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Prevalence and Incidence of Multiple Sclerosis in Panama (2000–2005)

F. Gracia[a] L.C. Castillo[b] A. Benzadón[b] M. Larreategui[c] F. Villareal[b] E. Triana[b]
A.C. Arango[d] D. Lee[a] J.M. Pascale[e] E. Gomez[b] B. Armien[e]

[a]Hospital Santo Tomás, [b]Caja de Seguro Social, [c]Ministerio de Salud, [d]Centro Médico Paitilla,
[e]Instituto Conmemorativo Gorgas de Estudios de la Salud, Panamá, Panamá

Key Words
Multiple sclerosis, prevalence and incidence · Panama

Abstract
Background: The first cases of multiple sclerosis (MS) in Panama were notified in the 1980s and it was considered a low-risk region for this disease. Between 2000 and 2005, a prevalence study was conducted to characterize MS in Panama. ***Methods:*** An instrument was developed to gather information from clinical files and interviews with previous informed consent. The diagnosis was confirmed by neurologists applying the Poser and McDonald criteria as per the inclusion period. ***Results:*** 178 patients from the public and private health sectors were captured between 1970 and 2005. The prevalence rate was 5.24/100,000 inhabitants, and the incidence was between 0.28 and 0.61/100,000 inhabitants. The disease was predominant among women, the mean age ± SD being 34.76 ± 10.909 years (1st crisis), and the average number of crises was 2.88. The most common clinical findings were motor, optic neuritis, sensitive and cerebellous. 52.4% presented monosymptomatic manifestations, 71.6% were clinically defined according to Poser's criteria and 55.6% had MS according to McDonald's criteria. 77.8% had their debut with the relapsing-remitting type and presented an Expanded Disability Status Scale score of 2.7 after the first crisis. ***Conclusion:*** MS is in Panama a neurological pathology with a low prevalence and the results of this investigation improved early treatment and diagnosis of this disease.

Introduction

In Latin America, the information related to the epidemiology of multiple sclerosis (MS) is yet scarce [1, 2] as is shown when consulting MEDLINE in search of publications in indexed journals during 1991–2006. This search reveals only 102 studies conducted by different investigators in the region [3]. This barely represents 1% of the world scientific production related to this topic [4].

Based on these recent data the worldwide prevalence of MS has been classified according to the following categories: countries with very high prevalence of MS (≥130 cases per 100,000), high prevalence (80–129 per 100,000), medium prevalence (30–79 per 100,000), low prevalence (5–29 per 100,000), and very low prevalence (0–4 per 100,000) [5].

Studies published in Latin America show that the prevalence of MS varies from low to medium [1, 2]. Research related to the epidemiology of MS in Central America is limited to nonindexed publications or per-

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Dr. Fernando Gracia
Sección de Neurologiá, Hospital Santo Tomas
Ave. Balboa y Calle 34 Este, Panamá (Panamá)
Tel. +507 227 4122/263 7977, Fax +507 206 2406
E-Mail fegra@medicospaitilla.com

sonal communications. The prevalence has been considered from low to very low [6]. The number of neurologists, information available, public awareness of MS, resources, investigators' interest, poor availability of and access to updated diagnostic technology, economic constraints and poverty have limited a better characterization of this problem in the region [7–9].

In Panama, the first cases of MS were reported in the 1980s, during studies carried out on human T-cell lymphotropic virus [10–12]. The prevalence was considered low, but there were no additional studies to confirm this observation. In this setting, in the year 2000, members of the Panamanian Society of Neurosurgery and Neurology put together a research team in order to begin a national registration to characterize MS.

Methods

Study Population

Between 2000 and 2005, we conducted a descriptive, cross-sectional study. It included all patients whose diagnosis of the disease was done between 1970 and 2005 in the Republic of Panama, located between latitude 7°12'07'' and 9°38'46'' (latitude north) and 77°9'24'' and 83°3'7'' (longitude west). The estimated population as of July 1st, 2005 is 3,228,186 inhabitants. In Panama, there is a public health system with two providers: the Social Security Fund 'Caja de Seguro Social' that covers approx. 70% of the working force and their beneficiaries, while the Ministry of Health (MINSA, for its Spanish acronym) covers the rest of the population. The study included all patients whose MS diagnosis had been confirmed by a panel of neurologists by clinical findings, neuroimaging such as magnetic resonance imaging (MRI), when cerebral spinal fluid (CSF) was available (authorized by patient isoelectrofocusing, a technique introduced in Panama in 2005) and visual evoked potentials (VEP). Up to 2002, diagnoses performed complied with the Poser criteria [13] and from 2003 until 2005, besides the former, diagnoses should also comply with McDonald's criteria [14]. Twelve patients who did not comply with the panel's criteria were excluded and patients who had not been referred with a diagnosis made by a neurologist were also excluded.

