

Review

# Epidemiology of Amyotrophic Lateral Sclerosis

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**Abstract:** We searched for full-text publications in Russian and English in the E-Library, PubMed, Springer, Clinical keys, Google Scholar databases, using keywords and combined word searches (amyotrophic lateral sclerosis - ALS, motor neuron disease, epidemiology, incidence, prevalence), for 2015 – 2020. In addition, the review included earlier publications of historical interest. Despite our comprehensive searches of these commonly used databases and search terms, it cannot be excluded that some publications may have been missed. A total of 74 publications were analyzed, reflecting epidemiological studies of ALS in 168 countries. The incidence of ALS worldwide varies from 0.4 per 100,000 per year (Ecuador) to 9.45 per 100,000 per year (Japan, Oshima region). Prevalence - from 0.1 per 100,000 population (Somalia) to 42.1 per 100,000 population (Canada). This data depends on many factors, including the quality of the diagnosis and the health care system.

**Keywords:** amyotrophic lateral sclerosis - ALS, motor neuron disease, epidemiology, incidence, prevalence.

## Introduction

Amyotrophic lateral sclerosis (ALS), or motor neurone disease (MND) is a severe progressive neurodegenerative disease that selectively affects the motor neurons of the spinal cord, brainstem and central motor neurons [1]. Usually the debut of ALS falls on 50-70 years of age [2]. Juvenile ALS is a rare form of the disease with a debut under the age of 25, occurring with variable phenotypic variants and rate of progression of the disease [3]. Clinically, the disease is characterized by weakness and atrophy of muscles in the extremities, fasciculations, dysarthria, dysphagia. There may be bulbar and pseudobulbar paralysis, lower paraparesis, central-peripheral paralysis, flaccid paralysis of the lower extremities, cognitive and mental disorders [4]. ALS is quite rare, but it progresses rapidly, causes disability and is characterized by high mortality [5]. The prognosis of the disease depends on the age of patients, the involvement of bulbar muscles, the rate of progression, but usually - it is unfavorable [6]. Timely diagnosis of ALS can reduce the rate of progression of the disease and improve the quality of life of patients at the initial stage. Due to the high mortality rate and the lack of specific therapy, ALS remains an urgent problem of modern neurology [7]. The study of the prevalence and incidence of ALS in different regions of Russia will help us to understand the cause of this disorder and develop a more accurate framework for identifying and combatting the disease.

## Methods

We have searched for full-text publications in Russian and English in the E-Library, PubMed, Springer, Clinical keys, Google Scholar databases, using keywords and combined word searches (amyotrophic lateral sclerosis – ALS, motor neuron disease, epidemiology, morbidity, prevalence), for 2015-2020. In addition, earlier publications of historical interest were included in the review. Despite our comprehensive research of these frequently used databases and search terms, it cannot be ruled out that some publications may have been missed. A total of 34 publications reflecting epidemiological studies of ALS in 166 countries were analyzed.

## Results

The incidence of ALS in the world varies from 0.4 per 100,000 per year (Ecuador) [8] to 3.83 per 100,000 per year [9] (Scotland), and the prevalence ranges from 0.1 (Somalia) [10] to 42.1 per 100,000 population (Canada) [10].

### *Russia*

We have analyzed 3 epidemiological studies conducted by Russian scientists and 1 study conducted in Russia as part of an international project. The variability of the incidence of ALS in Russia ranged from 1.25 per 100,000 per year (Moscow) [11] to 1.2 per 100,000 per year (Yakutia) [12]. The average incidence of ALS was 1.2 per 100,000 per year. The prevalence of ALS varied from 2.7 per 100,000 population [10] to 3.46 per 100,000 population (Novosibirsk) [13], the average level was 3.08 per 100,000 population.

### *North America*

In the North American region, epidemiological studies of ALS have been conducted in 3 countries (USA, Canada, Greenland). The incidence ranged from 1.4 per 100,000 per year (USA, state of California) [14] to 1.81 per 100,000 per year (USA, state of Florida) [15], the average incidence of ALS (excluding ethnic and racial affiliation of patients) in North America was 1.55 per 100,000 per year. The variability of the prevalence of ALS in the region was high: from 3.4 per 100,000 population (USA) [10] to 42.1 per 100,000 population (Canada) [10]. The average prevalence of ALS was 14.8 per 100,000 population,

