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Review

Multiple sclerosis in Colombia: A review of the literature

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Abstract

Background: The prevalence of multiple sclerosis (MS) in Latin America is generally considered low to moderate. However, accurate data regarding MS epidemiology in Colombia is lacking.

Objective: This study aims to discuss the situation of MS in Colombia.

Results: Analysis reveals a lack of accurate data regarding MS epidemiology in Colombia, however, there have been notable improvements in diagnosis and ultimately leading to better access to treatment for MS patients. While ethnic diversity may potentially influence MS prevalence, there is currently no strong data supporting this claim. MS treatment in Colombia, focuses on early disease-modifying therapy, nevertheless, MS is considered an orphan disease in Colombia, contributing to MS patients not receiving comprehensive evaluation in MS centers. Regional efforts are ongoing to improve diagnostic access and access to treatment for MS patients.

Conclusion: Despite the challenges in accurately defining MS epidemiology in Colombia, an increase in neurological training, diagnostic capabilities, and access to treatment has been observed. However, the status of MS as an orphan disease in Colombia poses challenges to comprehensive care for affected individuals. Further studies are needed to elucidate risk factors and improve care conditions for MS patients in the region.

Keywords: Epidemiology, genetics, multiple sclerosis, outcome measurement, treatment response, disease modifying therapies

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Introduction

Multiple sclerosis (MS) is an inflammatory, demyelinating disorder of the central nervous system that affects around 2 million people worldwide, with a reported increase in prevalence in Latin America over the past 20 years, particularly in regions like Puerto Rico and Argentina.[1–4] Colombia situated in the northwest of South America with a population of approximately 49 million, has very variable weather with temperatures between 8 °C in Andean regions and 32–33 °C at the coasts. A large majority of the population lives in urbanized cities such as Bogota, Medellin, Cali, and the Atlantic coast (Figure 1). The increase in the diagnosis of MS in Latin America and the significant economic burden associated with MS emphasizes the need to better understand the current state of MS in Colombia.[5]

Challenges in diagnosing and treating MS are pronounced in low and middle-income countries, encompassing scarcity of neuroimmunology-trained neurologists, limited magnetic resonance imaging (MRI) accessibility, centralized medical care primarily in larger cities, unidentified prevalence of MS-mimicking conditions, underreporting, and issues related to access to care.[6] These challenges are likely to be also experienced in Colombia. The aim of our article is to provide a comprehensive review of the epidemiology of MS in Colombia and identify the gaps therein.

Prevalence

Classically, high prevalence regions of MS are defined as >30 per each 100,000 inhabitants, medium prevalence is considered between 5 and 29 per each 100,000 inhabitants and low prevalence is said to be <4 per each 100,000 inhabitants,[7] with a latitudinal gradient, being higher as it moves away from equator.[8–10] In the recent years, this latitudinal gradient has been less consistent across studies.[9,11,12] Cities that lie at

