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A review on Parkinson Disease

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ABSTRACT
A neurodegenerative condition, Parkinson's disease (PD) often manifests itself between the ages of 55 and 65. Both motor and non-motor symptoms are progressive and have a significant impact on an individual's overall quality of life. Although there is no known cure for Parkinson's disease (PD), there are therapies available to assist control its symptoms. The area of PD management is expanding and aims to develop both novel and enhanced treatment approaches. Physicians may now address patient-specific issues as they emerge in addition to the primary motor symptoms of Parkinson's disease (PD) thanks to pharmaceutical, surgical, and therapy interventions. This study addresses the current and proven options for treating Parkinson's disease (PD) that can offer patient-specific care and lessen adverse effects from standard medicines.

Keywords: Parkinson's disease, Parkinson's treatment, substantia nigra, basal ganglia, Lewy bodies, α-synuclein, dopamine, levodopa

I. INTRODUCTION

Dr. James Parkinson first described Parkinson's disease (PD) as a "shaking palsy" in 1817. It is a neurodegenerative condition that progresses over time and has both motor and nonmotor symptoms. The disease's gradual degenerative effects on muscular control and movement have a major clinical impact on patients, families, and carers. The loss of striatal dopaminergic neurons is the cause of Parkinson's disease (PD) motor symptoms, while nonmotor symptoms also suggest neuronal loss in nondopaminergic regions. The motor characteristics of Parkinson's disease (PD), such as bradykinesia, muscle stiffness, and resting tremor, are collectively referred to as Parkinsonism. Parkinson's disease (PD) is the most prevalent cause of Parkinsonism, although there are several other reasons as well, such as disorders that mirror PD and drug-induced causes. [1-3] Studies indicate that the pathophysiological alterations linked to Parkinson's disease (PD) might precede the development of motor symptoms and encompass many non-motor manifestations; including depression, sleep disturbances, and cognitive impairments. Research on protective or preventive medicines is highly motivated due to evidence supporting this preclinical period. [4] PD is among the most prevalent neurological conditions. According to the Parkinson's Disease Foundation, one million or so Americans presently suffer from the condition. [5] In the United States, there are around 20 instances of Parkinson's disease (PD) for every 100,000 individuals, or 60,000 cases annually, and the average age of start is over 60 years old. According to reports, the prevalence of Parkinson's disease (PD) rises to 1% to 3% in those 80 years of age and older, from 1% in those 60 years of age and older. But it's crucial to remember that these figures don't include cases that go undetected. [6,7] Even though PD typically affects the elderly, people in their 30s and 40s have also been diagnosed with the condition. [7] The incidence of Parkinson's disease (PD) varies by gender, with a 3:2 ratio of males to females. The neuroprotective effects of oestrogen on the nigrostriatal dopaminergic pathway are thought to be the reason for the delayed start in females. [8,9] The erratic but noticeable course of Parkinson's disease has a profound effect on individuals, families, and the community. End-stage and advanced illness can cause major consequences, such as pneumonia, which are sometimes fatal. [10,11] The goal of current therapy is to control symptoms. [12,13] Research indicates that a multidisciplinary care team of movement experts, social workers, chemists, and other medical professionals may be beneficial for individuals with Parkinson's disease. [14,15] Parkinson's disease (PD) is linked to many genetic abnormalities and risk factors. Free radical production, oxidative stress, and other environmental pollutants are risk factors for the illness (Table 1). [16–17]

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Risk Factors associated with Parkinson Disease	
1.	Elevated cholesterol
2.	Environmental toxins
a)	Carbon disulfide
b)	Cyanide
c)	Herbicides
d)	Methanol and organic solvents
e)	Pesticides
3.	Head trauma
4.	High caloric intake
5.	Increased body mass index
6.	Inflammation associated with activation of microglia
7.	Methcathinone (manganese content)
8.	Methamphetamine/amphetamine abuse
9.	Mitochondrial dysfunction
10.	Nitric oxide toxicity
11.	Oxidative stress
a)	Formation of free radicals (e.g., hydrogen peroxide)
b)	Potent neurotoxins (e.g., 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)
12.	Post-infection states
13.	Signal-mediated apoptosis

Table – 1 : Risk Factors associated with Parkinson's Disease [16–20,22,23,29–38]

