

PROGRESSION ANALYSIS REPORT ON PARKINSON'S DISEASE

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1. INTRODUCTION

Parkinson's disease is a progressive neurological condition characterized by tremors, stiffness, and impaired movement. It also presents non-motor symptoms like cognitive decline and mood changes. Over time, symptoms worsen, affecting daily activities and quality of life. While the exact cause is unclear, it involves the loss of dopamine-producing neurons in the brain. Treatment aims to alleviate symptoms through medication, therapy, and lifestyle adjustments. Despite ongoing research, Parkinson's remains incurable, highlighting the importance of continued efforts in understanding and managing the disease.

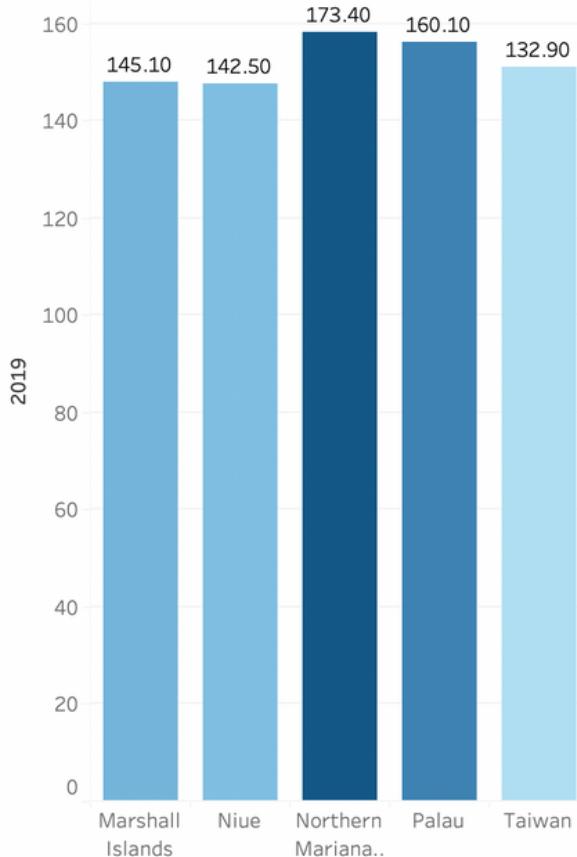


Fig 1. Top 5 countries of highest PD recorded in 2019

1.1. Prevalence

Globally, Parkinson's disease (PD) prevalence has doubled in the last 25 years, highlighting a concerning trend. Particularly noteworthy are regions like Marshall Islands (145.10), Niue (142.50), Northern Mariana (173.40), Palau (160.10), and Taiwan (132.90) per 100,000 people, exhibiting the highest rates. In India, although scientific literature is limited, significant disparities in PD prevalence are evident. The Parsi community in Mumbai displays the world's highest incidence of PD, with 328 cases per 100,000 people, while the general incidence in India is relatively lower, recorded at 70 per 100,000 individuals in 2016. These findings underscore the diverse and complex nature of PD distribution globally, emphasizing the need for further research and targeted interventions to address these disparities and mitigate the growing burden of the disease.

1.2. Aetiology

Parkinson's disease (PD) results from genetic susceptibilities, including α -synuclein and parkin gene mutations, and environmental factors like MPTP exposure. These trigger oxidative stress, mitochondrial dysfunction, and impaired proteasomal activity. Dopamine depletion in the brain's substantia nigra contributes to motor symptoms. The formation of Lewy bodies and abnormal protein aggregates primarily composed of α -synuclein disrupts the neuronal function. Emerging research explores the link between gut microbiota and PD, suggesting potential implications for disease progression and management.

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1.3. Pathophysiology

PD is characterized by the progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNpc) of the brain. This neuronal loss results in a marked reduction in dopamine levels within the basal ganglia, a key region involved in motor control. The pathophysiological hallmark of PD is the accumulation of abnormal protein aggregates known as Lewy bodies, primarily composed of α -synuclein, within the affected neurons. These aggregates disrupt cellular function and lead to neuronal dysfunction and death.

The loss of dopaminergic input from the SNpc to the striatum results in dysregulation of the basal ganglia circuitry, leading to the cardinal motor symptoms of PD, including bradykinesia, rigidity, resting tremor, and postural instability. Additionally, non-motor symptoms such as cognitive impairment, autonomic dysfunction, and psychiatric disturbances may also arise due to the widespread pathology affecting other brain regions. While the exact aetiology of PD remains elusive, a complex interplay of genetic susceptibility and environmental factors, such as oxidative stress and neuroinflammation, likely contributes to disease onset and progression. Furthermore, research suggests that dysfunction in non-dopaminergic neurotransmitter systems, such as noradrenergic, serotonergic, and cholinergic pathways, contributes to non-motor symptoms in PD. Understanding the intricate pathophysiological mechanisms underlying PD is crucial for developing targeted therapeutic interventions aimed at slowing or halting disease progression.

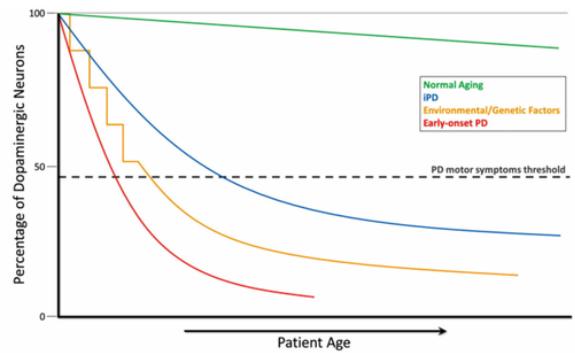


Image source: www.atrinceu.com

Fig 2. Evolution of dopamine depletion in Parkinson's Disease

During the course of normal aging (green line), small but slow dopaminergic degeneration occurs without any motor symptoms. Idiopathic PD (IPD, blue line) is of unknown origin but is thought to develop gradually, with a slow degeneration of dopaminergic neurons leading to the classic PD motor symptoms later in life. Another model of dopamine neurodegeneration leading to PD motor symptoms involves repeated exposure to environmental toxicants over time in combination with a genetic predisposition to dopaminergic neuron loss (yellow line). Early-onset PD (red line), as caused by mutations in the PARKIN gene, involves a precipitous decline in dopaminergic neurons, and PD motor symptoms can present decades prior to those in idiopathic PD. One more scenario (not shown) of PD motor symptom development involves possible in utero environmental toxicants or genetic factors leading to an atypically low number of dopaminergic neurons at birth and increased susceptibility to PD development (Haas et al., 2012).