Questionnaire and Data Collection

An investigation protocol was applied, whose questionnaire for collecting data included the following aspects: general information (age, sex, place of birth, economic income and ethnic groups phenotypically established); family and personal history; clinical findings; degree of disability [15–17]; diagnostic studies (oligoclonal bands in the CSF, MRI and VEP); differential diagnosis with other disease (HIV, human T-lymphotropic virus, neurosyphilis, collagenopathies, hypercoagulability syndrome, among others) classification [13, 14], and treatment.

Information was collected from patients' clinical files (attended by the neurologists of the study) from the national public health system (85%) or private practice (15%), and in some cases, the information was completed during patients' control visits. Patients had previously signed an informed consent, and confidentiality of information was respected. Before the application of this questionnaire, a procedure manual on how to apply the tool was prepared. Several meetings were held with neurologists participating in the study and criteria were unified for the application of the tool in different areas where information would be collected.

Once the forms were completed, they were revised by the primary investigator. Then another investigator (epidemiologist) did the data entry, coding and analysis without participating in collecting the information. Likewise, quality controls were applied to avoid duplication. All patients with the disease were included at the time of the study and those who have died were verified for analytical purposes.

Statistical Analysis

Analyses were conducted considering demographic variables such as age, gender and ethnicity. The geographic distribution of cases was determined, as well as availability of neurologists and diagnostic technology, level of education, socioeconomic level and family ties. Moreover, initial clinical findings were characterized (optical neuritis, brain stem, sensorial, motor, cerebellous, sphincters and others), as well as the Expanded Disability Status Scale score during the first crisis, number of crises, how long ago the disease was diagnosed, clinical type, classification and treatment. Data were analyzed in a descriptive manner by measuring central tendency (average) and dispersion measures [confidence interval (CI) and standard deviation (SD)] for analyzing age. For the analysis of categorical variables proportions were used and the χ^2 test was applied for comparison.

When calculating general and stratified prevalence by age and gender, the estimated population up to July 1st, 2005 was used. The CI of the general and stratified prevalence was calculated using S-Plus and the differences between them were assessed by using the χ^2 test. Incidence was estimated dividing the number of incident cases by the estimated population up to July 1st of the year of their detection. New cases per year were estimated by dividing the general prevalence by the mean time of the disease. Any variable with a p value <0.05 was considered statistically significant. EPIINFO 6.04 was used to build a database and S-Plus was used to conduct statistical analysis.

Results

During the study, 193 patients with a diagnosis of MS made between 1970 and 2005 were included. 92.2% (178/193) had been born in Panama of which 5.1% (9) had died. Only those born and living in Panama were included in the analysis carried out in the present publication.

56.2% of the cases were recruited in Panama city, 26.0% in the central region and 15.8% in the western region of the country (fig. 1). 65.2% (116/178) of the patients were attended at state institutions and 72.0% (128/178) had access to social security.

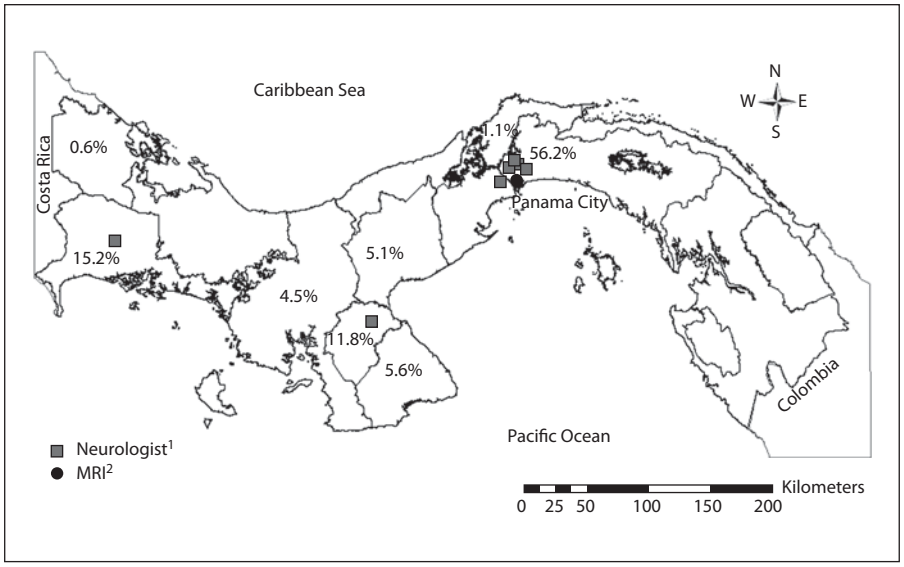

Fig. 1. Geographic distribution of patients diagnosed with MS and availability of neurologists by province in Panama. [1] Neurologists: 9 of 11 accredited and certified neurologists participated, of whom 7 were located in Panama City, 1 in the central region and the other one in the western region of the country. Pediatric neurologists that were invited to participate did not recruit any patients during the period of the study. [2] MRI is available in the country (private sector) since 1991.

