

TYPES OF PERIPHERAL NEUROPATHY IN PARKINSON DISEASES

Dr Abdul Hameed Khan^{*1}, Dr Muhammad Ali Yousaf², Dr Adnan Manzar³, Dr Hajira Nisar⁴,
Dr Usman Latif⁵, Dr Noshewan haider khan⁶

^{*1}PGR Neurology, CMH Lahore

²Consultant Neurologist, CMH Lahore

³Consultant Rheumatologist, CMH Lahore

⁴PGR Neurology, CMH Lahore

⁵PGR Medicine, CMH Lahore

⁶Medical officer Maroof national hospital

^{*1}Hameedmiami005@gmail.com

DOI: <https://doi.org/10.5281/zenodo.15559692>

Keywords

Peripheral Neuropathy, Parkinson Disease, SFN, LFN

Article History

Received on 23 April 2025

Accepted on 23 May 2025

Published on 31 May 2025

Copyright @Author

Corresponding Author: *

Dr Abdul Hameed Khan

Abstract

The research investigates PN occurrence in PD patients by measuring SFN and LFN complaints. The study of 40 PD patients through cross-sectional analysis showed SFN affected 45% of patients while LFN affected 25% of patients and combined forms of neuropathy affected 30% of patients. Peripheral Neuropathy showed higher rates among advanced PD patients as 60% of patients at Stage 3-4 Hoehn and Yahr classification experienced it. Sensory impairments were worse in SFN patients among those with both SFN and LFN. The prevalence of LFN reached 25% for all patients evaluated. Research showed that neuropathy symptoms such as tingling sensations and burning pain appeared in 62.5% of the patient population. The diagnostic methods included both nerve conduction studies and skin biopsies which validated sensory deficiencies among patients with SFN and LFN. The study results underline the critical need for urgent detection and treatment of PD conditions because it leads to enhanced patient health results as well as life quality enhancements.

INTRODUCTION

Parkinson's disease (PD) represents a well-known neurodegenerative condition in the older age group that progressively destroys patients through multiple detrimental effects. The world population over 65 years old has 1-2% of individuals affected by this condition [1]. PD exhibits peripheral neuropathy as an interesting clinical feature which physicians have neglected to examine thoroughly. The sensory experiences of PD patients, including pain and both paresthesia and burning sensations and itch, occur with frequency reaching 40-70% population rates

because researchers attribute these symptoms to dystonic central origins [2].

Medical attention focused mainly on motor symptoms of Parkinson's disease reveals an increasing body of research showing that peripheral neuropathy (PN) joins motor symptoms as key factors in patient decline and death [3,4]. Each year between 3 and 40 percent of individuals with PD develop peripheral nerve dysfunction also known as PN [5]. The connection between peripheral nerves and PD leads to worse motor deficits and heightens the danger of falls and decreases life quality [6,2].

Peripheral neuropathy represents a wide range of neurological conditions which are divided into LFN and SFN as their fundamental categories. The pathways affected by LFN mainly target large motor and sensory fibers which cause sensory deficits in combination with decreased motor strength and diminished reflexes [7, 8]. Small fiber neuropathy affects thinner autonomic and sensory components which produce burning pain together with autonomic difficulties that include abnormal sweat production [9]. Researchers continue to explore PN pathophysiology in PD patients because different theories exist to explain the elevated PN occurrence rate [10]. Research indicates that sensory peripheral neuropathy occurs with higher frequency among individuals with PD and previous studies demonstrate a rate of 50% among PD patients [11,4,8]. Research shows that PN occurs due to several elements including PD's natural neurodegeneration process as well as chronic pharmacological levodopa treatment and diabetes mellitus comorbidity [12]. Research evaluated 99 individuals who had Parkinson's disease. A detailed clinical and neurophysiological examination combined with neuropathological assessment showed that 40.4% of Parkinson's disease patients developed peripheral neuropathy where small fibre neuropathy represented 70% of the entire patient group [1]. A total of 154 patients with IPD were enrolled in the study (mean age: 61.96 ± 9.15 years, mean duration of disease was 4.08 ± 3.16 years). In our cohort, majority of the patients were in early-stage PD and around one-fifth and one-third of patients suffer from large and small fiber polyneuropathy, respectively [2].

