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ORIGINAL ARTICLE

Clinical epidemiology of multiple sclerosis in the Aran region of Azerbaijan

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ABSTRACT

Objective: To investigate the clinical and epidemiological characteristics of multiple sclerosis (MS) in the Aran region of Azerbaijan.

Methods: This prospective, single-center longitudinal study was conducted at Neurology Center under the Ministry of Health of Azerbaijan from January 2013 to December 2022. Patients from the Aran region were evaluated using standardized national diagnostic protocols based on the 2010 McDonald criteria. Of 267 individuals assessed, 241 with confirmed MS were included. Data on demographic characteristics, clinical features, and epidemiological indicators were collected. Incidence and prevalence rates per 100,000 population were calculated and age-standardized using World, European, and national reference populations. Statistical analysis was performed using SPSS version-27.

Results: Of the 241 patients, 150 (62.2%) were women and 91 (37.8%) were men. Mean age at diagnosis was 35.91±8.16 years, higher in men than women ($p<0.05$). The mean diagnostic delay was 5.90±5.27 years and was longer in rural residents ($p=0.009$). Relapsing-remitting MS was the predominant clinical subtype, observed in 190 patients (78.8%). The 10-year average incidence rate was 1.13±0.26 per 100,000 population, with no significant differences by gender or residence. By the end of 2022, the overall prevalence was 13.49±0.88 per 100,000 population (95% CI: 11.75-15.22), higher in women and urban populations ($p<0.001$). The highest prevalence was recorded in Central Aran Economic Region (16.20±1.50 per 100,000 population).

Conclusion: MS in Aran region shows moderate prevalence with female predominance, relapsing-remitting dominance, and diagnostic delays, particularly in rural populations. Findings highlight the disparities and need for improved access to neurological services and earlier referral.

Keywords: Azerbaijan (MeSH); Delayed Diagnosis (MeSH); Incidence (MeSH); Multiple Sclerosis (MeSH); Prevalence (MeSH); Neurology (MeSH); Multiple Sclerosis, Relapsing-Remitting (MeSH); Autoimmune Diseases of the Nervous System (MeSH); Demyelinating Autoimmune Diseases, CNS (MeSH).

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INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating autoimmune disease of the central nervous system, characterized by gliosis, axonal injury, and neuronal loss.[1] It most commonly begins between 20 and 40 years of age, affects women more frequently than men, with a female-to-male ratio of approximately 3:1,[2] and is one of the leading non-traumatic causes of disability in young adults.[3] The most common clinical phenotype is relapsing-remitting MS, accounting for 85-90% of cases, whereas primary progressive MS is characterized by gradual and continuous neurological deterioration without distinct relapses.[4] Recent epidemiological studies have shown increasing incidence and prevalence of MS in several regions of the world, emphasizing its growing public health importance.[5-8] The epidemiological characteristics of MS, including incidence, prevalence, clinical phenotypes, and demographic distribution, vary considerably across countries and populations under the influence of genetic, environmental, and healthcare-related factors.[2] One of the most distinctive epidemiological features of MS is its uneven geographical distribution.[9] For this reason, countries located at the intersection of different climatic zones, ethnic groups, and sociocultural environments are of particular interest for epidemiological investigation. Azerbaijan represents such a setting because of its geographical position between Europe and Asia, its climatic diversity ranging from subtropical to temperate zones, and its ethnically heterogeneous population. Despite this, epidemiological data on MS in Azerbaijan remain limited, and region-specific studies are scarce. In particular, there is insufficient information on the clinical and epidemiological characteristics of MS in the Aran region, including its demographic profile, diagnostic timing, clinical course, and disease frequency.

This lack of regional data represents an important knowledge gap and limits the ability to assess the local burden of MS and to plan healthcare services appropriately. Given the potential effect of regional differences in environment, healthcare access, and population structure on MS epidemiology, it is important to obtain reliable local data from different parts of the country. Therefore, the present study was undertaken to investigate the clinical epidemiology of MS in the Aran region of Azerbaijan by describing the demographic and clinical characteristics of patients and estimating disease incidence and prevalence.