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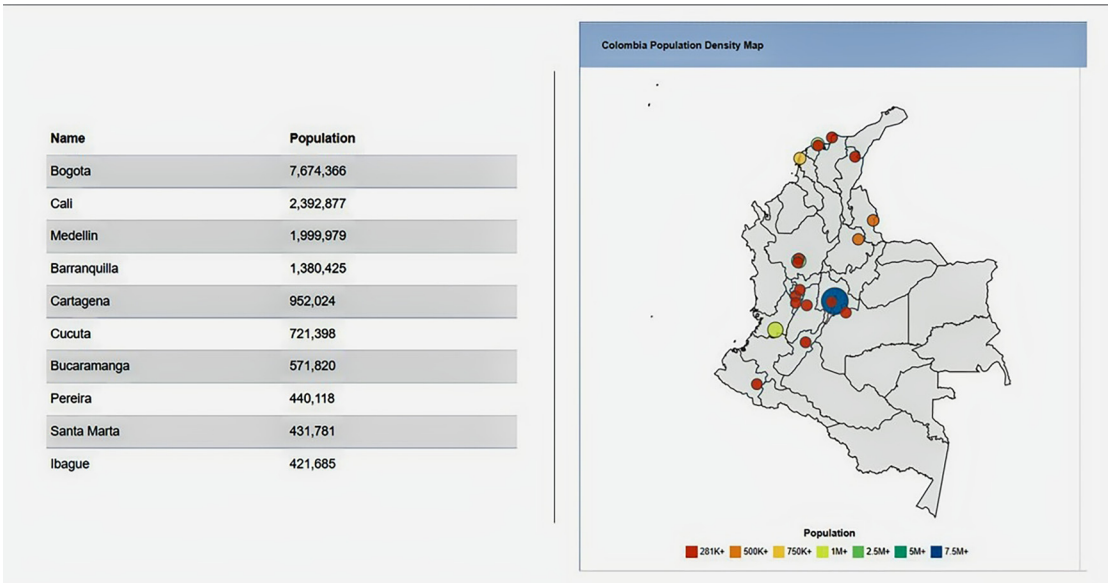

Name	Population
Bogota	7,674,366
Cali	2,392,877
Medellin	1,999,979
Barranquilla	1,380,425
Cartagena	952,024
Cucuta	721,398
Bucaramanga	571,820
Pereira	440,118
Santa Marta	431,781
Ibague	421,685

Figure 1. Colombia's population density map shows average-sized cities dominating urban areas.

the same latitudinal level, such as San Pedro Garza Garcia and Monterrey, show significant differences in prevalence. Specifically, the prevalence in San Pedro Garza Garcia is two to three times higher than in Monterrey. This finding suggests that factors other than latitude may play a more crucial role in determining the prevalence of MS, highlighting the importance of local environmental and possibly genetic influences.[12]

MS prevalence has dramatically risen[8] in large, urbanized countries like Argentina, where prevalence in Buenos Aires increased from 14 to 19/100,000 habitants to 38/10,000 habitants.[4] Puerto Rico has also noted a rise in cumulative prevalence, estimated at 68/100,000 habitants.[3] Colombia is situated in 12°N to 4°S latitude and is considered a low prevalence region for MS.[2,9–11] Due to the low prevalence, MS is considered an orphan disease in Colombia. Data reported by the National Institute of Health in February 2023 highlighted a total of 4263 documented MS cases recorded in Colombia spanning the period from 2016 to 2022.[13] The prevalence of MS in Colombia from 1995 to 2000 ranged from 1.48 to 4.89 cases per 100,000 inhabitants. This considerable difference in prevalence rates across the country may be attributed to various factors, including geographical variables, weather conditions, and altitude,[1] but it is unclear if altitude may influence in the odds of MS, a previous study did not find difference in regions regarding altitude when adjusted by latitude,[14] even though, additional studies are required to confirm it. Recent prevalence estimates (from 2009 to 2013) indicate higher rates in the Andean regions, such as Bogotá and Quindío, compared to the Pacific or Atlantic coast. Furthermore, an even higher prevalence is reported for Risaralda, at 10 per 100,000 inhabitants, which aligns closely with the prevalence estimated by Muñoz-Galindo in 2018.[15] Noteworthy, the limitations in these estimates are associated with: (I) inaccuracies in official governmental statistics, (II) heterogeneity in the published data, (III) small cohort sizes, (IV) different methodological approaches, (V) lack of access of the population to specialized neurological evaluation, (VI) lack of neuroimaging resources, and (VII) lack of laboratory resources for analysis of CSF biomarkers for MS.[6,8,16,17] These factors collectively make it challenging to comprehend the true prevalence of MS in the region.[17,18]