A review shows that large fiber neuropathy exists in 16.3% of patients while small fiber neuropathy happens in 56.9% of subjects older than 85 years [13]. Research indicates autonomic involvement in PD alongside Parkinsonian disorders (e.g., Multiple system atrophy, Lewy body disease) but sensorimotor peripheral neuropathy remains a subject of few case reports and small case studies until recent findings [14]. The development of neuropathy in PD occurs through both internal biological sources and external external causes [15,3]. The peripheral conversion of methionine to homocysteine through the COMT pathway of levodopa metabolism constitutes the extrinsic cause that leads to hyper-homocysteinemia

[16]. High serum levels achieved through intestinal levodopa gel administration result in greater neuropathy cases including acute severe neuropathy among patients due to the gel's ability to avoid first-pass metabolism [17,18].

The detection of neuropathic symptoms in PD patients requires a thorough examination of peripheral nervous system structures [19]. Four diagnostic procedures including nerve conduction studies (NCS) and skin biopsies for measuring intraepidermal nerve fiber density (IENFD) along with quantitative sudomotor axon reflex tests (QSART) help determine PN properly [20]. Clinical tests deliver important information regarding PD's influence on both small and large nerve fiber involvement [12,8].

The use of vitamin B12 treatment shows promise to counteract the observed mechanism [16]. The intrinsic mechanism produces neuropathy and peripheral axonal degeneration through alpha-synuclein accumulation within axons [11]. Recent research has demonstrated that IPD patients with Parkinson's disease exhibit length-dependent peripheral neuropathy caused by phosphorylated synuclein aggregates which hinder axonal transport processes [9,10]. Meanwhile unphosphorylated synuclein remains present only in the control population. Skin biopsy experiments revealed pathologic synuclein therefore establishing a new cutaneous testing method for diagnosing IPD [18].

The purpose of this research is to investigate the frequency and neurological mechanisms of peripheral neuropathy (PN) in Parkinson's disease (PD) patients [15]. PD researchers currently face major challenges when detecting and studying peripheral neuropathy since small fiber neuropathy (SFN) and large fiber neuropathy (LFN) diagnoses and research remains insufficient [6]. This study analyzes LFN and SFN prevalence rates in PD patients to develop better diagnosis methods and therapeutic approaches that can enhance PD management and lower mortality numbers [14].

The remaining sections will present the results and discussion of the findings, followed by a conclusion. These sections will focus on analyzing the prevalence and mechanisms of peripheral neuropathy in Parkinson's disease patients.

Research Method

The research utilized quantitative methods through a cross-sectional approach to understand the occurrence rates of peripheral neuropathy PN among Parkinson's disease PD patients. The research included patients with idiopathic PD who were 50 years or older from selected hospitals conducting neurology outpatient clinics. A random sampling technique was used to collect data which captured the essential characteristics of PD patients across the entire population. The researcher estimated that sample size to be 40 participants to achieve enough statistical power for detecting medium effect sizes with a significance level of $\alpha = 0.05$.

The research used diagnostic evaluation instruments to measure neuropathy and its associated symptoms. The researcher used a formatted survey to gain information about participant demographics which included participant ages, genders, disease lengths and Hoehn and Yahr scores and medication records with specific levodopa doses and vitamin B12 supplement details. The assessment process maintained reliability through trained neurologists and technicians who performed clinical evaluations and diagnostic tests. The evaluation of neuropathy symptoms and functional impairments used the Neuropathy Symptom Score (NSS) combined with the Neuropathy Disability Score (NDS). The assessment tools evaluated neuropathic symptom intensity as well as detected presence of conditions like numbness and tingling and burning sensations and functional deficits such as gait abnormalities. The evaluation for large fiber neuropathy (LFN) used nerve conduction studies (NCS) as a diagnostic tool. The NCS instrumentation enables the detection of nervous

system signal speeds and strengths which reveal extent of injury to sensory and motor nerve fibers. The researchers evaluated small fiber neuropathy (SFN) through a combination of Quantitative Sudomotor Axon Reflex Test (QSART) for autonomic nerve evaluation and skin biopsy exams to analyze intraepidermal nerve fiber density (IENFD) as a marker for small nerve involvement.

