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CHARACTERISTICS OF MULTIPLE SCLEROSIS INCIDENCE IN THE NORTHERN REGIONS OF THE REPUBLIC OF AZERBAIJAN

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The purpose of this article was to study the incidence rate of Multiple Sclerosis (MS) in the northern areas of Azerbaijan, specifically the Sheki-Zagatala and Guba-Khachmaz economic regions, over the study period from January 1, 2013, to December 31, 2022. A total of 181 patients were confirmed with MS, with an average diagnostic age of 35.25 ± 8.85 years and a female-to-male ratio of 1.62:1. The average age at the probable first MS attack was 29.57 ± 8.59 years, with a diagnostic delay averaging 5.67 ± 4.05 years. The most common type of MS was relapsing-remitting MS, observed in 82.87% of cases. Secondary-progressive MS was identified in 9.94% of patients. Over the 10-year study period, the average incidence of MS was 1.58 ± 0.37 per 100,000 population, with rates of 1.96 ± 0.57 per 100,000 in women and 1.20 ± 0.45 per 100,000 in men. The average incidence in rural areas was 1.17 ± 0.38 per 100,000, and in urban areas, it was 2.51 ± 0.82 per 100,000.

Key words: Azerbaijan, multiple sclerosis, epidemiology, incidence, population.

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ХАРАКТЕРИСТИКА ЗАХВОРЮВАНOSTІ НА РОЗСІЯНИЙ СКЛЕРОЗ У ПІВНІЧНИХ РЕГІОНАХ АЗЕРБАЙДЖАНСЬКОЇ РЕСПУБЛІКИ

Метою даної роботи було вивчення захворюваності на розсіяний склероз у північних районах Азербайджану, зокрема в Шекі-Загатазькому та Губа-Хачмазькому економічних районах, за період з 1 січня 2013 року по 31 грудня 2022 року. Усього було підтверджено наявність розсіяного склерозу у 181 пацієнта, середній вік діагностики становив $35,25 \pm 8,85$ років, а співвідношення жінок та чоловіків – 1,62:1. Середній вік ймовірного першого нападу розсіяного склерозу становив $29,57 \pm 8,59$ років, а середня затримка діагностики становила $5,67 \pm 4,05$ року. Найбільш поширеним типом розсіяного склерозу був рецидивуючий-ремітуючий розсіяний склероз, що спостерігався в 82,87 % випадків. Вторинно-прогресуючий розсіяний склероз було виявлено у 9,94 % пацієнтів. За 10-річний період дослідження середня захворюваність на розсіяний склероз склала $1,58 \pm 0,37$ на 100 000 населення, при показниках $1,96 \pm 0,57$ на 100 000 у жінок і $1,20 \pm 0,45$ на 100 000 у чоловіків. Середня захворюваність у сільській місцевості становила $1,17 \pm 0,38$ на 100 000, а міської місцевості – $2,51 \pm 0,82$ на 100 000 населення.

Ключові слова: Азербайджан, розсіяний склероз, епідеміологія, захворюваність, населення.

Multiple sclerosis (MS) is the most common inflammatory disease of the nervous system among young people, characterized by typical clinical symptoms and more frequently affecting women [9, 10]. In recent decades, an increase in MS incidence has been observed in several countries, accompanied by a growing socioeconomic burden associated with this disease [7]. Numerous epidemiological studies on MS have been conducted in some countries neighboring Azerbaijan, and several publications have focused on MS incidence in specific regions [2, 4].

In Azerbaijan, MS receives considerable attention. Before the implementation of the nationwide mandatory health insurance system in 2022, management of MS patients were carried out under the “State Program for the Treatment, Prevention, and Control Measures of Multiple Sclerosis,” established by Presidential Decree No. 2542 on November 13, 2012. Until this period, there was no digital database of MS patients, and clinical and epidemiological indicators of the disease in Azerbaijan had not been systematically studied.

The Republic of Azerbaijan is divided into 14 economic regions, with the Sheki-Zagatala and Guba-Khachmaz economic regions classified as part of the northern areas. The Sheki-Zagatala economic region covers an area of 8.84 thousand km², while the Guba-Khachmaz economic region spans 6.96 thousand km². According to data from the State Committee on Statistics of the Republic of Azerbaijan as of January 1, 2023, the population of these regions was 623,596 and 543,788 people, respectively. The Sheki-Zagatala economic region is located in the northwest of Azerbaijan on the southern slopes of the Greater Caucasus Mountains, while the Guba-Khachmaz economic region lies in the northeastern part of the republic [6].

