–42] However, estimating prevalence trends would be more challenging, because MS rates are very low in the region and most estimates were reported very recently, making it difficult to show any changes in incidence over time.

Methodological issues

Some methodological limitations still exist (i.e. uniform study design, well-defined and homogeneous populations). Most studies were based on a review of hospital records (not directly population-based) with the objective of identifying any potential cases of MS present in large cities, in order to evaluate the clinical profile of the disease and analyze its sociodemographic features.

Crude (overall) frequency rates may not be appropriate for accurately comparing different populations from different regions, given potential differences in age, gender, or ethnicity. Other differences may also affect the comparison of the disease rates across studies, including diagnostic criteria, case-finding methods, the availability of MRIs and access to specialists for early diagnosis. Future studies performed in the region should underline methodology standardization, to allow for more direct comparison of rates and to avoid bias.[43] Most studies in LAC countries do not show age-adjusted prevalence rates.[44] It is important to accurately estimate the denominator of the prevalence rates and to age-adjust those rates to a common standard population, for comparison with other rates.[45,46] The difficulties in comparing prevalence rates across studies are recognized, so efforts should be made to survey different geographical areas with similar methods and diagnostic criteria.

Geographic distribution, ethnicity and environmental factors

Due to the vast areas having different ethnic and environmental factors in combination with the varying geography, climate and UV radiation levels, we propose classifying LAC countries into two main regions for future epidemiological studies on MS (see Figure 1): . The *Intertropical zone* including areas north of the Equator having mainly Mestizo, African, and Mulatto populations, that has moderate (6–7) to very high (15–18) UV values, and measures altitudes between 540 and 3474 m above sea level (with the exception of Cienfuegos in Cuba, at 30 m); and areas south of the Equator with mainly Amerindian and Mestizo populations, moderate (6–7) to very high (15≥18) UV values, and altitudes between 154 and 4800 m above sea level, in the tropical Andes; and the *Southern Cone*, south of the Tropic of Capricorn, populated mainly by white and Mestizo populations, with intermediate UV values (5–7), and an average altitude between 6 and 260 m above sea level.

These proposed two areas also differ in climate, with the equatorial tropical rainforest characterized by heavy rainfall and an average annual temperature of 26 °C. This area does not experience distinct seasons, because the sun is always high in the sky. Only at the higher latitudes, north of the Tropic of Cancer and south of the Tropic of Capricorn, is there significant seasonal variation. In the *Southern Cone*, climate is mostly temperate with an average annual temperature of about 13°C, but this area may include regions that are: humid subtropical, Mediterranean, highland tropical, sub-Antarctic temperate, highland cold, or semi-arid temperate.

The Latin American population is characterized by a multi-ethnic and multicultural background. There are more than 60% Mestizos, a term used to refer to those individuals with mixed European and Amerindian ancestry, and these are mainly found in Paraguay, Colombia, Venezuela, Panama and Mexico. There, indigenous groups account for about 10% of the total regional population. Although most LAC ethnic groups are mixed, the percentage of Amerindians is highest in Guatemala, Bolivia, Peru and Ecuador.

In several studies, a protective role of solar radiation against MS has been hypothesized, due to the geographic distribution of disease. As UV light intensity is higher at high altitudes, the result is higher vitamin D synthesis, which appears to correlate with low MS rates.[11] In fact, UV levels increase about 10% every 1000 m, reaching 20 to 25 at the high-altitude tropical Andean zones, where a large proportion of Amerindians live.

A correlation between increasing latitude and increasing MS prevalence has been published elsewhere[46,47] with studies near the Equator consistently reporting low prevalence rates of MS. Epidemiological studies from both hemispheres support a positive correlation between frequency of MS and higher latitudes, with some exceptions in South America. For example, different Chilean regions between latitude 56°S (Magallanes region) and 17°S (Tarapacá region),[39] and the Argentinean Patagonia showed no gradient between parallels 55ºS (Ushuaia) and 36°S (their

Colorado River),[37] suggesting that other human factors such as genetics and ethnicity play important roles in determining the geographic distribution of MS.

Although there is a role for environmental factors in terms of the geographic distribution of people with MS, genetic factors are very important in determining the acquisition of MS. The low to medium prevalence rates found in LAC suggest that ethnicity (in particular, indigenous ancestry) influences the distribution of MS throughout the entire region. Despite the differences found throughout the studies we sourced for this review and the conditions under which such studies were performed (e.g. geography, economic structure, methodological differences), certain indigenous ethnicity does appear to emerge as a protective factor against MS, as specific resistance occurs regardless of the impact of latitude. Protection or resistance has also been observed in similar ethnic groups worldwide (e.g. both North and South Amerindians, the aboriginal peoples in Canada, the indigenous Samis from northernmost Norway, African Americans and the native Maoris of New Zealand).

The major limitations of this study derive from lack of homogeneity in the populations studied, as there are inequalities in the distribution of income, socioeconomic structure, and access to healthcare services in LAC countries. With a high percentage of rural populations and limited availability to modern day healthcare services, we expect that the prevalence of undiagnosed cases is high, so reliable MS rates are likely still underestimated.

Conclusions

There was general agreement among the participants of this collaborative study group that this regional initiative was successful in reviewing and updating MS prevalence data in LAC. This study further suggests that there is a potential relationship between a low prevalence of MS in the LAC region and ethnic factors, environmental factors, socioeconomic structure, and access of the general population to health care systems. This initiative will be followed by future collaborative epidemiological research in the region.

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Conflicts of interest

The authors have no conflicts of interest to report.

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