In the USA, the incidence of ALS ranged from 1.4 per 100,000 per year (California) [14] to 1.81 per 100,000 per year (Florida) [15], the average level was 1.55 per 100,000 per year. The prevalence ranged from 3.4 per 100,000 population [10] to 5.35 per 100,000 population (Atlanta State) [16], the average level was 4.25 per 100,000 population. According to epidemiological studies of ALS conducted in the United States, taking into account the ethnicity and race of samples, the incidence among Americans of European descent was higher (1.79 per 100,000 per year) compared to Americans of African descent (0.80 per 100,000 per year) and Asian Americans (0.76 per 100,000 per year). For non-Hispanic residents of the United States, the incidence of ALS was higher compared to Hispanics (1.65 vs. 0.57 per 100,000 population per year, respectively) [17].

In Canada, the prevalence rate was 42.1 per 100,000 population [10]. We have not found any studies on the incidence of ALS.

In Greenland, the prevalence of ALS was 29.8 per 100,000 population [10]. We have not found any studies on the incidence of ALS.

#### *South America*

In the South American region, we found and analyzed epidemiological studies of ALS in 33 countries (Argentina, Chile, Guadeloupe, Ecuador, Mexico, Brazil, Colombia, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama, Venezuela, Bolivia, Peru, Antigua and Barbuda, Barbados, Belize, Cuba, Dominica, Dominican Republic, Grenada, Guyana, Republic of Haiti, Jamaica, Puerto Rico, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Republic of Trinidad and Tobago, Virgin Islands, Paraguay). The incidence of ALS ranged from 0.4 per 100,000 per year (Ecuador) [8] to 0.93 per 100,000 per year (Guadeloupe, Caribbean Islands) [18]. The average incidence of ALS (excluding the ethnic and racial affiliation of patients) was 0.66 per 100,000 per year. The prevalence of ALS ranged from 2.7 per 100,000 population (Cuba) [10] to 27.8 per 100,000 population (Argentina) [10], the average level was 10.37 per 100,000 population.

The highest prevalence of ALS was in Argentina (27.8 per 100,000 population), Chile (27.6 per 100,000 population), Brazil (20.3 per 100,000 population), Virgin Islands (18.1 per 100,000 population), Costa Rica (17.2 per 100,000 population), Saint Lucia (14.8 per 100,000 population), Dominica (13.8 per 100,000 population), Saint Vincent and the Grenadines (13.1 per 100,000 population), Grenada (13.6 per 100,000 population), Colombia (12.4 per 100,000 population), Paraguay (10.8 per 100,000 population), Suriname (10.0 per 100,000 population), Mexico (9.8 per 100,000 population) and Belize (9.8 per 100,000) [10].

In contrast, in Guadeloupe (Caribbean Islands) and Ecuador, the incidence rate was low (0.4 per 100,000 per year [8] and 0.93 per 100,000 per year [18], respectively).

The average prevalence of ALS was observed in the Republic of Panama (9.4 per 100,000 population), Guyana (9.0 per 100,000 population), the Dominican Republic (8.5 per 100,000 population), Puerto Rico (8.0 per 100,000 population), Trinidad and Tobago (7.8 per 100,000 population), El Salvador (7.7 per 100,000 population), Bolivia (7.6 per 100,000 population), Honduras (6.3 per 100,000 population), Jamaica (5.8 per 100,000 population), Guatemala (5.7 per 100,000 population), Peru (5.6 per 100,000 population), Venezuela (5.1 per 100,000 population), Antigua and Barbuda (4.9 per 100,000 population), Barbados (4.3 per 100,000 population), Nicaragua (4.2 per 100,000 population) [10].

#### *Western Europe*

In Western Europe, we found and analyzed epidemiological studies of ALS in 19 countries (Austria, Andorra, Belgium, Great Britain, Germany, Denmark, Italy, Iceland, Spain, Luxembourg, Malta, the Netherlands, Norway, Portugal, Finland, France, Switzerland, Sweden, Scotland). The incidence of ALS ranged from 1.66 per 100,000 per year (Great Britain, London) [19] to 3.83 per 100,000 per year (Scotland) [9], the average

(excluding the ethnic and racial affiliation of patients) was 2.84 per 100,000 per year. The variability in the prevalence of ALS was high: from 4.1 per 100,000 population (Norway, Norland County) [20] to 37.6 (Portugal) [10]. The average prevalence of ALS in the region was 24.18 per 100,000 population.

