



# "THE RELATIONSHIP BETWEEN PARKINSON'S DISEASE AND TYPE 2 DIABETES MELLITUS: CLINICAL FEATURES AND PATHOPHYSIOLOGICAL MECHANISMS"

**Rakhimbayeva.G.S, Akramova D.T., Kasimova O.O.**

Tashkent Medical Academy, Department of Neurology and Medical Psychology. Uzbekistan, Tashkent.

## Article history:

**Received:** March 20<sup>th</sup> 2023  
**Accepted:** April 22<sup>nd</sup> 2023  
**Published:** May 24<sup>th</sup> 2023

## Abstract:

Parkinson's disease (PD) and type 2 diabetes mellitus (T2DM) are two widely prevalent chronic diseases that significantly affect the quality of life of patients. In recent years, the number of studies dedicated to analyzing the interaction between these diseases has been growing. In particular, clinical and neurological features of Parkinson's disease in the context of T2DM are being studied. This review article presents the results of an analysis of modern research on this topic. **Materials and methods:** Studies published in scientific journals over the last 10 years were used for analysis. Selection criteria for studies included originality, relevance, and methodological reliability. Studies were sought that focused on the clinical manifestations and neurological features of Parkinson's disease in patients with T2DM, as well as studies that examined the impact of Parkinson's disease on the manifestations of T2DM. **Results:** Analysis of the studies showed that the presence of T2DM in patients with PD may affect the clinical manifestations and course of the disease. In particular, it was found that patients with both PD and T2DM more often exhibit more severe motor symptoms and cognitive impairment. It was also found that pharmacological treatment of PD may be less effective in patients with coexisting T2DM. Studies in the field of the pathophysiology of PD and T2DM indicate possible common mechanisms underlying the development of these diseases, such as oxidative stress, chronic inflammatory processes, and mitochondrial dysfunction. **Conclusions:** The analysis of modern studies indicates that patients with Parkinson's disease and type 2 diabetes mellitus may exhibit specific clinical manifestations and course of the disease. This may be related to common pathophysiological mechanisms underlying the development of both diseases, as well as the influence of one disease on the other. Therefore, patients with coexisting PD and T2DM require a special approach to diagnosis, treatment, and monitoring of their condition.

**Keywords:** Parkinson's disease, Type 2 diabetes mellitus, Neurological features, Motor symptoms, Cognitive function, Oxidative stress, Inflammation, Mitochondrial dysfunction.

## INTRODUCTION:

Parkinson's disease (PD) and type 2 diabetes mellitus (T2DM) are two of the most prevalent chronic diseases that lead to a significant deterioration in the quality of life of patients (1,2). Parkinson's disease is a neurodegenerative disorder characterized by progressive impairment of motor functions and cognitive abilities (3). Type 2 diabetes mellitus is characterized by chronic hyperglycemia due to insulin secretion impairment and/or tissue resistance to insulin, which can lead to serious complications, including retinopathy, nephropathy, neuropathy, and cardiovascular diseases (4).

According to the statistics of the World Health Organization, more than 10 million people worldwide suffer from Parkinson's disease, and about 422 million people have type 2 diabetes mellitus (5,6). Due to the

increasing prevalence and deterioration of the quality of life of patients, studying the interaction between these two diseases becomes increasingly relevant (7,8).

## RELEVANCE:

**Wide prevalence:** Parkinson's disease and type 2 diabetes are two common chronic diseases that have a significant impact on the quality of life of patients. Therefore, studying the relationship between them has great clinical and scientific significance.

**Increase in research:** In recent years, the number of studies devoted to analyzing the interaction between Parkinson's disease and type 2 diabetes has been increasing. This indicates a growing interest in this issue and the need for a deeper understanding of their connection.



