



Prevalence of neuromyelitis optica spectrum disorder in Colombia: Analysis of the official Ministry of Health administrative registry

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ARTICLE INFO

Keywords:

Epidemiology
Neuromyelitis optica
Registries
Optic neuritis
Myelitis
Transverse

ABSTRACT

Background: Neuromyelitis optica spectrum disorder (NMOSD) is a rare entity with severe inflammatory demyelinating events of the central nervous system with debilitating sequelae. Its global prevalence ranges between 0.5 and 4/100,000 individuals, with variations by region and ethnicity. Latin America lacks epidemiological data on the disease, and Colombian prevalence is unknown.

Objective: Prevalence of NMOSD in Colombia was estimated between 2017 and 2021 using the official Ministry of Health administrative database (SISPRO).

Methods: This is an observational, cross-sectional retrospective study, using data between January 2017 and December 2021 in the SISPRO database using the International Classification of Disease code for NMOSD G36.0. Prevalence by gender, age and geographic distribution was estimated using official government statistics for 2019. World Health Organization (WHO) standard population was used to adjust using the direct method.

Results: 2,650 patients were diagnosed with NMOSD; the average age was 44.9 years with an overall unadjusted prevalence of 5.3/100,000 individuals, higher for females (7.8) than for males (2.8). No significant changes (from 5.3 to 5.4) were seen after adjusting to the WHO standard.

Conclusion: According to this study Colombia has one of the highest prevalence rates of NMOSD in Latin America, further studies are needed to elucidate the contributing factors.

1. Introduction

Neuromyelitis optica spectrum disorder (NMOSD) encompasses a group of severe inflammatory demyelinating events in the central nervous system, affecting both the optic nerve and spinal cord (Ma et al., 2020). As a demyelinating disease, it is characterized by relapses that result in demyelination plaques, leading to persistent neurological symptoms accumulating sequelae and disability, even after treatment (Jarius et al., 2020).

NMOSD is a relatively rare condition, with an estimated annual worldwide prevalence ranging from 0.5 to 4 cases per 100,000 individuals and an annual incidence of 0.5 to 0.8 per million people. These rates vary depending on the region and ethnicity (Ma et al., 2020; Jarius et al., 2020). In the Caucasian population, the estimated prevalence is around 1 case per 100,000 people, with an annual incidence of less than

1 case per million. However, in Asian populations, the prevalence is higher, with an approximate rate of 3.5 cases per 100,000. Additionally, individuals of African descent may experience an even higher prevalence, reaching up to 10 cases per 100,000 (Hor et al., 2020). While NMOSD can occur at any age, it predominantly affects young adults, with an average onset age of around 40 years, and a higher prevalence in females (Ma et al., 2020).

There is limited information available on the epidemiology of this disease in Latin America (Rivera et al., 2021), and there is currently no data on its current prevalence in Colombia. However, in recent years, there has been a growing interest in studying various aspects of this disease in our region. For instance, in 2008 Rivera et al., reported a prevalence of 1/100,000 in Mexican Mestizos (Rivera et al., 2008). In 2021 Lana-Peixoto et al. reported a prevalence of 4.5/100,000 in Belo Horizonte, Brazil (Lana-Peixoto et al., 2021). More recent studies from

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<https://doi.org/10.1016/j.msard.2023.104915>

Received 26 March 2023; Received in revised form 11 July 2023; Accepted 23 July 2023

Available online 24 July 2023

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Venezuela estimated a prevalence of 2.2/100,000, with a female-to-male ratio of 4:1 (Soto de Castillo et al., 2021). Lastly, a multicenter study on NMOSD in Central America and the Caribbean reported a prevalence of 1.6/100,000 in Panama and 0.7/100,000 in the Dominican Republic (Gracia et al., 2022). Last year, the first paper on NMOSD epidemiology in Colombia was published, gathering data from Antioquia between 2016 and 2019, with an estimated prevalence of 4.03/100.000 in this specific region (Monsalve et al., 2022).

The objective of our study was to estimate the prevalence of NMOSD in Colombia through the analysis of the official Ministry of Health administrative database.

