

## ANNOTATION

Dissertation of Abdraimova Saltanat Orynbasarovna on the topic "**Clinical and demographic analysis of Parkinson's disease in the Southern region of Kazakhstan**", submitted for the degree of Doctor of Philosophy (PhD) in the specialty 8D101141

**Relevance.** Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease (Tolosa et al, 2021). The disease affects almost 2% of the population over 65 years of age and 5% over 85 years of age, with 15% of PD cases debuting before the age of 45 years, being steadily progressive and leading to reduced activities of daily living and reduced quality of life (Riboldi et al, 2022).

The United Nations predicts that the number of people over 65 will double in the coming decades, from 761 million in 2021 to 1.6 billion in 2050, with the number of people over 80 growing even faster (<https://news.un.org/ru/>). This implies that the number of PD patients will increase in the coming years, both globally and in Kazakhstan.

The influence of external factors together with genetic predisposition on the development of PD has already been proven (Elsworth J.D., 2020). Given the rapid development of industrialisation and economy all over the world, including in our country with the predominance of industrial production, widespread use of pesticides in agriculture, general air pollution, we can expect an increase in the incidence of PD (Pandics et al, 2023). According to the United Nations Environment Programme (UNEP), which is the world's leading environmental organization. Currently, 100% (18,772,392 people) of Kazakhstan's population experience atmospheric air quality that does not meet the World Health Organization's annual standard for fine particulate matter ([www.unep.org/ru](http://www.unep.org/ru) 10.10.2024). The medical and social significance of the problem is due to the increasing incidence and prevalence of PD in the world and, as a consequence, the high level of disability and incapacity of different age groups of patients. However, diagnosing PD in the early stages faces a number of difficulties, as symptoms in the initial stages may be mild, limited to one side of the body and can be easily confused with signs of other diseases. Patients themselves may perceive them as a result of fatigue or age, rather than as a sign of a serious illness. The creation of screening forms will help to improve early detection of the disease (Sardar et al, 2023).

The obvious increase in the number of patients with PD, associated with increasing life expectancy of the population, progressive course of the disease, leading to severe clinical manifestations, and subsequently to disability, diagnostic difficulties actualized the present study in the Southern region of Kazakhstan.

The Movement Disorder Society has developed the UPDRS (Unified Parkinson's Disease Rating Scale) and UDysRS (Unified Dyskinesia Rating Scale) scales as standard tools for assessing the severity and for dynamic monitoring of the course of the disease, as well as for assessing dyskinesias that occur after prolonged use (3 years or more) of levodopa. All over the world, they are an effective tool in research and in the work of the practitioner. And for the first time in Kazakhstan as a result of cultural,

linguistic adaptation and validation of the international scales MDS-UPDRS and MDS-UDysRS its Kazakh-language version will be created with implementation in clinical and research practice (UPDRS: status and recommendations, 2003; Goetz et al, 2008).

**Aim of the study:** to investigate clinical and demographic characteristics of Parkinson's disease in the Southern region of Kazakhstan using measurement scales and to optimise diagnostic approaches.

**Objectives of the study:**

1. To identify the prevalence of Parkinson's disease in the Southern region of Kazakhstan, to assess the severity of clinical manifestations of the disease with the determination of the influence of external factors on the development of the disease.
2. To create and validate (approve) the Kazakh-language version of the MDS-UPDRS scale.
3. To create and validate (approve) the Kazakh-language version of the MDS-UDysRS scale.
4. To develop and implement a questionnaire for early detection of Parkinson's disease and digitalisation of the diagnostic stage.

**Object of the study.** Patients with Parkinson's disease and with suspected Parkinson's disease living in the Southern region of Kazakhstan, including Turkestan region: Turkestan city, Arys city, Kentau city, Zhetisay district, Baidibek district, Keles district, Kazygurt district, Mactaalar district, Ordabasy district, Otrar district. Kentau, Zhetisay district, Baidibek district, Keles district, Kazygurt district, Maktaalar district, Ordabasy district, Otrar district, Sairam district, Saryagash district, Suzak district, Tolebi district, Tulkubas district, Shardara district with a population over 45 years of age at the beginning of 2021 - 444,281 people and Shymkent city with a population over 45 years of age at the beginning of 2021 - 233,329 people.