1.4. Symptoms

1.4.1. Motor Symptoms

Tremors: Rhythmic shaking at rest, starting in one limb and spreading

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gradually. It occurs due to the degeneration of dopamine-producing neurons in the brain.

Rigidity: Stiffness in limbs or torso, often misattributed to arthritis. It results from increased muscle tone and resistance to movement.

Bradykinesia: Slowness of movement, leading to reduced facial expression and small handwriting. It's caused by impaired dopamine signaling in the basal ganglia, affecting motor coordination.

Changes in Handwriting: Micrographia, or small, cramped handwriting, develops due to bradykinesia affecting fine motor control.

Slowed Movement: Generalized slowing of movement, including turning in bed or performing daily tasks, caused by bradykinesia and rigidity.

Difficulty Walking: Impaired balance and coordination, making walking challenging. It's influenced by postural instability and bradykinesia.

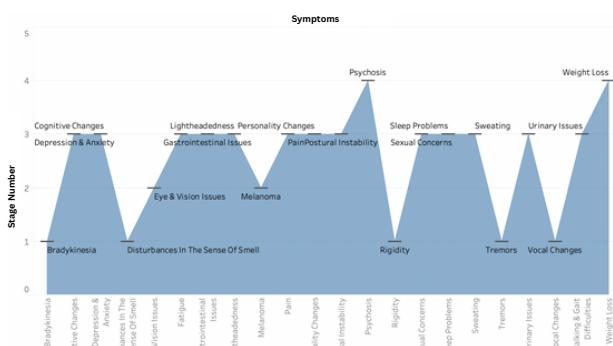


Fig 3. General occurrence of symptoms across different stages of Parkinson's disease

1.4.2. Non-Motor Symptoms

Cognitive Changes: Difficulties in thinking and judgment, linked to dopamine depletion and structural changes in the brain.

Depression and Anxiety: Common neuropsychiatric symptoms, possibly due

to dopamine imbalance and neurochemical changes.

Disturbances in the Sense of Smell: Reduced olfactory function, reflecting early involvement of the olfactory bulb in Parkinson's pathology.

Eye and Vision Issues: Reduced eye movement and blinking frequency, affecting visual perception and leading to dry eyes.

Fatigue: Associated with dysregulation of neurotransmitters and disruptions in sleep-wake cycles.

Gastrointestinal Issues: Constipation due to autonomic nervous system dysfunction and slowed gut motility.

Light-headedness: Resulting from autonomic dysfunction and impaired blood pressure regulation.

Melanoma: Elevated risk due to shared genetic susceptibility or environmental factors.

Pain: Various types of pain, possibly arising from altered sensory processing or musculoskeletal changes.

Personality Changes: Linked to neurochemical imbalances and structural brain changes.

Psychosis: Hallucinations and delusions, attributed to dopaminergic medications and altered brain function.

Sexual Concerns: Impaired libido and sexual dysfunction, potentially related to medication side effects or psychological factors.

Sleep Problems: Disruptions in sleep architecture and patterns, influenced by neurochemical changes and medication effects.

Sweating: Dysregulation of autonomic function, leading to excessive sweating episodes.

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Urinary Issues: Dysfunction of the autonomic nervous system affecting bladder control and urine flow.

Weight Loss: Multifactorial, including reduced appetite, swallowing difficulties, and metabolic changes.

1.5. Progression

Measuring the progression of Parkinson's disease is essential for evaluating treatment efficacy and guiding patient management. Various rating scales and assessment tools, spanning motor, cognitive, and functional domains, offer valuable insights into disease severity and prognosis over time.

1.5.1 Unified Parkinson's Disease Rating Scale (UPDRS)

The UPDRS provides a comprehensive assessment of both motor and non-motor symptoms, guiding treatment decisions and monitoring disease progression.

Part I assesses non-motor experiences of daily living, such as mood, sleep, and cognition.

Part II evaluates motor experiences of daily living, including speech, swallowing, and handwriting.

Part III focuses on motor examination, measuring tremors, rigidity, bradykinesia, and postural instability.

Part IV examines complications of therapy, such as dyskinesias and motor fluctuations.

1.5.2. Hoehn & Yahr Stages

This staging system offers a simple yet effective way to categorise the severity of Parkinson's disease, aiding in treatment planning and prognosis.

Stage 1: Mild symptoms affecting one side of the body.

Stage 2: Symptoms on both sides, with preserved balance.

Stage 3: Bilateral symptoms with impaired balance, but still able to stand and walk.

Stage 4: Severe disability, requiring assistance for mobility.

Stage 5: Wheelchair-bound or bedridden due to severe symptoms.

1.5.3. Mini-Mental State Examination (MMSE)

The MMSE is a widely used tool for detecting cognitive impairment in Parkinson's disease, helping clinicians evaluate patients' cognitive status and track changes over time.

MMSE assesses cognitive function across multiple domains, including orientation, memory, attention, and language.

1.5.4. Activities of Daily Living (ADL) Score

ADL scores reflect the impact of Parkinson's on functional independence, guiding interventions to optimize patients' daily functioning and quality of life.

ADL scores measure a person's ability to independently perform basic tasks like bathing, dressing, and eating.

1.5.5. Timed Up and Go (TUG) Test

The TUG test assesses mobility and fall risk, providing valuable information about a patient's functional capacity and guiding rehabilitation strategies.

