JOURNAL OF PHARMA INSIGHTS AND RESEARCH ISSN NO. 3048-5428

REVIEW ARTICLE

Current Perspectives on Pathogenesis, Clinical Manifestations, and Treatment of Parkinson's Disease

Chaudhari Sakshi Dattatraya*, Malgunde Swati Pandurang, Tamboli Najiya Jakir

UG Scholar, Sharadchandra Pawar College of Pharmacy, Dumbarwadi, Pune, Maharashtra, India

Publication history: Received on 30th Jan 2025; Revised on 10th Feb 2025; Accepted on 11th Feb 2025

Article DOI: 10.69613/t3q3nv23

Abstract: Parkinson's disease (PD) represents a progressive neurodegenerative disorder characterized by both motor and non-motor manifestations. The condition emerges through complex interactions between genetic susceptibility and environmental triggers, leading to the characteristic loss of dopaminergic neurons in the substantia nigra pars compacta. During the prodromal phase, patients often experience non-motor symptoms including rapid eye movement sleep disorder, anosmia, constipation, and depression. As the disease advances, motor symptoms become apparent, manifesting as tremor, rigidity, bradykinesia, and postural instability. The underlying molecular mechanisms involve α-synuclein aggregation, mitochondrial dysfunction, impaired protein clearance systems, neuroinflammation, and oxidative stress. Multiple neurotransmitter systems beyond dopamine, including noradrenergic, glutamatergic, serotonergic, and adenosine pathways, contribute to the diverse clinical presentation. Diagnosis remains primarily clinical, supported by neuroimaging and specific biomarker tests to differentiate PD from other parkinsonian syndromes. Current therapeutic strategies focus on symptom management through pharmacological interventions, particularly dopamine replacement therapy, along with surgical options like deep brain stimulation for advanced cases. While existing treatments effectively manage motor symptoms, they do not alter disease progression.

Keywords: Parkinson's disease; α-synuclein; Dopaminergic neurons; Motor symptoms; Neurodegeneration.

1. Introduction

Parkinson's disease (PD) has emerged as one of the most significant neurological disorders worldwide, ranking second only to Alzheimer's disease in prevalence among neurodegenerative conditions [1]. The historical milestone of PD recognition dates back to 1817 when James Parkinson first described the condition in his seminal "Essay on the Shaking Palsy," delineating the cardinal motor symptoms that would later become diagnostic hallmarks [2]. The global burden of PD has shown a striking increase, with current estimates indicating that over 6 million individuals are affected worldwide [3]. This number is projected to double by 2040, driven primarily by population aging and increased life expectancy [4]. The condition affects approximately 1% of individuals over 60 years of age, with incidence rates rising sharply after this age threshold [5].

At its core, PD manifests through the progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta, leading to the characteristic motor symptoms. However, the pathological process extends far beyond this classical understanding, involving multiple neural networks and neurotransmitter systems [6]. The presence of α-synuclein-containing Lewy bodies and Lewy neurites serves as the definitive pathological hallmark, though this can only be confirmed through post-mortem examination [7]. The clinical diagnosis of PD relies on the presence of specific motor manifestations, particularly the combination of resting tremor, bradykinesia, rigidity, and postural instability. However, the disease spectrum encompasses a wide range of non-motor symptoms that often precede the classical motor features by several years [8]. This prodromal phase, characterized by symptoms such as olfactory dysfunction, sleep disorders, and autonomic disturbances, has become increasingly recognized as crucial for early intervention strategies [9].

Recent advances in molecular biology and genetics have transformed our understanding of PD pathogenesis. The identification of multiple genetic risk factors, environmental influences, and cellular mechanisms has revealed PD as a complex disorder with multiple potential therapeutic targets [10, 11]. The regulations surrounding telemedicine continues to evolve, with healthcare organizations and governing bodies working to establish standards that ensure patient safety and care quality. These regulations address crucial aspects such as data privacy, security protocols, and professional licensing requirements across jurisdictional boundaries [10]. The development of comprehensive guidelines helps standardize telemedicine practice while maintaining flexibility for technological advancement and innovation. The aim of this review is to understand the current state of telemedicine, its various applications across medical specialties, and the challenges and opportunities that lie ahead in its continued evolution.

* Corresponding author: Chaudhari Sakshi Dattatraya

Copyright © 2025 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution Liscense 4.0.

2. Etiopathogenesis

2.1. Risk Factors

The etiology of PD represents a complex interplay between genetic predisposition and environmental factors, with age remaining the most significant risk factor [12]. Epidemiological studies have consistently demonstrated variations in disease prevalence across different geographical regions and populations, suggesting the influence of both genetic and environmental components [13]

2.1.1. Genetic Factors

The genetic landscape of PD has become increasingly complex with the identification of multiple genetic variants. Approximately 15% of PD patients report a positive family history, with several key genes implicated in both familial and sporadic cases [14]. The SNCA gene, encoding α-synuclein, represents one of the most significant genetic discoveries in PD research, with mutations leading to early-onset forms of the disease [15].