Clinical characteristics

The clinical characteristics of people with MS in Colombia appear to follow typical expected ranges described worldwide. Most MS patients in Colombia range between 25 and 60 years old, affecting mainly young and middle-aged adults.[2,6,18] An increase in the diagnosis of MS in recent years could be the result of an increase in neurological training, health literacy programs,[6,8] and better access to MRI and laboratory analysis (i.e. oligoclonal band testing). In fact, a regional study in Colombia (2011) suggested that 94% (192/204) of MS patients had access to brain and spinal cord MRI, 82% (167/204) of patients have had visual evoked potentials and approximately 45% (92/204) of patients have access to oligoclonal

bands in CSF and serum analysis[19] which has led to improved diagnosis and can directly influence prevalence in LATAM. Possibly, the changes to diagnostic criteria that have led to earlier diagnosis of MS could be contributing to the rise of MS in Latin America, however, it is not clear if the diagnostic criteria in MS are sensitive to the racial and ethnic variability seen in LATAM.[20,21] In 2017 Pagani-Cassara et al. found that the specificity and sensitivity of the 2017 McDonald criteria in MS patients in Argentina after a first demyelinating event was 67% and 53% respectively, and compared with the 2010 McDonald criteria, increasing two-fold the probability of diagnose MS after the first demyelinating event.[22] However, these studies are not generalizable to the rest of the LATAM population, because the ethnic and genetic ancestry, as a result of European, African, and Native-American admixture in LATAM, are not well reflected in the Argentinian cohorts.

The Colombian health system

The Colombian health system is made up of a large social security sector financed with public and private resources. The central axis of the model is the administrator of resources of the general social system security in health (ADRES, in Spanish). There are two healthcare regimens in Colombia, a contributory regime, built through contributions from employers and employees, and a subsidized regime, which receives contributions from the government and delivers care to the low-income population measured by unmet basic needs.[23] Medical care is provided through health-promoting entities (EPS), which receive the contributions, and through the institutions providing services, which offer the Health Benefits Plan (PBS).[24]

In 2019, the Colombian government, seeking better distribution and greater coverage of high-cost drugs, designed the law of "maximum recovery budget," which states that services and technologies not financed in the PBS (including certain disease-modifying therapy (DMT)) must be administered by EPS and financed by the ADRES. In Colombia, despite its low prevalence, the economic impact of MS is high. For the period 2002–2005, MS was the diagnosis that represented the highest cost covered by ADRES with an amount of about 19.5 million U.S. dollars.[25,26]

Currently, there is no large comprehensive patient database or local Colombian MS registry. This information gap poses challenges for health professionals, researchers, and policymakers in addressing the unique needs of MS patients. The absence of a solid knowledge base on the follow-up of MS patients, and whether differences exist in the public or private health sector, hinders the development of tailored interventions and personalized treatment plans. To address this problem, rigorous scientific research covering various aspects of MS is needed. Closing this knowledge gap is crucial to optimize the well-being and quality of life (QoL) of MS patients in Colombia.

Currently, despite increasing awareness through social media, MS is not considered a significant health burden.[27] Furthermore, sufficient priority is not given to making mandatory specialized MS programs a part of the health policy. Still, the growing number of MS cases in Colombia and the constant introduction of new DMTs would increase the disease cost, which makes it more important for neurologists, health insurance companies, and patients to pay more attention to MS. According to published estimates, there were approximately 5.2 neurologists per 100,000 inhabitants in the United States,[28] with notable variations from state to state. This mirrors the situation in Colombia, where neurologists tend to be concentrated in major cities. Additionally, there is a significant lack of training in neuroimmunology and the diagnosis of MS, with only a few university-based centers offering specialized care and diagnostic services in this domain. All these factors require well-designed strategies that facilitate patients to have wide access to specialized MS centers in Colombia.

