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Prevalence and incidence of multiple sclerosis in healthcare district IV of Asturias, Spain

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Abstract

Background Multiple sclerosis is an inflammatory demyelinating autoimmune disease of the central nervous system. Studies conducted in recent years point to an increase in its prevalence and a change in the age profile of patients. This study aims to analyse the prevalence and incidence of multiple sclerosis in healthcare district IV of the region of Asturias, in north-western Spain.

Methods We conducted a retrospective epidemiological study of the population of said healthcare district with a diagnosis of multiple sclerosis according to the 2017 McDonald criteria. The prevalence of the disease was calculated cross-sectionally (prevalence date: December 31, 2022), while the incidence was determined retrospectively over a six-year period, from 2017 to 2022. We gathered data from the registries and databases of the tertiary hospital in healthcare district IV, and from one private hospital. Relevant demographic and clinical data were gathered from electronic records.

Results The prevalence of multiple sclerosis in the population studied was 198 cases per 100 000 population. The incidence of multiple sclerosis during the study period (2017–2022) was 6.6 cases per 100 000 person-years. On the prevalence date, 66.5% of patients were women and 82.4% presented relapsing–remitting multiple sclerosis. Mean age was 33.98 years at symptom onset and 50.84 years on the prevalence date.

Conclusions Asturias currently presents the highest multiple sclerosis prevalence rate in Spain; the estimated rate represents an increase with respect to those reported in studies conducted in the same region in the 1990s.

Keywords Epidemiology, Multiple sclerosis, Prevalence, Incidence, Asturias, Spain

Introduction

Multiple sclerosis (MS) is a chronic disease of the central nervous system, characterised by an immune-mediated pathogenesis and onset mainly during early adulthood. Over the years, several studies have revealed changes in MS epidemiology, with increases in the prevalence and incidence of the disease [1, 2]. According to data from the Multiple Sclerosis International Federation, the number of people with MS worldwide has increased from 2.3 million in 2013 to 2.8 million in 2020 and 2.9 million

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in 2023 [1, 3]. In addition to the increase in MS prevalence, a change in the age profile of patients has also been observed; the available evidence points to a later disease onset and an older age in this patient group due to a wide range of causes [4, 5]. This has significant implications for the clinical presentation, progression, and treatment of the disease [6–8].

A total of 58 000 patients are estimated to have MS in Spain [3, 9]. Several epidemiological studies have been conducted over the years. Those conducted in the past decade reveal that Spain, and particularly north-western Spain, is a high-prevalence region for MS.

This study aims to analyse the prevalence, incidence, and geographical distribution of MS in the municipalities of healthcare district IV of Asturias, a region of north-western Spain. Results are compared against those reported by other studies conducted in the same region in the 1990s, as well as recent studies conducted in neighbouring regions.

Material and methods

Study region

A cross-sectional, observational, descriptive study was conducted to determine the prevalence and incidence of MS in healthcare district IV of Asturias, an Autonomous Community located in north-western Spain, with a total area of 10 603.57 km^2. According to the 2022 census, Asturias has a population of 1 004 686 [10]. For the purposes of healthcare planning, the region is divided into 8 healthcare districts. Hospital Universitario Central de Asturias (HUCA), located in Oviedo (N 43° 21′ 28.66″), is the only tertiary-level public hospital in Asturias, and is located in healthcare district IV. This healthcare district is divided into 22 municipalities and has an area of 2414.62 km^2 and a population of 325 577 inhabitants.

In 2022, the population density of Asturias was 94.76 people per km^2. An increasing imbalance has been observed in the geographical distribution of the region's inhabitants: the central area of Asturias presents continual growth in population density, whereas the eastern and western areas are experiencing progressive depopulation. Rural activities and tourism constitute the main economic activities in the eastern and western areas. In 2022, the central area of Asturias included the 3 most populated municipalities, accounting for approximately half of the Asturian population (55.61%) and barely 4% of the total area of Asturias [11].

Determination of cases and inclusion criteria

On the prevalence date, all included patients met the 2017 McDonald diagnostic criteria for MS [12]. Diagnosis of the different clinical phenotypes of MS was established according to Lublin's 2013 classification [13]. We excluded all patients with clinically isolated syndrome or other demyelinating diseases, as well as those not living in healthcare district IV of Asturias.