METHODS

The Aran region of Azerbaijan includes the Central Aran, Mil-Muğan, and Shirvan-Salyan economic regions. It has a favorable economic-geographical

position and a total area of 18.44 thousand square kilometers, accounting for 21.3% of the country's territory. More than half of the region consists of low-lying plains below sea level, while only the areas adjacent to the surrounding mountains have sloping terrain. The region is characterized by a dry subtropical climate, which, together with its natural and economic-geographical conditions, has influenced population distribution and settlement.[10] The total population of the region is 1,727,653, of whom 50.41% are women and 49.59% are men. The population is predominantly rural, with 61.95% (1,070,241) living in rural areas and 38.05% (657,412) residing in urban areas.[10] In 2022 the number of physicians per 10,000 population in the region was 12.2 and the outpatient clinic capacity was 84.13 (Table I).[11]

This was a prospective, single-center, longitudinal study conducted at the Neurology Center under the Ministry of Health (MoH) of the Republic of Azerbaijan. The study included individuals from the Aran region who were referred from regional healthcare facilities or who presented directly to the Neurology Center between January 1, 2013 and December 31, 2022. Comprehensive diagnostic evaluations were performed by a specially designated expert commission at the Neurology Center within the framework of the State Program on Measures for the Treatment, Prevention, and Control of Multiple Sclerosis, which ensured standardized diagnostic assessment nationwide. Multiple sclerosis was diagnosed according to the national Clinical Protocol for the Diagnosis and Treatment of Multiple Sclerosis, based on the 2010 McDonald criteria.[12,13]

During the study period, 267 individuals from the Aran region were evaluated at the center. Of these, 241 were confirmed to have multiple sclerosis, including both newly diagnosed patients and patients with a reconfirmed diagnosis, and were entered into a digital database. The remaining 26 individuals were excluded because differential diagnostic evaluation did not confirm multiple sclerosis; in some cases, alternative diagnoses were established. Thus, the study sample consisted of all eligible patients from the Aran region with a confirmed diagnosis of multiple sclerosis evaluated during the study period. Inclusion criteria were a confirmed diagnosis of multiple sclerosis established according to the national Clinical Protocol for the Diagnosis and Treatment of Multiple Sclerosis, based on the 2010 McDonald criteria. Exclusion criteria were failure to fulfill the 2010 McDonald criteria for multiple sclerosis at expert evaluation.

Data collected for analysis included demographic characteristics, place of residence, age at probable first attack, age at diagnosis, clinical course, and epidemiological indicators. Incidence and prevalence rates per 100,000 population were calculated, and age-standardized rates were determined using the direct standardization method. Reference populations included the World Health Organization (WHO) Standard Population (2000-2025),[14] the European Standard Population (2011-2030),[15] and the age and gender of the population of Azerbaijan as of January 1, 2023 for within-country regional comparisons.[10]

Statistical analysis was performed using IBM SPSS Statistics version 27 and Microsoft Excel 2016. Data distribution was assessed using the Kolmogorov-Smirnov test for large samples ($n>2000$) and the Shapiro-Wilk test for small and moderate samples ($n\leq2000$). In cases of discordant normality results, both parametric and non-parametric tests were applied to ensure robustness of the findings. Homogeneity of variances was assessed using Levene's test. For categorical variables, Pearson's chi-square test was used. For continuous variables with normal distribution, Student's t-test (pt) was used to compare two independent groups, and one-way ANOVA (pANOVA) for three or more groups. For non-normally distributed variables, the Mann-Whitney U test (p_U) was applied for two-group comparisons, and the Kruskal-Wallis H test (p_H) for comparisons involving three or more groups. A p-value of <0.05 was considered statistically significant. The 95% confidence intervals for incidence and prevalence rates were calculated using the Poisson method.[16]

The study was approved by the Ethics Committee of the Neurology Center of the Ministry of Health of the Republic of Azerbaijan (Reference #: 11/2012, dated: December 24, 2012), within the nationwide project entitled "Clinico-Epidemiological Study of Multiple Sclerosis in the Republic of Azerbaijan." The present manuscript reports findings specific to the Aran region within the scope of the approved protocol.