2. Methods

This is an observational, cross-sectional retrospective study which uses SISPRO, the official Ministry of Health administrative database, to estimate NMOSD prevalence in Colombia. SISPRO, which stands for *integral system of information for social protection*, is a comprehensive information system established in 1993 in Colombia that serves as a centralized platform that collects data related to social protection and healthcare services in the country (Rosselli and Pantoja-Ruiz, 2022). This system provides accurate and up to date information about the overall performance of the national health system, that provides nearly universal coverage, exceeding 99% of the population (Ministerio de Salud y Protección Social 2022), and helps policymakers and authorities monitor healthcare indicators and facilitates data-driven decision making. SISPRO obtains data from various sources that include government agencies, private and public healthcare providers, and social security institutions. This data, which is freely available for research purposes, is collected through standardized reporting mechanisms, electronic healthcare records and administrative databases (Rosselli and Pantoja-Ruiz, 2022) and has been used previously in other epidemiological studies (Justo et al., 2019; Fernández-Ávila et al., 2019).

Following the STROBE guidelines for observational studies, data was collected from the SISPRO database for patients who were diagnosed with NMOSD and assigned the ICD-10 code (G36.0) for NMOSD. Considering that the most recent diagnostic criteria for NMOSD were published in 2015 (Fujihara, 2019), and it took approximately a year for their implementation in our country, we chose to include data from starting from 2017 to 2021. The total number of cases detected during this time period was divided by the total Colombian population in 2019, according to SISPRO data, to estimate a crude national prevalence

expressed per 100,000 individuals. Additionally, prevalence was adjusted by age group, gender, and geographical location for every department in the country.

A final adjustment, using the “direct method”, was performed to allow international comparisons using the World Health Organization (WHO) standard population (Rosselli, 2023).

This research was approved by the Institutional Review Board of our university. According to the Declaration of Helsinki, informed consent was not required as the database does not contain variables that allow the identification of individual participants, thus respecting confidentiality.

3. Results

A total of 2650 cases of NMOSD were reported in Colombia between 2017 and 2021, with 73.1% of these cases being female, resulting in a female-to-male ratio of 2.8. The mean age of individuals affected by NMOSD was 45 years. The unadjusted crude prevalence of NMOSD in Colombia was calculated to be 5.3 cases per 100,000 individuals, higher for females (7.8) than for males (2.8). When considering age groups, the highest prevalence was observed among women between the ages of 50 and 59, with a prevalence rate of 19.8 cases per 100,000, as depicted in Fig. 1. After adjusting by age group, using the direct method and the WHO standard population, the prevalence did not suffer any significant change (moved from 5.3 to 5.4; 7.8 to 7.9 in females, and remained in 2.8 in males), due to the similarity in age distribution of the Colombian population and the WHO standard population (Rosselli, 2023).

In terms of geographic distribution, the prevalence rates for each political division of the country unveiled the highest prevalence in Sucre, a department in the Caribbean region, with a rate of 10.5 cases per 100,000. This was followed by Bogotá and Risaralda, both in the central Andean region, which reported prevalence rates of 10.3 and 10.2 cases per 100,000, respectively (See Table 1)

4. Discussion

NMOSD is an uncommon disease worldwide. Variations in prevalence have been described among different geographic regions and ethnicities (Papp et al., 2021). In this study, we identified a crude prevalence rate of 5.3 cases per 100,000 inhabitants for Colombia (5.4 after adjusting to the WHO standard population), which is among the highest reported prevalence rates not only in Latin America, but globally.