The TUG Tests measure the time taken to stand up from a chair, walk a short distance, turn around, return, and sit down.

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1.5.6. 10-Meter Walk Test (10MWT)

The 10MWT is a reliable measure of walking ability in Parkinson's disease, helping clinicians monitor disease progression and assess the effectiveness of interventions aimed at improving mobility.

The 10WT measures the time taken to walk 10 meters, evaluating gait speed and mobility.

1.5.7. Berg Balance Scale

The Berg Balance Scale is a standardized tool for identifying individuals at risk of falls and guiding interventions to improve balance and prevent injuries.

The Berg Balance scale assesses balance by evaluating a person's ability to perform specific tasks related to maintaining a stable posture.

1.5.8. Finger Tapping Speed

This test provides objective data on motor function, particularly useful for monitoring the progression of Parkinson's-related motor symptoms and evaluating treatment efficacy.

It measures the speed and rhythm of repetitive finger tapping, assessing fine motor control and coordination.

1.5.9. Parkinson's Disease Questionnaire (PDQ-39)

The PDQ-39 offers a comprehensive assessment of the physical, emotional, and social aspects of living with Parkinson's disease, guiding holistic care planning and management strategies.

The PDQ-39 assesses the impact of Parkinson's disease on quality of life across various domains, including mobility, activities of daily living,

emotional well-being, and social support.

1.5.10. Geriatric Depression Scale (GDS)

The GDS helps identify individuals at risk of depression, enabling timely intervention and improving overall management of Parkinson's disease by addressing mental health concerns.

The GDS screens for depressive symptoms in older adults, including those with Parkinson's disease.

1.5.11. Progression of symptoms during different stages

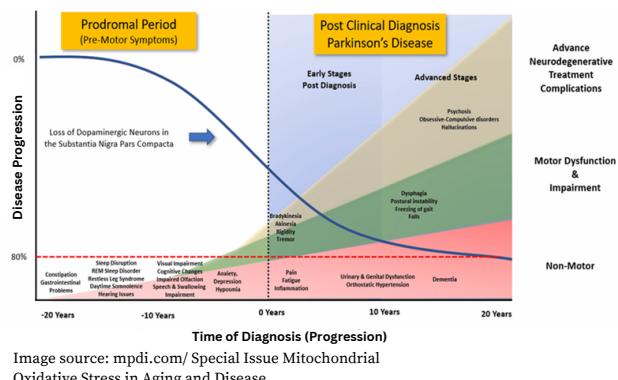


Fig 4. Progression of Parkinson's Disease

Parkinson's disease progression unfolds over a prodromal period, characterized by gastrointestinal issues and sleep disturbances up to 20 years pre-diagnosis. Cognitive alterations, mood fluctuations, and sensory impairments emerge a decade before diagnosis. The clinical diagnosis of Parkinson's disease accepts that there is a potential loss of up to 80% of the dopaminergic neurons in the Substantia Nigra Pars Compacta. However, prior to the emergence of any significant motor impairment, a wide variety of symptoms associated with non-motor dysfunction and disability usually precede the clinical diagnosis of Parkinson's disease by 10–20 years. Post-

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diagnosis, motor symptoms escalate, with bradykinesia, tremor, and rigidity worsening. Urinary dysfunction arises at the 10-year mark, followed by gait instability, falls, and cognitive decline at 20 years post-diagnosis. These manifestations correspond to the loss of dopaminergic neurons in the substantia nigra pars compacta. As the disease advances, dysphagia, freezing of gait, and psychiatric symptoms like hallucinations and obsessive-compulsive behaviors become pronounced. Understanding this progressive trajectory is crucial for tailoring interventions and managing the multifaceted manifestations of Parkinson's disease effectively.

1.6. Treatment and Management

1.6.1 Medications

Levodopa/Carbidopa: Increases dopamine levels in the brain to alleviate motor symptoms.

Dopamine Agonists: Mimic the action of dopamine in the brain to improve motor function.

MAO-B Inhibitors: Inhibit the breakdown of dopamine in the brain, helping to increase dopamine levels and improve motor symptoms.

COMT Inhibitors: Extend the duration of action of levodopa by inhibiting its breakdown in the body, leading to more consistent symptom control.

Anticholinergics: Reduce tremors and muscle stiffness by blocking the action of acetylcholine in the brain.

Amantadine: Provides relief from dyskineticias and may improve motor symptoms in some patients.

Apomorphine: Acts rapidly to improve motor fluctuations and "off" episodes in advanced Parkinson's disease.

NMDA Receptor Antagonists: Modulate glutamate levels in the brain to reduce motor fluctuations and dyskineticias.

Medications, including Levodopa-Carbidopa, Ropinirole, Pramipexole, Rasagiline, Selegiline, Bromocriptine, and Placebo, play vital roles in managing Parkinson's disease, alleviating motor symptoms, and improving patients' quality of life through various mechanisms of action.

Levodopa-Carbidopa: Replenishes dopamine levels and reduces motor symptoms by converting to dopamine and inhibiting its breakdown.

Ropinirole: Directly stimulates dopamine receptors in the brain, alleviating motor symptoms like tremors and rigidity.

Pramipexole: Acts as a dopamine agonist, mimicking dopamine's effects and improving motor symptoms.

Rasagiline: Inhibits the breakdown of dopamine, helping maintain dopamine levels and improve motor function.

Selegiline: Blocks dopamine degradation, preserving dopamine levels and enhancing motor function.

Bromocriptine: Stimulates dopamine receptors in the brain, alleviating motor symptoms associated with Parkinson's disease.

1.6.2 Drug Analysis

A drug analysis was conducted using

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Levodopa-Carbidopa, Ropinirole, Pramipexole, Rasagiline, Selegiline, Bromocriptine, and Placebo to assess their effectiveness based on the UPDRS III scale improvement score.