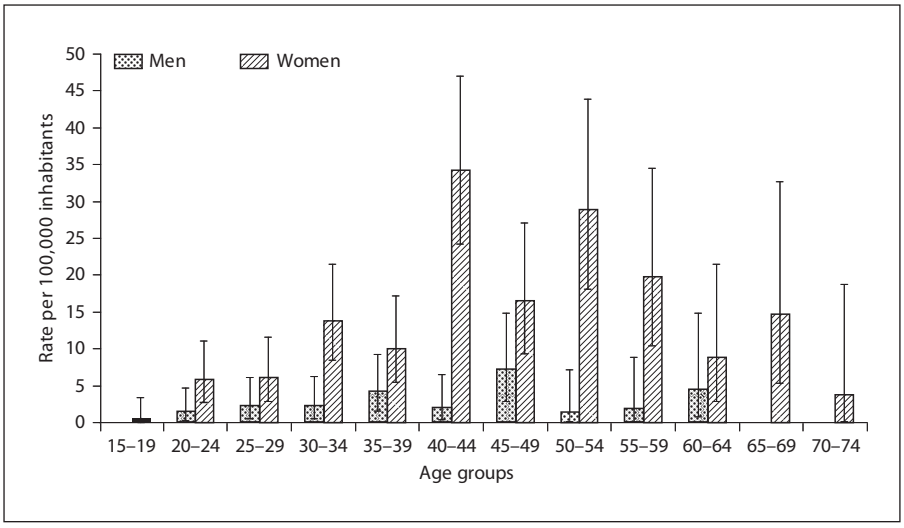

Fig. 2. Prevalence rate of MS in Panama by age group according to gender in 2005. The error bars correspond to 95% CIs.

The rate of the general prevalence was 5.24/100,000 inhabitants (95% CI 4.49–6.07); among women it was 8.94/100,000 (95% CI 7.56–10.50) and in men it was 1.60/100,000 inhabitants (95% CI 1.07–2.21). This difference was statistically significant ($p < 0.001$). When disaggregating by age group and gender, prevalence among women predominated (fig. 2).

The incidence during 1990–1999 (n = 65) fluctuated between 0.15 and 0.40, and during 2000–2005 (n = 79) it fluctuated between 0.28 and 0.61/100,000 inhabitants per year (fig. 3). The average time of duration after onset of the disease in this series was 8.67 years (SD ±8.709) and fluctuated between 1 month and 49 years. Incident cases of MS were estimated at approx. 19 cases per year.

Of the subjects, 49.4% (n = 88) were mestizos, and 30.3% (n = 54), 7.9% (n = 14) and 12.4% (n = 22) were Caucasians, African descendants and of undetermined ethnicity, respectively. Patients' mean level of education was 13.59 years (SD ±3.934). 47.0% (64/136) were professionals, 28.0% (38/136) were housewives, 5.0% students (7/136) and 20.0% had other occupations. Of the 85 patients who agreed to give information on family income, 68.2% (n = 58) stated it was less than USD 1,000.00 per month. 7.8% (n = 11) had a relative with MS; of these, 4 were first-degree and 7 were second-degree relatives.

The mean age of the cases at the time of estimating the general prevalence was 42.96 years (SD ±11.571]. On the other hand, the mean age of patients during the first cri-