Other crucial genetic players include LRRK2 (leucine-rich repeat kinase 2), which predominantly causes late-onset PD, and recessive genes such as Parkin (PARK2), PINK1, and DJ-1 (PARK7), associated with early-onset forms [16]. The LRRK2 G2019S mutation, in particular, represents the most common genetic cause of PD, showing variable penetrance across different populations [17].

2.1.2. Environmental Risk Factors

Environmental factors have demonstrated significant associations with PD development, though the precise mechanisms remain under investigation [18]. Pesticide exposure, particularly to compounds such as rotenone and paraquat, has shown consistent links to increased PD risk. These agents typically interfere with mitochondrial function and promote oxidative stress, mirroring cellular pathologies observed in PD [19].

Recent attention has focused on the potential role of viral infections in PD pathogenesis. The COVID-19 pandemic has renewed interest in this area, drawing parallels with historical observations of post-encephalitic parkinsonism following the 1918 influenza pandemic [20]. Meta-analyses have identified associations between PD risk and various viral infections, including influenza, herpes simplex virus, and hepatitis viruses [21].

2.1.3. Occupational and Lifestyle Factors

Occupational exposures to specific metals and solvents have emerged as potential risk factors. Manganese exposure in welding occupations has been linked to a distinct form of parkinsonism, while chronic exposure to industrial solvents like trichloroethylene (TCE) shows associations with increased PD risk [22]. The mechanism likely involves oxidative stress and mitochondrial dysfunction, leading to selective dopaminergic neuron vulnerability [23].

2.1.4. Epigenetic Modifications

Epigenetic alterations represent an important bridge between environmental exposures and genetic susceptibility. DNA methylation patterns in PD-related genes, histone modifications, and microRNA expression changes have been documented in PD pathogenesis [24]. These modifications can affect gene expression without altering the DNA sequence, potentially explaining some of the environmental influences on disease development [25].

Table 1. Major Genetic and Environmental Risk Factors in Parkinson's Disease

Category	Factor	Association	Features
Genetic Mutations	SNCA	Strong	Early-onset, autosomal dominant
	LRRK2	Strong	Most common genetic cause, variable penetrance
	Parkin	Strong	Early-onset, autosomal recessive
	PINK1	Strong	Early-onset, mitochondrial dysfunction
Environmental	Pesticide exposure	Moderate	Particularly rotenone and paraquat
	Heavy metals	Moderate	Industrial exposure, especially manganese
	Head trauma	Weak to Moderate	Repeated injury increases risk
Protective Factors	Caffeine consumption	Moderate	Inverse relationship with PD risk
	Physical activity	Moderate	Regular exercise reduces risk
	Smoking	Moderate	Inverse relationship (not recommended)

3. Pathophysiology

3.1. Cellular and Molecular Pathways

The pathophysiology of PD involves multiple interconnected cellular processes that ultimately lead to dopaminergic neuron death [26]. The sequential progression of pathological changes involves several key mechanisms that operate both independently and synergistically.

3.1.1. a-Synuclein Aggregation

α-Synuclein misfolding and aggregation represent central events in PD pathogenesis. The protein accumulates in characteristic fibrillar inclusions known as Lewy bodies and Lewy neurites [27]. Recent evidence suggests that α-synuclein aggregates can spread between neurons in a prion-like manner, potentially explaining the progressive nature of PD pathology [28]. The aggregation process begins with the formation of oligomers, which may be more neurotoxic than the final fibrillar forms [29].

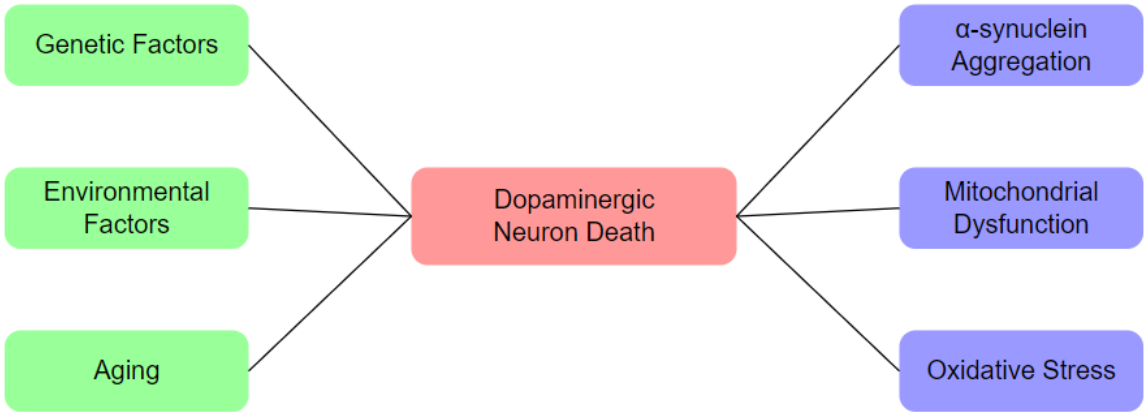

Figure 1. Pathophysiology of Parkinson's disease

3.1.2. Mitochondrial Dysfunction

Mitochondrial impairment plays a crucial role in PD pathogenesis, affecting both sporadic and genetic forms of the disease [30]. Defects in mitochondrial complex I activity, increased oxidative stress, and compromised mitochondrial quality control mechanisms contribute to cellular dysfunction. The selective vulnerability of dopaminergic neurons may partly relate to their high energy demands and exposure to oxidative stress from dopamine metabolism [31].