Inclusion criteria: patients diagnosed with clinically possible and clinically probable PD according to the current MDS diagnostic criteria (2015).

Exclusion criteria: patients with secondary parkinsonism syndrome, patients with other specified basal ganglia diseases, patients with congenital and hereditary hyperkinesias, patients with other neurodegenerative brain diseases.

**Research Methods:**

1. A cross sectional descriptive study to collect demographic and clinical data.
2. Cross-sectional observational quantitative analysis using standardised scales for disease assessment
3. Creation and development of clinical questionnaire by Survey Design method.
4. Cross-sectional questionnaire - quantitative data collection for the study using the designed questionnaire

**Scientific novelty:**

1. For the first time in the Southern region of Kazakhstan were identified patients with Parkinson's disease, the diagnosis of which was confirmed on the basis of MDS criteria (2015).
2. For the first time the clinical and demographic characteristics of Parkinson's disease in the Southern region of Kazakhstan were analysed, taking into account the age of debut, duration of the disease, sex differences, motor and non-motor manifestations with the determination of their influence on the severity of the disease and the prevalence of the disease was revealed.
3. For the first time in Kazakhstan the scales MDS-UPDRS and MDS-UDysRS were translated into Kazakh language and validation of the scales on patients with Parkinson's disease and on patients with complicated levodopa-induced dyskinesia was carried out with the subsequent official confirmation of the Movement Disorder Society (Movement Disorder Society).
4. For the first time a study was conducted to determine the influence of external factors on the development of PD in the Southern region of Kazakhstan.
5. For the first time a questionnaire was developed to detect PD in the early stages of the disease.

#### **Practical significance of the results.**

1. Application of the registry of patients with a confirmed diagnosis of PD based on the MDS 2015 diagnostic criteria to optimise the procurement of antiparkinsonian drugs and ensure their rational use
2. Application of the approved Kazakh-language versions of the international scales MDS UPDRS and MDS UDysRS in practical healthcare, clinical trials and scientific research.
3. Developed and tested a specialised questionnaire for early detection of Parkinson's disease.
4. The obtained results can become the basis for the creation of recommendations and leaflets on the prevention and treatment of Parkinson's disease.

#### **The main points put forward for defence:**

1. The approved Kazakh-language version of the MDS-UPDRS scale is effective in clinical assessment of PD severity, including in dynamics.
2. The approved Kazakh-language version of the MDS-UDysRS scale is effective in clinical evaluation of dyskinesia manifestations occurring at the unfolded stages of PD.
3. Prolonged influence of harmful environmental factors can be considered as predictors of PD occurrence.
4. The developed questionnaire as a tool for diagnosing PD at the initial manifestations can be used by clinicians to improve the detection of the disease and also increase public awareness of the signs and risk factors of PD.

**The results of the study were presented and discussed at the following conferences:** International Scientific and Practical Conference 'Brain Diseases: the challenge of the XXI century', Shymkent, 3.12.2020, International Scientific and

Practical Conference 'Interdisciplinary Neurology', dedicated to the 30th anniversary of independence of the Republic of Kazakhstan, Shymkent, 18.11.2021, International scientific-practical conference 'Actual issues of clinical neurology and psychiatry', Shymkent, 10.11.2022, with the receipt of a diploma II place for the best report, IX International Scientific Conference of young scientists and students 'Prospects of development of biology, medicine and pharmacy', Shymkent, 8.12.2022, Annual International Congress of Motor Disorders Society (MDS) in Copenhagen (Denmark) from 27 to 31 August 2023, International Scientific and Practical Conference 'Interdisciplinary Neurology', Shymkent, 09.11.2023, International scientific-practical conference 'Neurology and therapy: points of contact', 25.04.2024 Russia (Republic of Bashkortostan), Ufa, 10th Congress of the European Academy of Neurology in Helsinki (Finland) from 29 June to 2 July 2024, 2 poster presentations, Regional scientific-practical conference 'Orphan diseases of CNS in the Southern region of Kazakhstan', Shymkent, 13 September 2024, Annual International Congress of the Movement Disorders Society (MDS) in Philadelphia (USA) from 27 September to 1 October 2024 Poster presentation.