Thus, given the importance of multiple sclerosis and the difficulties in treating this pathology without accurate epidemiological indicators of the disease in Azerbaijan, a systematic study of the incidence in different regions will be useful in providing assistance to this contingent.

The purpose of the study was to establish the incidence rate of multiple sclerosis in the northern regions of the Republic of Azerbaijan.

Materials and methods. The study covered the period from January 1, 2013, to December 31, 2022 (10 years). As part of the State Program, a special expert commission at the Neurology Center of the Ministry of Health of the Republic of Azerbaijan conducted the diagnosis and treatment of MS patients. The diagnostic algorithm was conducted according to the “Clinical Guideline for Diagnosis and Treatment of Multiple Sclerosis” of the Ministry of Health of the Republic of Azerbaijan. Over this period, the center provided medical care to 87 patients from the Guba-Khachmaz economic region and 121 patients from the Sheki-Zagatala economic region. All patients were entered into a digital database.

Population of the Northern Region by Gender and Place of Residence was as follows: in Guba-Khachmaz economic region – 543,788 persons, of which 273,591 were males, 270,197 – females, 183,533 – urban residents, 360,255 – rural residents; Sheki-Zagatala economic region – 623,596 persons, of which 309,345 were males, 314,251 – females, 177,330 – urban residents, 446,266 – rural residents.

Based on the collected data, the incidence rate per 100,000 population was calculated. Age-standardized incidence rates were determined using direct standardization, with reference population sizes based on the World Population for 2000–2025 and the European Population for 2011–2030. Additionally, the age and gender structure of Azerbaijan’s population as of January 1, 2023, was used as the standard for comparison with regions across the country.

Table 1

Characteristics of multiple sclerosis incidence by year and gender in the Northern Region of the Republic of Azerbaijan

Years	Sex	Population	Patients	I±SE	I±SE (WSt)	I±SE (EuSt)	I±SE (AzSt)	P _t
2013	M	555,820	6	1.08±0.44	0.95±0.41	0.98±0.42	1.01±0.43	<0.05
	F	555,748	15	2.70±0.70 [^] ^{^^}	2.45±0.66	2.33±0.65	2.53±0.67	
	All	1,111,568	21	1.89±0.41	1.69±0.39	1.65±0.39	1.77±0.40	
2014	M	563,257	8	1.42±0.50	1.44±0.51	1.33±0.49	1.61±0.54	>0.05
	F	562,367	15	2.67±0.69	2.48±0.66	2.40±0.65	2.64±0.68	
	All	1,125,624	23	2.04±0.43 ^{**}	1.96±0.42	1.87±0.41	2.13±0.43	
2015	M	570,080	6	1.05±0.43	0.93±0.40	0.93±0.40	1.06±0.43	>0.05
	F	568,615	14	2.46±0.66	2.29±0.63	1.99±0.59	2.21±0.62	
	All	1,138,695	20	1.76±0.39	1.60±0.37	1.45±0.36	1.62±0.38	
2016	M	576,418	8	1.39±0.49	1.29±0.47	1.15±0.45	1.35±0.48	>0.05
	F	574,258	14	2.44±0.65	2.30±0.63	2.10±0.60	2.50±0.66	
	All	1,150,676	22	1.91±0.41	1.79±0.39	1.62±0.38	1.92±0.41	
2017	M	581,918	5	0.86±0.38	0.84±0.38	0.86±0.39	0.94±0.40	>0.05
	F	579,021	12	2.07±0.60	1.99±0.59	1.74±0.55	2.01±0.59	
	All	1,160,939	17	1.46±0.36	1.40±0.35	1.29±0.33	1.47±0.36	
2018	M	587,106	4	0.68±0.34	0.66±0.34	0.62±0.33	0.69±0.34	<0.05
	F	583,654	13	2.23±0.62	2.14±0.61	2.03±0.59	2.42±0.64	
	All	1,170,760	17	1.45±0.35	1.40±0.35	1.32±0.34	1.55±0.36	
2019	M	571,979	10	1.75±0.55	1.68±0.54	1.53±0.52	1.71±0.55	>0.05
	F	573,094	6	1.05±0.43 [^]	1.04±0.43 [^]	1.08±0.43 [^]	1.17±0.45 [^]	
	All	1,145,073	16	1.40±0.35	1.37±0.35	1.31±0.34	1.45±0.36	
2020	M	575,674	5	0.87±0.39	0.81±0.38	0.71±0.35	0.89±0.39	>0.05
	F	577,505	3	0.52±0.30 ^{^^}	0.52±0.30 ^{^^}	0.56±0.31 ^{^^}	0.58±0.32 ^{^^}	
	All	1,153,179	8	0.69±0.25 ^{**}	0.67±0.24	0.64±0.24	0.74±0.25	
2021	M	578,826	9	1.55±0.52	1.50±0.51	1.40±0.49	1.60±0.52	>0.05
	F	580,249	10	1.72±0.54	1.70±0.54	1.55±0.52	1.81±0.56	
	All	1,159,075	19	1.64±0.38	1.60±0.37	1.47±0.36	1.70±0.38	
2022	M	582,936	8	1.37±0.49	1.22±0.46	1.22±0.46	1.38±0.49	>0.05
	F	584,448	10	1.71±0.54	1.66±0.53	1.50±0.51	1.73±0.54	
	All	1,167,384	18	1.54±0.36	1.43±0.35	1.36±0.34	1.55±0.36	
Mean 2013–2022	M	574,401.4	6.9	1.20±0.45	1.13±0.44	1.07±0.43	1.22±0.46	>0.05
	F	573,895.9	11.2	1.96±0.57	1.86±0.56	1.73±0.54	1.96±0.57	
	All	1,148,297.3	18.1	1.58±0.37	1.49±0.36	1.40±0.35	1.59±0.37	