3.1.3. Protein Clearance Systems

Two major protein degradation pathways show dysfunction in PD:

The ubiquitin-proteasome system (UPS) demonstrates reduced efficiency in protein degradation, particularly affecting α-synuclein clearance [32]. The autophagy-lysosomal pathway exhibits impairments in both macro-autophagy and chaperone-mediated autophagy, crucial processes for removing damaged cellular components and protein aggregates [33].

3.2. Neural Circuit Dysfunction

3.2.1. Basal Ganglia Circuitry

The loss of dopaminergic neurons disrupts the normal functioning of basal ganglia circuits, leading to characteristic motor symptoms [34]. The progressive degeneration of substantia nigra neurons results in dopamine depletion in the striatum, altering the balance between direct and indirect pathways of movement control [35].

3.2.2. Neurotransmitter Systems

While dopamine deficiency remains central to PD pathophysiology, multiple neurotransmitter systems show involvement:

- Cholinergic system alterations contribute to cognitive decline and gait disorders
- Noradrenergic deficits affect attention and arousal

- Serotonergic dysfunction relates to depression and anxiety
- GABAergic and glutamatergic changes influence motor control [36]

4. Clinical Manifestations

4.1. Motor Symptoms

The cardinal motor manifestations of PD emerge from the progressive loss of dopaminergic neurons and subsequent disruption of motor control circuits [37]. Bradykinesia, considered the most characteristic feature, manifests as slowness in movement initiation and execution. Patients experience difficulty with sequential and simultaneous tasks, showing progressive reduction in speed and amplitude of repetitive movements [38].

Resting tremor, typically beginning unilaterally, presents as a characteristic 4-6 Hz "pill-rolling" movement of the hands. This tremor typically diminishes with voluntary movement and disappears during sleep, distinguishing it from other tremor disorders [39]. Rigidity manifests as increased muscle tone, often described as "lead-pipe" or "cogwheel" resistance during passive limb movement, frequently accompanied by pain and discomfort [40].

Postural instability, typically emerging in later disease stages, represents a significant source of disability and fall risk. This manifestation proves particularly challenging as it often shows limited response to dopaminergic therapy [41]. Additional motor features include hypomimia (reduced facial expression), micrographia (small handwriting), and festinating gait characterized by small, rapid steps [42].

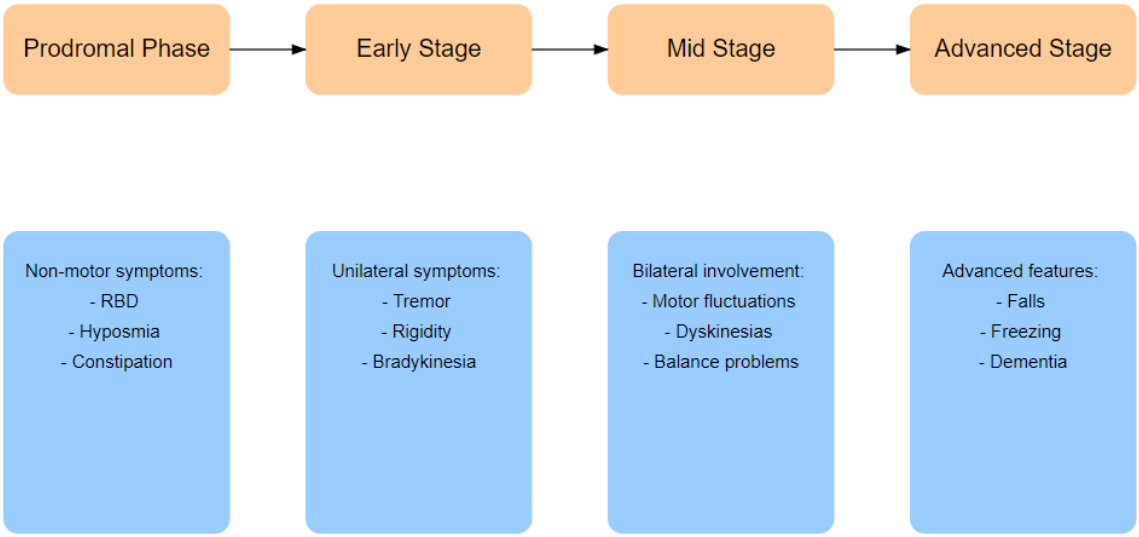

Figure 2. Clinical Progression in PD

4.2. Non-Motor Manifestations

4.2.1. Autonomic Dysfunction

Autonomic disturbances significantly impact quality of life in PD patients. Gastrointestinal dysfunction manifests early, with constipation often preceding motor symptoms by years. Dysphagia becomes increasingly prominent as the disease progresses, raising aspiration risk [43]. Cardiovascular autonomic dysfunction presents as orthostatic hypotension, while urinary symptoms include urgency, frequency, and nocturia. Thermoregulatory disturbances lead to excessive sweating and temperature sensitivity [44].