RESULTS

The overall demographic indicators for the Aran region are shown in Table II, while detailed data for the three economic regions are provided in Supplementary Table S-1. At the time of diagnosis, the average age of MS patients in the Aran region was 35.91±8.16 years. The mean age at diagnosis differed significantly between men and women($p_t=0.001$, $p_U=0.004$).

Table I: Socio-demographic characteristics of the region and study subjects

Indicators	Regions			
	Central Aran	Mil-Mughan	Shirvan-Salyan	Total
Population	716,187	520,205	491,261	1,727,653
Physicians[1]	14.4	8.4	13.9	12.2
Outpatient clinic capacity[1]	77.7	62.4	112.3	84.13
All patients	134	65	68	267
Multiple sclerosis patients	120	59	62	241
Excluded patients	14	6	6	26

[1]: per 10,000 population

Table II: Demographic indicators of multiple sclerosis patients in the Aran region (prevalence day 31.12.2022)

Indicator		N	Min.	Max.	Me	Mean±SD (95% CI)	SE	p-value
Age at diagnosis	Men	91	18	56	38.00	38.04±7.99 (36.38-39.71)	0.84	p_t=0.001 p_U=0.004
	Women	150	15	54	34.00	34.61±8.01 (33.32-35.91)	0.65	
	Urban	129	15	56	35.00	34.99±8.62 (33.49-36.49)	0.76	p_t=0.061
	Rural	112	18	55	38.00	36.96±7.50 (35.56-38.37)	0.71	
	Total	241	15	56	36.00	35.91±8.16 (34.87-36.94)	0.53	—
Age on the prevalence date	Men	88	27	73	44.00	44.42±9.60 (42.39-46.45)	1.02	p_U=0.032
	Women	145	24	67	41.00	41.52±9.84 (39.90-43.13)	0.82	
	Urban	124	24	63	42.00	42.06±10.31 (40.22-43.89)	0.93	p_U=0.375
	Rural	109	27	73	43.00	43.25±9.26 (41.49-45.01)	0.89	
	Total	233	24	73	42.00	42.61±9.83 (41.35-43.88)	0.64	—
Age at the probable first attack	Men	91	16	50	32.00	31.43±7.81 (29.80-33.05)	0.82	p_U=0.029
	Women	150	14	49	29.00	29.15±8.09 (27.84-30.45)	0.66	
	Urban	129	14	49	30.00	29.84±8.15 (28.42-31.26)	0.72	p_U=0.729
	Rural	112	15	50	30.00	30.21±7.96 (28.71-31.70)	0.75	
	Total	241	14	50	30.00	30.01±8.05 (28.99-31.03)	0.52	—
Diagnostic delay (years)	Men	91	0	35	5.00	6.62±6.13 (5.34-7.89)	0.64	p_U=0.263
	Women	150	0	23	4.00	5.47±4.63 (4.72-6.21)	0.38	
	Urban	129	0	24	4.00	5.16±4.84 (4.31-6.00)	0.43	p_U=0.009
	Rural	112	0	35	6.00	6.76±5.61 (5.71-7.81)	0.53	
	Total	241	0	35	5.00	5.90±5.27 (5.23-6.57)	0.34	—
Disease Duration (years)	Men	91	4	38	11.00	13.36±6.58 (11.99-14.73)	0.69	p_U=0.876
	Women	150	3	29	12.00	13.11±5.81 (12.18-14.05)	0.47	
	Urban	129	3	29	12.00	13.03±5.92 (12.00-14.06)	0.52	p_U=0.778
	Rural	112	5	38	12.00	13.41±6.32 (12.23-14.59)	0.60	
	Total	241	3	38	12.00	13.21±6.10 (12.43-13.98)	0.39	—
Age at death	Men	3	51	62	54.00	55.67±5.69 (41.54-69.79)	3.28	p_U=0.143
	Women	5	58	71	62.00	63.80±6.34 (55.93-71.67)	2.84	
	Urban	5	54	71	62.00	63.00±7.42 (53.79-72.21)	3.32	p_U=0.393
	Rural	8	51	62	58.00	57.00±5.57 (43.17-70.83)	3.21	
	Total	3	51	71	60.00	60.75±7.07 (54.84-66.66)	2.50	—
Life span (years)	Men	3	13	22	18.00	17.67±4.51 (6.47-28.87)	2.60	p_U=0.786
	Women	5	14	26	19.00	19.40±4.51 (13.81-24.99)	2.01	
	Urban	5	17	26	19.00	20.20±3.56 (15.78-24.62)	1.59	p_U=0.393
	Rural	8	13	22	14.00	16.33±4.93 (4.08-28.59)	2.85	
	Total	3	13	26	18.50	18.75±4.27 (15.18-22.32)	1.51	—