*Clinical significance:* Studying the relationship between these two diseases can help optimize the diagnosis, treatment, and monitoring of patients suffering from both conditions. Understanding the clinical features, the impact of one disease on the other, and the common pathophysiological mechanisms may lead to the development of more effective management strategies for these conditions. Based on these factors, the article will be relevant to researchers, medical specialists, and practicing physicians who are interested in the fields of neurology and endocrinology, as well as in improving the diagnosis and treatment of patients with Parkinson's disease and type 2 diabetes. We will examine the clinical manifestations of Parkinson's disease in patients with type 2 diabetes, the peculiarities of the course of Parkinson's disease against the backdrop of type 2 diabetes, the impact of diabetes on the pharmacological treatment of Parkinson's disease, as well as the neurological features of Parkinson's disease in patients with diabetes.

Additionally, the interrelation of the pathophysiological mechanisms of Parkinson's disease and type 2 diabetes will be explored, including oxidative stress, chronic inflammatory processes, and mitochondrial dysfunction (9,10). The impact of type 2 diabetes on cognitive function in patients with Parkinson's disease is also a subject of study, as both conditions can lead to cognitive impairment (11,12).

An analysis of scientific research published in academic journals over the past 10 years has been conducted. The criteria for selecting studies include originality, relevance, and methodological reliability. Studies dedicated to the clinical findings and neurological features of Parkinson's disease in patients with type 2 diabetes, as well as studies examining the impact of Parkinson's disease on the manifestations of type 2 diabetes, will be considered.

**AIM:** The aim of the article is to summarize the findings of contemporary research investigating the relationship between these two chronic diseases, with the goal of gaining a deeper understanding of their mutual influence, clinical signs, and treatment effectiveness.

#### **MATERIALS AND METHODS:**

To conduct this review article, a systematic search of scientific research published in academic journals over the past 10 years was conducted. The following databases were used: PubMed, Web of Science, Medscape, Oxford Academic, and Google Scholar. The search was performed using keywords and

combinations such as "Parkinson's disease", "type 2 diabetes", "clinical manifestations", "neurological features", "pathophysiological mechanisms", "oxidative stress", "chronic inflammatory processes", "mitochondrial dysfunction", "glycemic control", and "diabetes complications".

The selection and analysis of studies were conducted in two stages. In the first stage, studies dedicated to the clinical picture and neurological observations of Parkinson's disease in patients with type 2 diabetes, as well as studies examining the impact of Parkinson's disease on the manifestations of type 2 diabetes, were selected. In the second stage, studies focusing on the pathophysiological mechanisms underlying the course of both disorders and their possible interrelation were selected. After choosing the studies, their critical evaluation was carried out to determine their scientific value, methodological reliability, and relevance of the obtained results. The following criteria were taken into account during the analysis: the quality of the research methodology, sample size, degree of control over possible confounding factors, statistical significance of the results obtained, and their interpretation. Based on the analysis within the chosen studies, the following key aspects have been identified for further consideration in this review article:

Clinical manifestations of BP in patients with type 2 diabetes (T2D): comparison with clinical manifestations of BP in patients without T2D, peculiarities of the disease course, possible differences in symptoms and severity of the disease. Neurological features of BP in patients with T2D: the effect of diabetes on the evolution and worsening of neurodegenerative processes associated with BP, as well as on cognitive function and other neurological aspects of the disease. Pathophysiological mechanisms of BP and T2D onset: common and specific mechanisms, their interrelationship and influence on each other, including oxidative stress, chronic inflammatory processes, and mitochondrial dysfunction. The impact of BP on T2D manifestations and course: glycemic control, development of diabetes complications, impact on the effectiveness and safety of T2D pharmacotherapy. Interaction of pharmacological agents used to treat BP and T2D: possible synergistic or antagonistic effects, peculiarities of combined therapeutic methods, impact of T2D on the effectiveness and safety of BP pharmacotherapy. Strategies for patients with both BP and T2D: the demand for an individualized method to identify, address, and observe patients, in addition to the establishment of interdisciplinary guidelines and clinical protocols for such patients.



---

Using comparative analysis, systematization, and generalization of scientific data, the following main aspects were identified, which require further consideration in this review article.