Quality of life

Currently, there are very few studies about QoL in Colombian MS patients, a single center study using a small cohort of patients ($n = 55$) revealed a good baseline QoL, which was maintained at similar levels at the six-month and 12-month follow-ups, measured by MusiQol score, however, an inversely proportional correlation was observed between the Expanded Disability Status Scale (EDSS) and QoL indices.[29] Interestingly, symptoms of fatigue and depression were lower (27% and 7% respectively) than described in published studies.[30–34]

Mortality rate

Characterized as a neuroinflammatory condition with a relapsing and/or chronic nature leading to neurodegeneration, MS is marked by a significant incidence of morbidity and disability. Additionally, various studies have indicated a reduced lifespan for MS patients, typically ranging from 7 to 14 years when compared to the general population.[35] The mortality rate in MS has been estimated from two to three-fold compared with

the general population. However, it is highly variable according to age, sex, race, duration of the disease, or geographical region.[36–38] In Colombia, a retrospective observational study conducted between 2008 and 2013 that included approximately 7000 orphan disease-related deaths found that MS was the orphan disease with the highest mortality rate in patients older than 45-year-old which represents the leading cause of death at all ages in female patients with orphan diseases.[39] It is important to note the potential limitations of the mortality estimate in Colombia. These findings are based on death certificates and not necessarily on a comprehensive autopsy analysis.

Health costs

The cost of MS in the health care system worldwide has risen in the last 20 years, since the advent of new DMTs, modern diagnostic tools (MRI), or wider and more sensitive diagnostic criteria to increase early disease detection.[40–42] For instance, in the United States, annual costs range from 30,000 to 60,000 USD per patient depending on disability level or DMT prescribed, and the total cost for all MS patients represents around 28 billion annually.[40,41,43,44] In Europe, the annual cost per patient with MS has been estimated from 22,800 € to 60,000 €, being higher in patients with higher disability level.[45] In 2011, Romero et al., found that between 2002 and 2005 total public health cost for MS patients in Colombia was approximately 19.5 million USD, being approximately 20.000 USD patient/year in patients with EDSS <3 and ~30.000 USD patient/year in those with EDSS 6 or higher.[25] This data supports that in Colombia, related MS costs increase with the disability level, as described in previous studies worldwide[44] with DMTs representing around 90% of the costs.[15] More recent data show that the total health cost of MS therapies was estimated around 40 million USD.[2] However, the approval of newer MS therapies in the last 10 years may have led to increased MS costs in Colombia.

Genomic and ethnicity

Colombians are very diverse, not just in terms of geographical distribution, but also in terms of genetics and ethnicity. The country has a large ethnic diversity, throughout all the territory.[46,47] Ossa et al. (2016), found that in Colombia, European ancestry genes are more prevalent in cities like Bogota, Medellin, Manizales, and Tunja, where they constitute around 58%, whereas in other regions, such as Amazonia, most ascending genes come from native ancestry, accounting for approximately 65%, or the Pacific Coast, where Afro-descendant ancestry genes equate to 63% of total genes.[48] On the other hand, Hispanic and Asian populations share quite a genetic similarity, especially regarding HLA.[49] Many haplotypes have been described previously in NA and Asian populations, mainly those from northeast Asia and Japan, including HLA DRB1*14 and HLA B*39, HLA DRB1*08, HLA A31, and HLA B5.[49] This is remarkable given the low MS prevalence in both areas, which might indicate how the haplotypes HLA distribution may draw the global MS map. Also, it has been described that some of these HLA, especially HLA DRB1*14, HLA-DRB1*11-, HLA-DRB1*01-, and HLA-DRB1*10 may have a protective effect.[50] Among Colombians, a study found that HLA-DRB1*14 and DQA1*103 were associated with lower risk,[51–53] despite these data, the knowledge, and available evidence about genomic factors in Colombian MS patients is still relatively scarce. There is a big gap in understanding the ancestry of many Latin American countries that could potentially explain the disease variability in the region (disease phenotype, risk factors for higher disability, etc.), as well as the role of other tropical infections (not limited to Epstein Barr virus (EBV) or parasitic infections) in neuroimmunological disorders.