Note: N:number of patients; Min.: minimum value; Max.: maximum value; Me: Median; Mean: average value; SD: standard deviation; CI: confidence interval; SE: standard error; p: statistical significance of differences within-region comparison by Pt – Student's t-test and pU –Mann-Whitney U test for comparison by gender or place of residence; between-regions comparison by pANOVA – one way ANOVA and p_H – Kruskal-Wallis H-test).

Table III: Characteristics of multiple sclerosis patients by gender and residence

Region	Indicator	Region				Total	
		Urban		Rural			
		Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Central Aran Economic region	Male	22	46.8	25	53.2	47	100
	Female	36	49.3	37	50.7	73	100
	Total	58	48.3	62	51.7	120	100
	px^2	0.789				—	
Mil-Mughan Economic region	Male	11	57.9	8	42.1	19	100
	Female	19	47.5	21	52.5	40	100
	Total	30	50.8	29	49.2	59	100
	px^2	0.456				—	
	Fisher exact px^2	0.580				—	
Shirvan-Salyan Economic Region	Male	14	56.0	11	44.0	25	100
	Female	27	73.0	10	27.0	37	100
	Total	41	66.1	21	33.9	62	100
	px^2	0.166				—	
	Fisher exact px^2	0.184				—	
Aran Region (total)	Male	47	51.6	44	48.4	91	100
	Female	82	54.7	68	46.5	150	100
	Total	129	53.5	112	46.5	241	100
	px^2	0.649				—	

Note: N: number of patients; Statistical significance of differences (comparison by gender); px^2: by Pearson's chi-square test and Fisher's exact test

Although patients residing in rural areas were diagnosed at a higher average age compared to urban residents, this difference was not statistically significant (p_t=0.061). Additionally, the average age at the time of the presumed first attack was higher in men than in women (p_U=0.029). The period between the probable first attack and the diagnosis of MS (diagnosis delay) in the Aran region was 5.90±5.27 years (Table II). There was no statistically significant difference in diagnosis delay between men and women. However, rural residents had a significantly longer diagnosis delay compared to urban residents (p_U=0.009). By the end of the study, the average age of patients registered in the database was 42.61±9.83 years, with disease durations ranging from 3 to 38 years. The average disease duration was 13.21±6.10 years. The average life span of patients was 18.75±4.27 years, and the average age at death was 60.75±7.07 years.

When comparing the demographic indicators of patients across the economic regions, no statistically significant differences were identified (Supplementary Table S-1). In the Central Aran economic region, the diagnosis delay among the urban population (4.67±5.41 years) was shorter than the other two regions, but this difference was not statistically significant (p_H=0.124).