A database was created with the historical records of patients attended at HUCA, a tertiary-level public hospital with an MS unit, and Centro Médico de Asturias, a private hospital, both of which are located in Oviedo. Patients' demographic data and vital status were extracted by the IT department at HUCA. We reviewed the clinical histories and gathered data on the clinical variables of interest. Analysis was conducted for the period from 1 January 2017 to 31 December 2022 (the prevalence date). Patients not attending the healthcare centre in the 2 years prior to the prevalence date were considered lost to follow-up. Data were accessed for research purposes in December 2023.

We gathered population data by municipality and year, in the period 2017–2022, from the local population register (Spain's National Statistics Institute [INE], https://www.ine.es/). Healthcare district population data for 2020 and 2021 were gathered by the Asturian Society of Economic and Industrial Studies (https://www.sadei.es/) using INE's local population registry data.

The prevalence date was established on 31 December 2022. A descriptive study was conducted to analyse relevant demographic and clinical variables of prevalent patients with MS on that date. The most relevant characteristics of the patients who died until 31 December 2022 were also described.

We calculated the incidence of the disease over period from 2017 to 2022 by summing all cases in the region based on the year of symptom onset and then dividing by the total person-years at risk. Person-years at risk were calculated by summing the population for each year over the study period. We used population data from the local population register (INE) and fluctuations are not sizeable in the region.

Statistical analysis was conducted using the R statistics software (version 4.3.3). Both prevalence and incidence confidence intervals were determined using exact method [14] implemented in *epiR* library [15]. Maps were created using *QGis* (v3.34).

The study was approved by the local ethics committee and complied with personal data protection law and human research guidelines.

Results

Of all the patients diagnosed with MS who were considered for inclusion in our study (693), 28 died during the study period (1 January 2017 to 31 December 2022). An additional 18 patients (12 women and 6 men) were lost to follow-up.

On 31 December 2022, there were a total of 647 prevalent patients with MS in healthcare district IV of Asturias (430 women [66.5%] and 217 men [33.5%], with a female-male ratio of 2:1) (Table 1). The prevalence of MS in the whole region was 198.4 cases per 100 000 population (140.6 cases for men and 250.5 cases for women) (Fig. 1). We calculated prevalence rates for each municipality in healthcare district IV of Asturias and created a map of the frequency distribution across these municipalities (Figs. 1 and Additional File 1). Additionally, an analysis of the prevalence was conducted using the Queen contiguity method. The Moran's I value of −0.00144 indicates a very weak and negative spatial autocorrelation, suggesting that there is no significant clustering of MS prevalence across the municipalities in the study area. The Z-score of 0.31814 and the *P*-value of 0.750375 further support this finding, as they indicate that the observed spatial pattern does not significantly differ from a random distribution.

The mean incidence of MS for the period 2017–2022 was 6.61 (95%CI 5.53- 7.85) cases per 100 000 person-years (5.74 cases for men and 7.36 cases for women).

Map of the municipalities that constitute health area IV of the Principality of Asturias. The variations in color intensity illustrate the differences in the prevalence of Multiple Sclerosis (MS) across the different localities.

The figure illustrates the age-related patterns observed in the cohort, emphasizing the intervals between symptom onset and diagnosis, as well as the age demographic at the time of prevalence assessment.

Mean age at symptom onset was 33.98 years (standard deviation [SD]: 10.95; range, 5–74) in the total sample, and 33.73 years (SD: 10.72) in women and 34.48 years (SD: 11.40) in men. Mean age at diagnosis was 36.03 years (SD: 11.45; range, 5–78) (Fig. 2).

In our sample of patients with MS, mean age on the prevalence date was 50.84 years (SD: 12.25) for the total sample, and 50.99 years among women and 50.53 years among men (Fig. 2), whereas the median age was 50.0 years (50.0 in women and 51.0 in men). Approximately 75% of patients were aged 40–70 years.

Mean time from symptom onset to diagnosis of MS was 2.06 years (SD: 5.03) in the total sample, and 1.96 years (SD: 4.42) in women and 2.24 years (SD: 6.08) in men (Fig. 2). Mean disease progression time on the prevalence date was 16.86 years (SD: 11.04) in the total sample, and 17.27 years (SD: 10.85) in women and 16.04 years (SD:11.40) in men.