There is no evidence to establish genetic links between PD and some gene alterations (Table 2). [18-20] Remarkably, there is a negative correlation between coffee use, cigarette smoking, and the chance of Parkinson's disease. The beneficial effects of coffee may be attributed to its adenosine antagonist action, whereas the protective effects of tobacco smoking may be explained by inhibition of the enzyme monoamine oxidase (MAO). [21] The varying global frequency of Parkinson's disease (PD) raises the possibility that genetic, environmental, and ethnic variables all contribute to the illness's pathophysiology. [22–23] Research on biomedical aspects of Parkinson's disease (PD) is still ongoing and might lead to the identification of new risk factors as well as future therapy and preventative choices. [24-28]

Gene Mutations Associated With Parkinson's Disease
• Alpha-synuclein gene (SNCA)
• Eukaryotic translation initiation factor 4 gamma 1 gene (EIF4G1)
• Glucocerebrosidase gene (GBA)
• Leucine-rich repeat kinase 2 (LRRK2) gene loci
• PTEN-induced putative kinase 1 (PINK1) gene loci
• Superoxide dismutase 2 gene (SOD2)
• Vacuolar protein sorting 35 homolog gene (VPS35)

Table – 2: Gene Mutations Associated With Parkinson's disease

Pathophysiology

Parkinson's disease (PD) is an illness of the extrapyramidal system, which includes basal ganglia motor structures. It is typified by a decrease in motor function resulting from dopaminergic function loss, which drives the disease's clinical characteristics. [4, 30] The presence of nonmotor features suggests the involvement of other neurotransmitters of the glutamatergic, cholinergic, serotonergic, and adrenergic systems, in addition to the neuromodulators adenosine and enkephalins. Research conducted in the late 1950s identified striatal dopamine depletion as the primary cause of the motor symptoms of Parkinson's disease (PD). [39–44] According to further data, Parkinson's disease (PD) may have its start in the anterior

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olfactory nucleus, the dorsal motor nucleus of the vagal and glossopharyngeal nerves, or the brain stem. This indicates that the illness may follow a pattern of onset in the brain stem and progress to higher cortical levels. [45] Lewy bodies (LBs) and the loss of pigmented dopaminergic neurons are two of the histological characteristics of Parkinson's disease (PD). [47,46]

People with Parkinson's disease (PD) lose their dopaminergic function due to progressive degradation of dopaminergic neurons in the substantia nigra pars compacta (SNpc), which project to the striatum (the nigrostriatal pathway). Patients often don't get the motor symptoms of Parkinson's disease (PD) until between 50% and 80% of their dopaminergic neurons have been destroyed. This suggests that a compensatory mechanism may be involved in the illness's early stages. D1 (excitatory type) and D2 (inhibitory type) dopamine receptors affect motor activity in the extrapyramidal system. This system consists of the pars reticulata section of the substantia nigra (SNpr) and the basal ganglia, which includes the internal globus pallidal segment (GPi) of the ventral striatum. These elements are a part of bigger circuits found in the cortex and thalamus. Patients with Parkinson's disease (PD) have dopamine depletion in the striatum, which causes the GPi/SNpr circuits to become more active. This leads to gamma aminobutyric acid (GABA) malfunction, which in turn inhibits the thalamus. The ultimate consequence is a reduction in the thalamus's capacity to stimulate the frontal cortex, which leads to the diminished motor activity that is indicative of Parkinson's disease.

Therefore, clinical improvement in the motor symptoms of Parkinson's disease (PD) is mediated by restoring dopamine activity in the striatum through D2 and D1 receptor activation with dopaminergic treatments. [48] Furthermore, because dopamine no longer has the same inhibitory effect, dopaminergic depletion causes both an increase in cholinergic activity and a decrease in thalamic activation. [49,50] Research keeps confirming the notion that several levels of diffuse global network failure in the neurological system underlie Parkinson's disease (PD). [51]

The presence of LBs, which are defined as internal cytoplasmic aggregates made of proteins, lipids, and other components, is another important histological characteristic of Parkinson's disease (PD). Moreover, LBs have been found to be important indicators of long-term neurodegenerative illnesses, such as Parkinson's disease. [46,52] LBs are spherical bodies with radiating fibrils that are identified in dopaminergic neurons in the substantia nigra of PD patients. [46,47] According to research, refractory proteolytic processes involving aberrant breakdown or overproduction affected by genetic mutations may be the secondary cause of their development. [46,47] Alpha-synuclein (αSyn) gene mutations have been observed to aggregate and produce insoluble fibrils linked to LBs;53 Future Parkinson's disease (PD) treatments may target αSyn proteins. [53,54]