In the Aran region, 53.5% (129 patients) of the cases were urban residents, while 46.5% (112 patients) were rural residents (Table III). Although the proportion of urban residents was slightly higher, the difference in gender distribution between urban and rural areas was not statistically significant (χ^2=0.207, df=1, p=0.649). Similarly, when analyzing gender distribution by economic regions, there were differences in proportions based on residence, but none of these differences were statistically significant: Central Aran Economic Region (χ^2=0.072, df=1, p=0.789), Mil-Mughan Economic Region (χ^2=0.557, df=1, p=0.456), and Shirvan-Salyan Economic Region (χ^2=1.919, df=1, p=0.166). When comparing the clinical course of MS, the most prevalent subtype was Relapsing-Remitting MS (RRMS), accounting for 78.8% (190 patients) of cases [Figure 1]. This was followed by Secondary-Progressive MS (SPMS) at 14.9% [36 patients]. The least common subtypes were Primary Progressive MS (PPMS) and Progressive-Relapsing MS [PRMS]. Additionally, 3.3% of patients were diagnosed with Clinically Isolated Syndrome (CIS). The 10-year average

Table IV: Multiple sclerosis incidence by gender and place of residence

Indicator		Population (mean)	Patients (mean)	Incidence±SE, crude (95% CI)	Incidence±SE, WSt (95% CI)	Incidence±SE, EuSt (95% CI)	Incidence±SE, AzSt (95% CI)	p-value
Mean 2013-2022	Males	841,545.6	7.5	0.89±0.33 (0.25-1.53)	0.85±0.32 (0.22-1.47)	0.84±0.32 (0.22-1.46)	0.93±0.33 (0.28-1.58)	0.352[1] 0.382[2] 0.511[3] 0.404[4]
	Females	852,997.7	11.7	1.37±0.40 (0.59-2.16)	1.28±0.39 (0.52-2.04)	1.16±0.37 (0.43-1.88)	1.36±0.40 (0.58-2.14)	
	Rural	1,043,088.8	9.1	0.87±0.29 (0.31-1.44)	0.82±0.28 (0.27-1.37)	0.79±0.28 (0.25-1.34)	0.90±0.29 (0.33-1.48)	0.232[1] 0.251[2] 0.319[3] 0.268[4]
	Urban	651,454.5	10.1	1.55±0.49 (0.59-2.51)	1.46±0.47 (0.53-2.38)	1.32±0.45 (0.44-2.20)	1.53±0.49 (0.58-2.48)	
	All patients	1,694,543.3	19.2	1.13±0.26 (0.63-1.64)	1.06±0.25 (0.57-1.55)	1.00±0.24 (0.52-1.47)	1.14±0.26 (0.63-1.65)	—
Mean 2013-2022 (2020 excluded)	Males	841,284.8	8.1	0.96±0.34 (0.30-1.63)	0.92±0.33 (0.27-1.56)	0.91±0.33 (0.27-1.56)	1.01±0.35 (0.33-1.68)	0.341[1] 0.378[2] 0.517[3] 0.200[4]
	Females	852,335.9	12.6	1.47±0.42 (0.66-2.29)	1.38±0.40 (0.59-2.16)	1.24±0.38 (0.49-1.99)	1.46±0.41 (0.65-2.27)	
	Rural	1,042,173.8	9.7	0.93±0.30 (0.35-1.52)	0.88±0.29 (0.31-1.45)	0.85±0.29 (0.29-1.41)	0.96±0.30 (0.37-1.56)	0.199[1] 0.220[2] 0.288[3] 0.232[4]
	Urban	651,446.9	11.0	1.69±0.51 (0.69-2.69)	1.58±0.49 (0.61-2.54)	1.43±0.47 (0.51-2.35)	1.67±0.51 (0.68-2.66)	
	All patients	1,693,620.7	20.7	1.22±0.27 (0.70-1.75)	1.15±0.26 (0.64-1.65)	1.07±0.25 (0.58-1.57)	1.23±0.27 (0.70-1.76)	—