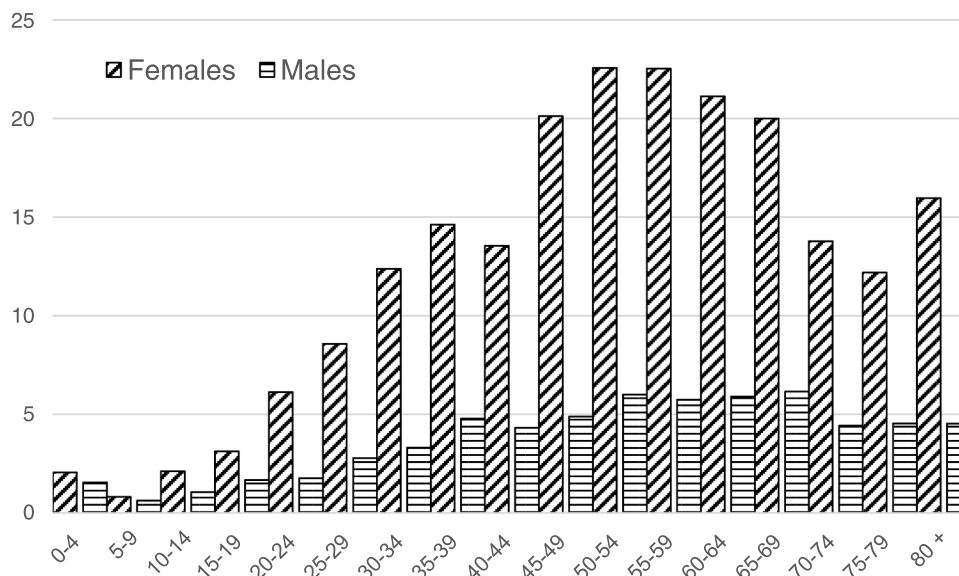


Fig. 1. Age distribution, by five-year age groups, of NMOSD prevalence in Colombia, expressed as cases per 100,000 inhabitants.

Table 1

List of the 20 departments of Colombia with higher prevalence rates (cases per 100,000 inhabitants).

	Females	Males	Total
Sucre	13.95	7.13	10.50
Bogotá	14.63	5.68	10.29
Risaralda	14.82	5.28	10.17
Quindío	12.57	4.93	8.82
Atlántico	12.61	4.40	8.55
Córdoba	10.38	4.07	7.22
Valle del Cauca	9.72	3.87	6.89
Antioquia	11.07	2.48	6.87
Norte de Santander	7.77	5.33	6.56
Tolima	7.99	2.96	5.48
Bolívar	6.92	3.28	5.10
Caldas	7.47	1.64	4.62
Santander	6.50	1.93	4.24
Cundinamarca	4.90	2.33	3.62
Magdalena	5.40	1.51	3.43
Boyacá	5.47	1.24	3.35
Cesar	5.00	1.30	3.15
Huila	3.98	2.30	3.14
Chocó	3.47	2.30	2.88
Cauca	4.54	1.25	2.87

Although NMOSD can occur at any age, it is more frequent in young adults and middle-aged individuals, with an average age of onset around 40 years (Ma et al., 2020). However, there are studies on that reveal a significant proportion of cases, ranging from 20% to 28%, with late onset presentation over the age of 60 (Papp et al., 2021). In a meta-analysis conducted by Hor et al. (2020), different presentation ages were observed, with African descendants typically presenting between 28 and 33 years of age, Asians between 35 and 40 years, and Caucasians around 44 years. Another meta-analysis by Papp et al. (2021) found the highest prevalence in India between 30 and 39 years and in Catalonia and Hungary between 40 and 59 years. These findings are consistent with our data, which shows that most cases of NMOSD are

found between the ages of 40 and 69 in both men and women; the age group with the highest prevalence in women is between 50 and 59 years.

Previous papers have indicated that the majority of affected individuals are women, with female-to-male ratios ranging from 2.3 to 7.6 (Papp et al., 2021), consistent with our 2.8 ratio.

Different ethnicities and geographical regions have reported varying prevalence rates that range from 0.5 to 4 per 100,000 individuals, with East Asians (Japanese, Chinese, and Koreans) and Afro-descendant populations being more susceptible to NMOSD compared to Caucasians and other Asian racial groups (Ma et al., 2020; Hor et al., 2020). Interestingly, the lowest prevalence rates have been found in Australia and New Zealand, with 0.7/100,000 inhabitants (Papp et al., 2021) (Fig. 2). These variations in prevalence rates suggest that there are underlying factors, including genetic and environmental influences, contributing to the differences observed among different ethnicities and geographical regions.