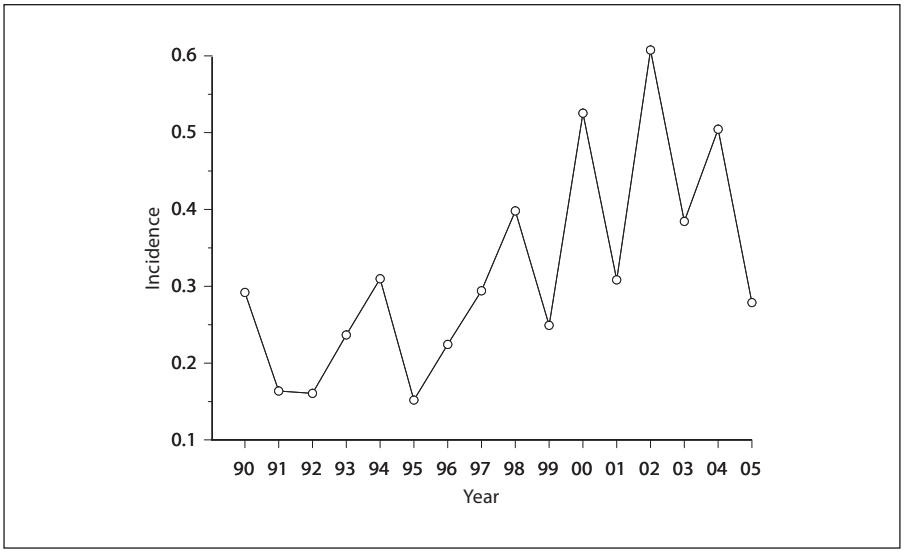

Fig. 3. Incidence rate of MS per year during the period between 1990 and 2005 in Panama. During 1990–1999 and 2000–2005, 65 and 79 MS cases were diagnosed, respectively.

Table 1. Neurologic manifestations prevalent during the 1st crisis (MS patients = 170)

Manifestation	Number	Percent
Motor	81	47.6
Optical neuritis	53	31.2
Sensitive	46	27.1
Cerebellous syndrome	46	27.1
Brain stem	30	17.6
Sphincters	14	8.2
Myelitis	12	7.1
Neuropsychiatric disorders	4	2.4

sis was 34.27 years (SD ±10.786), and the range fluctuated between 13 and 59 years, being more frequent between 20 and 49 years (90% in the series). Men had the first crisis at a mean age of 31.82 years (SD ±9.971) and women at a mean age of 34.76 years (SD ±10.909). No statistically significant differences were observed (p = 0.1883).

The mean number of crises was 2.88 (SD ±2.148). When stratified by gender, it was 2.75 (SD ±1.456) among women and in men it was 3.50 (SD ±4.086), but this difference was not statistically significant (Kruskal-Wallis test $\chi^2_1 = 0.129$, p = 0.7198). The mean time span between the first crisis and the diagnosis of MS was 27.15 months (SD ±50.643). When assessing this time during 1990–1999 (n = 57) and during 2000–2005 (n = 67), the mean time was 23.72 months (SD ±24.844) and 9.63 months (SD ±13.020), respectively, with a statistically significant difference (Kruskal-Wallis test $\chi^2_1 = 11.168$, p = 0.0008).

During the first crisis, the most frequent neurological manifestations (n = 170 patients) were motor disorders (47.6%), optical neuritis (31.2%), sensory disorders (27.1%) and cerebellous syndrome (27.1%) (table 1). 52.4% (89/170) had a single clinical manifestation (monosymptomatic) during the first crisis, i.e. motor disorders (28.7%), optical neuritis (27.6%) or sensory disorders (12.6%).

Ninety-five percent (75/79) of the patients were followed up during the period spanning between 2000 and 2005. Of these, 43.0% (34/79) had a monosymptomatic clinical manifestation. Information related to the evolution of the disease was obtained in 88.2% (30/34) of the monosymptomatic cases; 47.0% (14/30) developed a second symptom after 18.85 months (SD ±14.544).

Throughout this series, the type of MS was defined in 86.0% (153/178) of the cases, of which 77.8% were of the relapsing-remitting type; 11.8% were secondary progressive and 10.4% primary progressive. 97.0% (148/153) were classified according to Poser criteria. 71.6% (106/148) were clinically defined and 23.0% (34/148) were defined according to laboratory results. After 2002, McDonald criteria were also applied and 55.6% (15/27) were classified as MS while 44.4% (12/27) were considered probable cases.

Diagnostic studies included: MRI of the brain and/or spine (when indicated) performed in 92.0% (164/178) of the patients, of whom 163 (99.4%) had demyelinating disease after being reviewed by a neuroradiologist. Evoked

potentials were done in 102 patients, of whom 77.4% (79) had optical neuritis. 46.8% (37/79) had clinical symptoms of visual disturbance associated with clinical optical neuritis and 92.5% (37/40) had an abnormal VEP. On the other hand, 53.2% (42/79) had an abnormal VEP which was clinically asymptomatic. CSF from patients diagnosed with MS in 2004 and 2005 was tested with the isoelectrofocusing technique and 85.7% (12/14) were positive for oligoclonal band.