Overproduction of misfolded ubiquitin proteins—which are important in protein recycling—contributes to the creation of leukemia bodies (LBs). The ubiquitin proteasome system's (UPS) dysfunction is the secondary cause of the buildup of these proteins. [52,55] Different lesion patterns are observed at different phases of Parkinson's disease (PD), suggesting that the creation of LBs may play a part in the neurodegeneration that characterizes the illness. Early (premotor) olfactory and rapid eye movement (REM) aspects of Parkinson's disease (PD) may be supported by lesion patterns in the dorsal nucleus, medulla, and pons. The prevalent motor symptoms of Parkinson's disease (PD) are partly caused by lesions in the nigrostriatal area later in the illness. [57, 56] Similar to their existence in individuals with dementia with LBs (DLB), LBs are also linked to the dementia of Parkinson's disease (PD). The clinical presentations of PD and DLB are distinct from one another because in PD, motor characteristics are more pronounced and manifest earlier than in DLB. (47, 52, 55)

While amyloid beta 1-42 has been linked to the pathophysiology of Alzheimer's disease (AD), new research indicates that cerebral spinal fluid carrying this biomarker may also be able to predict cognitive impairment in Parkinson's disease (PD). [59, 58] These findings are in line with other studies that suggested AD pathology exacerbates cognitive impairment in Parkinson's disease (PD) and may be useful in forecasting the cognitive decline linked to PD. In [58]

Studies are also being conducted on the role of inflammation, particularly cytokines and other mediators, in the etiology of Parkinson's disease (PD). The pathophysiology of Parkinson's disease (PD) may involve the involvement of inflammatory responses resulting from the loss of dopaminergic neurons. Data obtained in vitro have validated the activation of astrocytes and microglia

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as a result of damage to dopaminergic neurons. [64–60]

In conclusion, several molecular pathways are involved in Parkinson's disease (PD), which is a complicated neurodegenerative illness that may have a role in the neuropathophysiology of the condition. [60]

Diagnosis

A thorough history and physical examination should be part of the differential diagnosis for Parkinson's disease (PD). Cases that are challenging or dubious should be referred to a movement disorder expert for further assessment. Since there are no conclusive tests to establish a PD diagnosis, a physician must get a clinical diagnosis by reviewing the patient's medical history, evaluating the patient's symptoms, and ruling out other possible diagnoses such multiple-system atrophy, DLB illness, and essential tremor (Table 3). [65, 70]

Diseases and Conditions That May Require Differentiation From Parkinson's Disease [65 – 79]
• Alzheimer's disease
• Basal ganglia tumor
• Benign essential tremor
• Cerebrovascular disease
• Corticobasal degeneration
• Creutzfeldt–Jakob disease
• Dementia with Lewy bodies
• Drug-induced parkinsonism
• Metabolic causes (e.g., hypoparathyroidism, thyroid dysfunction, nutritional deficiencies)
• Multiple-system atrophy
• Normal-pressure hydrocephalus
• Olfactory dysfunction
• Olivopontocerebellar atrophy
• Post-traumatic brain injury Parkinson's disease
• Progressive supranuclear palsy
• Shy–Drager syndrome
• Subdural hematoma
• Wilson's disease

Table - 3 : Diseases and Conditions That May Require Differentiation From Parkinson's Disease [65–79]

The "classical triad"—a 4-Hz to 6-Hz resting tremor, "cogwheel" stiffness, and bradykinesia—are the three main motor characteristics of Parkinson's disease (PD) (Table 4). These essential characteristics are frequently cited as the illness's initial clinical findings. About 50% of PD patients get postural instability (Table 4) as a fourth sign within five years of diagnosis.77–71 Even though Parkinson's disease (PD) is thought to mostly affect the elderly, younger people can have certain genetic variations. Clinically, younger patients (those under 60 years old) could have less bradykinesia and stiffness at presentation, which could cause a missed or delayed diagnosis. [77, 76]