4.2.2. Neuropsychiatric Features

Depression affects approximately 40% of PD patients, often emerging before motor symptoms and significantly impacting quality of life [45]. Anxiety frequently co-exists with depression, while apathy may occur independently. Cognitive impairment ranges from mild executive dysfunction to frank dementia, with up to 80% of patients developing dementia in advanced disease stages [46].

4.2.3. Sleep Disorders

REM sleep behavior disorder (RBD) represents a significant early marker of PD, often preceding motor symptoms by years. Patients may act out their dreams, potentially causing injury to themselves or bed partners [47]. Excessive daytime sleepiness, insomnia, and restless legs syndrome frequently complicate the disease course, contributing to reduced quality of life [48].

Table 2. Clinical Features and Their Prevalence in PD

Category	Manifestation	Prevalence (%)	Typical Onset
Cardinal Motor	Bradykinesia	95-100	Early
	Resting tremor	75-85	Early
	Rigidity	85-95	Early
	Postural instability	70-80	Late
Non-Motor	Depression	40-50	Any stage
	REM sleep disorder	30-40	Often precedes motor
	Cognitive impairment	20-80	Usually late
	Autonomic dysfunction	70-80	Variable

4.3. Disease progression

The natural history of PD follows a progressive course, though the rate and pattern of progression vary considerably among individuals [49]. The disease trajectory can be conceptualized in several phases, beginning with a prolonged prodromal period characterized by non-motor symptoms. This period may extend 10-20 years before the emergence of classical motor features [50].

Early-stage PD typically presents with unilateral motor symptoms, gradually progressing to bilateral involvement. The initial response to dopaminergic therapy tends to be excellent, often termed the "honeymoon period" [51]. As the disease advances, motor complications emerge, including motor fluctuations and dyskinesias, reflecting both disease progression and long-term levodopa therapy effects [52].

5. Diagnosis

5.1. Clinical Diagnosis

The diagnosis of PD remains primarily clinical, based on the presence of cardinal motor features and supporting criteria [53]. The Movement Disorder Society Clinical Diagnostic Criteria for PD establish a systematic approach to diagnosis, incorporating both motor and non-motor features. The criteria define categories of clinically established PD and probable PD, considering absolute exclusion criteria and red flags [54].

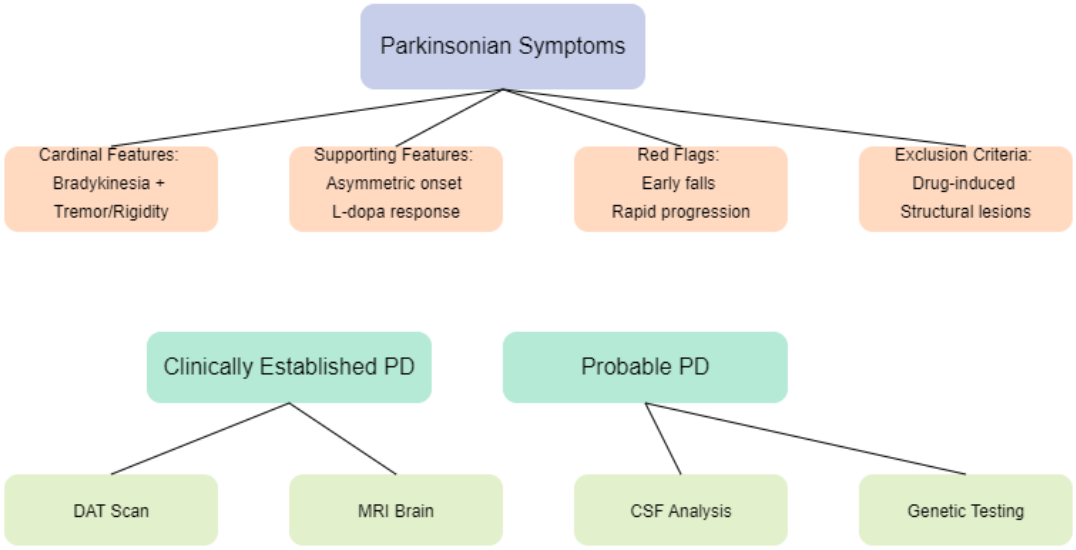

Figure 3. Diagnostic Decision Tree for PD

5.2. Diagnostic Tools and Biomarkers

5.2.1. Neuroimaging

Structural neuroimaging with MRI helps exclude secondary causes of parkinsonism and may reveal specific patterns associated with PD. Advanced MRI techniques, including diffusion tensor imaging and functional connectivity studies, provide insights into disease-related brain changes [55]. Nuclear imaging techniques, particularly DaTscan (123I-ioflupane SPECT), demonstrate dopaminergic terminal loss in the striatum, helping differentiate PD from essential tremor and drug-induced parkinsonism [56].

