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COMPARATIVE ANALYSIS OF THE DURATION OF SPORADIC FORMS OF MOTOR NEURON DISEASE IN THE REPUBLIC OF SAKHA (YAKUTIA)

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УДК 616.8

The article describes a study of the duration of the disease in patients with different forms of motor neuron disease (MND) in the Republic of Sakha (Yakutia). Motor neuron disease is a group of neurodegenerative diseases of unknown etiology and pathogenesis, accompanied by the death of central and / or peripheral motor neurons, steady progression and inevitable death. The results obtained correlate with the data of researchers in the world and depend on the combined or isolated damage to the motor neuron (p = 0.00001).

Aim: to study the duration of the cases of illness in different forms of motor neuron disease in the RS (Y), depending on ethnicity, age and gender.

Keywords: motor neuron diseases, amyotrophic lateral sclerosis, progressive muscle atrophy, primary lateral sclerosis.

Introduction. Motor neuron disease (MND) is a group of neurodegenerative diseases of unclear etiology, characterized by selective damage to central and / or peripheral motor neurons with an invariable lethal outcome.

MND classification

Currently, there is no uniform accepted international classification of MND

In the most common North American [16] and British [27] classifications of MND, in addition to the division into sporadic and familial forms of MND, its varieties are indicated, depending on the isolated peripheral lesion (progressive bulbar palsy, progressive muscle atrophy) of the central (primary lateral sclerosis) or mixed motor neuron lesion (amyotrophic lateral sclerosis). In the Russian modified classification of ALS (MND) by G. Levitsky and V. Skvortsova (2006), progressive bulbar palsy, progressive muscle atrophy, primary lateral sclerosis are also separated from ALS, in which there is a combined lesion of the motor neuron [2]. In the classification of O.A. Hondkarian ALS is not differentiated from the degree of motor neuron involvement, but its forms have been described, depending on the onset of the disease [4]. Many researchers adhere to the principle of separation in which MND is divided into a disease with a "pure" lesion of the lower motor neuron - progressive muscle atrophy (PMA), with a "pure" lesion of the upper motor neuron - primary lateral sclerosis (PLS) and a combined lesion of the lower and upper motor neurons, amyotrophic lateral sclerosis (ALS) [6, 7, 19, 20, 21, 24, 25]. Some authors consider PMA and PLS to be atypical forms of ALS or its variants of the course, believing that a single molecular mechanism may be compatible with clinical heterogeneity. [6, 10, 24].

Epidemiology of ALS.

Since ALS is the most common motor neuron disease in comparison with PMA and PLS, we present data on its prevalence. PMA and PLS are rare forms of MND and we have not found data on their prevalence in the available literature. According to researchers and co-authors from the Institute of Neuroepidemiology and Tropical Neurology (France), who published in 2017 a comparative meta-analysis on the prevalence of MND in the world, the total cumulative incidence of ALS in the world was 1.68 (1.50-1.85) per 100,000 population after standardization. Heterogeneity was found in the standardized incidence of ALS between Northern Europe 1.89 (1.46–2.32) per 100,000 population and East Asia (China, Japan) 0.83 (0.42–1.24) per 100,000 population (p = 0.00) and South Asia (Iran) 0.73 (0.58-0.89) / 100,000 population (p = 0.02). In contrast, homogeneous rates were reported in populations from Europe, North America and New Zealand: pooled standardized ALS incidence 1.81 (1.66–1.97) / 100,000 population for these regions [18]. In Yakutia, the incidence as of 2018. was 0.5 cases per 100,000 population. Taking into account the severity of the patient's condition and the absence of biomarkers for early detection of MND, specific treatment, a group of these diseases is a medical and social problem for public health authorities and social protection of the population and requires the organization of a multidisciplinary approach in the management of such patients.

Materials and methods. Materials: We retrospectively analyzed the hospital register of patients with MND, as well

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as their medical records for the period from 2006 to 2019, who received medical care at the neurological department of the republican hospital № 2 and the neurological department of the Clinic of the Yakutsk Scientific Center for Complex Medical Problems. All patients were diagnosed with MND after excluding other diseases that might have a similar clinical picture.