Cardinal Motor Features ("Classical Triad")
• **Bradykinesia**
✓ Occurs in 80% to 90% of patients
✓ Slowness of movement
✓ Decreased amplitude of movement
• **Rigidity**
✓ Occurs in 80% to 90% of patients

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✓	Resistance to passive movement in both flexor and extensor muscles with limb relaxed
✓	Often accompanied by "cogwheel" phenomenon
•	**Tremor at rest**
✓	Common initial symptom (70% to 90% of patients)
✓	Often resolves with action or during sleep
✓	Primarily distal, involving hands
✓	May also involve jaw, tongue, lips, chin, or legs
Others	
•	**Postural instability**
✓	Predisposes patients to falls and injuries
✓	Occurs in later stages of Parkinson's disease
✓	Results from loss of postural reflexes
•	**Dysarthria**
•	**Dystonia**

Table - 4 : Motor Symptoms of Parkinson's Disease [71–78,90–101,120–128]

Finding illnesses whose symptoms resemble Parkinson's disease is a crucial step in the diagnosis procedure. A few of the illnesses and ailments included in Table 3 are those that need to be considered in the differential diagnosis and may need further testing to rule them out. A frequent appearance of benign essential tremor is an intention-type tremor, which is a tremor with movement and a higher degree of head involvement. [77–71] While patients with DLB often have concomitant cognitive changes and visual hallucinations, they may also exhibit PD-like symptoms. [78] Movement disorder specialists may be needed to confirm the diagnosis because many other illnesses can have symptoms similar to Parkinson's disease. Furthermore, when the patient's history points to a potential exposure, laboratory testing may be required to rule out nutritional deficits and other anomalies, such as thyroid illness. To rule out Wilson's illness, measuring the levels of ceruloplasmin and copper in the plasma may also be necessary. [71, 72, 75, 79] Additional diagnostic techniques include levodopa or apomorphine bedside dopaminergic challenge tests, while some neurology professionals oppose their usage. [72–75] Neuropsychiatric tests, sleep investigations, and visual examinations in response to visual abnormalities noted in certain Parkinson's disease patients—such as aberrant colour vision resulting from altered intraretinal dopaminergic transmission—may be further diagnostic tools. [71,72]

Since drug-induced parkinsonism (DIP) is one of the few reversible causes of Parkinson's disease (PD), it should be taken into account in the differential diagnosis of the illness. A thorough medication review is thus required for all patients who are suspected of having Parkinson's disease (PD) in order to prevent treating them improperly. This is because identifying DIP is crucial. Patients with various comorbidities, older women, and patients taking several drugs at high doses for prolonged periods of time are at-risk populations for DIP. [80,81]

The medications that have the ability to inhibit dopamine receptors, such as risperidone, thiothixene, and haloperidol, are the ones that are most frequently linked to DIP. [82–85] Antipsychotic medications having a lower risk of DIP, including quetiapine and clozapine, are suggested if PD patients need them. [84,85] Metoclopramide, a gastrointestinal prokinetic drug, and antiemetics containing a phenothiazine core (such as prochlorperazine or promethazine) are also linked to DIP. [80,81,86] Numerous additional medicines, such as antidepressants, lithium, anticonvulsants, and some antihypertensive treatments like methyldopa and calcium-channel blockers, can also result in DIP. [80,81,87] In order to manage DIP, the contributory medication(s) must be found and stopped. This typically eliminates the symptoms, though occasionally they may persist for a few months or perhaps a year or two. [81,82]

The fact that the clinical motor symptoms of Parkinson's disease (PD) may not appear until

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between 50% and 80% of dopaminergic neurons have been destroyed presents a diagnostic problem. Unfortunately, there may already be severe disease progression at this stage. [88–90] The requirement to detect minute motor characteristics that are prone to being overlooked, including the lack of arm swing or jerky movements, exacerbates this issue. [91–93] The existence of nonmotor comorbidities, such as anosmia, lethargy, constipation, melancholy, anxiety, and sleep disturbances (Table 5), which the doctor might not recognise as being related with Parkinson's disease (PD), further complicates an early diagnosis. [4, 94–97] It could be easier to diagnose Parkinson's disease (PD) earlier if certain characteristics are identified early and linked to the disease. [90-93] Because PD is often identified and treated at the outset of motor characteristics, researchers are still looking for biomarkers that might enable a quicker diagnosis. [101–111] If PD patients receive the right care after their diagnosis, their life expectancy may be comparable to that of healthy people. [70, 77]