1.6.2.1. Objective

The drug analysis aimed to evaluate the effectiveness of various Parkinson's disease medications compared to a placebo based on the UPDRS III improvement score. The analysis sought to provide insights into which medications show the most promising outcomes in alleviating motor symptoms associated with Parkinson's disease.

1.6.2.2. Methodology

The analysis utilized a dataset named "Medications.csv" containing medication names and corresponding improvement scores. Python programming language, along with libraries such as pandas, matplotlib, and seaborn, was employed for data manipulation, visualization, and analysis. Bar charts were used to visually represent the mean improvement scores of each medication category.

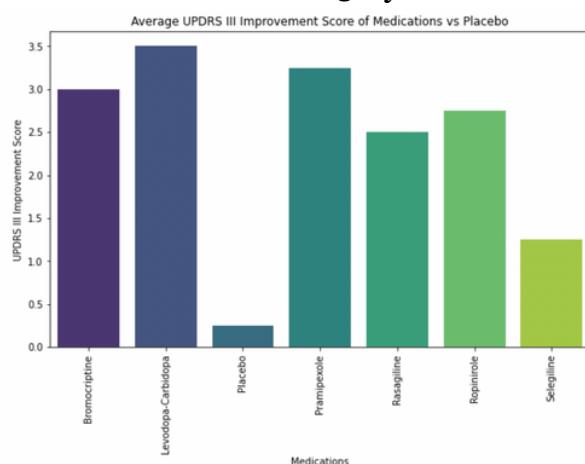


Fig 5. Comparison of improvement score of medications

1.6.2.3. Findings

The findings revealed that Levodopa-Carbidopa and Bromocriptine exhibited higher mean improvement scores

compared to Ropinirole, Pramipexole, Rasagiline, Selegiline, and the placebo. Dopamine agonists and MAO-B inhibitors demonstrated relatively lower improvement scores.

1.6.2.4. Interpretation

These results suggest that Levodopa-Carbidopa and Bromocriptine may be more effective in managing motor symptoms of Parkinson's disease compared to other medications analyzed. However, further research and clinical trials are warranted to validate these findings and assess long-term efficacy and safety.

1.6.2.5. Conclusion

In conclusion, the drug analysis highlights the potential effectiveness of certain medications, particularly Levodopa-Carbidopa and Bromocriptine, in improving motor symptoms in Parkinson's disease patients. Clinicians may consider these medications as primary treatment options, but individual patient factors and preferences should also be taken into account.

1.6.3. Disease Management

Physical Therapy: Tailored exercise regimens in physical therapy improve motor function, balance, and flexibility, crucial for managing Parkinson's symptoms. Therapists focus on gait training, strength exercises, and stretching to enhance mobility and prevent falls, promoting independence and overall well-being.

Occupational Therapy: Occupational therapists assess functional abilities and design personalised strategies to overcome challenges in daily activities like

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dressing, cooking, and writing. They may suggest adaptive equipment and environmental modifications to promote safety and efficiency, enabling individuals to maintain autonomy and quality of life.

Speech Therapy: Speech therapists address speech, voice, and swallowing difficulties common in Parkinson's disease, employing exercises to strengthen facial muscles and improve articulation. Techniques such as respiratory training and swallowing exercises enhance communication and prevent aspiration, ensuring optimal swallowing function and nutrition.

Nutritional Counseling: Expert guidance ensures individuals with Parkinson's disease maintain a balanced diet to manage weight fluctuations, alleviate constipation, and minimize adverse interactions with medications, supporting overall health and well-being.

Exercise Programs: Tailored exercise regimens, including yoga, Tai Chi, and dance, improve flexibility, posture, and mood, fostering physical and mental wellness while effectively managing Parkinson's symptoms and enhancing quality of life.

Support Groups: These provide a vital network for patients and caregivers, offering emotional support, educational resources, and coping strategies to navigate the challenges of Parkinson's disease, reducing feelings of isolation and promoting holistic well-being.

Deep Brain Stimulation (DBS): This surgical procedure involves implanting

electrodes in specific brain areas to regulate abnormal neural activity, effectively mitigating motor symptoms in eligible patients, offering a promising therapeutic option for advanced Parkinson's management.

2. PROJECT OVERVIEW

2.1. Objective

- To assess the progression of Parkinson's disease (PD) over time, focusing on both motor and non-motor symptoms.
- To identify and analyze factors influencing disease progression, including demographic, clinical, and lifestyle variables.
- To evaluate the effectiveness of current management strategies in slowing disease progression and improving quality of life for PD patients.
- To investigate the relationship between baseline characteristics and the rate of disease progression in PD.
- To provide recommendations for optimizing treatment approaches and addressing challenges in managing PD progression.

2.2. Methodology

- Define key performance indicators (KPIs) related to PD progression, such as UPDRS scores, quality of life assessments, and cognitive function tests.
- Establish criteria for measuring and tracking disease progression over time, including baseline assessments and follow-up evaluations.
- Conduct comprehensive baseline assessments of PD patients, including demographic information, medical history, and initial symptom severity.
- Analyze baseline data to identify

- patterns and trends in disease presentation and progression, using statistical methods and data visualization techniques.
- Implement longitudinal data collection methods to track changes in motor and non-motor symptoms of PD over time.
- Utilize standardized assessment tools, such as UPDRS scales and neuropsychological tests, to quantify disease progression and monitor treatment response.
- Identify potential factors influencing the rate and severity of PD progression, including genetic predisposition, environmental exposures, and comorbidities.
- Identify potential factors influencing the rate and severity of PD progression, including genetic predisposition, environmental exposures, and comorbidities.
- Analyze the relationship between various demographic, clinical, and lifestyle factors and disease progression outcomes through regression analysis and correlation studies. Incorporating feature importance analysis to find the most important variable in disease progression
- Assess the selected participant's medical history, including onset and progression of symptoms, current treatment regimen, and any comorbidities, to understand the contextual factors influencing their disease.