During the period from 2000 to 2005, the Expanded Disability Status Scale was applied in 45.6% (36/79) of the patients 1 month after the beginning of the first crisis, and a median of 2.7 points was obtained. Approximately 60 patients in our series received immunomodulator medication with an estimated monthly cost per patient of USD 1,200.00, i.e., USD 72,000.00 were invested in these patients per year [Castillo, unpublished data].

Discussion

This is the first study on MS conducted in Panama, where a low prevalence was observed. Traditionally, the frequency of MS is considered moderate to high in countries with a mild climate above 42° north, whereas in the tropical zone it is considered an infrequent neurological pathology [18].

During the last 30 years of the past century, in tropical countries such as Panama, MS was occasionally diagnosed and at times these diagnoses could not be confirmed. Except for the cases of MS reported during the 1990s [11], epidemiological information in Panama was scarce. This might suggest that the disease was infrequent [18]. However, our study shows that MS is a public health problem to bear in mind due to its socioeconomic impact despite the observed low prevalence and the same has been seen in other countries with similar characteristics, such as Colombia [19, 20], Brazil [7], Mexico [21] and Cuba [22]. However, it is difficult to make comparisons in the Central American subregion due to a lack of formal studies.

The foundation of the Latin American Committee for Treatment and Research in Multiple Sclerosis (LACTRIMS) in 1999 renewed interest and allowed the characterization of MS in some countries in the region [2]. Although these studies were of different designs, type of population and ethnic groups [2, 23], we now have a clearer idea about the prevalence in countries such as Colombia (Bogota) [19], Peru [24] and Venezuela [24] where the prevalence is low according to Kurtzke [18]; Mexico [21], Brazil (San Paulo and Rio de Janeiro) [7, 25, 26], Chile [27], Puerto Rico [28], Argentina (Buenos Aires) [29], Cuba [22] and Uruguay [30] where there is a medium prevalence, and Argentina (Córdoba) [31] where the prevalence is high. In Central America, information related to MS is obtained through nonindexed publications or personal communications; however, prevalence fluctuates between 1 and 7.1/100,000 inhabitants [6]. Poor availability and access to cutting-edge diagnostic technology, number of neurologists, information, public awareness of MS, resources, interest among investigators [7], economic constraints [8] and poverty [9] have limited further investigations that would allow for a better characterization of this problem in the region.

The Panamanian population has been composed of multiple ethnic groups since colonial times. Over two thirds of the cases in our series were Caucasians and Mestizos, and no cases were identified in native populations. This probably explains the low prevalence of MS in contrast with the findings in other regions where Caucasian groups prevail [18]. Genetic and average disease duration studies would be required to establish this link.

Clinical findings are not different to those described in other series in which motor and visual disorders are most frequent during the first crisis and mainly affect young adults, particularly women [18, 20–22, 32–34]. Kinship association was not found in our series. When comparing the age in which the first crisis occurred and the number of crisis, no gender differences were observed [32, 33]. This suggests gender does not affect the behavior of the disease.

The most common clinical manifestations were motor compromise and optic neuritis; the relapsing-remitting type predominated and most cases were classified as clinically defined. This is similar to what has been reported in other series [20–22, 32, 34].

Inclusion of patients during the study allowed us to estimate the annual incidence which increased after 2000; time to diagnosis during the period between 1990 and 1999 was 13 months and it was significantly reduced to 4 months in the period between 2000 and 2005. This was mainly due to the interest generated upon the creation of the MS research group as well as access to diagnostic technology by the end of the 1990s [8, 24].

An underreporting undoubtedly exists. This is suggested by the fact that diagnoses were geographically distributed in Health Regions located in the central and western areas of the country which had the human re-

sources (neurologists) and diagnostic technology [9, 24]. Poverty and educational level [35] were factors that probably limited capturing capacity, since the vast majority of the patients identified in the study were those with better socioeconomic and educational levels [24]. Another limiting factor was incomplete data in clinical files in 17% of our series depending on the variable, the methodology employed and the length of time the study lasted which somehow reduced cost-effectiveness. It would be advisable to apply the capture-recapture methodology for future studies of low-prevalence pathologies [36].

As interest grows in diagnosing this pathology and diagnostic technology is made available, more new cases are detected. This may play an important role in the increased incidence of MS in developing countries. The availability of drugs that modify the course of the disease demand an early diagnosis and treatment of MS, to delay the natural course as much as possible, reduce disability and economic burden.

Throughout this study's findings, we can conclude that MS in Panama can be considered a health problem among the chronic degenerating diseases that cause morbidity and permanent disability. We will be able to present the necessary evidence to generate new health policies by decision makers. Additional studies must be developed in order to determine the therapeutic response, disease burden, immunologic and genetic characterization as well as the development of educational programs in the scientific community and general population of Panama.

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