• **Autonomic Dysfunction***
✓ Constipation (parasympathetic nervous system cholinergic)
✓ Orthostatic hypotension (sympathetic nervous system noradrenergic)
✓ Sexual dysfunction (parasympathetic nervous system cholinergic)
✓ Sweating (sympathetic nervous system cholinergic)
✓ Urinary retention (parasympathetic nervous system cholinergic)
• **Neuropsychiatric Symptoms**
✓ Anxiety
✓ Cognitive impairment (mild)
✓ Dementia
✓ Depression (e.g., dysphoria, suicidal ideation, apathy)
✓ Impulse-control disorders (e.g., preoccupations, hypersexuality, compulsive shopping, binge eating)**
✓ Panic disorder
✓ Psychosis (e.g., hallucinations, delusions)
• **Sensory Symptoms**
✓ Olfactory dysfunction (hyposmia)
✓ Paresthesias
✓ Pain
• **Sleep Disturbance*** **
✓ Daytime somnolence
✓ Insomnia
✓ Rapid eye movement disorder
✓ Restless legs syndrome
✓ Sleep attacks
✓ Sleep apnea
• **Others**
✓ Fatigue
✓ Sialorrhea
✓ Weight loss

Table – 2 : Nonmotor Symptoms of Parkinson's Disease [71–78,90–101,120–128]

*Depends on components of nervous system that are affected
**Usually associated with use of dopamine agonists
***Complex etiology; linked to neurodegenerative process, motor features, and drug therapy

Because olfactory anomalies can have numerous aetiologies, olfactory screening should not be regarded a diagnostic tool in and of itself. However, it may be helpful in identifying Parkinson's disease (PD). [96–94] Protein indicators from biopsy or other techniques, such as spinal fluid, salivary gland, rectal, and intestinal samples, may also be utilised in the future. [105,

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109, 111, 104] Imaging methods are mainly used to rule out other neurological conditions in the diagnosis of Parkinson's disease (PD); for example, normal-pressure hydrocephalus can be identified with magnetic resonance imaging (MRI).112. In the future, 7-T MRI may be used to assess the substantia nigra's (SN) anatomy in order to detect PD patients.113- Alzheimer's disease and other non-LB dementias can be distinguished from LB-type dementias (PD and DLB) using dopamine transporter scans (DaT scans).1104–112. At the moment, there is disagreement on the efficacy of genetic testing in the diagnosis of Parkinson's disease (PD) due to uncertainty about the populations to test, the implications of the test results, and cost concerns. [24-26,117]

Clinical Presentation

Parkinson's disease (PD) can have a sneaky start. Up to 90% of individuals experience mild symptoms at first, such trouble rising from a chair. The identification of nonmotor symptoms may be delayed if they are mistakenly believed to be associated with comorbidities or natural ageing. As previously mentioned, the early stages of the illness might involve nonmotor characteristics and endure an average of four to six years. [89-94] Additional clinical symptoms, such as thermoregulatory dysfunction, may appear as the condition worsens. Sweating excessively is one example of thermoregulatory disorders, although sensitivity to cold is more prevalent. Some individuals may have neuropathic and nociceptive pain (musculoskeletal) in the early or late phases of the illness.79, 90-93, 118-121.

Bradykinesia, stiffness, and tremor are the three clinical motor symptoms of Parkinson's disease (PD) patients, as was mentioned in the diagnostic section. Among these three fundamental characteristics, tremor is the one that patients and carers identify with more frequency, particularly in those who have the tremor-predominant PD subtype.121–127, 122–125 The age of the patient at the commencement of Parkinson's disease (PD) may be related to the motor presentations of the disease. Specifically, tremor is twice as likely in people over 64 years old as in those under 45 years old at the onset of PD. Furthermore, individuals diagnosed between the ages of 45 and 55 are more likely to experience treatment-related problems, such as the correlation between the duration of levodopa medication and the development of dystonias and dyskinesias.77%