MND inclusion criteria:

1. Patients with "significant ALS" were included according to the revised El Escorial criteria [12].

2. The presence of clinical signs of an isolated lesion of the lower motor neuron, confirmed by the electromyography (ENMG) method, without signs of damage to the upper motor neuron within 4 years after the onset of the first symptoms;

3. The presence of clinical signs of an isolated lesion of the upper motor neuron without signs of damage to the lower motor neuron;

MND exclusion criteria:

1. A family history of Kennedy disease, spinal muscular atrophy, and hereditary spastic paraplegia;

Research methods. When making a diagnosis, the clinical picture of the disease took into account the combination of signs of damage to the lower and central motor neurons or its absence, the rate of development of the disease. In this case, the defeat of the lower motor neuron, if possible, was confirmed by the electrophysiological method. The diagnosis was made only after excluding other diseases that mimic the MND clinic. The clinical method included the study of the demographic data of the patients, the age of onset, the duration of the disease and its clinical manifestations; neuroimaging techniques included magnetic resonance imaging of the brain and spinal cord; electroneuromyography was performed to confirm damage to the lower motor neuron;

Statistical analysis was carried out using the STATISTICA 13.3 software (developed by StatSoft.Inc). Quantitative indicators were assessed for compliance with the normal distribution, for this, the Kolmogorov-Smirnov test was used. In the case of describing quantitative indicators with a normal distribution, the obtained data were combined into variational series in which the arithmetic mean values (M) and standard deviations (SD) were calculated. Aggregates of quantitative indicators, the distribution of which differed from normal, were described using the values of the median (Me) and the lower and upper quartiles (Q1-Q3). The

Frequency of MND by gender

Gender	Form DMN PLS	Form DMN ALS	Form DMN PMA
Female (n=41)	7	30	4
	17.07%	73.17%	9.76%
Male (n=57)	1	50	6
	1.75%	87.72%	10.53%
All Grps	8	80	10
	χ^2 =7.46; p=0.006	χ^2 =3.37; p=0.067	χ^2 =0.02; p=0.9

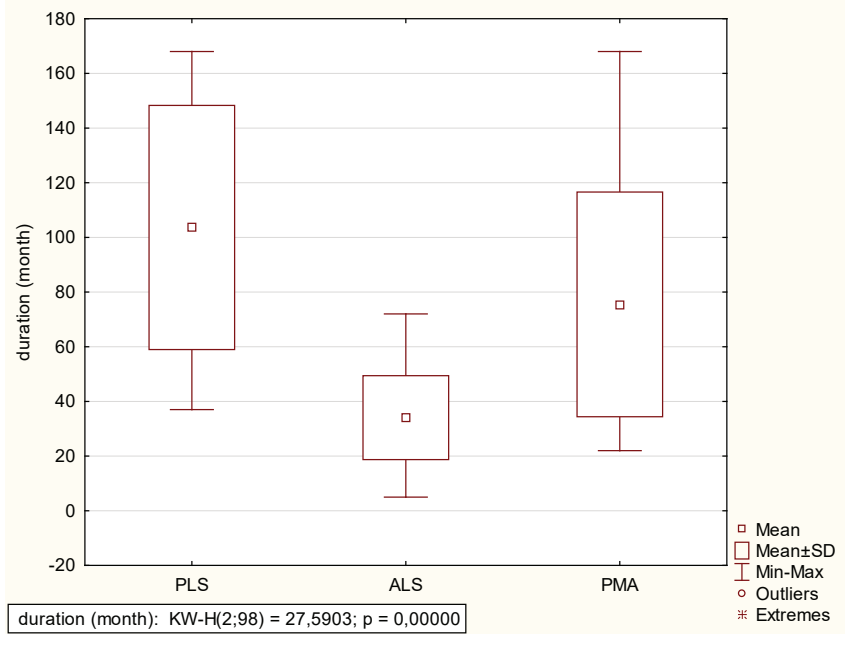

Fig. 1. Duration of the disease with different forms of MND (months)