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- Conduct thorough neurological evaluations, including motor and non-motor symptom assessments, cognitive function tests, and quality of life surveys, to comprehensively capture the participant's Parkinson's disease profile and its impact on daily functioning.
 - Summarize key findings from the progression analysis, highlighting significant trends, correlations, and associations identified.
 - Present a concise overview of the main results and their implications for understanding PD progression and informing clinical management strategies.
 - Interpret the findings in the context of existing literature and current understanding of PD pathophysiology and treatment.
 - Discuss the clinical implications of the study findings, including potential implications for patient care, research, and policy.
 - Identify limitations of the study design, data collection methods, and analysis techniques used in the progression analysis.
 - Discuss challenges encountered during the study, such as sample size limitations, data variability, and confounding factors.
 - Provide recommendations for future research directions, including the need for larger longitudinal studies, novel biomarker discovery, and targeted therapeutic interventions.
 - Offer practical recommendations for improving clinical practice and patient care based on the study findings and identified gaps in knowledge.
 - Summarize the main findings of the progression analysis and their implications for understanding PD progression and management.
 - Reiterate the significance of the study results and their potential impact on advancing knowledge and improving outcomes for PD patients.
-

3. DATASET OVERVIEW

To obtain the dataset for Parkinson's disease progression analysis, collaboration with a movement disorders neurologist was achieved. Through comprehensive patient evaluations, including motor symptoms, cognitive function, and quality of life assessments, KPIs like UPDRS scores, Hoehn and Yahr stage, MMSE score, ADL score, and medication dosages were collected. This ensured dataset accuracy and reliability.

Age: Age is an essential demographic factor influencing disease progression in Parkinson's disease (PD). Younger age at onset is associated with a more aggressive disease course, while older age may be linked to increased risk of cognitive decline and motor complications.

Gender: Gender differences exist in PD, with males generally having a higher incidence and earlier onset compared to females. Gender can influence disease presentation, symptom severity, and treatment response, making it a relevant factor to consider in progression analysis.

Date of Diagnosis: The date of PD diagnosis provides a baseline reference point for tracking disease progression over time. Longitudinal assessments relative to the diagnosis date enable clinicians to monitor changes in symptoms, functional abilities, and treatment response, facilitating personalized management strategies.

Disease Duration (Years): Disease duration reflects the length of time since PD diagnosis and serves as a critical indicator of disease progression. Longer disease duration is associated with increased motor and non-motor symptom burden, functional decline, and treatment complications, highlighting the progressive nature of PD.

Family History: Family history of PD indicates a potential genetic predisposition to the disease, influencing disease susceptibility and progression. Individuals with a positive family history may experience earlier onset and more severe symptoms, warranting closer monitoring and tailored intervention strategies.

UPDRS (Unified Parkinson's Disease Rating Scale) Parts I-IV: The UPDRS assesses various aspects of motor and non-motor symptoms, providing a comprehensive evaluation of disease severity and progression. Each part evaluates specific domains such as mentation, mood, motor function, and complications of therapy, offering valuable insights into disease trajectory.

Hoehn and Yahr Stage: The Hoehn and Yahr staging system categorizes PD based on motor symptoms and functional impairment, offering a standardized measure of disease severity and progression. Advancement through stages reflects worsening motor symptoms and increasing disability,

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guiding treatment decisions and prognosis estimation.

MMSE Score (Mini-Mental State Examination): The MMSE evaluates cognitive function across multiple domains, detecting changes indicative of cognitive decline in PD. Declining MMSE scores over time suggest progression of cognitive impairment, impacting treatment decisions and patient management.

ADL Score (Activities of Daily Living): ADL assessments measure functional independence in performing daily tasks, reflecting disease impact on daily functioning. Declining ADL scores signify worsening functional impairment and disease progression, guiding interventions to maintain quality of life and independence.

TUG Test (Timed Up and Go Test): The TUG test assesses mobility and balance by measuring the time taken to rise from a chair, walk a short distance, and return to a seated position. Prolonged TUG test durations indicate impaired mobility and balance, reflecting disease progression and fall risk in PD.

10-Meter Walk Test: The 10-meter walk test evaluates gait speed and mobility, reflecting motor function and disease progression in PD. Slower walk test times indicate gait disturbances and mobility limitations, guiding interventions to improve ambulation and functional mobility.

Berg Balance Scale: The Berg Balance Scale assesses balance and fall risk by

evaluating performance on various balance-related tasks. Lower Berg Balance Scale scores indicate impaired balance and increased fall risk, reflecting disease progression and functional decline in PD.

Finger Tapping Speed: Finger tapping speed measures manual dexterity and bradykinesia, key motor symptoms of PD. Slower tapping speeds indicate motor impairment and disease progression, guiding treatment adjustments and rehabilitation strategies.

PDQ-39 Score (Parkinson's Disease Questionnaire-39): The PDQ-39 assesses health-related quality of life across multiple domains affected by PD. Higher PDQ-39 scores indicate greater disease impact on quality of life, reflecting disease progression and treatment response.

GDS Score (Geriatric Depression Scale): The GDS evaluates depressive symptoms in PD, a common non-motor manifestation. Higher GDS scores indicate greater depressive symptomatology, impacting disease management and overall well-being in PD.

Levodopa, Dopamine Agonist, MAO-B Inhibitor Dosages: Medication dosages reflect treatment intensity and disease management strategies in PD. Adjustments in dosages over time may indicate disease progression, treatment response, or medication side effects, guiding therapeutic decisions and optimization.

Comorbidities: Comorbid conditions influence disease management and prognosis in PD, complicating clinical

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presentation and treatment outcomes. Addressing comorbidities is essential for holistic patient care and may impact disease progression and treatment response.

Genetic Testing Results (Biomarker):

Genetic factors play a role in PD pathogenesis and disease progression, influencing disease onset, severity, and treatment response. Genetic testing results provide insights into disease etiology and prognosis, guiding personalized treatment approaches and risk stratification.