Clinical manifestations of patients with type 2 diabetes: a comparison with the clinical picture of patients without type 2 diabetes, the course of the disease, possible differences in symptoms, and its severity.

---

Neurological features of Parkinson's disease in patients with type 2 diabetes: the impact of diabetes on the development and progression of neurodegenerative processes associated with Parkinson's disease, as well as on cognitive functions and other neurological aspects.

---

Pathophysiological pathways involved in the pathogenesis of both Parkinson's disease and type 2 diabetes: overlapping and distinctive mechanisms, their interdependence and impact on each other, encompassing oxidative stress, chronic inflammation, and mitochondrial impairment.

---

### **RESULTS:**

As a result of the analysis of scientific studies in the field of clinical and neurological features of Parkinson's disease (PD) in the context of type 2 diabetes (T2D), the following results were obtained: Comparing the clinical manifestations of PD in patients with and without T2D, it was found that patients with both conditions have more pronounced symptoms and worsened quality of life (Schapira et al., 2017) [13]. It was also revealed that T2D may accelerate the progression of neurodegenerative changes associated with PD, which may lead to earlier onset and worsening of motor symptoms (Santiago et al., 2016) [14].

Neurological features of BP in patients with type 2 diabetes: Based on the analysis of research, it has been found that patients with a combination of BP and type 2 diabetes often experience cognitive function impairments such as memory loss, attention deficits, and information processing speed reduction (Aviles-Olmos et al., 2013) [15] (Petrou et al., 2016) This is likely due to the shared pathophysiological mechanisms of both diseases, such as oxidative stress, chronic inflammatory processes, and mitochondrial dysfunction (Santiago et al., 2016) [16] Cereda et al., 2012). [17] Furthermore, evidence has been found to suggest that insulin resistance and reduced insulin levels in the CNS may contribute to the development and progression of BP, as insulin plays an important role in neuroplasticity processes, synaptic transmission,

and the formation of new neuronal connections (Angela De Iuliis et al., 2021). [18]

Thus, there is a mutual influence of the pathophysiological mechanisms of BP and type 2 diabetes, which can lead to the intensification of negative consequences of each disease. The impact of BP on the manifestations and course of type 2 diabetes: Analysis of research has shown that BP may have a negative impact on glycemic control in patients with type 2 diabetes, which can lead to the deterioration of diabetes and the development of its complications (Cereda et al., 2012) [17]. This may be due to motor function impairments in patients with BP, which reduces their physical activity and affects the effectiveness of glycemic control. Interaction of pharmacological agents used to treat BP and type 2 diabetes: Analysis of research has revealed that some medications used to treat BP can affect glycemic control and metabolic exchange in patients with type 2 diabetes (Aviles-Olmos et al., 2013) [15]. It has also been found that some anti-diabetic medications can have neuroprotective effects and thus slow down the progression of BP (Santiago et al., 2016) [14] (Eman A Elbassuoni et al., Neurochem 2019) [19]. Based on the analysis of research, it has been found that patients with a combination of BP and type 2 diabetes require an individualized approach to diagnosis, treatment, and monitoring of their condition (Kim et al., 2017). [20] It is important to develop interdisciplinary recommendations and clinical protocols for such



patients, taking into account the characteristics of both diseases and possible interactions between them. A comprehensive approach to treatment, including pharmacotherapy, non-pharmacological methods

(physical activity, diet therapy), and psychological support, can contribute to improving the quality of life and slowing down the progression of both diseases (Santiago et al., 2016).[14]

The pathophysiological mechanisms underlying Parkinson's disease and type 2 diabetes are interrelated and can mutually influence each other, potentially leading to the development and progression of both diseases

It is important to consider the possible interactions of pharmacological agents used for the treatment of Parkinson's disease and type 2 diabetes when selecting a therapeutic strategy for patients with both conditions.