Regarding the clinical phenotype of prevalent patients with MS, 82.27% had relapsing–remitting MS (571 patients, 66.54% of whom were women), 12.8% had secondary progressive MS (84 patients, 71.42% of whom were women), and 5.61% had primary progressive MS (39 patients, 56.41% of whom were men).

Table 1 Prevalence of multiple sclerosis in healthcare district IV of Asturias, by age group and sex

Age (years)	Cases of MS			Population			Prevalence Men[a]	Prevalence Women[a]	Prevalence Total[a]
	Men	Women	Total (%)	Men	Women	Total (%)			
0–14	0	0	0 (0)	18 811	17 777	36 588 (9.23)	0 (0.0–19.6)	0 (0.0–20.7)	0 (0.0–10.08)
15–19	1	2	3 (0.46)	6984	6640	13 624 (4.18)	14.32 (0.3–79.7)	30.12 (3.6–108.8)	22.02 (4.5–64.3)
20–24	3	1	4 (0.62)	6851	6412	13 263 (4.07)	43.79 (9.0–127.9)	15.60 (0.4–86.9)	30.16 (8.22–77.2)
25–29	4	14	18 (2.78)	6662	6682	13 344 (4.1)	60.04 (16.3–153.6)	209.52 (114.6–351.3)	134.89 (79.9–213.1)
30–34	15	25	40 (6.18)	7509	7773	15 282 (4.69)	199.76 (111.8–329.2)	321.63 (208.2–474.4)	261.75 (187.1–356.2)
35–39	19	33	52 (8.04)	9794	9961	19 755 (6.07)	194.0 (116.8–302.7)	331.29 (228.1–464.9)	263.22 (196.6–345.0)
40–44	28	58	86 (13.29)	12 645	13 344	25 989 (7.98)	221.43 (116.8–302.8)	434.65 (330.2–561.5)	330.91 (264.8–408.5)
45–49	30	65	95 (14.68)	14 041	14 448	28 489 (8.75)	213.66 (144.2–304.9)	449.89 (347.4–573.1)	333.46 (269.9–407.4)
50–54	34	65	99 (15.3)	12 894	13 575	26 469 (8.13)	263.69 (182.7–368.3)	478.82 (369.7–609.9)	374.02 (304.1–455.2)
55–59	36	53	89 (13.76)	12 273	13 602	25 875 (7.95)	293.33 (205.5–405.7)	389.65 (292.0–509.4)	343.96 (276.3–423.1)
60–64	19	57	76 (11.75)	11 948	13 563	25 511 (7.84)	159.02 (95.8–248.2)	420.26 (318.45–544.2)	297.9 (234.8–372.7)
65–69	15	29	44 (6.8)	10 411	12 299	22 710 (6.98)	144.08 (80.6–237.5)	235.79 (158–338.5)	193.75 (140.8–260.0)
70–74	8	19	27 (4.17)	8489	10 448	18 937 (5.82)	94.24 (40.7–185.6)	181.85 (109.5–283.8)	142.58 (94–207.4)
75–79	2	3	5 (0.77)	6377	8600	14 977 (4.6)	31.36 (3.8–113.2)	34.88 (7.2–101.9)	33.38 (10.8–77.9)
80–84	3	6	9 (1.39)	3793	5815	9608 (2.95)	79.09 (16.3–231)	103.18 (37.9–224.4)	93.67 (42.8–177.7)
≥ 85	0	0	0	4702	10 454	15 156 (4.66)	0 (0–78.4)	0 (0–35.28)	0 (0.0–24.3)
Total	**217**	**430**	**647**	**154 184**	**171 393**	**325 577**	**140.74 (122.6–160.7)**	**250.89 (227.8–275.7)**	**198.72 (183.7–214.6)**

[a] The results are expressed in number of cases for 100 000 inhabitants with the confidence interval at 95%