Environmental factors

Along with previous data about genetic factors in the risk and the course of the disease, it has been widely recognized that genes by themselves are not sufficient to develop MS and it is likely caused by a complex interaction between genetic predisposition and environmental factors.[54] Previous studies have shown that some patients who migrated from a low prevalence MS region to a higher one, increase the risk of developing MS and vice versa, which would indicate that the environment may modify the individual risk.[7,55] Several environmental risk factors have been proposed as triggers of MS including infections, vitamin D levels, UV radiation, or "Western diet."[7,54] For instance, large data and several studies have shown that EBV infection is closely related to the risk of MS[55–57] and even more, some authors have found that close to 100% of MS patients are EBV-positive[58] which suggest that EBV virus is a crucial environmental factor in the risk of the disease, being even higher when is associated to HLA-DRB1*1501.[59] In Colombia the findings are similar, in 2020 Toro et al., found that MS patients have higher antibody titers against EBV nuclear antigen 1 (anti-EBNA1) compared to non-MS patients, which is consistent with worldwide data.[60] Moreover, in LATAM some studies have found that MS is less likely to develop in populations with high *Trichuris trichiura* prevalence,[61,62] which might be associated with the "hygiene hypothesis," previously described in patients with MS.[61] Furthermore, Correale et al., found that MS patients with *T. trichiura* infestation have lower

disease activity compared with noninfected MS patients.[62] In Colombia this finding has not been studied yet, nevertheless, it is known that the prevalence of the *T. trichiura* infestation can reach up to 90% in some areas,[63] and even more the presence of polyparasitism defined as the presence of two or more parasites is around 85% of the population in the Amazonia region.[64] Vitamin D and sun exposure are also relevant in the risk of developing MS[65] since previous studies have shown that these factors are linked, nevertheless, the pathophysiological mechanism is not completely clear, but it seems to have a regulatory effect in immune cells such as T and B cells.[66] MS prevalence maps show that areas with lower MS prevalence are predominantly those with higher sun exposure which is also linked to vitamin D metabolism, and they could be related to MS risk. This link between vitamin D and MS has been inconsistently demonstrated in LATAM. In Argentina, Correale et al. found that MS patients with lower vitamin D levels have a higher relapse rate[67] but recent studies from Mexico[68,69] and Colombia[60] found no differences in vitamin D levels between MS and non-MS patients, and no association of disease activity and vitamin D levels among MS patients.[60,69] Further studies regarding vitamin D levels and MS risk need to be performed in LATAM to have more accurate data.

Diet and intestinal microbiota have been highlighted as important environmental factors for MS development in recent years.[17] The higher adoption of "Western diet" in LATAM, not only in big cities but also in rural regions, has contributed to the risk of developing both cardiovascular and autoimmune diseases.[70,71] The changing diet in the last 20 years may have affected the risk of MS. Previous research has shown childhood obesity to increase the risk of MS over the years in comparison to those with normal weight.[72,73] These findings are crucial considering that obesity prevalence has rapidly increased in LATAM countries such as Colombia where obesity and overweight represent around 57% of the adult population.[74] Likewise, evidence suggests that high consumption of saturated fat, salt, sugar, or even animal protein results in a higher inflammatory response involving proinflammatory cytokines[75] and induces intestinal microbiota changes to a higher proportion of *Firmicutes phylum* which also increases the "inflammatory state" in MS.[76,77] Therefore, it is interesting to find out that intestinal microbiotas in Latinos are different from those in the United States. In 2019, Kaplan et al. showed that immigrants who had arrived in the United States after their 40s have a higher proportion of *Bacteroidetes phylum/Prevotella* and *Firmicutes* than Latinos who had migrated during childhood or those born in the United States from Latino parents,[78] which highlight the impact of the "western diet" and environment in the intestinal microbiota. Furthermore, gut microbiota in the Colombian population is different from North Americans, Europeans, or Asians, being predominantly *Firmicutes and Bacteroidetes phylum*.[79–81] The microbiota, diet, and lifestyle may be factors in the development of MS in the Colombian population, but additional studies are necessary to gain a deeper understanding.