Ethnicity, geography, and culture are likely to be associated with human leukocyte antigens (HLA) and the microbiome. Several studies have demonstrated a significant link between HLA alleles and NMOSD. For example, in the Netherlands, patients with IgG AQP4 (aquaporin 4) were found to have HLA DRB103, along with HLA A01 and HLA B08 (Jarius et al., 2020). Similar associations were reported in Mexico and Spain, where HLA DRB110 and HLA DRB103 were implicated (Alonso et al., 2018; Blanco et al., 2011), as well as in the French Afro-Caribbean population with HLA DRB103 (Deschamps et al., 2011), and in Brazil with HLA DRB1×03:01 (Alvarenga et al., 2017). It is plausible that in Colombia, there may be a high frequency of HLA antigens associated with an increased risk of developing NMOSD, an aspect that warrants investigation in future studies.

Dysbiosis of the gut microbiota has been observed in individuals with NMOSD, characterized by an imbalance between pathogenic bacteria and decreased levels of beneficial commensal bacteria (Shi et al., 2020). Preliminary studies investigating gut microbiota in NMOSD patients have indicated a strong association with Clostridium perfringens. Additionally, certain Clostridium strains in the gut have been found to

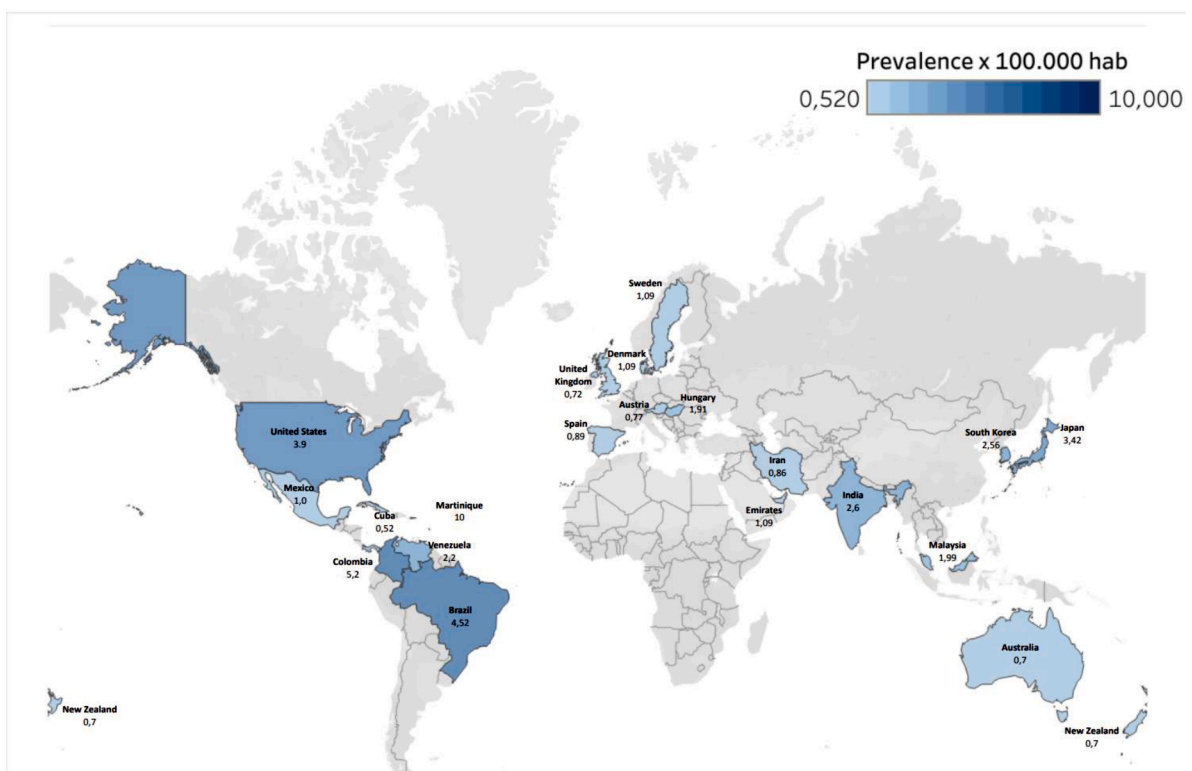


Fig. 2. World distribution of NMO prevalence per country (cases per 100,000 inhabitants).