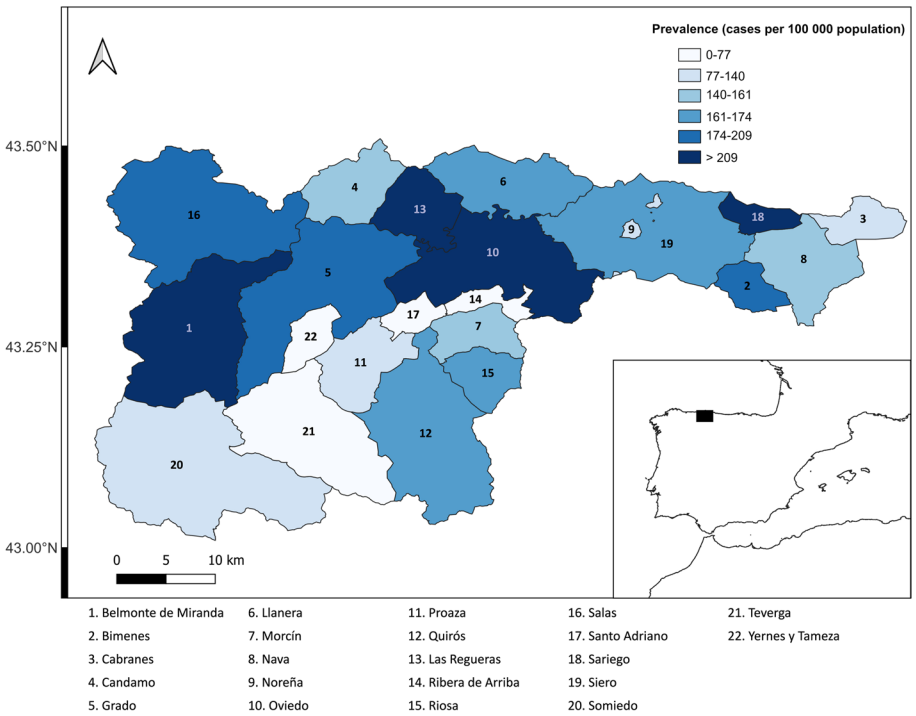

Fig. 1 Maps of the crude MS prevalence per 100 000 inhabitants in each municipality of healthcare district IV of Asturias at December 31, 2022

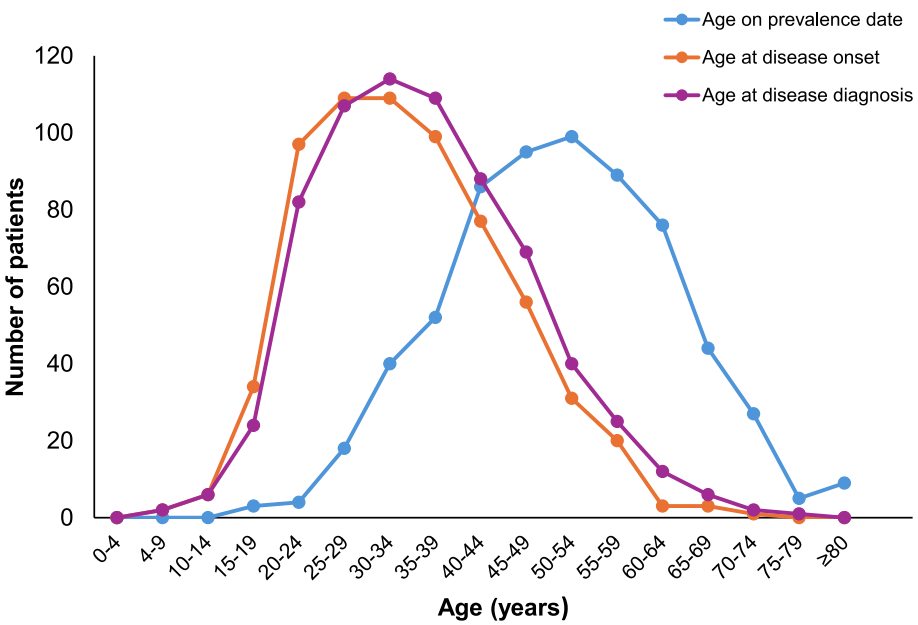

Fig. 2 Age on the prevalence date, age at symptom onset, and age at diagnosis

Between 2017 and 2022, 28 patients died (15 women and 13 men), amounting to a case fatality rate of 4.0%. Mean age in the subgroup of deceased patients was 66.04 years (SD: 13.54), and the mean EDSS (Expanded Disability Status Scale) [16] score was 7.75 (SD: 1.84).