Disease-modifying therapy access in Colombia

MS is a growing health problem in LATAM, and regional efforts continue to achieve timely access to both diagnostic tests and treatment options for the disease.[17,18,28] Colombia has a privileged position among other LATAM countries regarding the availability of DMTs,[82] providing almost all the options currently approved (except ublituximab, ozanimod, ponesimod, and monometil/diroximel fumarate). In the United States, First DMTs, approved in 1993, were three different preparations of beta-interferon (IFNβ) and shortly thereafter, glatiramer acetate (GA) was approved.[83,84] In Colombia, DMTs were introduced more than 20 years ago and by 2015 Jimenez et al. described that beta interferon 1A was responsible for 32% of the total cost of DMTs.[2] Regarding safety profile, the most common adverse events (AEs) with a consistently higher incidence with INF than with placebo are injection site erythema, influenza-like illness, pyrexia, headache, myalgia, chills, and injection site pain.[83,84] The first oral treatment, fingolimod, was approved in the United States in 2010; it is an analog of sphingosine and induced migration and sequestration of lymphocytes in the lymph nodes.[83] In Colombia, it was approved in 2012 and since then has been widely prescribed. Rosselli et al. designed a budget impact model to determine the effect that the introduction of fingolimod for patients with relapsing-remitting MS would have on the resources of the health system. They revealed that the introduction of fingolimod in the Colombian healthcare system does not imply a significant budget impact but represents an important reduction in the number of MS relapses.[85] New oral sphingosine modulators have been approved, such as siponimod and ozanimod,[86,87] and it is possible to have them in Colombia in the short term. Fingolimod has evidence regarding its efficacy, reducing annualized relapse rates by 48% compared to placebo. The reduction in Gd-enhancing T1 lesion counts for fingolimod versus placebo was 65%. Furthermore, fingolimod

reduced the number of new or newly enlarged T2 lesions by 69% relative to placebo.[86] Some adverse effects mentioned include bradyarrhythmia, ventricular tachycardia, hemorrhagic focal encephalitis, decreased hemoglobin level, and lymphoma. Recently, cases of progressive multifocal leukoencephalopathy (PML) due to the John Cunningham (JC) virus were reported with fingolimod.[86] Other oral therapies such as teriflunomide (TFN), an oral drug that inhibits the biosynthesis of pyrimidine, was introduced in 2012.[83] Dimethyl fumarate (DMF) was introduced in 2013, activating the nuclear factor erythroid 2–related factor 2 pathways and demonstrating moderate efficacy. However, it is associated with a high rate of gastrointestinal (GI) symptoms, and additionally, higher-risk adverse effects such as lymphopenia, risk of infection, and the need for laboratory monitoring. To address these concerns, diroximel fumarate was developed and approved. It shares the same pharmacologically active metabolite as DMF but is associated with fewer GI AEs. In 2020, Monometil fumarate received approval, showcasing fewer GI AEs compared with DMF. It's important to note that while these fumarates may have reduced GI AEs, other risks, and considerations such as lymphopenia and infection risk, as well as the necessity for lab monitoring, should be considered.[88–90] The newer fumarates are not yet available in Colombia. Cladribine, a new oral agent with an immune-suppressing effect derived from inhibiting DNA synthesis was approved by the FDA in 2019 and it is considered a highly effective DMT. It is recommended for patients who have had inadequate response to other therapies or naïve patients with highly active disease.[91] In Colombia, TFN and DMF have been used since 2014 and 2016 respectively. Also, Cladribine obtained approval in 2020 and it has been used lately.[92]

Novel therapeutic options such as monoclonal antibodies (mAbs) that suppress or modulate the immune system by acting against B and T cells and other components of cell migration through the blood–brain barrier are available in Colombia[93,94] (see Table 1). First approved was natalizumab[83] which showed a significant increase in treatment efficacy compared with injectable therapies, but there are some considerations regarding the safety and profiling of patients, to reduce the risks associated with disease-

Table 1. A comparison of Food and Drug Administration (FDA) and Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA), which is the national institute for food and drug surveillance, approval years for every multiple sclerosis therapy available in Colombia.