Note: SE: standard error of the mean; CI: confidence interval; WSt: World Standard Population (using the world population as the standard); EuSt: European Standard Population (using the European population as the standard); AzSt: Azerbaijan Standard Population. Statistical significance of differences: p_t: determined by Student's t-test. 1: applicable to crude prevalence rates; 2: applicable to WSt; 3: applicable to EuSt; 4: applicable to AzSt

Table V: Prevalence of multiple sclerosis in the Aran region of Azerbaijan by the end of 2022

Indicator	Population	N	Prevalence±SE, crude (95% CI)	Prevalence±SE, WSt (95% CI)	Prevalence±SE, EuSt (95% CI)	Prevalence±SE, AzSt (95% CI)	p-value
Males	856,728	88	10.27±1.09 (8.13-12.42)	9.48±1.0 (7.42-11.54)	10.77±1.12 (8.58-12.97)	10.72±1.12 (8.53-12.92)	<0.001[1] 0.001[2,4] 0.002[3]
Female	870,925	145	16.65±1.38 (13.94-19.36)	15.21±1.32 (12.62-17.80)	16.15±1.36 (13.48-18.82)	16.75±1.39 (14.03-19.47)	
Urban	657,412	124	18.86±1.69 (15.54-22.18)	17.35±1.62 (14.17-20.53)	18.42±1.67 (15.14-21.70)	19.27±1.71 (15.91-22.62)	<0.001[1-4]
Rural	1,070,241	109	10.18±0.98 (8.27-12.10)	9.42±0.94 (7.58-11.26)	10.55±0.99 (8.60-12.49)	10.47±0.99 (8.53-12.41)	
Total	1,727,653	233	13.49±0.88 (11.75-15.22)	12.39±0.85 (10.73-14.05)	13.50±0.88 (11.77-15.24)	13.79±0.89 (12.04-15.54)	—

Note: N: number of patients; Prevalence: crude prevalence per 100,000 population; SE: standard error of the mean; CI: confidence interval; WSt: World Standard Population (using the world population as the standard); EuSt: European Standard Population (using the European population as the standard); AzSt: Azerbaijan Standard Population. Statistical significance of differences: pt: determined by Student's t-test. 1: applicable to crude prevalence rates; 2: applicable to WSt; 3: applicable to EuSt; 4: applicable to AzSt

incidence rate of MS in the region was 1.13±0.26 cases per 100,000 population (Table IV). Although the incidence rate among men was lower than among women, the difference was not statistically significant (p=0.352). Similarly, the incidence rate in rural areas was lower than in urban areas, but this difference was also not statistically significant (p=0.232). In 2020, due to the strict quarantine measures associated with the COVID-19 pandemic, there was a decrease in patient visits. Excluding 2020 from the analysis slightly increased the average incidence rate to 1.22±0.27 cases per 100,000 population. However, comparisons of incidence rates by gender and residence still did not reveal statistically significant differences. The overlapping confidence intervals further confirm the closeness of these values and the absence of statistically significant differences.