The highest prevalence of ALS was in Belgium (37.2 per 100,000 population), Great Britain (34.5 per 100,000 population), Austria (36.9 per 100,000 population), Portugal (37.6 per 100,000 population), Malta (32.2 per 100,000 population), the Netherlands (28.1 per 100,000 population), Luxembourg (27.2 per 100,000 population), Iceland (25.1 per 100,000 population), Switzerland (22.8 per 100,000 population), Andorra (21.0 per 100,000 population) and Finland (19.5 per 100,000 population) [10].

In the UK, the incidence of ALS was 1.66 per 100,000 per year, 1.97 per 100,000 among the population of European descent and 1.35 per 100,000 among the population of African descent (London)[20]. The prevalence rate in the UK was 34.5 per 100,000 population[10]. In Scotland, the incidence rate was 3.83 per 100,000 per year [9], the prevalence ranged from 7.61 to 7.81 per 100,000 population [9], the average level was 7.71 per 100,000 population.

In France, the incidence of ALS was 3.32 per 100,000 per year [21], and the prevalence was 27.3 per 100,000 population [10].

The prevalence rate of ALS in Germany was 27.5 per 100,000 per year [10], we have not found any data on incidence.

The largest number of epidemiological studies of ALS have been conducted in Italy. The incidence rate ranged from 2.81 per 100,000 per year (Friuli, Venice, Giulia) [22] to 3.11 per 100,000 per year (Liguria) [23], the average was 2.9 per 100,000 per year. The prevalence of ALS in Italy varied in a wide range: from 7.85 per 100,000 population (Liguria) [24] to 12.3 per 100,000 population (Piedmont) [24]. The average prevalence of ALS in the country was 9.37 per 100,000 population.

In Norway, the incidence rate was 2.1 per 100,000 per year (Norland County) [21], the prevalence rate was 4.1 per 100,000 population (Norland County) [21].

#### *Eastern Europe*

In Eastern Europe, we found and analyzed epidemiological studies of ALS in 13 countries (Albania, Belarus, Bosnia and Herzegovina, Greece, Lithuania, Moldova, Cyprus, Poland, Slovakia, Romania, Montenegro, Estonia, Ukraine). The prevalence of ALS varied in a wide range: from 1.1 per 100,000 population (Moldova) [10] to 29.4 per 100,000 population (Greece) [10], the average was 8.8 per 100,000 population.

The prevalence of ALS is high in Greece (29.4 per 100,000 population), Lithuania (21.3 per 100,000 population), Cyprus (19.7 per 100,000 population) [10], the average prevalence of ALS is noted in Bosnia and Herzegovina (10.1 per 100,000 population), Poland (6.5 per 100,000 population), Albania (6.8 per 100,000 population), Romania (6.4 per 100,000 population), Slovakia (6.1 per 100,000 population), Montenegro (4.1 per 100,000 population) [10].

In Belarus, the prevalence of ALS varied from 2.0 per 100,000 population [25] to 5.4 per 100,000 population [10], the average prevalence was 3.7 per 100,000 population. In Ukraine and Moldova, the prevalence rates of ALS were lower (1.8 and 1.1 per 100,000 population, respectively) [10].

### *Asia*

In Asia, we have found and analyzed epidemiological studies of ALS in 34 countries (Armenia, Azerbaijan, Georgia, Kazakhstan, Mongolia, Turkmenistan, Uzbekistan, Turkey, Israel, China, Singapore, Brunei, South Korea, North Korea, Japan, Taiwan, Cambodia, Indonesia, Laos, Maldives, Mauritius, Myanmar, Philippines, Sri Lanka, Seychelles, Thailand, East Timor, Vietnam, Bangladesh, Bhutan, India, Nepal, Pakistan, Malaysia). The incidence rate of ALS in the region ranged from 1.2 per 100,000 per year (Korea) [26] to 1.8 per 100,000 per year (Israel) [27], the average (excluding ethnic and racial affiliation of patients) was 1.51 per 100,000 per year. The prevalence of ALS varied from 1.7 per 100,000 population (Georgia) [10] to 26.3 per 100,000 population (South Korea) [10], the average was 9.4 per 100,000 population.

In Turkey, the incidence of ALS varied from 1.3 per 100,000 per year (Antalya) [28] to 1.9 per 100,000 per year (Fraction) [29], the average incidence rate was 1.6 per 100,000 per year. The prevalence of ALS in Turkey varied from 4.6 per 100,000 population (Antalya) [29] to 7.3 per 100,000 population (Fraction) [30]. The average prevalence of ALS in the country was 5.9 per 100,000 population.