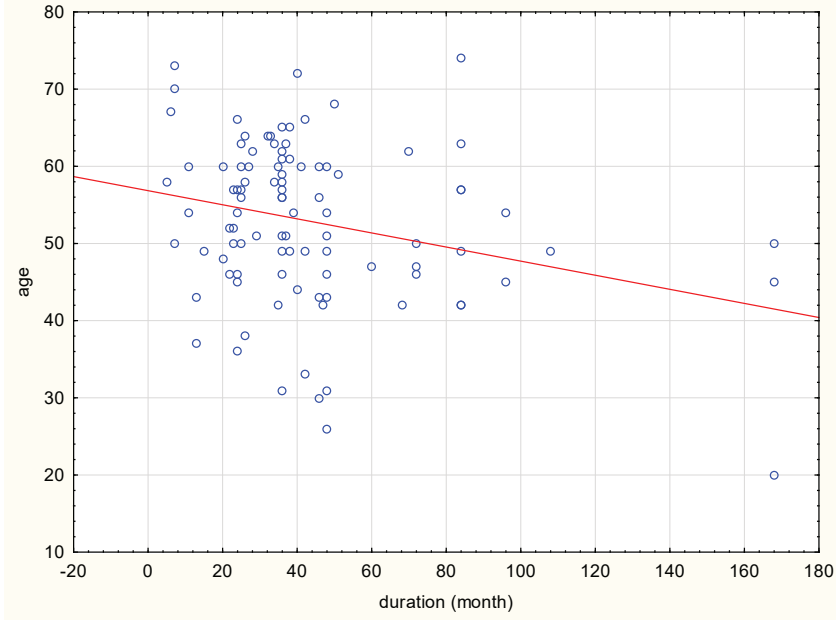

Fig. 2. Relationship between age and duration of disease in MND (n = 98)

nominal data were described with the indication of absolute values and percentages. When comparing the means in normally distributed populations of quantitative data, Student's t-test and Fisher's F test were calculated. The Mann-Whitney U-test and the Kruskal-Wallis test were used to compare independent populations in cases where there were no signs of normal distribution of the data, while the comparison of nominal data was carried out using the Pearson χ2 test. In the case of the analysis of four-field tables with the expected phenomenon in at least one cell less than 10, we calculated the χ2 criterion with the Yates correction. In cases where the number of expected observations in any of the cells of the four-field table was less than 5, Fisher's exact test was used to assess the level of significance of the differences. Differences in indicators were considered statistically significant at a significance level of p <0.05.

Informed consent was obtained from all patients before the study.

Results and discussion. Results: The observation period for the patients averaged 48 months. The male to female ratio was 1: 1.4. Patients with ALS accounted for 81.6% (n = 80), with PLS 8.6% (n = 8), with PMA 10.2% (n = 10). At the same time, no significant differences in age depending on gender were found (p> 0.05).

But when analyzing by forms, it turned out that PBS is much more common in women than in men - 17.07% versus 1.75% (p = 0.006). There were no gender differences in the frequency of ALS and PMA (p> 0.05) - Table.

The mean age of onset was 52.8 ± 10.42 years, with the oldest patient being 74 years old at the time of symptom onset.

The median duration of MND in the entire group (n = 98) was 36 months, while the minimum duration was 5 months, and the maximum duration was 168 months. In PBS (n = 8), the median duration was 90 months, while the minimum duration was 37 months, the maximum duration was 168 months. With PMA (n = 10), the median duration was 84 months, while the minimum duration was 22 months, the maximum duration was 168 months. From fig. 1 shows that the duration of the disease in ALS is statistically highly significantly less than in other forms: the median duration is 36 months in ALS versus 90 months in PLS and 84 months in PMA (p <0.00001). In ALS, death occurred on average after 36 months from respiratory failure.