5.2.2. Molecular and Biochemical Markers

Recent advances in biomarker development have yielded promising tools for PD diagnosis and monitoring. The α-synuclein seed amplification assay in cerebrospinal fluid demonstrates high sensitivity and specificity for PD diagnosis [57]. Emerging blood-based biomarkers, including measures of α-synuclein species and inflammatory markers, show potential for early disease detection and progression monitoring [58].

Table 4. Diagnostic Tools and Their Clinical Utility

Diagnostic Method	Application	Sensitivity	Specificity
Clinical Criteria	Initial diagnosis	80-90%	80-90%
DaTscan	Differential diagnosis	95%	90%
MRI	Structural changes	70-80%	85-95%
CSF α-synuclein	Biochemical marker	85-95%	80-90%
Genetic testing	Familial cases	Variable	95-100%
Olfactory testing	Early detection	75-85%	60-70%

5.3. Differential Diagnosis

Multiple conditions can mimic PD, necessitating careful diagnostic consideration. Essential tremor, drug-induced parkinsonism, and atypical parkinsonian syndromes (multiple system atrophy, progressive supranuclear palsy, corticobasal degeneration) require differentiation through specific clinical features and diagnostic tests [59].

6. Therapeutic Management

6.1. Pharmacological Treatment

6.1.1. Levodopa

Levodopa remains the gold standard treatment for motor symptoms in PD, providing the most effective symptomatic relief [60]. Modern formulations combine levodopa with peripheral decarboxylase inhibitors (carbidopa or benserazide) to enhance central nervous system availability. The timing of levodopa initiation requires individualization, considering factors such as age, symptom severity, and impact on quality of life [61].

Table 4. Current Treatment Options for PD

Treatment	Intervention	Primary Use	Considerations
Pharmacological	Levodopa	Motor symptoms	Gold standard, motor fluctuations
	Dopamine agonists	Motor symptoms	Impulse control disorders
	MAO-B inhibitors	Early treatment	Modest effect
Advanced Therapies	DBS	Advanced motor	Careful patient selection
	LCIG	Motor fluctuations	Requires jejunal tube
	Apomorphine	Rescue therapy	Subcutaneous delivery
Non-pharmacological	Physical therapy	Mobility/balance	Regular adjustment needed
	Speech therapy	Communication	Early intervention beneficial

6.1.2. Dopamine Agonists

Dopamine agonists serve as either initial monotherapy in younger patients or adjunct therapy with levodopa. These agents, including pramipexole, ropinirole, and rotigotine, offer the advantage of delayed motor complications but carry risks of impulse control disorders and other psychiatric symptoms [62]. The newer agent apomorphine, available in injectable and infusion forms, provides rescue therapy for severe "off" periods [63].

6.1.3. MAO-B Inhibitors

Monoamine oxidase B inhibitors (selegiline, rasagiline) provide modest symptomatic benefit and may have disease-modifying potential. Anticholinergic medications, while historically significant, now play a limited role due to cognitive side effects. COMT inhibitors (entacapone, opicapone) extend levodopa's duration of action by reducing peripheral metabolism [64].

6.2. Recent advances

6.2.1. Deep Brain Stimulation

Deep Brain Stimulation (DBS) has revolutionized the management of advanced PD. Targeting primarily the subthalamic nucleus or globus pallidus interna, DBS provides significant improvement in motor symptoms and reduces medication requirements [65]. Patient selection criteria have evolved, with earlier intervention showing promising results in appropriately selected candidates [66].

6.2.2. Continuous Delivery Systems

Device-aided therapies include:

- Levodopa-carbidopa intestinal gel infusion via jejunal tube
- Continuous subcutaneous apomorphine infusion

These approaches aim to provide more consistent dopaminergic stimulation, reducing motor fluctuations in advanced disease [67].

6.3. Non-pharmacological Interventions

6.3.1. Rehabilitation Strategies

Physiotherapy focuses on maintaining mobility, balance, and preventing falls. Speech therapy addresses both communication and swallowing difficulties. Occupational therapy helps maintain independence in daily activities. Exercise programs, particularly those incorporating aerobic and resistance training, show benefits for both motor and non-motor symptoms [68].

6.3.2. Psychological Support

Cognitive behavioral therapy helps manage depression, anxiety, and adjustment to chronic illness. Support groups provide valuable peer support and practical coping strategies. Mindfulness-based interventions show promise in managing both motor and non-motor symptoms [69].