**14 printed works were published on the subject of the thesis:** 1 article in the journal 'Clinical Parkinsonism and Related Disorders', indexed in the Scopus database with a percentile of 39 (Cite Score 2.7); 1 letter to the editor in the journal 'Lancet Neurology', indexed in the Scopus database with a percentile of 99 (Cite Score 58.7); 3 articles in journals recommended by the Science and Higher Education Quality Assurance Committee of the Ministry Science and Higher Education of the of the Republic of Kazakhstan; 3 articles in the materials of International scientific-practical conferences; 5 abstracts in the materials of International conferences, including 2 abstracts in the journal 'Movement Disorders', indexed in Scopus with a percentile of 96 (Cite Score 13.3) and 2 abstracts in the journal 'European Journal of Neurology', indexed in Scopus with a percentile of 88% (Cite Score 9.7) and 1 teaching manual.

### **Conclusions:**

1. The prevalence rate of PD among the population of Turkestan region and Shymkent city was 67 and 65 cases per 100,000 population, respectively. At the same time, high prevalence among the regions of Turkestan region was noted in Zhetisay city 85 cases and in Maktaaral district 88 cases per 100,000 population.

2. Analysis of 450 patients showed that 64% lived in rural areas, and women were 57.4% among urban and 55.2% among rural residents. The age of disease debut in urban was  $58.5 \pm 9.83$  years and in rural was  $56.9 \pm 10.1$ . The earliest debut was observed at 27 years of age and the latest at 80 years of age. In men the debut of the disease was more often at 50-59 years of age, in women - at 60-69 years of age. According to the forms of the disease: akinetic-rigid-tremor - 62%, akinetic-rigid - 27%, tremor - 11%. According to Hoehn-Yahr stages: I - 32%, II - 24.4%, III - 28.7%, IV - 12.2%, V - 2.7%. 70% were on levodopa therapy, 25.1% were untreated, and 4.9% used other antiparkinsonian drugs. Dyskinesias were found in 42.4% on levodopa and 1.6% on other drugs. Levodopa-induced dyskinesias developed  $6.02 \pm 2.59$  years after the onset of the disease, slightly earlier in urban residents ( $5.83 \pm 2.85$ ) than in rural residents ( $6.11 \pm 2.46$ ). Women developed dyskinesias later ( $6.07 \pm 2.7$ ) than men ( $5.97 \pm 2.49$ ).

3. Analysis of PD risk factors showed that living in rural areas ( $p < 0.001$ ) and drinking well water ( $p < 0.001$ ) were associated with earlier disease debut. Rural residence increased the risk of early debut by 2.47 times (OR = 2.47,  $p = 0.006$ ), whereas tap water use reduced it by 3.87 times (OR = 0.26,  $p = 0.0001$ ). Gender ( $p = 0.068$ ) and family history ( $p = 0.683$ ) had no significant effect.

4. The Kazakh-language versions of the MDS UPDRS and MDS UDysRS scales validated as part of the thesis research were approved by the official developers of the scales, the International Movement Disorders Society (MDS), and are available on the MDS website (<https://www.movementdisorders.org/>)

5. The developed PD questionnaire has proven to be reliable when used in GP practice, incorporating a website with a medical calculator, brief information about the disease and the ability to self-diagnose, promoting patient awareness and referral to a neurologist when necessary.