In China, the incidence of ALS was 1.65 per 100,000 per year [30]. The prevalence of ALS in China was 2.91 per 100,000 population [31]. In Korea, the incidence of ALS was 1.2 per 100,000 per year [27], and the prevalence ranged from 2.6 per 100,000 population (North Korea) [10] to 26.3 per 100,000 population (South Korea) [10]. The average prevalence of ALS in Korea was 10.7 per 100,000 population.

The prevalence of ALS is high in Singapore (20.6 per 100,000 population), Brunei (16.2 per 100,000 population), India (16.1 per 100,000 population), East Timor (13.6 per 100,000 population), Myanmar (13.3 per 100,000 population), Taiwan (13.5 per 100,000 population), Bhutan (11.8 per 100,000 population), Vietnam (11.4 per 100,000 population), Laos (11.1 per 100,000 population), Indonesia (10.6 per 100,000 population), Cambodia (10.6 per 100,000 population), Thailand (10.0 per 100,000 population), Sri Lanka (9.6 per 100,000 population) [10].

The average prevalence rates of ALS are found in the Maldives (8.7 per 100,000 population), Malaysia (8.6 per 100,000 population), Mauritius (8.6 per 100,000 population), Bangladesh (8.6 per 100,000 population), Nepal (8.1 per 100,000 population), Seychelles (7.5 per 100,000 population), Pakistan (7.0 per 100,000), Mongolia (6.8 per 100,000 population), Philippines (6.7 per 100,000 population), Turkmenistan (5.7 per 100,000 population), Azerbaijan (5.2 per 100,000 population), Kazakhstan (4.0 per 100,000 population), Uzbekistan (4.0 per 100,000 population), Armenia (3.7 per 100,000 population) [10].

The lowest prevalence rates of ALS were noted in Georgia (1.7 per 100,000 population) [10]. In Israel, the incidence rate was 1.8 per 100,000 per year [28], the prevalence rate was 8.1 per 100,000 population [28].

#### *Middle East and Africa*

In the Middle East and Africa region, we found and analyzed epidemiological studies of ALS in 59 countries (Afghanistan, Algeria, Bahrain, Egypt, Iran, Iraq, Jordan, Lebanon, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Sudan, Syria, Tunisia, UAE, Yemen, Botswana, Lesotho, Namibia, Swaziland, Benin, Burkina Faso, Cameroon, Cape Verde, Chad, Ivory Coast, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Sao Tome and Principe, Senegal, Sierra Leone, Togo, Burundi, Eritrea, Ethiopia, Kenya, Madagascar, Malawi, Mozambique, Rwanda, Somalia, South Sudan, Tanzania, Uganda, Zambia, Angola, Congo, Equatorial Guinea, Gabon, South Africa). The incidence rate of ALS in South Africa was 1.09 per 100,000 per year (South Africa) [31], we have not found data on the incidence in other regions. The prevalence rates of ALS ranged from 0.1 per 100,000 population (Somalia) [10] to 24.6 per 100,000 population (Equatorial Guinea) [10]. The average prevalence of ALS in the region was 4.2 per 100,000 population.

The highest prevalence rates of ALS were in Equatorial Guinea, where the prevalence rate of ALS was 24.6 per 100,000 population [10]. We have not found epidemiological studies of the incidence of ALS in the region for the analyzed period of time.

Average prevalence rates of ALS are shown in Cape Verde (8.2 per 100,000 population), Oman (7.2 per 100,000 population), Egypt (7.1 per 100,000 population), Iran (7.3 per 100,000 population), Saudi Arabia (7.1 per 100,000 population), Mozambique (7.1 per 100,000 population), Sudan (6.9 per 100,000 population), Botswana (6.6 per 100,000 population), Lesotho (6.5 per 100,000 population), Mali (6.2 per 100,000 population), Ghana (6.2 per 100,000 population), Nigeria (6.0 per 100,000 population), Uganda (5.9 per 100,000 population), Chad (5.2 per 100,000 population), Tunisia (5.1 per 100,000 population) [10]. The prevalence of ALS in Burkina Faso, Morocco and Yemen was comparable - 5.1 per 100,000 population [10]. The prevalence rates of ALS were lower in Swaziland and Angola (5.0 per 100,000 population), Namibia (4.8 per 100,000 population), Jordan (4.5 per 100,000 population), Qatar (4.4 per 100,000 population), Iran (4.4 per 100,000 population), Bahrain (4.1 per 100,000 population), Syria and Tanzania (4.0 per 100,000 population), Ethiopia (3.9 per 100,000 population), Iraq (3.6 per 100,000 population), Benin (3.4 per 100,000 population), Mauritania (3.3 per 100,000 population), Afghanistan and Lebanon (3.2 per 100,000 population), Palestine (3.0 per 100,000 population), Algeria and Rwanda (2.9 per 100,000 population), Sierra Leone, Sao Tome and Principe (2.8 per 100,000 population), Senegal (2.1 per 100,000 population) [10].