influence the equilibrium between regulatory T cells and Th17 cells, suggesting a potential involvement of gut microbiota, including *C. perfringens*, in the development of NMOSD (Zamvil et al., 2018). Further investigations comparing the microbiota composition between NMOSD patients and healthy individuals are essential to elucidate the possible role of microbiota in NMOSD pathogenesis.

The only previous prevalence study in Colombia was conducted in Antioquia, a department of the Andean region of the country, which reported a prevalence rate of 4.0/100,000 for that specific region (Monsalve et al., 2022). Although slightly lower than the prevalence reported in this study, it still remains one of the highest in Latin America and worldwide. Additionally, this study revealed that the department with the highest prevalence was Sucre, followed by Bogota and Risaralda. In Colombia, as well as in many other countries in Latin America, peripheral and smaller cities face barriers in terms of access to healthcare and specialists, such as neurologists. Therefore, areas with higher prevalence are correlated with larger cities that have access to magnetic resonance and specialized neurologists for accurate diagnoses. Individuals from remote areas often need to travel to these larger cities to undergo NMOSD diagnostic tests.

4.1. Limitations

The SISPRO database offers national-level data; however, the absence of a unified electronic medical records system makes it impossible to review the complete clinical data of each patient. Consequently, it is not feasible to determine how many of them are seropositive for anti-AQP4 antibodies or to ascertain the specific diagnostic criteria utilized in each case. Furthermore, it is not possible to determine who made the diagnosis of the disease, as SISPRO captures records of all healthcare encounters in the country. However, in Colombia, NMOSD is classified as a rare disease and falls under the national rare diseases law. Consequently, its notification as a rare disease requires rigorous registration and a medical board, which includes a neurologist, potentially reducing biases.

4.2. Strengths

The most notable strength of this study is its national representation. By utilizing the SISPRO database, which includes data from every region of the country, the study achieved a comprehensive understanding of the prevalence of the disease in Colombia. Furthermore, this study is the only one to date that assesses the nationwide prevalence of this disease in Colombia.

4.3. Conclusion

This study reveals that Colombia has one of the highest prevalence rates of NMOSD in Latin America, trailing only behind the rates found in the French islands. Understanding the disease's prevalence in the country can facilitate the development of public policies to ensure adequate treatment for affected patients.

While the study benefits from its national representation and use of the SISPRO database, it is important to acknowledge its limitations. The absence of a unified electronic medical records system limits the ability to review complete clinical histories. Nevertheless, the classification of NMOSD as a rare disease in Colombia ensures rigorous registration and the involvement of neurologists in the diagnostic process, thereby mitigating potential biases.

In conclusion, this study provides valuable insights into the epidemiological characteristics of NMOSD in Colombia and emphasizes the need for additional research to better understand the underlying factors driving its prevalence, particularly in relation to genetic and environmental influences. Given the high prevalence identified, future studies

on seropositivity, the diagnostic process, and risk and prognostic factors are needed to enhance our understanding, diagnosis, and management of this complex neurological disorder.

Funding

This research did not receive help from any funding agency in the public, commercial or not-for-profit sectors.

CRediT authorship contribution statement

Isabel Torres-Camacho: Writing – original draft, Data curation, Formal analysis, Writing – review & editing. **María Camila Pantoja:** Data curation, Formal analysis, Writing – original draft. **Luis Alfonso Zarco:** Writing – original draft, Data curation, Formal analysis, Writing – review & editing. **José Luis Peralta:** Writing – original draft, Writing – review & editing. **Carolina García-Alfonso:** Writing – original draft, Writing – review & editing. **Diego Rosselli:** Data curation, Formal analysis, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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