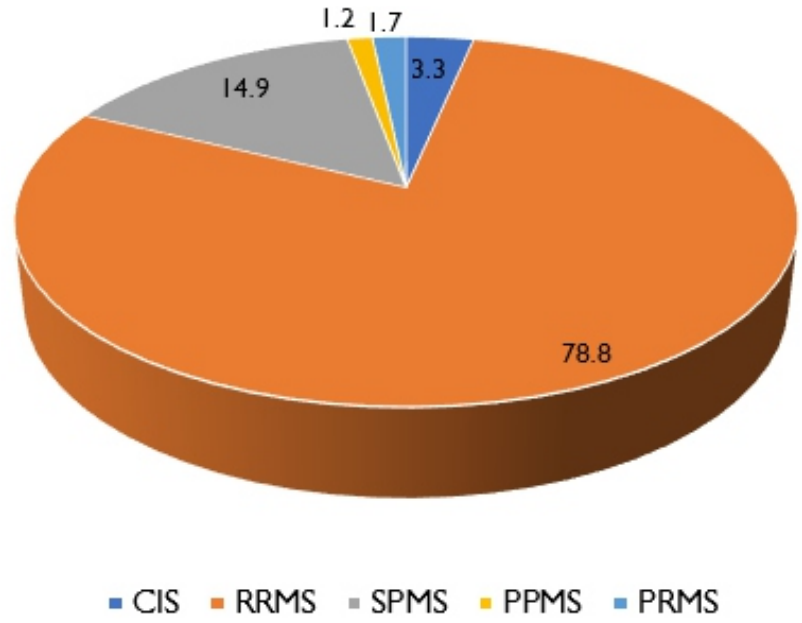

Figure 1. Proportion of multiple sclerosis (MS) types by clinical course (in %).Note: CIS: Clinically Isolated Syndrome; RRMS: Relapsing-Remitting MS; SPMS: Secondary-Progressive MS; PPMS: Primary Progressive MS; PRMS: Progressive-Relapsing MS.

The overall prevalence estimates are presented in Table V; region-specific prevalence estimates are shown in Supplementary Table S-II. By the end of the study period, the prevalence of MS in the region was 13.49±0.88 cases per 100,000 population (95% CI: 11.75-15.22). Significant differences in MS prevalence by gender and residence were observed. Specifically, MS prevalence was higher among women and urban residents compared to men and rural residents. These differences remained statistically significant when age-standardized rates were compared.

Interesting results were observed when prevalence rates were analyzed across economic regions (Supplementary Table S-I). In the Central Aran and Mil-Muğan economic regions, MS prevalence among women was significantly higher than among men ($p<0.05$).

In the Mil-Muğan and Shirvan-Salyan economic regions, MS prevalence among urban residents was significantly higher than among rural residents ($p<0.05$). However, no statistically significant differences in prevalence were found by residence in the Central Aran region or by gender in the Shirvan-Salyan region ($p>0.05$). The highest prevalence of MS was observed in the Central Aran Economic Region, with a rate of 16.20±1.50 cases per 100,000 population (95% CI: 13.25-19.14). This difference was statistically significant only when compared to the Mil-Muğan Economic Region ($p=0.012$).

When the World and Azerbaijan populations were used as standards, the difference became even more pronounced ($p=0.008$ and $p=0.009$, respectively). Comparisons based on the European standard also demonstrated that the prevalence of MS in the Central Aran Economic Region was statistically significantly higher than in both other economic regions ($p=0.002$ and $p=0.038$, respectively).

DISCUSSION

This study provides the first comprehensive clinical-epidemiological description of MS in the Aran region of Azerbaijan. The principal findings were a marked female predominance, with a female-to-male ratio of 3.1:1, a mean age at diagnosis of 35.91±8.16 years, a mean diagnostic delay of 5.90±5.27 years, and predominance of the relapsing-remitting form, which accounted for 78.8% of cases. The 10-year average incidence rate was 1.13±0.26 per 100,000 population, while the prevalence by the end of 2022 reached 13.49±0.88 per 100,000 population. Significant differences were observed according to gender and place of residence, and the highest prevalence was recorded in the Central Aran Economic Region. These findings indicate that MS in the Aran region shares the major epidemiological characteristics reported internationally, while also demonstrating region-specific features relevant to healthcare planning.

One of the most important findings of the present study was the prolonged interval between the probable first attack and confirmed diagnosis. In the Aran region, the mean diagnostic delay was 5.90±5.27 years, which was slightly higher than the national average previously reported for Azerbaijan and longer than that reported in some other settings, including India.[17,18] This finding suggests that, despite the existence of a centralized diagnostic system, delays in referral, access to MRI, and access to specialist neurological evaluation may still influence timely diagnosis. Because early diagnosis and early initiation of disease-modifying treatment are associated with more favorable long-term outcomes and slower disability progression, the observed diagnostic delay is clinically important and may have implications for disease burden and long-term care needs.