Discussion

Our study found an MS prevalence rate of 198.4 cases per 100 000 population, and a mean incidence rate of 6.6 cases per 100 000 person-years for the period 2017–2022 in healthcare district IV of Asturias. This is the highest

prevalence rate for MS reported to date in Spain. MS predominantly affects women, and the most frequent clinical phenotype is relapsing–remitting MS (82.38%). Our study adopted a geospatial epidemiological approach, which allowed us to analyse the distribution of the disease across municipalities. A total of 28 patients died during the study period, amounting to a case fatality rate of 4%.

Comparing our results with those reported in previous studies of Spanish populations is not straightforward due to differences in methodology and the years of study (Table 2). An epidemiological study conducted in the 1990s in the city of Gijón, located 24.48 km from Oviedo, estimated MS prevalence at 65 cases per 100 000 population [17]. The study analysed the area covered by 2 primary care centres, with a total population of 33 775. Despite the potential methodological differences, we may conclude that the prevalence of MS has increased significantly in our region over a period of little more than 2 decades. This increase is presumably due to a combination of multiple causes, such as changes in diagnostic criteria, the increasingly widespread use of magnetic resonance imaging, which enables the identification of milder cases, and improvements in disease prognosis due to the development of specific treatments [2]. Furthermore, the implementation of digital clinical records [18] and the provision of specialised care in MS units has improved the identification of new cases.

Research conducted in recent years reflects high prevalence of MS in Spain, and particularly north-western Spain (Table 2 and Fig. 3). The existence of a north–south gradient in prevalence rates has been suggested, based on the results from studies conducted in Asturias and such neighbouring regions as Galicia [19–21]. The lower cumulative sun exposure in the north of Spain has been proposed as a probable cause of the higher prevalence of MS in this region [19]. At the same time, low levels of vitamin D have been shown in northern Spain [22]. Numerous studies have linked the variation in the prevalence of the disease to latitude, such that the frequency of the disease rises with latitude, both in the northern and southern hemispheres [23–25]. Although there are studies that relate the latitudinal variation to exposure to the Epstein-Barr virus [26, 27] or genetic factors [28–31], the main factor proposed to explain this phenomenon is exposure to ultraviolet radiation and vitamin D levels [24, 25, 30]. Nevertheless, it is important to consider that there may be multiple factors that contribute to fully explaining geographical variations in the prevalence of the disease. On the other hand, there may be other methodological factors [32, 33] or those related to the temporal variation of prevalence [34] that could distort an adequate comparison between epidemiological data. A study conducted in Santiago de Compostela in 2015 reported a prevalence of 152 cases per 100 000 population [19], and another study conducted in Ourense in 2016 reported a rate of 184.1 cases per 100 000 population [20]. These rates stand in contrast with findings from other studies conducted in the past decade, such as the one conducted in San Vicente de Raspeig (Alicante) in 2017, with a reported prevalence rate of 102 cases per 100 000 population [35]. In any case, regarding Spain, it is necessary to confirm the hypothesis of a latitudinal prevalence gradient through updates of the epidemiological studies carried out in the Spanish regions located at lower latitudes.

While there may be differences between the various geographical locations of cities in northwest Spain where epidemiological studies on multiple sclerosis (MS) are conducted (Table 2 and Fig. 3), they generally share

Table 2 Characteristics of the most recent prevalence studies conducted in north-western Spain and a previous study conducted in Asturias (Gijón, 1994)

	Healthcare district IV, Asturias	Gijón, Asturias [17]	Santiago de Compostela, Galicia [19]	Ourense, Galicia [20]	Healthcare district of Ferrol [21]
Prevalence date	31 December 2022	1 March 1994	31 December 2015	31 December 2016	31 December 2015
Latitude	43° 21′ N	43° 31′ N	42° 52′	42° 34′ N	42° 29′ N
Reference population	325 577	33 775[c]	95 612	105 892	194 834
Cases	647	22	145	195	214
Prevalence[a]	198.4	65	152	184.1	109
Incidence[b]	6.6 Retrospective 2017–2022	3.7 Retrospective 1987–1990 Prospective 1991–1995	8 Retrospective 2010–2015	7.86 Retrospective 2002–2016	5.5 Retrospective 2001–2015