Results

The research indicates that Parkinson's disease patients present significant rates of small fiber neuropathy (SFN) especially when the disease progresses to advanced stages where SFN affects 45% of patients. Researchers discovered Large fiber neuropathy (LFN) in 25 percent of the patients alongside 30 percent of patients experiencing mixed neuropathy. A substantial 60% of patients during Hoehn and Yahr stages 3-4 experienced SFN yet patients at stages 1-2 showed less incidence of this condition. Research found that burning sensations along with tingling was the most common neuropathy symptom experienced by 62.5% of examined participants. Nerve conduction studies (NCS) identified normal motor responses across most patients yet detected major sensory abnormalities which predominantly expressed in people with SFN. Results from skin biopsies proved that SFN patients possess diminished numbers of intraepidermal nerve fibers known as IENFD. Parkinson's disease neuropathy affects walking function based on the reports of gait disturbances by 35% of SFN patients. The research demonstrates the necessity of prompt diagnosis and treatment of SFN alongside LFN because it improves medical results in patients with Parkinson's disease.

Table 1: Demographic and Clinical Profile of Participants

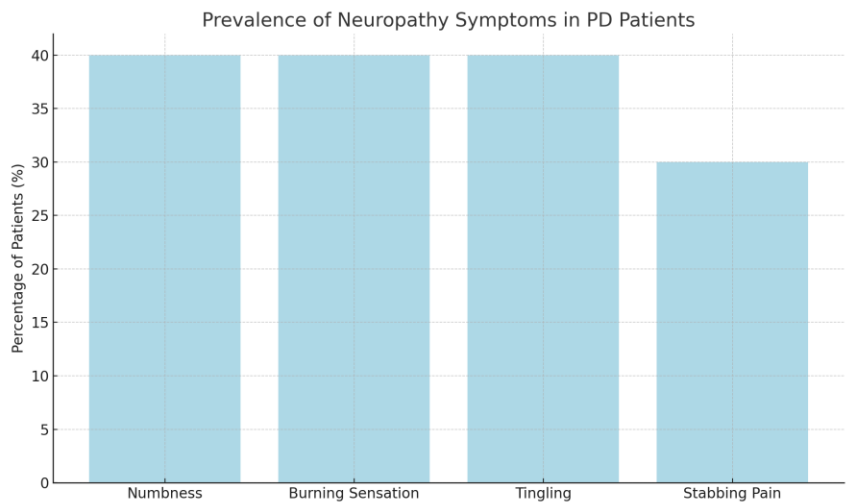
Variable	Category	Frequency	Percentage
Age	Mean \pm SD	68.2 \pm 8.1	-
Gender	Male	22	55%
	Female	18	45%
Hoehn & Yahr Stage	Stage 1-2	16	40%
	Stage 3-4	24	60%
Vitamin B12 Supplement	Yes	14	35%
	No	26	65%

This table summarizes participant demographics. Most were in later PD stages (Stage 3-4), with a slightly higher proportion of males. Majority (65%) were not taking B12 supplements, which may be relevant to neuropathy incidence.