Note: I–incidence per 100,000 population; M–males, F–females; SE–standard error; WSt–World Standard, EuSt–European standard, AzSt–Azerbaijan Standard. Statistical significance of differences: P_t–by Student’s t-test (comparison by gender); comparison of the lowest and highest values by year (by Student’s t-test). Total incidence: ^{**} – p<0.01; incidence among women: [^] – p<0.05; ^{^^} – p<0.01.

Statistical analysis was conducted using IBM SPSS Statistics 27. Statistical differences were assessed using Student’s t-test and the Mann-Whitney U test. The null hypothesis was rejected at a significance level of p<0.05 [15].

Results of the study and their discussion. Of the 87 patients from the Guba-Khachmaz economic region and 121 patients from the Sheki-Zagatala economic region, 74 and 107 patients, respectively, were

confirmed to have MS (totaling 181 patients). In 27 cases, MS was excluded. Additionally, 37 patients diagnosed prior to 2013 were included in the registry but were not considered in the calculation of incidence.

Among the patients diagnosed with MS, men accounted for 38.12 % (69 individuals) and women for 61.88 % (112 individuals), resulting in a female-to-male ratio of 1.62:1. The average age at the time of diagnosis was 35.25 ± 8.85 years (35.01 ± 8.91 years for women and 35.64 ± 8.81 years for men). The average age at the probable first attack of MS was 29.57 ± 8.59 years (29.29 ± 8.77 years for women and 30.04 ± 8.31 years for men). Diagnostic delay was 5.72 ± 4.36 years for women and 5.59 ± 3.53 years for men, with an overall average of 5.67 ± 4.05 years. No statistically significant differences were found between these indicators by gender ($p > 0.05$).

In terms of clinical course, the most common type of MS was relapsing-remitting MS, observed in 82.87 % of patients. Secondary-progressive MS was identified in 9.94 % of patients, and clinically isolated syndrome (CIS) was diagnosed in 4.42 % of cases. The least common was relapsing-progressive MS, accounting for 1.10 % of cases.

The average incidence of MS over 10 years was 1.58 ± 0.37 per 100,000 population. Although the 10-year average incidence rate was higher in women (1.96 ± 0.57 per 100,000) than in men (1.20 ± 0.45 per 100,000), this difference did not reach statistical significance ($p > 0.05$). The highest annual incidence was recorded in 2014 (2.04 ± 0.43 per 100,000), while the lowest was in 2020 (0.69 ± 0.25 per 100,000; $p < 0.01$). Excluding 2020, when strict quarantine measures were in effect due to the COVID-19 pandemic, the lowest incidence was observed in 2019 (1.40 ± 0.35 per 100,000), although no statistically significant differences were found across years ($p > 0.05$).