[a] No. cases per 100 000 population

[b] No. cases per 100 000 person-years

[c] Population from 2 primary care centres

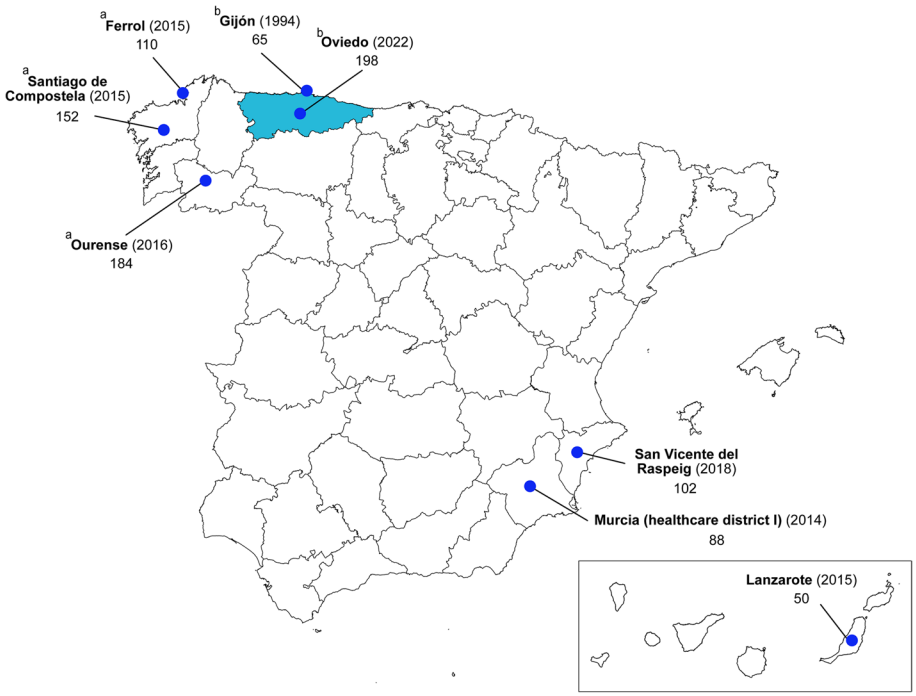

Fig. 3 Locations of the prevalence studies of multiple sclerosis conducted in Spain in the past 10 years and the study conducted in Asturias in the 1990s

The following studies are represented: Ourense: García-Estévez et al. [20]; Santiago de Compostela: Costa-Arpín et al. [19]; Ferrol: Llaneza-González [21]; Gijón: Uría et al. [17]; San Vicente del Raspeig: Pérez-Carmona et al. [35]; Murcia: Carreón-Guarnizo et al. [36]; Lanzarote: Pérez-Pérez et al. [37]

The map highlights the epidemiological studies conducted in the autonomous communities of Galicia (a) and Asturias (b). Prevalence is expressed as the number of cases per 100,000 population

geographical and climatic characteristics. Therefore, the environmental risk factors could be comparable. However, Galicia and Asturias have had different migratory patterns throughout history; in Asturias, migration has been more internal and less diversified, which may have contributed to lower genetic variability [38, 39]. In terms of access to health care, specialized medical care is available in both regions. In the case of the Ferrol health area [40], there is a significant difference, as it is classified as a second-level hospital. Furthermore, a common aspect of Oviedo, compared to other Spanish and European localities, is the aging of the population pyramid. This phenomenon is similarly observed in neighboring regions, although it is minimized in urban environments due to the presence of the service sector and universities.

The use of geographical information systems and spatial analysis enable researchers to better understand patterns in the spatio-temporal distribution of diseases, risk factors, and geographical disparities, and to improve healthcare planning [41]. The size and sociodemographic profile of the population may have a significant impact on the epidemiology of a disease [42]. Our study analysed the distribution of cases in different municipalities (see Addicional File 1); the study region only contains 2 municipalities with populations greater than 50 000.

An increase in age at diagnosis has been observed in recent years [4, 43, 44]. This phenomenon, together with improvements in MS prognosis and other factors, has led to an increase in the mean age of the population with the disease. This is extremely relevant for disease management, as most patients will be receiving immunosuppressant or immunomodulatory drugs [45]. Age-related aspects of safety and efficacy and the presence of comorbidities must be taken into account. Regardless of immunosenescence, we must be aware that patients older than 50–60 years are underrepresented in clinical trials. However, some studies, like our own, show that this age group represents a considerable percentage of the current population with MS.