In PLS, spastic tetraparesis with symptoms of pseudobulbar paralysis, leading to real estate and complete dependence on others, was observed in 3 female patients and 1 male patient. In the remaining 4 cases, spastic lower paraparesis and tendon insufficiency in the upper extremities were observed with a moderate revival of oral automatism symptoms. At the same time, none of the patients had bedsores. In 2 cases, the death occurred as a result of acute cerebrovascular accident, in 1 case from pulmonary tuberculosis and in 1 case from complications of hypostatic pneumonia

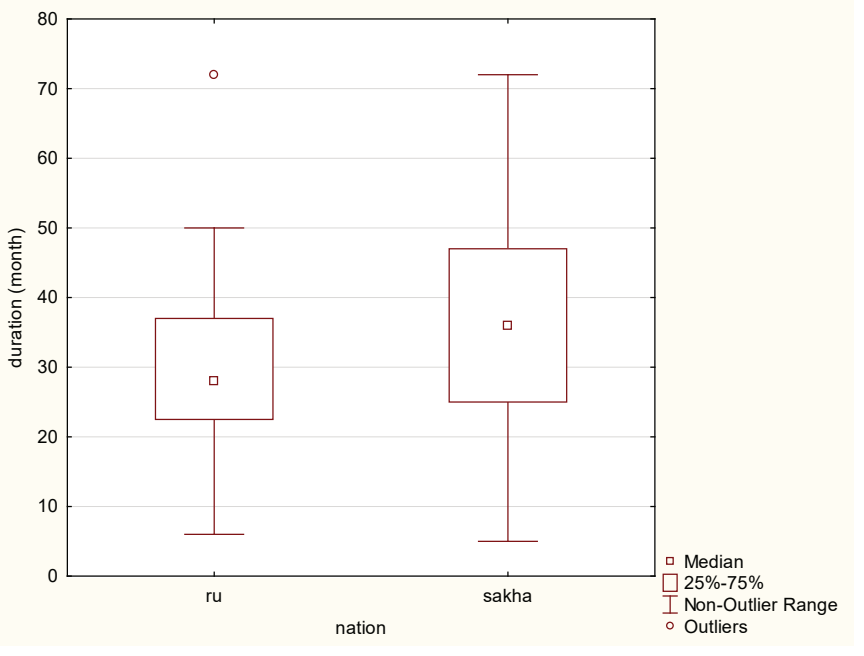

Fig. 3. Duration of MND (months) in ethnic groups

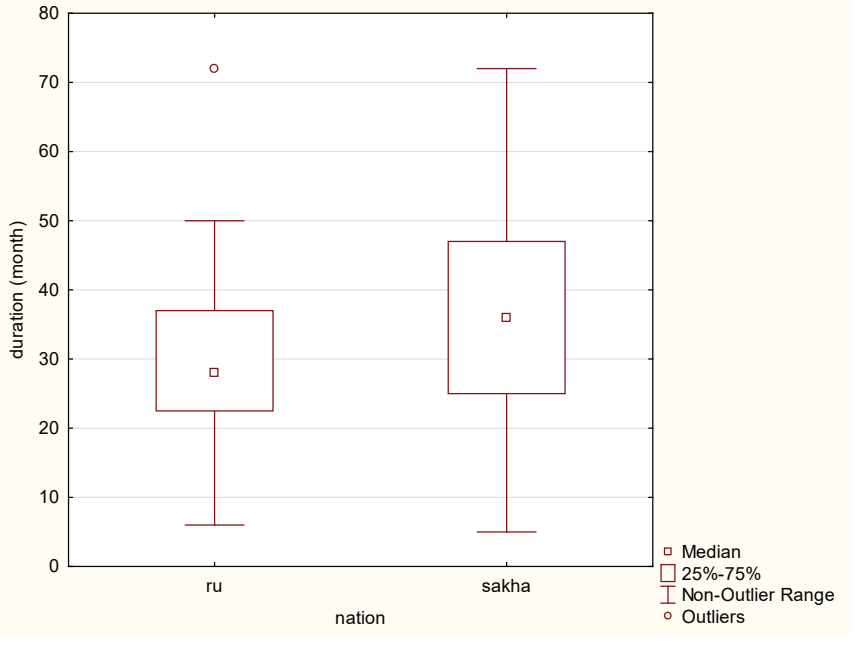

Fig. 4. Duration of ALS (months) in ethnic groups

With PMA (n = 10), in 1 case the disease had a rapidly progressive course and was 38 months. At the first visit of the patient, a clinically isolated lesion of the lower motor neuron at all levels of the spinal cord attracted attention. Flaccid tetraparesis with low reflexes was noted; the patient turned when the disease became generalized. Symptoms of bulbar palsy and a symptom of damage to the upper motor neuron were absent. The neuronal lesion was confirmed by needle electromyography. 6 months after the first visit, the patient was re-hospitalized due to

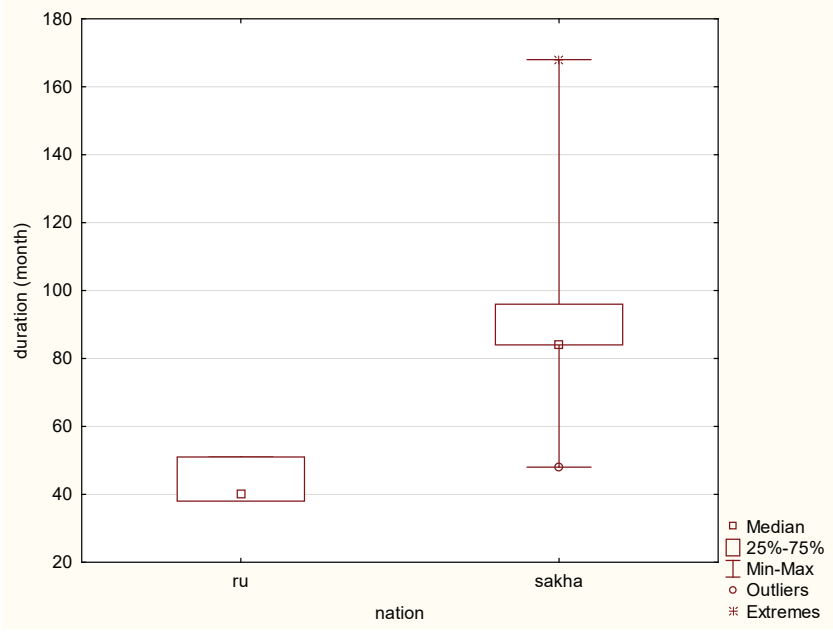

Fig. 5. Duration of PMA (months) in ethnic groups