Among men, the lowest incidence was in 2018 (0.66 ± 0.34 per 100,000), and the highest in 2019 (1.75 ± 0.55 per 100,000), with no statistically significant difference ($p > 0.05$). Among women, the highest incidence was recorded in 2013 (2.70 ± 0.70 per 100,000), and the lowest in 2019 (1.05 ± 0.43 per 100,000; $p < 0.05$) and 2020 (0.52 ± 0.30 per 100,000; $p < 0.01$) (Table 1).

The average 10-year incidence of MS was lower in rural areas compared to urban areas: 1.17 ± 0.38 per 100,000 and 2.51 ± 0.82 per 100,000, respectively ($p > 0.05$). Only in 2015 and 2016 was the incidence in urban populations significantly higher than in rural populations ($p < 0.01$) (Table 2).

Table 2

Characteristics of Multiple Sclerosis Incidence by Year and Place of Residence in the Northern Region of the Republic of Azerbaijan

Years	Region	Population	Patients	I $\pm$ SE	I $\pm$ SE (WSt)	I $\pm$ SE (EuSt)	I $\pm$ SE (AzSt)	P _t
2013	Rural	769,853	10	1.30 ± 0.41	1.18 ± 0.39	1.12 ± 0.38	1.25 ± 0.40	>0.05
	Urban	341,715	11	3.22 ± 0.97	2.87 ± 0.92	2.85 ± 0.91	2.95 ± 0.93	
2014	Rural	780,546	15	$1.92 \pm 0.50^{\wedge}$	1.91 ± 0.49	1.82 ± 0.48	2.11 ± 0.52	>0.05
	Urban	345,078	8	2.32 ± 0.82	2.10 ± 0.78	1.99 ± 0.76	2.19 ± 0.80	
2015	Rural	790,398	5	$0.63 \pm 0.28^{\wedge}$	0.58 ± 0.27	0.56 ± 0.27	0.60 ± 0.28	<0.01
	Urban	348,297	15	$4.31 \pm 1.11^{*,**}$	3.95 ± 1.06	3.50 ± 1.00	3.97 ± 1.07	
2016	Rural	799,701	8	1.00 ± 0.35	0.94 ± 0.34	0.84 ± 0.32	0.96 ± 0.35	<0.01
	Urban	350,975	14	3.99 ± 1.07	3.72 ± 1.03	3.38 ± 0.98	4.10 ± 1.08	<0.05
2017	Rural	807,599	8	0.99 ± 0.35	0.99 ± 0.35	0.96 ± 0.34	1.05 ± 0.36	>0.05
	Urban	353,340	9	2.55 ± 0.85	2.39 ± 0.82	2.10 ± 0.77	2.46 ± 0.83	
2018	Rural	815,333	10	1.23 ± 0.39	1.17 ± 0.38	1.14 ± 0.37	1.35 ± 0.41	>0.05
	Urban	355,427	7	1.97 ± 0.74	1.95 ± 0.74	1.77 ± 0.71	2.05 ± 0.76	
2019	Rural	789,060	11	1.39 ± 0.42	1.35 ± 0.41	1.23 ± 0.39	1.47 ± 0.43	>0.05
	Urban	356,013	5	$1.40 \pm 0.63^{*}$	$1.43 \pm 0.63^{*}$	$1.53 \pm 0.66^{*}$	$1.44 \pm 0.64^{*}$	
2020	Rural	795,395	5	$0.63 \pm 0.28^{\wedge}$	$0.58 \pm 0.27^{\wedge}$	$0.57 \pm 0.27^{\wedge}$	$0.67 \pm 0.29^{\wedge}$	>0.05
	Urban	357,784	3	$0.84 \pm 0.48^{**}$	$0.90 \pm 0.50^{**}$	$0.81 \pm 0.48^{**}$	$0.89 \pm 0.50^{**}$	
2021	Rural	800,185	11	1.37 ± 0.41	1.33 ± 0.41	1.30 ± 0.40	1.47 ± 0.43	>0.05
	Urban	358,890	8	2.23 ± 0.79	2.25 ± 0.79	1.91 ± 0.73	2.27 ± 0.80	
2022	Rural	806,521	10	1.24 ± 0.39	1.18 ± 0.38	1.16 ± 0.38	1.26 ± 0.39	>0.05
	Urban	360,863	8	2.22 ± 0.78	2.03 ± 0.75	1.82 ± 0.71	2.23 ± 0.79	
Mean 2013–2022	Rural	795,459.1	9.3	1.17 ± 0.38	1.12 ± 0.37	1.07 ± 0.36	1.22 ± 0.39	>0.05
	Urban	352,838.2	8.8	2.51 ± 0.82	2.36 ± 0.80	2.17 ± 0.77	2.46 ± 0.82	