The gender distribution observed in this study is consistent with the known epidemiology of MS. Women constituted the majority of patients, and prevalence was significantly higher among women than men, in agreement with the well-established female predominance described in the literature.[2,4,8] Men, however, had a higher mean age at diagnosis and a higher mean age at the probable first attack. These differences may reflect variation in disease recognition, healthcare-seeking behavior, referral timing, or biological factors influencing disease onset and detection. Although the present study was not designed to investigate the mechanisms underlying such differences, the findings confirm the importance of considering gender-specific epidemiological patterns in MS surveillance and health-service planning. Residence-related and

subregional differences were also notable. Rural residents had a significantly longer diagnostic delay, whereas overall prevalence was significantly higher among urban residents. This pattern may reflect more complete case ascertainment in urban settings due to better access to neurologists, imaging facilities, and follow-up systems, while delayed diagnosis in rural populations raises the possibility of under-recognition or under-registration outside major population centers. Regional analysis also demonstrated heterogeneity within Aran, with the highest prevalence observed in the Central Aran Economic Region. These findings support the view that place of residence and regional healthcare infrastructure may influence not only access to diagnosis but also the registered epidemiological profile of MS. Comparison with national, regional, and international studies places these findings into broader context. The mean age at diagnosis in the Aran region was slightly higher than the previously reported national average for Azerbaijan but close to that reported in the southern region of the country and in Türkiye.[8,17,19] Similarly, the incidence and prevalence observed in the Aran region were lower than those reported in Türkiye, southeastern Iran, and many European countries, but higher than those reported in some Asian populations.[4,5,8,18,20-27] These similarities and differences may reflect variation in genetic background, environmental exposures, access to healthcare services, diagnostic capacity, and case-registration systems. Overall, the findings suggest that the Aran region represents a relatively lower-prevalence setting than many European populations, while still bearing a measurable and clinically important burden of MS. The clinical and public health relevance of these findings is considerable. The prolonged diagnostic delay, particularly among rural residents, indicates the need to strengthen early referral pathways and improve access to specialist neurological assessment and MRI. The observed gender- and region-related differences also suggest that national averages alone may not fully reflect the epidemiological burden of MS in different parts of the country. Improved public and professional awareness, stronger regional registration systems, and more equitable access to diagnostic services may contribute to earlier detection and more effective planning of MS care in Azerbaijan.

This study has several limitations. First, its single-center design may not fully capture the diversity of MS cases across the entire Aran region. Second, reliance on data from patients who presented to the Neurology Center may have introduced selection bias, as individuals with limited access to healthcare may have been underrepresented. Third, diagnostic evaluation procedures and data completeness may have influenced case inclusion. Finally, the COVID-19 pandemic may have affected access to healthcare and diagnostic services during part of the study period. In future studies, these limitations could be addressed by conducting multicenter or population-based investigations, expanding regional registry coverage, and incorporating more detailed data on healthcare access, environmental factors, and socioeconomic characteristics.

CONCLUSION

In the Aran region of Azerbaijan, MS was characterized by female predominance, predominance of the relapsing-remitting form, and a substantial diagnostic delay. Significant differences by gender, residence, and economic region were identified, with the highest prevalence observed in the Central Aran Economic Region and longer diagnostic delay among rural residents. These findings highlight the need to improve access to specialized neurological assessment and diagnostic services, particularly outside urban areas, and support the importance of strengthened regional surveillance and healthcare planning for MS in Azerbaijan. Future studies should include broader multicenter and region-based investigations to clarify the effect of healthcare access, environmental conditions, and population factors on the epidemiology of MS in the country.

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SUPPLEMENTARY INFORMATION

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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

RRA: Conception and study design, acquisition, analysis and interpretation of data, drafting the manuscript, critical review, approval of the final version to be published

SNM: Acquisition, analysis and interpretation of data, critical review, approval of the final version to be published

RKS: Conception and study design, acquisition of data, drafting the manuscript, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

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