worsening of his condition. Examination revealed bulbar disorders in the form of choking and swallowing disorders, flaccid deep tetraparesis, pronounced manifestations of respiratory failure. The patient was bedridden, completely dependent on others. No symptoms of central motor neuron involvement were found. Due to the development of restrictive respiratory failure, the patient was transferred to a ventilator, which he continued after being discharged from the neurological hospital at home. Death occurred 18 months after the 1st treatment [1]. In this case, despite the fact that the duration of the disease was slightly more than 3 years, given the clinical picture with “pure” damage to the lower motor neuron and the rapid development rate of neurodegeneration of motor neurons, this patient was included in the PMA group. The postmortem examination was not carried out due to the refusal of relatives from this study. All patients with PMA also had no pelvic abnormalities or pressure ulcers.

Figure 2 shows that with increasing age, the duration of the disease in MND decreased statistically significantly, i.e. negative correlation of duration with age was obtained (rsp = -0.22; p = 0.03).

When studying the incidence of diseases in ethnic groups Sakha (n = 58) and Russians (n = 40) with ALS, PMA and PLS, despite the predominance of the Yakut ethnic group (Sakha), no differences were found depending on belonging to a particular ethnic group (p> 0.05).

Figure 3 shows that the duration of MND in the Sakha group is significantly higher than in the group of patients belonging to the Russian ethnic group and is 38.5 months versus 33.5 months, respectively (p = 0.03).