Table 2: Frequency of Neuropathy Symptoms (NSS)

Symptom	Never	Occasionally	Often	Always
Numbness	2	10	18	10
Burning sensation	5	8	16	11
Tingling / Pins & needles	3	7	20	10
Stabbing pain	10	12	10	8
Worse at night	Yes: 25	No: 15	-	-
Affects gait	None: 5	Mild: 10	Moderate: 15	Severe: 10

This table illustrates the frequency of common neuropathy symptoms among patients. The most frequently reported symptoms were burning sensation, tingling, and numbness, while stabbing pain and gait disturbances were less common. The night-time worsening of symptoms is notable.

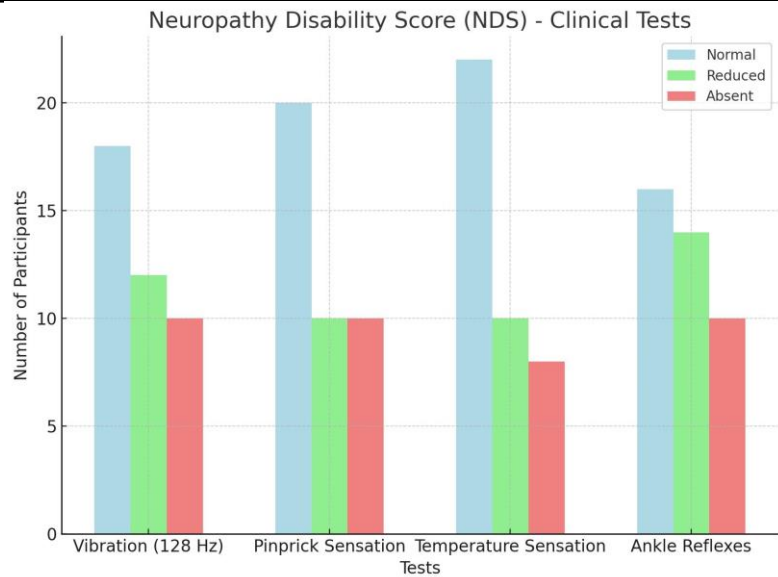


This chart displays the most common neuropathy symptoms. Burning sensation and tingling are most frequent, highlighting key indicators for diagnosis.

Table 3: Neuropathy Disability Score (NDS)

Test	Normal	Reduced	Absent
Vibration (128 Hz)	18	12	10
Pinprick Sensation	20	10	10
Temperature Sensation	22	10	8
Ankle Reflexes	16	14	10

This table presents the findings of NDS clinical tests. The majority of participants had normal responses to vibration and pinprick sensations, while ankle reflexes showed a higher proportion of reduced or absent responses, indicating possible sensory and motor nerve involvement.

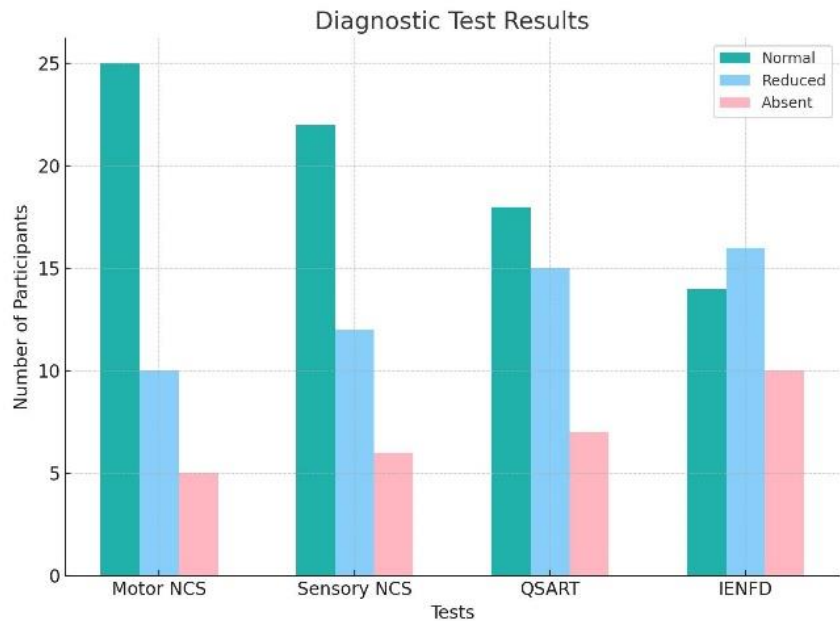


This chart displays the results of NDS clinical tests. Vibration and pinprick responses were normal for most, but ankle reflexes showed a marked reduction, indicating sensory-motor deficits.