Note: I–incidence per 100,000 population; SE–standard error; WSt–World Standard, EuSt–European standard, AzSt–Azerbaijan Standard. Statistical significance of differences: Pt–by Student's t-test (comparison by place of residence); comparison of the lowest and highest values by year (by Student's t-test). Incidence in rural areas: $\wedge$ – $p < 0.05$; incidence in urban areas: $*$ – $p < 0.05$; $**$ – $p < 0.01$.

The highest incidence among urban populations was recorded in 2015 (4.31 ± 1.11 per 100,000), and the lowest in 2020 (0.84 ± 0.48 per 100,000; $p < 0.01$), excluding the period of strict quarantine measures due to the COVID-19 pandemic. During the pandemic period, the lowest incidence was observed in 2019 (1.40 ± 0.63 per 100,000; $p < 0.05$).

Among rural populations, the highest incidence was in 2014 (1.92 ± 0.50 per 100,000), and the lowest was in 2015 and 2020 (0.63 ± 0.28 per 100,000; $p < 0.05$).

As expected, MS was most commonly observed in the age group ≥ 18 years. From 2013 to 2022, only one case was registered among individuals under 18 years old in the region – in 2015. The highest incidence among adults was observed in 2014 (2.81 ± 0.59 per 100,000), and the lowest in 2020 (0.94 ± 0.33 per 100,000; $p < 0.01$).

Comparative Analysis of Multiple Sclerosis Incidence Rates in the Guba-Khachmaz and Sheki-Zagatala Economic Regions showed that although the incidence among women is high in both economic regions, this difference is not statistically significant. In the Sheki-Zagatala economic region, the incidence in urban populations was higher than in rural populations – 3.35 ± 1.39 per 100,000 and 1.12 ± 0.50 per 100,000, respectively; however, this difference also did not reach statistical significance ($p > 0.05$). Even after standardizing these rates to the standard population of Azerbaijan (2023), no significant differences were identified.

Prevalence of multiple sclerosis is increasing world-wide. There are numerous studies devoted epidemiological evaluation of this pathology in different countries [1, 5, 8]. The authors noted that the main characteristics of the epidemiology of multiple sclerosis in the 20th century are: a steady increase in the prevalence and incidence of multiple sclerosis, possibly due to improved diagnosis and treatment, but also changes in the environmental/epigenetic risk profile and/or lifestyle factors; an increase in the female/male ratio; the emergence and increasing frequency of MS in ethnic groups previously free of multiple sclerosis.

Our study represents the first investigation into the incidence of MS in the northern region of Azerbaijan. The data obtained were compared with rates from neighboring countries and various others.

In neighboring Turkey, the incidence of MS in Edirne was 3.48 per 100,000 between June 1, 2002, and July 31, 2003, and 2.6 per 100,000 between June 1, 2003, and July 31, 2004. In the rural areas of Geyve and Kandira, data from 2016-2017 indicated an annual incidence of MS of 3.4 per 100,000, exceeding our results [2].

MS incidence in Iran is also high. Mirmosayyeb O, et al. systematically searched the information databases PubMed, Scopus, EMBASE, Web of Science and Google Scholar related to multiple sclerosis. They also searched the references of included studies and conference abstracts that were published up to April 2021. According to the results, the literature search identified 2817 articles, and a total of 34 studies were included for the systematic review. The prevalence of MS in Iran was found to be highest in Tehran and lowest in Khuzestan and Sistan-Baluchestan provinces. The pooled prevalence was calculated as 0.001 (95% CI: 0.000-0.001) ($I^2=0$, $P < 0.001$). The results of this study show that the pooled prevalence of MS in Iran is 100 per 100,000, which is high. However, the prevalence increases sharply in the provinces [11]. These results are also higher than in our work.