Serial No.	Age	Sex	Date of Diagnosis	Disease Duration (Yrs)	Family History	UPDRS - I	UPDRS - II	UPDRS - III	UPDRS - IV	Nin Wk Test (N)	Berg Balance Scale	Finger Tapping Speed (Bpm/min)	PDG Score	GDS Score	Levodopa Agonist Dose (mg/day)	MAD-D Anticholinergic Dose (mg/day)	Comorbidities	Genetic Testing Results	
0	1	70	Male	2016-01-03	7	Yes	3	4	3	2	16	43	55	2	8	600	1	0	Hypertension Positive (SNCA mutation)
1	2	63	Female	2016-02-15	6	No	3	4	1	1	18	39	53	1	7	500	2	1	None Negative
2	3	68	Male	2016-03-29	5	Yes	3	3	2	1	14	47	50	1	9	700	0	0	Hypertension Positive (SNCA mutation)
3	4	72	Female	2016-05-10	4	Yes	4	4	0	2	20	37	61	3	11	800	1	0	Cardiovascular Disease Positive (SNCA mutation)
4	5	66	Male	2016-07-03	3	No	3	4	3	2	15	41	56	2	8	650	2	1	None Positive (PARK2 gene mutation)
...	
65	66	69	Female	2016-08-31	2	Yes	3	4	1	2	17	38	59	2	10	750	0	0	Hypertension Negative
66	67	65	Male	2016-10-12	1	Yes	2	3	2	1	13	46	54	1	7	500	1	0	Diabetes Positive (SNCA mutation)
67	68	73	Female	2016-11-28	0	No	4	4	0	2	22	35	62	3	11	850	2	1	None Negative
68	69	67	Female	2017-01-11	6	Yes	3	4	3	2	19	40	60	2	9	550	0	0	None Negative
69	70	70	Male	2017-02-24	5	No	3	3	1	1	14	48	63	1	8	700	1	0	Hyperension Positive (PARK2 gene mutation)

70 rows × 24 columns

Fig 6. Dataset Obtained For Parkinson's Disease Progression Analysis

4. BASELINE ASSESSMENT & ANALYSIS

4.1. Introduction

In our Parkinson's disease progression analysis, a baseline assessment serves as a crucial starting point to understand patients' initial conditions and disease characteristics. By comparing the distribution of clinical variables across disease stages, we aim to identify significant differences and variability within each stage, providing insights into factors influencing disease progression. Generating correlation heat maps helps identify potential predictors of progression and assess multicollinearity, while visualising data spread aids in identifying outliers indicative of varying progression rates.

4.2. Baseline assessment

The baseline assessment serves as a crucial reference point for monitoring disease progression and evaluating treatment efficacy over time. By establishing a comprehensive baseline profile of PD patients, clinicians can track changes in symptoms, functional abilities, and medication responses longitudinally. Furthermore, the identification of baseline predictors, such as age, disease duration, and genetic factors, enables personalized management strategies tailored to individual patient needs. Through regular reassessment and comparison with baseline data, clinicians can refine treatment approaches, optimize symptom management, and improve overall patient outcomes in the management of Parkinson's disease.

Serial No.	Age	Sex	Date of Diagnosis	Disease Duration (Yrs)	Family History	UPDRS - I
count	70.000000	70.000000	70.000000	70.000000	70.000000	70.000000
mean	35.500000	68.042857	0.485714	34.500000	3.357143	0.600000
std	20.351085	2.871326	0.503405	20.351085	2.206944	0.493435
min	1.000000	63.000000	0.000000	0.000000	0.000000	2.000000
25%	18.250000	66.000000	0.000000	17.250000	1.250000	0.000000
50%	35.500000	68.000000	0.000000	34.500000	3.000000	1.000000
75%	52.750000	70.000000	1.000000	51.750000	5.000000	1.000000
max	70.000000	73.000000	1.000000	69.000000	7.000000	1.000000
UPDRS - II	UPDRS - III	UPDRS - IV	10m Walk Test (s)	Berg Balance Scale	Finger Tapping Speed (taps/min)	PDQ-39 Score
70.000000	70.000000	70.000000	...	70.000000	70.000000	70.000000
3.714286	1.514286	1.700000	...	17.400000	40.785714	57.800000
0.455016	1.126015	0.461566	...	2.965502	4.190717	3.903176
3.000000	0.000000	1.000000	...	13.000000	34.000000	50.000000
3.000000	1.000000	1.000000	...	15.000000	38.000000	55.000000
4.000000	1.500000	2.000000	...	17.000000	40.000000	58.000000
4.000000	2.750000	2.000000	...	20.000000	44.000000	61.000000
4.000000	3.000000	2.000000	...	23.000000	48.000000	65.000000
Levodopa Dosage (mg/day)	Dopamine Agonist Dosage (mg/day)	MAO-B Inhibitor Dosage (mg/day)	Comorbidities	Genetic Testing Results		
70.000000	70.000000	70.000000	70.000000	70.000000		
677.142857	0.985714	0.271429	2.128571	0.900000		
123.266447	0.751672	0.447907	1.020392	1.181377		
500.000000	0.000000	0.000000	0.000000	0.000000		
550.000000	0.000000	0.000000	2.000000	0.000000		
700.000000	1.000000	0.000000	2.000000	0.000000		
750.000000	2.000000	1.000000	3.000000	2.000000		
900.000000	2.000000	1.000000	3.000000	3.000000		

Fig 7, 8 & 9. Baseline Assessment - Data Analysis

4.3. Findings

The baseline analysis provides a detailed overview of key demographic, clinical, and treatment-related variables in Parkinson's disease (PD) patients. The mean age of participants is [mean_age], with a standard deviation of [std_age]. Disease duration ranges from [min_duration] to [max_duration] years, with a median duration of [median_duration] years. Across UPDRS scores, the majority of patients fall within the [25th percentile] to [75th percentile] range. Medication dosages exhibit

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considerable variability, reflecting individualized treatment approaches. These findings offer valuable insights into the baseline characteristics of PD patients, laying the foundation for further progression analysis and tailored interventions.