The MS Unit of the Central University Hospital of Asturias, as it belongs to a tertiary care center, acts as a reference for the region. Access to specialized care is available regardless of the patient's place of residence. Additionally, the selection of patients has been restricted

to those who reside in health area IV, located in the central area of Asturias, which ensures easy accessibility. Therefore, a significant impact on prevalence data derived from difficulties in accessing specific health care is not expected. Moreover, the collaboration between a public and a private centre in data collection has allowed for a more global estimation of the frequency of the disease in our area. In any case, our health system is eminently public, which allows economic coverage of the use of disease-modifying drugs.

Although several epidemiological studies have been conducted in neighbouring regions, one limitation of our study is the fact that we lack prior data on the same reference area and with the same methodology. Long-term longitudinal follow-up data are needed to analyse the changes in MS epidemiology in Asturias. Another limitation arises from the application of a frequentist approach when creating disease distribution maps, as results may be affected by the random variation of the disease. For example, the detection of a single case of a rare disease in an area with a small population may result in an overestimation of its prevalence [46]. Our data are extremely valuable for healthcare planning as they provide real-time information about the current needs in our region. After applying a spatial autocorrelation analysis using the Moran index to our area, the results suggest that the distribution of MS cases is considered random and is not influenced by geographic proximity. Therefore, it is necessary to investigate other determining factors that may influence the prevalence of the disease. In any case, long-term follow-up would enable the application of other statistical approaches, such as Bayesian methods, which allow for separate modelling of random and true variation [47, 48].

Conclusions

Our results support the hypothesis that Spain is a high-prevalence region for MS. We should underscore the need for long-term follow-up studies to analyse the factors influencing the progression of MS epidemiology, as well as the importance of implementing public health strategies specifically designed for each population. In this regard, the use of a geospatial epidemiological approach may help us to better understand the distribution and determinants of MS in different geographical settings, and to adequately plan healthcare resource allocation for targeted interventions.

Abbreviations

MS	Multiple sclerosis
HUCA	Hospital Universitario Central de Asturias
INE	Spain's National Statistics Institute
SADEI	Asturian Society of Economic and Industrial Studies
SD	Standard deviation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-025-04108-5.

Additional file 1. Prevalence data for the different municipalities of healthcare district IV of Asturias. Table legend: Prevalence is expressed as number of patients per 100 000 population.

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Authors' contributions

Study concept and design: PON; Acquisition of data: PON, MSA, CSV, JVE, JFD, RGD; Analysis and interpretation of data: PON; Drafting of the manuscript: PON; Revising it for intellectual content: MALG, JVE, JFD, AOD; Final approval of the completed manuscript: All authors.

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Data availability

Not applicable. The datasets generated and/or analyzed during the current study are not publicly available due to the recommendation of our Ethics Committee but are available from the corresponding author on reasonable request and with permission from the Ethics and Research Committee of the Principality of Asturias (ceim.asturias@asturias.org).

Declarations

Ethics approval and consent to participate

This study complied with personal data protection laws and human research guidelines and was approved by the ethics committee of our institution, the Ethics and Research Committee of the Principality of Asturias, with the code CEImPA 2023.120. Our dataset is not publicly available. To carry out our project, we requested and obtained a waiver of informed consent due to the nature of the study, which was explicitly approved by the ethics committee. This waiver specifically included the renunciation of the requirement for participants to sign informed consent forms. The committee recommended restricting access to the data, as there may be sensitive information that could compromise the anonymity of the participants. If the editorial committee or readers of our work wish to have direct access to the dataset, we recommend that they contact the Ethics and Research Committee of the Principality of Asturias (ceim.asturias@asturias.org). Our institution's committee will attend to any requests in this regard, in accordance with local ethical policies and procedures.

Consent for publication

Not applicable. The Ethics and Research Committee of the Principality of Asturias has waived the requirement for informed consent for publication based on the use of anonymized data that does not compromise participant privacy.

Competing interests

Pedro Oliva-Nacarino has received lecture honoraria and consultancy fees from Almirall, Biogen Idec, Bristol Myers, Merck, Novartis, Roche, Sanofi, and Teva.
Marina Simal Antuña has no conflicts of interest.
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