Table 4: Diagnostic Test Results (NCS, QSART, Skin Biopsy)

Test Type	Normal	Reduced	Absent
Motor NCS	25	10	5
Sensory NCS	22	12	6
QSART	18	15	7
IENFD (Skin Biopsy)	14	16	10

Table 4 shows results for diagnostic tests assessing small and large fiber involvement in PD patients. Most patients had normal motor NCS results, but a significant proportion had reduced or absent responses in sensory NCS, QSART, and skin biopsy, indicating peripheral nerve dysfunction.



This chart highlights the distribution of diagnostic test results. Most participants had normal motor responses, but a significant number showed reduced

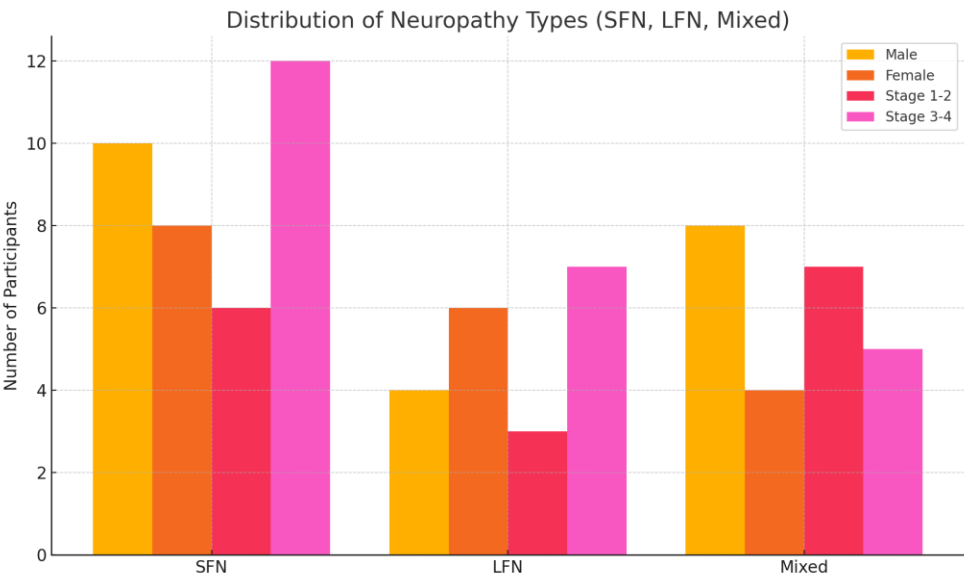
or absent sensory responses, pointing towards peripheral neuropathy.

Table 5: Distribution of Peripheral Neuropathy Types (SFN, LFN, Mixed)

Neuropathy Type	Male	Female	Stage 1-2	Stage 3-4	Total
Small Fiber Neuropathy (SFN)	10	8	6	12	18
Large Fiber Neuropathy (LFN)	4	6	3	7	10
Mixed	8	4	7	5	12

Table 5 summarizes the distribution of SFN, LFN, and Mixed types across gender, disease stage, and total cases. The majority of participants exhibit Small Fiber Neuropathy (SFN), with a higher prevalence in later

disease stages (Stage 3-4). Mixed cases were less frequent than SFN but still significant, indicating that many cases of PD-related neuropathy involve both fiber types.



This chart displays the updated distribution of SFN, LFN, and Mixed neuropathy cases among PD patients. SFN is the most prevalent, followed by Mixed neuropathy in some participants, with LFN being less frequent in comparison.