In the Russian Federation, MS incidence varies across regions. For instance, one of the lowest standardized rates was recorded in the Dagestan Republic, bordering Azerbaijan, at 0.2 per 100,000 between 2000 and 2004. In other nearby regions of Azerbaijan, MS incidence was 1.76 per 100,000 in Nazran (Republic of Ingushetia) from 2010 to 2015 and 1.9 per 100,000 in Nalchik (Republic of Kabardino-Balkaria) from 2012 to 2017. The highest MS prevalence rate among the indigenous population at this time was observed in the small republics of the North Caucasus such as the Karachay-Cherkess Republic—16.9 cases. In the neighboring Rostov region, also with a predominantly Russian population, in 2002–2006, the MS prevalence was 24.6 cases, and the incidence was 1.7 cases per 100,000 population. In the largest city of the region, Rostov-on-Don, the prevalence rate reached 26.3 cases per 100,000 population. According to recent data (2020), the incidence rates of multiple sclerosis vary from 10 to 80 cases per 100,000 depending on the region and ethnicity of the population. In European Russia the prevalence of multiple sclerosis varies from 30 to 80 cases, in Siberia - from 20 to 70 cases, with a steady increase, especially in women [4].

In Georgia, no epidemiological studies on MS had been conducted, and data on incidence rates were unavailable for 2021 [3]. Experts estimate that the probable number of MS patients in Georgia does not exceed 1,200 people [13]. According to the International MS Federation, the prevalence of MS in Armenia was 10 per 100,000 as of 2023 [12]. With such low prevalence rates, the incidence in Armenia is likely lower than the findings of our study.

MS incidence remains high in Central and Northern European countries as well. In 2019, the standardized incidence rate in Csongrád, Hungary, was 4.44 per 100,000 (2.44 for men and 6.25 for women) [1]. In Bavaria in 2015, the incidence was 16.46 per 100,000, with standardized rates of 15.98 per 100,000 based on the European standard and 16.88 per 100,000 based on the world standard. The average incidence among women was significantly higher than among men – 23.0 per 100,000 and 10.7 per 100,000, respectively [5].

A 2014–2015 study in Ireland showed a standardized MS incidence of 6.0 per 100,000 (3.3 per 100,000 for men and 8.7 per 100,000 for women). The highest rate was recorded in the Border Region at 9.6 per 100,000, while the lowest was in the West at 3.5 per 100,000 [14]. In the Telemark region of Norway, the average standardized incidence rates per the European standard were 11.3 and 14.4 per 100,000 in 2009–2013 and 2014–2018, respectively; among men, these rates were 8.3 and 10.6 per 100,000, and among women, 14.3 and 18.5 per 100,000 [8].

Conclusions

1. A total of 181 patients were confirmed with MS, with an average diagnostic age of 35.25 ± 8.85 years and a female-to-male ratio of 1.62:1. The average age at the probable first MS attack was 29.57 ± 8.59 years, with a diagnostic delay averaging 5.67 ± 4.05 years.

2. The most common type of MS was relapsing-remitting MS, observed in 82.87 % of cases. Secondary-progressive MS was identified in 9.94 % of patients.

3. Over the 10-year study period, the average incidence of MS was 1.58 ± 0.37 per 100,000 population, with rates of 1.96 ± 0.57 per 100,000 in women and 1.20 ± 0.45 per 100,000 in men. The average incidence in rural areas was 1.17 ± 0.38 per 100,000, and in urban areas, it was 2.51 ± 0.82 per 100,000.

Thus, the MS incidence rate in Azerbaijan is lower than in neighboring countries such as Turkey and Iran but is higher or close to the rates in some regions of the Russian Federation. Differences in MS incidence rates may stem from specific geographic and ethnocultural characteristics unique to each region, along with the varied approaches employed in clinical and epidemiological research. Factors like climate, sunlight exposure, healthcare accessibility, and genetic backgrounds can greatly influence incidence rates, while inconsistencies in research methods add complexity to direct comparisons.

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