In South Africa, the incidence rate of ALS was 1.09 per 100,000 per year [31], and the prevalence rate was 5.9 per 100,000 population [10].

The prevalence of ALS was low in Guinea-Bissau (2.0 per 100,000 population), the United Arab Emirates (1.7 per 100,000 population), Cameroon (1.5 per 100,000 population), Ivory Coast (1.4 per 100,000 population), Gambia (1.3 per 100,000 population), Togo (1.1

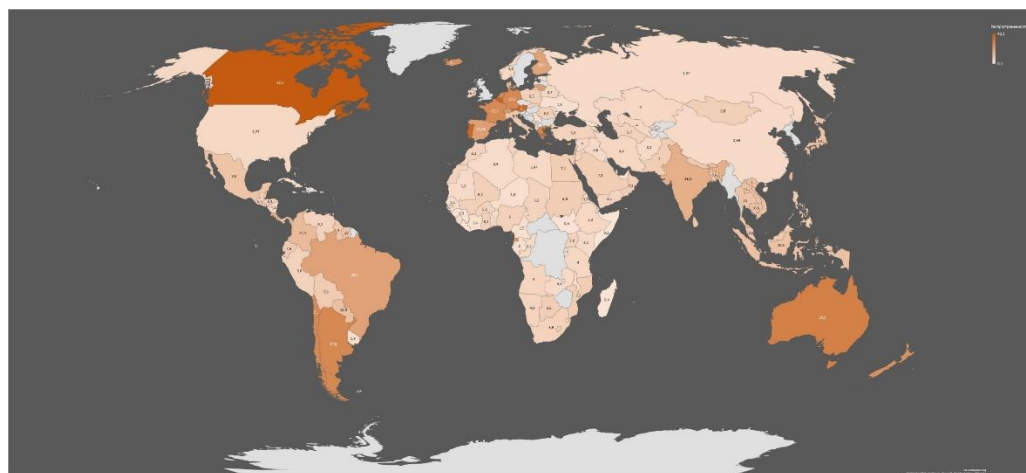
per 100,000 population), Guinea (0.9 per 100,000 population), Liberia (0.4 per 100,000 population), South Sudan (0.6 per 100,000 population), Burundi (0.7 per 100,000 population), Madagascar (0.4 per 100,000 population), Somalia (0.1 per 100,000 population) [10].

#### *Australia*

In the Australia region, we found and analyzed epidemiological studies on ALS in 2 countries (Australia and New Zealand). The prevalence of ALS was high and ranged from 25.1 per 100,000 population (New Zealand) [10] to 30.3 per 100,000 population (Australia) [10], the average level was 27.7 per 100,000 population. We have not found any data on morbidity in this region.

### **Discussion**

The analysis of epidemiological studies of ALS indicates that the neuromuscular disease in question is an urgent medical problem. The incidence and prevalence of ALS depends on many factors, including the quality of diagnosis and management of healthcare systems. Climatic, geographical, ethnic and racial risk factors of ALS affect epidemiological indicators, however, in general, we have not found significant epidemiological dynamics of ALS in the west-east direction and from north to south (Figure 1). The problem of ALS requires improving approaches to early diagnosis, which is important for reducing the rate of progression of the disease and improving the quality of life of patients.



**Figure 1.** Epidemiology of amyotrophic lateral sclerosis.

### **Conclusions**

The epidemiology of ALS is being actively studied in Russia and worldwide. According to our meta-analysis, the incidence and prevalence of ALS in the world is variable, which is probably genetically determined in some racial and ethnic groups of the population. ALS is a severe neurodegenerative disease which despite the low frequency of occurrence are characterized by high mortality. It is important to understand which

regions are characterized by a high prevalence and incidence of ALS in order to improve the quality of diagnosis and patient care.

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