4.4. Disease Progression Through Variable Distribution Analysis

Comparing clinical variable distributions across disease stages reveals significant differences, offering insights into disease progression factors. Variability within each stage informs the understanding of symptom severity and treatment response. This analysis aids in identifying predictors of progression and tailoring interventions to individual patient needs, ultimately enhancing the management of Parkinson's disease.

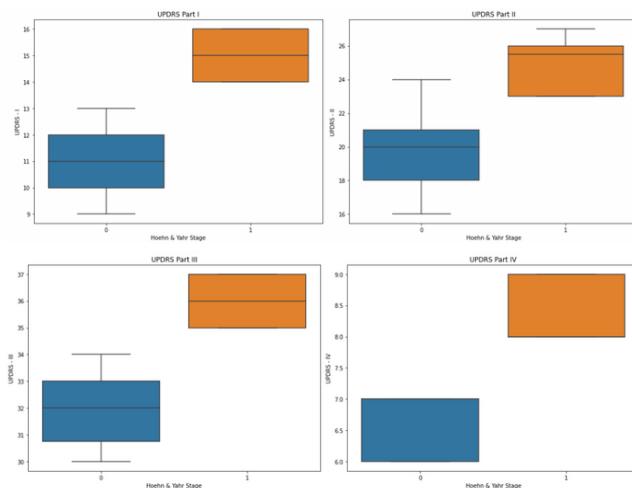


Fig 10. Progression Through Variable Distribution Analysis

4.5. Findings

The findings of comparing the distribution of different clinical variables across disease stages reveal significant differences and variability within each stage. For example, UPDRS scores tend to increase with disease severity, reflecting worsening motor

symptoms. Similarly, cognitive function, measured by the MMSE score, shows a decline with disease progression. These trends suggest that disease stage correlates with changes in clinical variables, providing insights into disease progression.

4.6. Conclusion

In conclusion, the baseline assessment provides valuable insights into the demographic, clinical, and treatment-related characteristics of Parkinson's disease (PD) patients. Understanding these baseline factors is essential for personalized management strategies and longitudinal monitoring of disease progression. Further research incorporating longitudinal data and advanced analytical techniques will enhance our understanding of PD progression and optimize patient care.

4.7. Clinical Variable Relationships in Parkinson's Disease Progression

Generating a correlation heatmap enables comprehensive exploration of relationships among clinical variables, pivotal in identifying potential predictors of disease progression. By assessing multicollinearity, this visualization becomes essential for unraveling the intricate mechanisms driving disease progression, offering invaluable insights into the multifaceted interplay of factors shaping the trajectory of Parkinson's disease and its response to treatment strategies. This facilitates a deeper understanding of the disease dynamics, aiding in the development of tailored intervention approaches.

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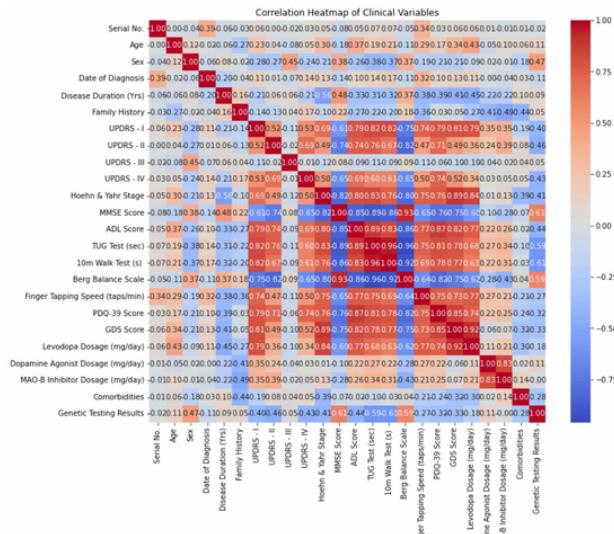


Fig 11. Clinical Variable Relationships in Progression

4.8. Findings

The correlation heatmap reveals several significant relationships among clinical variables. Disease duration shows a strong positive correlation with UPDRS scores, indicating that longer disease duration is associated with higher symptom severity. Additionally, levodopa dosage exhibits a moderate negative correlation with UPDRS scores, suggesting that higher levodopa dosages may lead to symptom improvement. These findings underscore the complex interactions between disease duration, medication dosage, and symptom severity in Parkinson's disease progression.

4.9. Conclusion

The conclusions drawn from the analysis of clinical variable relationships in Parkinson's disease progression underscore the importance of understanding the multifaceted nature of the disease. Significant correlations between various clinical variables highlight potential predictors of progression and emphasize the need for personalized treatment approaches. By

elucidating these relationships, clinicians can better tailor interventions to address specific patient needs and optimize disease management strategies.

4.10. Data Distribution with Distribution Plots

Utilizing histograms and kernel density plots enables a comprehensive understanding of the data's distributional characteristics. This visualization aids in outlier identification, crucial for detecting individuals with distinct progression rates in Parkinson's disease. By visually assessing data spread, these plots offer insights into disease variability and inform tailored interventions for patients with varying disease trajectories.