Tailored strategies are essential for the diagnosis, treatment, and surveillance of patients who have both Parkinson's disease and type 2 diabetes, as well as the establishment of interdisciplinary recommendations and clinical protocols designed specifically for this patient group.

Parkinson's disease and type 2 diabetes have several clinical and neurological peculiarities when they coexist, which can result in a more severe course of both diseases and a decline in the patients' quality of life.

Further research on the relationship between Parkinson's disease and type 2 diabetes may uncover new avenues for preventive and therapeutic interventions, as well as improvements in quality of life and prognosis for patients with both conditions.

The findings suggest that the combination of Parkinson's disease (PD) and type 2 diabetes (T2D) has a significant impact on the clinical manifestations, course, and prognosis of both diseases. One key aspect is the exacerbation of PD symptoms in patients with T2D (Cereda et al., 2012)[17]Furthermore, insulin resistance and hypofunction of insulin in the CNS may accelerate the progression of PD, as insulin plays an important role in neuroplasticity, synaptic transmission, and the formation of new neuronal connections (Angela De Iuliis et al., 2021)[18]Therefore, patients with a combination of PD and T2D require a more active and personalized strategy to identify their condition, provide therapy, and follow their progress. In addition, the impact of PD on the manifestations and course of T2D needs to be considered. PD may have a negative impact on glycemic control in patients with T2D, which can lead to the deterioration of diabetes and the increasing of its complications (Cereda et al., 2012).[17]This highlights the need for an interdisciplinary approach to managing patients with a combination of PD and T2D, considering the potential interactions between the two.

The study's results suggest that a personalized and all-inclusive approach is crucial in managing patients with both PD and T2D to enhance their health outcomes

and quality of life. Further research is needed to establish effective treatment modalities for this specific patient population.

Possible reasons for such an influence include motor function impairment in patients with hypertension, decreased physical activity, and reduced effectiveness of glycemic control. Further research is needed to determine optimal management strategies for patients with both hypertension and type 2 diabetes in order to achieve effective glycemic control and prevent complications. The interaction of pharmacological agents used to treat hypertension and type 2 diabetes: Studies have shown that some drugs used to treat hypertension may affect glycemic control and metabolism in patients with type 2 diabetes (Aviles-Olmos et al., 2013) [15].

It has also been found that some anti-diabetic drugs may have neuroprotective effects and thus slow the progression of hypertension (Santiago et al., 2016) [14]. These data emphasize the importance of an individualized approach to selecting pharmacotherapy for patients with both hypertension and type 2 diabetes (Aviles-Olmos et al., 2013) [21]. In the future, new pharmacological agents may be developed that take into account the interaction between hypertension and type 2 diabetes and promote improvement in the



course of both diseases. Management strategies for patients with both hypertension and type 2 diabetes: It is important to formulate recommendations and clinical guidelines for such patients, taking into consideration the peculiarities of both and possible interactions between them.

A comprehensive approach to treatment that includes pharmacotherapy, non-pharmacological methods (physical activity, diet therapy), and psychological support may contribute to improving the quality of life and slowing the progression of both diseases (Santiago et al., 2016) [14]. Further research could be directed towards studying the molecular and cellular mechanisms underlying the interrelationship between these diseases, as well as determining possible biomarkers and predictors of the development and progression of hypertension and type 2 diabetes (Schernhammer et al., 2011) [22]. Moreover, conducting clinical trials aimed at expanding new pharmacological and non-pharmacological therapeutic strategies for patients with both hypertension and type 2 diabetes may lead to improvements in the quality of life and prognosis for such patients.

In summary, research conducted in the area of the correlation between Parkinson's disease and type 2 diabetes have recognized several clinical and neurological patterns when these conditions coexist, which could lead to a more severe progression of both illnesses (Pagano et al., 2018) [23] and deteriorate the well-being of patients. These discoveries underscore the importance of an individualized strategy for the diagnosis, treatment, and surveillance of patients with comorbid hypertension and type 2 diabetes, as well as the imperative for multidisciplinary collaboration between neurology and endocrinology experts.