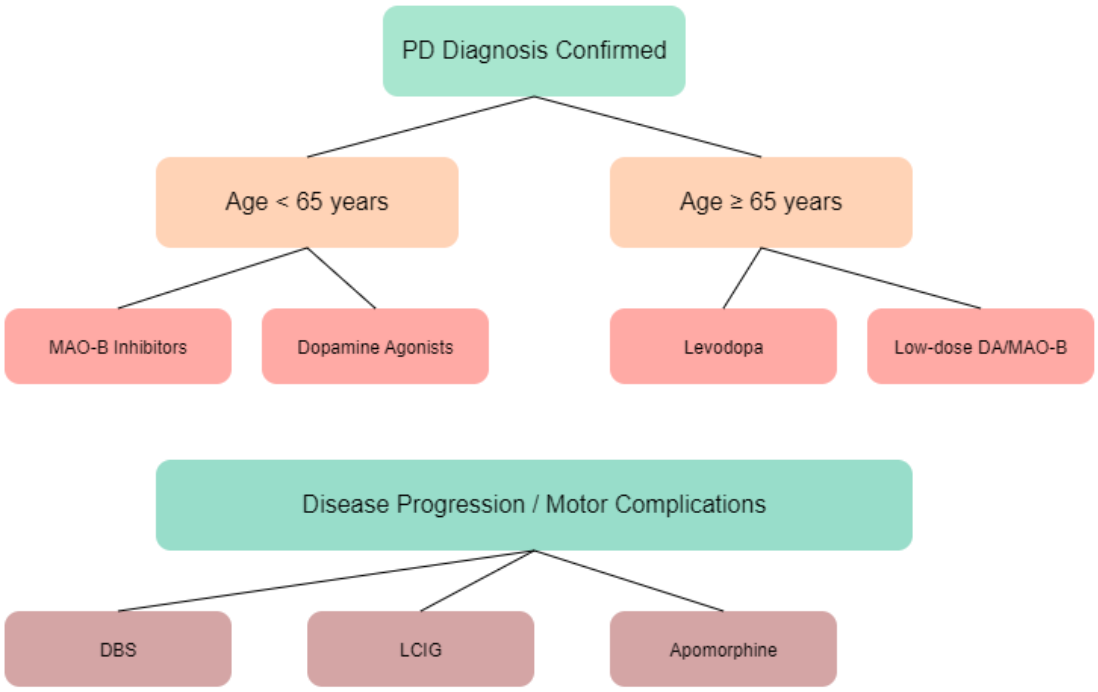

Figure 4. Treatment Algorithm for PD

7. Conclusion

Parkinson's disease is a complex neurodegenerative disorder whose understanding has evolved significantly from its initial description as a pure motor syndrome to recognition as a multisystem disorder with diverse clinical manifestations. The identification of multiple pathogenic mechanisms, genetic factors, and environmental influences has opened new avenues for therapeutic intervention, though a definitive disease-modifying treatment remains elusive. Current management approaches combine pharmacological treatments, advanced therapies, and comprehensive rehabilitation strategies to address both motor and non-motor manifestations. The emergence of promising biomarkers and development of targeted molecular therapies suggest a future where earlier intervention and personalized treatment approaches may become possible.

References

[1] Dorsey ER, Bloem BR. The Parkinson pandemic—a call to action. JAMA Neurol. 2018;75(1):9-10.

[2] Goetz CG. The history of Parkinson's disease: early clinical descriptions and neurological therapies. Cold Spring Harb Perspect Med. 2011;1(1):a008862.

[3] GBD 2019 Parkinson's Disease Collaborators. Global, regional, and national burden of Parkinson's disease, 1990-2019. Lancet Neurol. 2022;21(10):860-881.

[4] Marras C, Beck JC, Bower JH, et al. Prevalence of Parkinson's disease across North America. NPJ Parkinsons Dis. 2018;4:21.

[5] Poewe W, Seppi K, Tanner CM, et al. Parkinson disease. Nat Rev Dis Primers. 2017;3:17013.

[6] Surmeier DJ, Obeso JA, Halliday GM. Selective neuronal vulnerability in Parkinson disease. Nat Rev Neurosci. 2017;18(2):101-113.

[7] Spillantini MG, Goedert M. Synucleinopathies: past, present and future. Neuropathol Appl Neurobiol. 2016;42(1):3-5.

[8] Postuma RB, Berg D. Prodromal Parkinson's disease: the decade past, the decade to come. Mov Disord. 2019;34(5):665-675.

[9] Berg D, Postuma RB, Adler CH, et al. MDS research criteria for prodromal Parkinson's disease. Mov Disord. 2015;30(12):1600-1611.

[10] Blauwendraat C, Nalls MA, Singleton AB. The genetic architecture of Parkinson's disease. Lancet Neurol. 2020;19(2):170-178.

[11] Kalia LV, Lang AE. Parkinson's disease. Lancet. 2015;386(9996):896-912.

[12] Cookson MR. Mechanisms of Parkinson's disease. Mol Neurodegener. 2022;17(1):34.

[13] Dorsey ER, Sherer T, Okun MS, Bloem BR. The emerging evidence of the Parkinson pandemic. J Parkinsons Dis. 2018;8(s1):S3-S8.

[14] Billingsley KJ, Bandres-Ciga S, Saez-Atienzar S, Singleton AB. Genetic risk factors in Parkinson's disease. Cell Tissue Res. 2018;373(1):9-20.

[15] Del Rey NL, Quiroga-Varela A, Garbayo E, et al. Advances in Parkinson's disease: 200 years later. Front Neuroanat. 2018;12:113.