About two thirds of PD patients experience tremor, which frequently manifests as the first symptom. It normally begins mildly and intermittently, and at rest, its level is commonly recorded between 4 and 6 Hz. Typically, the condition starts off with a unilateral tremor and escalates to bilateral involvement over time.A-125 The Parkinson's disease (PD) tremor is commonly characterised as a pill-rolling tremor, which is a resting tremor of the hand, however it can also affect the lower limbs, toes, and jaws. While movement or sleep help to lessen the symptoms, stressful events or expecting the patient to complete a mental activity may intensify and worsen a PD tremor. Younger individuals could only exhibit tremor or variable presentations when they are really tired. [122,124] While the most prevalent kind of tremor in Parkinson's disease (PD) is resting tremor, some people may exhibit action tremor, or tremor that manifests during activity. In addition to the possibility of resting tremor later in the course of the disease, individuals with benign essential tremor (BET) also present with mixed tremor, which complicates the diagnostic procedure. Tremor was seen to decrease in the latter stages of the illness in imaging investigations of Parkinson's disease patients, and it was not always linked to pathologic dopaminergic loss. [68,124] Despite being prevalent in Parkinson's disease, tremor is thought to be the least incapacitating motor characteristic when compared to rigidity and bradykinesia, the other two cardinal aspects. [122,125]

One of the main clinical motor characteristics of Parkinson's disease (PD) is bradykinesia, which is characterised by a decrease in the amplitude, gait, and speed of repeated voluntary movements. [126] The most prevalent clinical characteristic seen in PD patients is bradykinesia, which is regarded as a crucial diagnostic factor. The condition (i.e., the akinetic–rigid subtype of PD) typically manifests after tremor, yet in some cases it may be the first symptom and tremor may never occur. [123,125] A sluggish, shuffling stride and difficulties starting or beginning movements are prominent clinical presentations linked to this characteristic. Bradykinesia patients may also have a hastened gait, wherein they walk faster and take smaller, more rapid steps to try and "catch up" with their shifted centre of gravity. [123-126] Bradykinesia-related immobility can also occur in patients; this usually happens when turning or trying to fit through a small door. [121]. "Freezing" episodes

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are severe PD symptoms that often appear in advanced stages of the disease. [125] Rigidity is the third main characteristic of Parkinson's disease (PD). It manifests as either elevated muscular tone or greater resistance to a passive range of motion. This characteristic in persons with Parkinson's disease is usually referred to as "cogwheel rigidity." [72,73,123] The easiest way to explain this is as muscular tension, which manifests as little jerks or a ratchet-like sensation when moved passively. Since cogwheeling is a symptom of benign essential tremor, a clear diagnosis is necessary for cogwheel stiffness. [71,74] In addition to the limbs, other body regions affected by Parkinson's disease (PD) rigidity include the face, which may have a "masked" look (hypomimia). [73-75,125] Postural instability is a fourth characteristic that often appears later in the course of Parkinson's disease (PD). The aetiology of this symptom is complex and includes neuronal degeneration in the hypothalamus brainstem or peripheral nervous system, as well as stiffness and other motor complaints. Because postural instability is linked to loss of balance and an increased risk of falling, it can be extremely incapacitating. [94,120,127]

Other distinct characteristics of Parkinson's disease (PD) include quiet voice (hypophonia) and handwriting difficulties (micrographia). [73,74,119,123] To evaluate the course of Parkinson's disease (PD) and set guidelines for the application of various management techniques, a variety of staging instruments are employed. The Unified Parkinson's Disease Rating Scale (UPDRS) is the most widely used scale for evaluating the clinical state of individuals with Parkinson's disease (PD), encompassing both motor and nonmotor symptoms. This four-part instrument evaluates problems associated with therapy as well as motor characteristics, psychological characteristics, and activities of daily life. [129]

It has been determined that increases in the UPDRS motor and total scores of 2.5 and 4.3 points, respectively, are clinically significant. [129]

Although it has been around since the 1960s, the staging scale created by Hoehn and Yahr is another instrument that is not frequently utilised in clinical practise. This scale ranges from moderate symptoms to a bedridden state, with five phases denoting different levels of disability. [130]