### **CONCLUSIONS:**

Based on the analysis of modern research related to the clinical and neurological features of Parkinson's disease (PD) in the context of type 2 diabetes (T2D), the following interpretation can be made:

PD and T2D have similar pathophysiological mechanisms (Cereda et al., 2012; Kim et al., 2017) [17][20]. The presence of T2D may worsen PD symptoms and accelerate its progression, which may be related to insulin resistance, CNS insulin hypofunction, and impaired neuroplasticity (Angela De Iulii, 2021) [18]. Therefore, patients with both PD and T2D require a more active and individualized path to diagnosis, therapy, and observing of their condition. PD may negatively affect glycemic control in patients with T2D, which could result in worsening of diabetes and its complications (Cereda et al., 2012) [17]. In the

future, new pharmacological drugs (Eman A Elbassuoni 2019)[19] may be formulated that allow for the interaction between BP and DM2 and contribute to improving the course of both diseases.

Interdisciplinary recommendations and clinical protocols for handling patients with both BP and SD-2 should be established taking into account the characteristics of both diseases and possible interactions between them (Kim et al., 2017)[20]. A comprehensive approach to treatment, including pharmacotherapy, non-pharmacological methods (physical activity, diet therapy), as well as psychological support, may offer an improvement in quality of life and slowing the progression of both diseases (Santiago et al., 2016)[14].

On a final note, given all the above conclusions, special attention should be paid to patients with a correlation of Parkinson's disease and type 2 diabetes. Customized therapeutic approaches and regular patient surveillance for those with concurrent medical conditions, along with the creation of multidisciplinary guidelines, are critical components for achieving favorable treatment outcomes in such individuals

### **REFERENCES:**

1. Zoler, M. L. (2021). Type 2 Diabetes Worsens Parkinson's Disease. Medscape. <https://www.medscape.com/viewarticle/962501>
2. Sazonova, O. V., Goldobina, Y. V., Degtyar, N. S., & Lasovskaya, T. Y. (2018). Evaluation of the quality of life of patients with type 2 diabetes. *Diabetes mellitus*, 21(1), 36-43. <https://doi.org/10.14341/DM8837>
3. World Health Organization. (2021). Parkinson's Disease. <https://www.who.int/ru/news-room/fact-sheets/detail/parkinson-disease>
4. Lukyanchikov, V. S. (2016). Diabetic neuropathy. *Russian Medical Journal*, 24(7), 440-444. [https://www.rmj.ru/articles/obshchie-stati/Diabeticheskaya\\_nevropatiya/](https://www.rmj.ru/articles/obshchie-stati/Diabeticheskaya_nevropatiya/)
5. Cell therapy for Alzheimer's disease, Parkinson's disease, and vascular dementia. (n.d.). MedTour Help. <https://medtour.help/ru/disease/kletochnaya-terapiya-bolezni-alczejmera-sindroma-parkinsona-i-sosudistoj-demenczii>
6. The number of people with diabetes has reached 422 million, according to Reuters. (2016). *Russian Medical Journal*. <https://www.rmj.ru/news/chislo-bolnykh-diabetom-dostiglo-422-mln-chelovek/>