[16] Nalls MA, Blauwendraat C, Vallerga CL, et al. Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease. Lancet Neurol. 2019;18(12):1091-1102.

[17] Gan-Or Z, Giladi N, Rozovski U, et al. Genotype-phenotype correlations between GBA mutations and Parkinson disease risk and onset. Neurology. 2008;70(24):2277-2283.

[18] Goldman SM. Environmental toxins and Parkinson's disease. Annu Rev Pharmacol Toxicol. 2014;54:141-164.

[19] Tanner CM, Kamel F, Ross GW, et al. Rotenone, paraquat, and Parkinson's disease. Environ Health Perspect. 2011;119(6):866-872.

[20] Pavel A, Murray DK, Stoessl AJ. COVID-19 and selective vulnerability to Parkinson's disease. Lancet Neurol. 2020;19(9):719

[21] Fang F, Wirdefeldt K, Jacks A, et al. CNS infections, sepsis and risk of Parkinson's disease. Int J Epidemiol. 2012;41(4):1042-1049.

[22] Racette BA, Nielsen SS, Criswell SR, et al. Dose-dependent progression of parkinsonism in manganese-exposed welders. Neurology. 2017;88(4):344-351.

[23] Ascherio A, Schwarzschild MA. The epidemiology of Parkinson's disease: risk factors and prevention. Lancet Neurol. 2016;15(12):1257-1272.

[24] Pavlou MAS, Outeiro TF. Epigenetics in Parkinson's disease. Adv Exp Med Biol. 2017;978:363-390.

[25] Miranda-Morales E, Meier K, Sandoval-Carrillo A, et al. Implications of DNA methylation in Parkinson's disease. Front Mol Neurosci. 2017;10:225.

[26] Przedborski S. The two-century journey of Parkinson disease research. Nat Rev Neurosci. 2017;18(4):251-259.

[27] Wong YC, Krainc D. α-synuclein toxicity in neurodegeneration: mechanism and therapeutic strategies. Nat Med. 2017;23(2):1-13.

[28] Brundin P, Melki R. Prying into the prion hypothesis for Parkinson's disease. J Neurosci. 2017;37(41):9808-9818.

[29] Lashuel HA, Overk CR, Oueslati A, Masliah E. The many faces of α-synuclein: from structure and toxicity to therapeutic target. Nat Rev Neurosci. 2013;14(1):38-48.

[30] Bose A, Beal MF. Mitochondrial dysfunction in Parkinson's disease. J Neurochem. 2016;139:216-231.

[31] Schapira AHV, Gegg M. Mitochondrial contribution to Parkinson's disease pathogenesis. Parkinsons Dis. 2011;2011:159160.

[32] McNaught KS, Olanow CW. Protein aggregation in the pathogenesis of familial and sporadic Parkinson's disease. Neurobiol Aging. 2006;27(4):530-545.

[33] Moors TE, Hoozemans JJ, Ingrassia A, et al. Therapeutic potential of autophagy-enhancing agents in Parkinson's disease. Mol Neurodegener. 2017;12(1):11.

[34] DeLong MR, Wichmann T. Circuits and circuit disorders of the basal ganglia. Arch Neurol. 2007;64(1):20-24.

[35] Lanciego JL, Luquin N, Obeso JA. Functional neuroanatomy of the basal ganglia. Cold Spring Harb Perspect Med. 2012;2(12):a009621.

[36] Bohnen NI, Albin RL. The cholinergic system and Parkinson disease. Behav Brain Res. 2011;221(2):564-573.

[37] Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord. 2015;30(12):1591-1601.

[38] Jankovic J. Parkinson's disease: clinical features and diagnosis. J Neurol Neurosurg Psychiatry. 2008;79(4):368-376.

[39] Hallett M. Tremor: pathophysiology. Parkinsonism Relat Disord. 2014;20 Suppl 1:S85-86.

[40] Rodriguez-Oroz MC, Jahanshahi M, Krack P, et al. Initial clinical manifestations of Parkinson's disease: features and pathophysiological mechanisms. Lancet Neurol. 2009;8(12):1128-1139

[41] Kim SD, Allen NE, Canning CG, Fung VSC. Postural instability in patients with Parkinson's disease: epidemiology, pathophysiology and management. CNS Drugs. 2013;27(2):97-112.

[42] Sveinbjornsdottir S. The clinical symptoms of Parkinson's disease. J Neurochem. 2016;139 Suppl 1:318-324.

[43] Sarella PN, Dadishetti JP, Asogwa PO, Kakarparthy R. A Case Report on Organic Psychosis Induced by Antitubercular Drugs in A Young Female. Asian Journal of Hospital Pharmacy. 2023 May 28:1-3.

[44] Pfeiffer RF. Non-motor symptoms in Parkinson's disease. Parkinsonism Relat Disord. 2016;22 Suppl 1:S119-122.

[45] Schrag A, Taddei RN. Depression and anxiety in Parkinson's disease. Int Rev Neurobiol. 2017;133:623-655.