Disease modifying therapy	Year of FDA* approval	Year of INVIMA** approval
INFB-1b	1993	1997
INFß-1 a	1996	2007
INFß-1 a	2002	2010
Galatiramer acetate	1996	2015***
Natalizumab	2004	2010
Fingolimod	2010	2011
Teriflunomide	2012	2014
Alemtuzumab	2014	2015
Dimethyl-fumarate	2013	2016
PEG-INFß-1 a	2014	2017
Ocrelizumab	2017	2019
Cladribine	2019	2020
Ofatumumab	2020	2022

*The FDA (Food and Drug Administration) serves as the regulatory authority for medications in the United States.
**In Colombia, a similar role is undertaken by INVIMA (Instituto Nacional de Vigilancia de Medicamentos y Alimentos) which is the national institute for food and drug surveillance
***The official approval for Galatiramer acetate in Colombia pertains to the concentration of Galatiramer acetate at 40 mg/ml, as per the information provided by INVIMA (Instituto Nacional de Vigilancia de Medicamentos y Alimentos), the regulatory authority in Colombia.
You can find information about FDA-approved drugs at the following link: [FDA Drug Approval] (https://www.accessdata.fda.gov/scrips/cder/daf/). Additionally, data on currently valid medications in Colombia can be accessed via the following link: [Unique Code for Valid Medications on datos.gov.co] (https://datos.gov.co/en/Salud-y-Protecci-n-Social/C-DIGO-NICO-DE-MEDICAMENTOS-VIGENTES/i7cb-raxc/data).

modifying treatment, such as PML, a serious potential AE[94] In Colombia, its use has shown good outcomes since its approval in 2010. García-Bonitto et al.[95] showed that more than 80% of the individuals on Natalizumab therapy reached NEDA (no evidence of disease activity) status during a mean time of 9.2 years, with no evidence of PML; the risk can be assessed with JCV status, available in our country. Rosselli et al. estimated the cost-effectiveness of natalizumab compared with fingolimod for relapsing-remitting MS (RRMS) with high disease activity or failure of the interferon therapy as first-line therapy based on a Markov economic model. This result showed natalizumab had lower costs and higher quality adjusted life year (QALY) than fingolimod in patients with high-activity RRMS,[85] similar findings have been found in other studies.[96,97]

The mAb Alemtuzumab was FDA-approved in 2014. Alemtuzumab targets and depletes CD52-expressing cells including T and B cells, natural killer cells, and monocytes. Alemtuzumab has demonstrated higher efficacy compared to interferon beta 1-a in clinical and MRI outcomes (CARE-MS I and II). The most frequent AEs described with Alemtuzumab include infusion-related reactions, autoimmune disease, and thyroid dysfunction. Immune thrombocytopenia and nephropathies are less frequent. Rare opportunistic infections including but not limited to listeriosis, cytomegalovirus infection, and pulmonary aspergillosis have been described.[98]

The anti-CD20 mAb Ocrelizumab was FDA-approved in 2017, leading to B cell depletion. Ocrelizumab efficacy was compared with interferon beta-1a in the OPERA and ORATORIO pivotal trials, demonstrating reduced clinical and radiological progression in the Ocrelizumab arm, with infusion-related reactions accounting for the main AE. It is noteworthy to mention hypogammaglobulinemia and severe B cell depletion as AEs that need to be monitored to minimize infections among MS patients. These tests are widely available. The infections related to Ocrelizumab were mainly mild or moderate. A slightly increased risk of malignancies has been observed.[83,99]