Deficits in everyday life tasks cause the patient to lose their capacity to remain independent as Parkinson's disease (PD) worsens, requiring more carer help. The risk factors that may impact Parkinson's disease (PD) progression have been recognised by the American Academy of Neurology. Patients who initially appear with tremor, for instance, can have a slower illness progression and a longer response to medication. Patients who exhibit postural instability, motor characteristics, and gait abnormalities early in the disease may see a higher rate of disease development than those who come with Parkinson's disease in their late 50s or later. Individuals with severe dementia who do not respond well to medication therapy frequently need to be sent to an institution right once. [131, 125] Complications from immobility, such pneumonia, pulmonary embolism, and falls, are frequently linked to mortality. [10,11,75]

Clinical Management

Treating the motor and nonmotor symptoms of Parkinson's disease (PD) is the main aim of the disease management strategy, which also aims to enhance the patient's overall quality of life. An initial assessment and diagnosis by a multidisciplinary team made up of neurologists, primary care physicians, nurses, physical therapists, social workers, and chemists is necessary for appropriate management. [132, 14] Input from the patient and their family into management decisions is also crucial. [133 -135]

To optimise therapeutic results, effective therapy should combine pharmacological and nonpharmacological techniques. There are currently no known treatments that halt the advancement of Parkinson's disease (PD) or have a neuroprotective impact. [135] The development of potential disease-modifying therapies and the identification of biomarkers that may be helpful in the early detection of illness have been the main goals of current research. [136,137]

Avoided Drugs

Drugs that block dopamine receptors have the potential to cause neuroleptic malignant syndrome, parkinsonism, or a significant worsening of motor symptoms in Parkinson disease patients. These include antiemetics like prochlorperazine and metoclopramide, tetrabenazine, promethazine, fluphenazine, risperidone, and olanzapine; neuroleptics like haloperidol, thioridazine, chlorpromazine, promethazine, fluphenazine, and olanzapine; and antihypertensives like

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methyldopa. Monoamine oxidase B inhibitor users should refrain from using meperidine.

Prognosis

Parkinson disease patients have a lower life expectancy (odds ratio 2.56, meaning that their mortality risk is 2.56 times higher than that of age-matched individuals without Parkinson disease), and medical interventions do not seem to change this mortality or postpone the development of nonmotor symptoms. Early-onset patients had a longer absolute survival and slower advancement, but at the cost of more years lost from life (11 years lost in early-onset vs. 4 years in late-onset illness). A deficiency of compensatory measures to prevent cell death may be the reason for the faster disease progression and cognitive deterioration observed in late-onset Parkinson PD. There is a dearth of information on the elderly population and long-term results.

II. DISCUSSION

Parkinson's disease (PD) is a progressive, long-term neurological illness with both motor and nonmotor symptoms.1-3 The primary reason behind the motor symptoms of the condition, such as bradykinesia, "cogwheel" stiffness, and resting tremor, has been determined to be striatal dopamine depletion [39–44.77–71] Cognitive alterations, sadness, and sleep difficulties are examples of nonmotor symptoms. [4]

A thorough history and physical examination should be part of the differential diagnosis for Parkinson's disease (PD). [65-70] Finding illnesses with symptoms comparable to Parkinson's disease (PD) is a crucial step in the diagnosis procedure. [77–71] There are no conclusive tests to support a PD diagnosis. [65-70] The most widely used scale for evaluating the clinical state of people with Parkinson's disease is the UPDRS. [128] Treatment of the PD's symptomatic motor and nonmotor aspects is the main aim of the disorder's management, with the ultimate goal being to enhance the patient's quality of life overall. [14,132] No known therapies have been found to slow the disease's progression or have a neuroprotective effect. [134,135]

III. CONCLUSION

It is common to identify nonmotor signs of Parkinson disease, a neurodegenerative ailment that is clinically diagnosed mainly on its motor aspects. Although the exact cause is still unknown, it is thought to be a result of a mix of environmental and genetic risk factors, most notably sex and age. Parkinsonism intensity, pace of progression, levodopa sensitivity, early gait abnormalities, and parkinsonia symmetry are all potential risk factors for higher death. Several characteristics might lead to a mistaken diagnosis of idiopathic Parkinson disease instead of Parkinson-plus syndrome, and it's critical to identify this difficulty while making a differential diagnosis.

Numerous medicinal and surgical therapies are available for the symptomatic treatment of both motor and nonmotor characteristics at different phases of the disease course, even if neuroprotective treatments are not yet accessible. Better choices could be available soon given the range of ongoing trials on novel medicines.

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