When studying the duration of PLS, ethnic differences were not revealed (p> 0.05)

The duration of ALS was significantly higher in Yakuts than in Russians: the median duration was 36.0 (25.0-47.0) months and 28.0 (22.5-37.0) months, respectively (p = 0.03).

In fig. 4 it can be seen that when studying the duration of PMA, it turned out that the median of PMA duration was more than 2 times higher in Sakha than in Russians: 84.0 (84.0-96.0) months versus 40.0 (38, 0-51.0) months, respectively (p = 0.03).

Thus, the study revealed a feature in the duration of the disease in MND: the duration in ALS and PMA was significantly higher in representatives of the Yakut nationality than in Russians.

Conclusion. Despite the probable unity of the pathogenesis of diseases of the MND group, there is still a need for the clinical separation of diseases of this group, both for solving bioethical problems when presenting a diagnosis to a patient, and for organizing multicenter scientific studies in PBS and PMA to determine the causes affecting the duration of the disease.

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POST-COVID 19 SYNDROME OF CHRONIC FATIGUE AND EMOTIONAL DISORDERS IN RESIDENTS OF YAKUTSK

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УДК 61.616-06

The analysis of chronic fatigue syndrome and the level of anxiety and depression in 161 patients aged 20 to 72 years was conducted who had an acute infection with COVID-19 from 3 to 12 months ago. Young and middle-aged women are more susceptible to COVID-19 viral pneumonia in a severe and critically severe form. Men are more severely affected by COVID-19 compared to women aged 32-51 and 61-70. Anxiety-depressive disorders and chronic fatigue syndrome can develop at any time in the post-ovarian period, from 3 months to 12 months.

Keywords: COVID-19, post-COVID 19 syndrome, anxiety-depressive syndrome, chronic fatigue syndrome, HADS scale.

Relevance: In March 2020, the World Health Organization (WHO) announced the global COVID-19 pandemic. Like any major epidemic outbreak, it has caused negative consequences for individuals and society as a whole, covering almost all aspects of life. Neurological disorders caused by human coronaviruses, including SARS-CoV-2, are attracting the attention of researchers.

Thus, chronic angioencephalopathy, structural epilepsy, parkinsonism, leukoencephalopathy, and other progressive forms of neurodegenerative and autoimmune pathology are long-term complications from the central and peripheral nervous system in persons who have undergone COVID-19 [2]. Neurological syndromes that develop during the acute period are also described. diseases and after, which last more than 12 weeks - long-COVID hypostolic syndrome (PCS). PMS is included in the new edition of the International Classification of Diseases, revision 10, where it is designated as "post-COVID-19 condition" under the code U09.9 [1, 9].

E.M. Amenta et al. [12], classifying the manifestations of COVID-19, identified residual symptoms that persist after recovery from an acute infection, organ dysfunction that persists after initial recovery, and new symptoms or syndromes that develop after an initial asymptomatic or mild infection. The incidence of postcoid syndrome as a whole is 10–35%, while for hospitalized patients it can reach 85% [10]. The possibility of developing postcoid syndrome in patients with a mild form of the disease or asymptomatic course is very important, which must be taken into account when managing these patients [11]. The clinical picture of postcoid syndrome is very diverse. Fatigue is the most common symptom after COVID-19, with an incidence of 17.5% to 72% among hospitalized patients, and duration in some cases exceeding 7 months. after the onset of the disease [13]. Up to 40% of patients hospitalized with COVID-19 within 2-4 months. after discharge, a decrease in exercise tolerance is noted [5]. These symptoms, as well as pain in joints and muscles for no apparent reason, headaches, decreased memory and concentration, insomnia, lack of feeling of rest after a full night's sleep, dizziness, can be attributed to chronic fatigue syndrome (CFS), which can develop after suffering viral infection [4]. Also, patients with postcoid syndrome may experience emotional disturbances such as anxiety and depression, which are detected in 40% of patients even after 6 months. after COVID-19 [1]. According to foreign and domestic studies, during the first wave of COVID-19, clinically completed anxiety and depressive disorders (TDR) were diagnosed in 20-40% of the population, in 20-35%

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