The latest therapy approved and available for RRMS in Colombia is Ofatumumab (OMB) which also targets CD-20 but binds to different epitopes in the receptor than Ocrelizumab. The efficacy of Ofatumumab was compared to Teriflunomide in ASCLEPIOS I/II trials,[100] improving clinical and radiological outcomes with a higher proportion of patients achieving NEDA-3. Common AEs included infusion-related systemic reactions which were mild to moderate. It is important to remark that this mAb is designed for subcutaneous administration[101] and hence could improve access in cities without infusion centers. The cost-effectiveness of this therapy was evaluated by Tamayo et al. with a Markov model predicting that OMB is a dominant alternative (with lower expected costs and higher number of QALYs) in most of the simulations carried out: 72% compared to Fingolimod and in 54% compared to Natalizumab.[102]

Furthermore, concerning the safe use of immunosuppressive therapy, it is important to note that in Colombia the incidence rate of tuberculosis of all forms is estimated to be 25.96/100,000 inhabitants, showing a 4.61 increase compared to 2020.[103] As per the Tuberculosis Panel of National expert recommendations, it is considered good clinical practice to carry out tuberculosis testing to rule out latent forms before prescribing MS medications. The recommended tests for latent tuberculosis are tuberculin and interferon-gamma release.[104] Given Colombia's endemic status for *Strongyloides stercoralis* and other helminthic infections, it is important to consider these infections in the differential work-up of MS before prescribing steroids or antiparasitics.[105]

Unfortunately, there is no current real-world data about safety and effectiveness in the Colombian population. The therapeutic approach decision regarding how to treat an MS patient lies directly on treating physicians, based on their knowledge and clinical expertise.[106,107] Given the complexities of MS and the difficulties in treatment decision-making when considering DMTs, the LACTRIMS released guidelines in 2012, encompassing recommendations to assist clinicians when they start, switch, and stop DMTs for their patients,[108] nevertheless, it is important to highlight the heterogeneity in LATAM population which make difficult to extrapolate guidelines to the whole region. The use of generic (nonproprietary) medications has been increasing in recent years. Since several developing countries produce drugs at similar costs as brand names benefiting from more flexible rules and regulations in the health system,[17] this could also impact the management of MS patients. Saposnik et al. reported that the formulation of bioequivalent medicines is strongly related to therapeutic inertia, which is defined as the lack of treatment initiation or intensification when treatment goals are not met.[109] In LATAM, access to MS therapies depends on several factors such as socioeconomic status,

social security system, or the availability of MS centers: In fact, a recent study suggested that MS patients from lower socioeconomic groups have difficulties accessing higher efficacy DMTs.[110] Currently, there is no available data on prescription practices in Colombia, or information about the accessibility of infusion centers, especially in rural areas. These factors could impact individualized therapeutic decisions, underscoring the necessity for additional research on this topic.

Conclusion

In summary, MS in Colombia is an orphan disease associated with a meaningful morbidity and mortality rate in young adults. This review highlights country-specific epidemiological data, prevalence rates, and healthcare infrastructure relevant to Colombia. Additionally, it highlights the barriers to access which include the lack of resources, lack of awareness of MS symptoms among the general population and health care professionals, and the difficulties in accessing MS centers or neurologists with the knowledge to diagnose MS. Taken together, this review underlines the relative paucity of available MS data in the Colombian population. Although the use of several DMTs has been approved in Colombia, there remain significant challenges to effectively deliver these treatments and to ultimately understand the impact they will have for the MS community across the country. The unique racial/ethnic, cultural, ancestral, and environmental landscape of Colombia may provide researchers an opportunity to discover new genetic and environmental risk factors that may help to specifically address the needs of the Latin-American population and more generally to better understand the underlying biology of MS. Future regional studies will undoubtedly allow us to expand our knowledge about patients living with MS in Colombia.

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