[46] Aarsland D, Creese B, Politis M, et al. Cognitive decline in Parkinson disease. Nat Rev Neurol. 2017;13(4):217-231.

[47] Postuma RB, Iranzo A, Hu M, et al. Risk and predictors of dementia and parkinsonism in idiopathic REM sleep behaviour disorder. Brain. 2019;142(3):744-759.

[48] Chahine LM, Amara AW, Videnovic A. A systematic review of the literature on disorders of sleep and wakefulness in Parkinson's disease from 2005 to 2015. Sleep Med Rev. 2017;35:33-50.

[49] Fereshtehnejad SM, Postuma RB. Subtypes of Parkinson's disease: what do they tell us about disease progression? Curr Neurol Neurosci Rep. 2017;17(4):34.

[50] Mahlknecht P, Seppi K, Poewe W. The concept of prodromal Parkinson's disease. J Parkinsons Dis. 2015;5(4):681-697.

[51] Cenci MA. Presynaptic mechanisms of l-DOPA-induced dyskinesia: the findings, the debate, and the therapeutic implications. Front Neurol. 2014;5:242.

[52] Antonini A, Moro E, Godeiro C, Reichmann H. Medical and surgical management of advanced Parkinson's disease. Mov Disord. 2018;33(6):900-908.

[53] Berg D, Adler CH, Bloem BR, et al. Movement disorder society criteria for clinically established early Parkinson's disease. Mov Disord. 2018;33(10):1643-1646.

[54] Heinzel S, Berg D, Gasser T, et al. Update of the MDS research criteria for prodromal Parkinson's disease. Mov Disord. 2019;34(10):1464-1470.

[55] Pyatigorskaya N, Gallea C, Garcia-Lorenzo D, et al. A review of the use of magnetic resonance imaging in Parkinson's disease. Ther Adv Neurol Disord. 2014;7(4):206-220.

[56] Lotankar S, Prabhavalkar KS, Bhatt LK. Biomarkers for Parkinson's disease: recent advancement. Neurosci Bull. 2017;33(5):585-597.

[57] Shahnawaz M, Mukherjee A, Pritzkow S, et al. Discriminating α-synuclein strains in Parkinson's disease and multiple system atrophy. Nature. 2020;578(7794):273-277.

[58] Parnetti L, Gaetani L, Eusebi P, et al. CSF and blood biomarkers for Parkinson's disease. Lancet Neurol. 2019;18(6):573-586.

[59] McFarland NR, Hess CW. Recognizing atypical parkinsonisms: "red flags" and therapeutic approaches. Semin Neurol. 2017;37(2):215-227.

[60] LeWitt PA, Fahn S. Levodopa therapy for Parkinson disease: a look backward and forward. Neurology. 2016;86(14 Suppl 1):S3-12.

[61] Fox SH, Katzenschlager R, Lim SY, et al. International Parkinson and movement disorder society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease. Mov Disord. 2018;33(8):1248-1266.

[62] Connolly BS, Lang AE. Pharmacological treatment of Parkinson disease: a review. JAMA. 2014;311(16):1670-1683.

[63] Sarella PN, Dadishetti JP, Asogwa PO, Kakarparthy R. Pharmacological and Non-pharmacological Management of Bipolar Disorder with Comorbid Huntington's Disease: A Case Report. Journal of Clinical and Pharmaceutical Research. 2023 Apr 30:5-8.

[64] Cerri S, Siani F, Blandini F. Investigational drugs in Phase II clinical trials for the treatment of Parkinson's disease. Expert Opin Investig Drugs. 2019;28(7):587-598.

[65] Deuschl G, Schade-Brittinger C, Krack P, et al. A randomized trial of deep-brain stimulation for Parkinson's disease. N Engl J Med. 2006;355(9):896-908.

[66] Schuepbach WM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. N Engl J Med. 2013;368(7):610-622.

[67] Antonini A, Poewe W, Chaudhuri KR, et al. Levodopa-carbidopa intestinal gel in advanced Parkinson's: Final results of the GLORIA registry. Parkinsonism Relat Disord. 2017;45:13-20.

[68] van der Kolk NM, de Vries NM, Kessels RPC, et al. Effectiveness of home-based and remotely supervised aerobic exercise in Parkinson's disease: a double-blind, randomised controlled trial. Lancet Neurol. 2019;18(11):998-1008.

[69] Pickut BA, Van Hecke W, Kerckhofs E, et al. Mindfulness based intervention in Parkinson's disease leads to structural brain changes on MRI: a randomized controlled longitudinal trial. Clin Neurol Neurosurg. 2013;115(12):2419-2425.

Author's short biography

Miss Chaudhari Sakshi Dattatraya

Miss Chaudhari Sakshi Dattatraya is pursuing her Bachelor of Pharmacy at Sharadchandra Pawar College of Pharmacy in Dumbarwadi, Otur, Pune. She completed her Diploma in Pharmacy from Samarth College of Pharmacy, Belhe. With three months of medical training experience, she has published a review article and participated in national-level conferences and presentations.