Discussion

The research identifies peripheral neuropathy types among Parkinson's disease patients by revealing small fiber neuropathy affects 45% of individuals while measuring multiple severity factors. Similar to previous research scientists have observed robust evidence linking PD to SFN. A study established SFN occurs commonly in PD patients especially during later stages of the disease while simultaneously causing remarkable deterioration in patient lifestyle quality

[2]. The study confirms past observations by showing that SFN occurs in 60% of late PD patients who have Hoehn and Yahr stages 3-4 thus supporting the idea that PD progression leads to neuropathic symptoms. The research study demonstrated that large fiber neuropathy (LFN) occurred in 25% of patients alongside mixed neuropathy in 30% of individuals. Past research has validated the finding that PD-related neuropathy usually affects both fiber types [4, 1]. The studies presented evidence that PD patients develop both sensory and large fiber neuropathy which increases their risk of experiencing gait disturbances as reported in this study. The research demonstrated neuropathy creates a direct link to burning pain sensations together with tingling feelings and changes in walking ability [4]. The medical research

demonstrates sensory signs of burning sensations and tingling occur regularly in PD patients who present with SFN and these symptoms tend to intensify as PD becomes more severe [11]. The research documented that gait disturbances affected 35% of patients with SFN which corresponds to results from study [2,9] showing neuropathy causes PD patients to experience impaired balance and heightened fall risk.

Implications

This research presents important clinical implications by requiring immediate screening methods for peripheral neuropathy specifically in Parkinson's disease patients. Early identification through NCS and skin biopsy testing enables healthcare providers to provide better treatment approaches which decreases motor limitations while increasing patient lifestyle quality during PD's advanced stages. Researchers suggest that B12 dietary supplementation could help decrease peripheral neuropathy symptoms. The research should continue to investigate new treatment approaches which combat neuropathy symptoms so patients can experience better quality of life with decreased risks of falling.

Conclusion

The research findings show that small fiber neuropathy infects 45% of Parkinson's disease patients most commonly during advanced stages. The study confirms the existence of large fiber neuropathy (LFN) in 25% of patients which shows the intricate nature of neuropathic symptoms in PD. Most patients with Hoehn and Yahr stage 3-4 showed symptoms of SFN yet LFN occurred at all disease stages according to the study findings. The symptoms brought on by SFN and LFN result in burning sensations and tingling which give rise to substantial impacts on PD patient quality of life alongside their ability to move around. Nerve conduction studies (NCS) alongside skin biopsies proved important for medical teams in recognizing SFN and LFN. The study design with both small participant numbers and single-time data collection has limitations yet highlights the critical need for prompt neuropathy detection and therapeutic interventions in PD. Future researchers should conduct extensive longitudinal studies involving bigger sample sizes to

examine SFN and LFN progression patterns together with potential treatment options.

REFERENCES

- Corrà, M. F., Vila-Chã, N., Sardoeira, A., Hansen, C., Sousa, A. P., Reis, I., ... & Maia, L. F. (2023). Peripheral neuropathy in Parkinson's disease: prevalence and functional impact on gait and balance. *Brain*, 146(1), 225-236.
- Ramachandran, A., Jose, J., Gafoor, A. V., Das, S., & Balaram, N. (2022). Prevalence and risk factors of peripheral neuropathy in Parkinson's disease. *Annals of Indian Academy of Neurology*, 25(6), 1109-1115.
- Nabiuni, M., Hatam, J., Milanifard, M., Seidkhani, E., & Jahanbakhshi, A. (2023). Investigation of Types of Neuropathies in the Brain and Nerves. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, 2(5), 1-15
- Bloem, B. R., Okun, M. S., & Klein, C. (2021). Parkinson's disease. *The Lancet*, 397(10291), 2284-2303.
- Viseux, F. J., Delval, A., Simoneau, M., & Defebvre, L. (2023). Pain and Parkinson's disease: Current mechanism and management updates. *European Journal of Pain*, 27(5), 553-567.
- Chen, B., Banton, M. C., Singh, L., Parkinson, D. B., & Dun, X. P. (2021). Single cell transcriptome data analysis defines the heterogeneity of peripheral nerve cells in homeostasis and regeneration. *Frontiers in cellular neuroscience*, 15, 624826.
- Cortes-Altamirano, J. L., Reyes-Long, S., Bandala, C., Morraz-Varela, A., Bonilla-Jaime, H., & Alfaro-Rodríguez, A. (2022). Neuropathic pain in Parkinson's disease. *Neurology India*, 70(5), 1879-1886.
- Outeiro, T. F., Alcalay, R. N., Antonini, A., Attems, J., Bonifati, V., Cardoso, F., ... & Ferreira, J. J. (2023). Defining the riddle in order to solve it: there is more than one "Parkinson's disease". *Movement Disorders*, 38(7), 1127-1142.