7. Troshneva, A. Y., Levin, O. S., & Ametov, A. S. (2016). The relationship between Parkinson's disease and type 2 diabetes. *Ural Medical Journal*, 11(140), 102-106. <https://umedp.ru/articles/vzaimosvyaz-bolezni-parkinsona-i-sakharnogo-diabeta-2-tipa>
8. Komici K, et al. *J Parkinsons Dis*. 2021;11(4):1585-1596. [https://internist.ru/publications/detail/sa-kharnyy-diabet-uskoryaet-progressirovanie-bolezni-parkinsona/?sphrase\\_id=366225](https://internist.ru/publications/detail/sa-kharnyy-diabet-uskoryaet-progressirovanie-bolezni-parkinsona/?sphrase_id=366225)
9. Mitochondrial Dysfunction, Oxidative Stress A.Picca · 2020 · <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7466131/>
10. The Role of Oxidative Stress in Parkinson's Disease Vera Dias, Eunsung Junn, and M. Maral Mouradian <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4135313/>
11. Parkinson's Disease, Diabetes and Cognitive Impairment Mohammad R Ashraghi, Gennaro Pagano, Sotirios Polychronis, Flavia Niccolini, Marios Politis <https://pubmed.ncbi.nlm.nih.gov/27396477/>
12. Novel Treatment Opportunities Against Cognitive Impairment in Parkinson's Disease with an Emphasis on Diabetes-Related Pathways Holly Green, Panagiota Tsitsi, Ioanna Markaki, Dag Aarsland, and Per Svenningsson <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6373401/>
13. Non-motor features of Parkinson disease Schapira et al <https://pubmed.ncbi.nlm.nih.gov/28720825/> [https://www.researchgate.net/publication/317441933\\_Non-motor\\_features\\_of\\_Parkinson\\_disease](https://www.researchgate.net/publication/317441933_Non-motor_features_of_Parkinson_disease)
14. Deficits in cholinergic neurotransmission and their clinical correlates in Parkinson's disease Santiago Perez-Lloret et al. *NPJ Parkinsons Dis*. 2016 <https://pubmed.ncbi.nlm.nih.gov/28725692/>
15. Parkinson's disease, insulin resistance and novel agents of neuroprotect on 2013
16. Iciar Aviles-Olmos, Patricia Limousin, Andrew Lees, Thomas Foltynie <https://academic.oup.com/brain/article/136/2/374/287025>
17. Petrou M, Davatzikos C, Hsieh M, Albin R, Kotagal V, Müller M, Koeppe RA, Herman WH, Frey KA, Bohnen NI (2016) Diabetes, gray matter loss and cognition in the setting of Parkinson Disease, *Acad Radiol* 23, 577–581 <https://pubmed.ncbi.nlm.nih.gov/26874576/>
18. Shared dysregulated pathways lead to Parkinson's disease and diabetes Jose A Santiago, Judith A Potashkin 2013, 2016 <https://pubmed.ncbi.nlm.nih.gov/23375873/>
19. Clinical features of Parkinson disease when onset of diabetes came first E. Cereda, M. Barichella, E. Cassani, R. Caccialanza, G. Pezzoli <https://n.neurology.org/content/78/19/1507>
20. Diabetes mellitus and Parkinson's disease: dangerous liaisons between insulin and dopamine
21. Angela De Iulii, 1 Ennio Montinaro, 2 Giuseppe Fatati, 3 Mario Plebani, 1, 4 and Carlo Colosimo 2021 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8504381/>
22. Mechanism of the neuroprotective effect of GLP-1 in a rat model of Parkinson's with pre-existing diabetes Eman A Elbassuoni et al. *Neurochem Int*. 2019 Dec. <https://pubmed.ncbi.nlm.nih.gov/31654678/>
23. A New Treatment Strategy for Parkinson's Disease through the Gut–Brain Axis The Glucagon-Like Peptide-1 Receptor Pathway Dong Seok Kim, Ho-Il Choi, Yun Wang, Yu Luo, Barry J. Hoffer, and Nigel H. 2017 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5680957/>
24. Exenatide and the treatment of patients with Parkinson's disease Aviales-Olmos et al. 2013 <https://pubmed.ncbi.nlm.nih.gov/23728174/>
25. Diabetes and the risk of developing Parkinson's disease in Denmark Eva Schernhammer et al. *Diabetes Care* <https://pubmed.ncbi.nlm.nih.gov/21411503/>
26. Diabetes mellitus and Parkinson disease Gennaro Pagano, Sotirios Polychronis, Heather Wilson, Beniamino Giordano, Nicola Ferrara, Flavia Niccolini, Marios Politis <https://pubmed.ncbi.nlm.nih.gov/29626177/> 2018