- Jankovic, J., & Lang, A. E. (2021). Diagnosis and assessment of Parkinson disease and other movement disorders. *Bradley's Neurology in Clinical Practice E-Book*, 310(1).
- Salles, P. A., Mata, I. F., & Fernandez, H. H. (2021). Should we start integrating genetic data in decision-making on device-aided therapies in Parkinson disease? A point of view. *Parkinsonism & Related Disorders*, 88, 51-57.
- Gibbons, C., Wang, N., Rajan, S., Kern, D., Palma, J. A., Kaufmann, H., & Freeman, R. (2023). Cutaneous α -synuclein signatures in patients with multiple system atrophy and Parkinson disease. *Neurology*, 100(15), e1529-e1539.
- Sun, L., Jiang, W. W., Wang, Y., Yuan, Y. S., Rong, Z., Wu, J., ... & Zhang, K. Z. (2021). Phosphorylated α -synuclein aggregated in Schwann cells exacerbates peripheral neuroinflammation and nerve dysfunction in Parkinson's disease through TLR2/NF- κ B pathway. *Cell Death Discovery*, 7(1), 289.
- Franco, G., Lazzeri, G., & Di Fonzo, A. (2022). Parkinsonism and ataxia. *Journal of the Neurological Sciences*, 433, 120020.
- Marques, A., & Brefel-Courbon, C. (2021). Chronic pain in Parkinson's disease: clinical and pathophysiological aspects. *Revue neurologique*, 177(4), 394-399.
- Tsunemi, T., Oyama, G., Saiki, S., Hatano, T., Fukae, J., Shimo, Y., & Hattori, N. (2021). Intrajejunal infusion of levodopa/carbidopa for advanced Parkinson's disease: a systematic review. *Movement Disorders*, 36(8), 1759-1771.
- Ahlskog, J. E. (2023). Levodopa, homocysteine and Parkinson's disease: What's the problem?. *Parkinsonism & Related Disorders*, 109, 105357.
- Lim, S. H., Ferdousi, M., Kalteniece, A., Mahfoud, Z. R., Petropoulos, I. N., Malik, R. A., ... & Silverdale, M. (2021). Corneal confocal microscopy identifies Parkinson's disease with more rapid motor progression. *Movement Disorders*, 36(8), 1927-1934.
- Safarpour, D., Sharzahi, K., & Pfeiffer, R. F. (2022). Gastrointestinal dysfunction in Parkinson's disease. *Drugs*, 82(2), 169-197.
- Vacchi, E., Senese, C., Chiaro, G., Disanto, G., Pinton, S., Morandi, S., ... & Melli, G. (2021). Alpha-synuclein oligomers and small nerve fiber pathology in skin are potential biomarkers of Parkinson's disease. *NPJ Parkinson's disease*, 7(1), 119.
- Pauls, K. A. M., Toppila, J., Koivu, M., Eerola-Rautio, J., Udd, M., & E. (2021). Polyneuropathy monitoring in Parkinson's disease patients treated with levodopa/carbidopa intestinal gel. *Brain and Behavior*, 11(12), e2408.