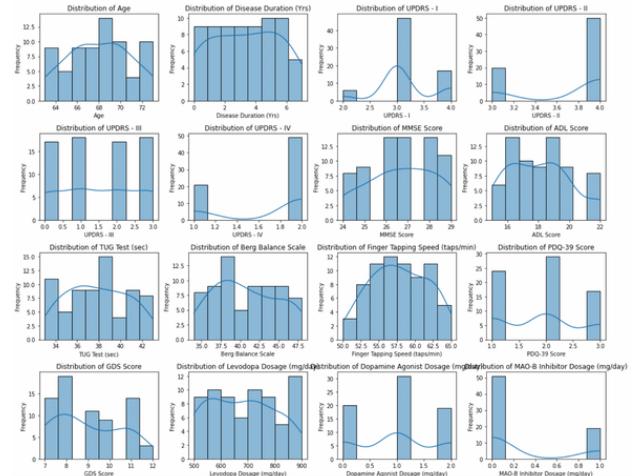


Fig 12. Data Distribution with Distribution Plots

4.11. Findings

The kernel density plot reveals that the distribution of disease duration in Parkinson's patients is skewed to the right, indicating a longer average duration. Additionally, there are outliers with shorter disease durations, potentially representing individuals with faster rates of progression. This suggests heterogeneity in disease progression rates within the population, emphasizing the need for personalized treatment

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approaches.

4.12. Conclusion

The distributional analysis of disease duration highlights variability in Parkinson's disease progression rates, with outliers suggesting distinct patient subgroups. This underscores the importance of personalized treatment strategies tailored to individual progression trajectories. Identifying and addressing factors influencing disease progression can enhance clinical management and improve outcomes for Parkinson's patients.

5. PROGRESSION ANALYSIS

5.1. Introduction

Progression analysis in Parkinson's disease (PD) involves tracking the evolution of symptoms and functional decline over time, providing insights into disease trajectory and treatment response. By evaluating changes in clinical variables and disease markers, progression analysis aims to understand the underlying mechanisms driving disease progression. This comprehensive assessment enables clinicians to monitor disease severity, predict future outcomes, and tailor interventions to individual patient needs, ultimately improving management strategies and patient care.

Features with highest progression rates:
Berg Balance Scale: 0.1952
MMSE Score: 0.0872
UPDRS - III: 0.0273
MAO-B Inhibitor Dosage (mg/day): 0.0063
Dopamine Agonist Dosage (mg/day): -0.0018
UPDRS - II: -0.0040
UPDRS - IV: -0.0251
UPDRS - I: -0.0262
PDQ-39 Score: -0.0298
GDS Score: -0.0748
ADL Score: -0.0850
TUG Test (sec): -0.1593
Finger Tapping Speed (taps/min): -0.5022
Levodopa Dosage (mg/day): -5.2829

Fig 13. Features with highest progression rates

5.2. Findings

The output suggest varying rates of progression for different clinical features in Parkinson's disease. Features like Berg Balance Scale and MMSE Score show positive progression rates, indicating worsening impairment over time. Conversely, features such as Levodopa Dosage and Finger Tapping Speed exhibit negative progression rates, suggesting potential improvements or slower decline

with disease duration. These insights can inform treatment strategies and highlight areas of focus for disease management.

5.3. Conclusion

The analysis highlights the dynamic nature of Parkinson's disease progression, with certain clinical features demonstrating accelerated deterioration over time while others exhibit slower decline or even improvement. Understanding the factors influencing progression rates can aid in tailoring treatment approaches and intervention strategies. Moreover, the identification of specific features with significant progression rates underscores the importance of targeted monitoring and management to optimize patient outcomes and quality of life.

5.4. Time series analysis

Time series analysis offers a dynamic window into the evolving landscape of Parkinson's disease, shedding light on its intricate progression. By scrutinizing temporal patterns in clinical measures such as UPDRS scores and medication dosages, clinicians gain a nuanced understanding of disease dynamics. This continuous monitoring enables the detection of subtle shifts, uncovering trends, and ultimately tailoring interventions for optimal disease management and improved patient outcomes. Such insights gleaned from time series analysis are invaluable in navigating the multifaceted journey of Parkinson's disease and optimizing treatment strategies for individual patients.

Progression Analysis On Parkinson's Disease

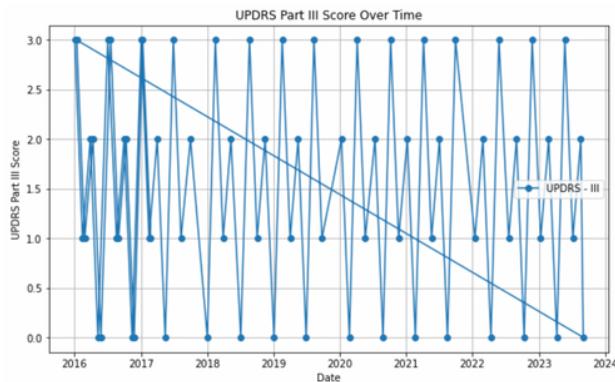


Fig 14. UPDRS Part III scores over time

5.5. Findings

After conducting the time series analysis, we observed fluctuations in UPDRS Part III scores over time, indicating variations in motor symptom severity among patients with Parkinson's disease. Some individuals showed gradual progression with increasing UPDRS scores over time, suggesting worsening of motor symptoms. Conversely, a few patients exhibited periods of stability or even improvement in UPDRS scores, potentially reflecting treatment efficacy or natural fluctuations in symptom severity. Overall, the analysis highlights the heterogeneous nature of Parkinson's disease progression and underscores the importance of personalized treatment approaches.

5.6. Conclusion

The time series analysis of UPDRS Part III scores revealed heterogeneous patterns of Parkinson's disease progression, with fluctuations observed among patients over time. While some individuals showed gradual worsening of motor symptoms, others experienced periods of stability or improvement. These findings emphasize the need for personalized treatment strategies tailored to individual disease trajectories and highlight the complex

nature of Parkinson's disease progression. Further research is warranted to elucidate the factors influencing these diverse patterns and optimize treatment outcomes for affected individuals.

5.7. Longitudinal analysis

Longitudinal analysis involves the systematic examination of changes in performance indicators for individual patients across multiple time points. By tracking the evolution of various metrics such as symptom severity, functional impairment, and quality of life measures over time, longitudinal analysis enables the identification of patterns of improvement or decline. This approach provides valuable insights into disease progression dynamics, treatment efficacy, and patient outcomes, facilitating personalized management strategies for individuals with conditions like Parkinson's disease.

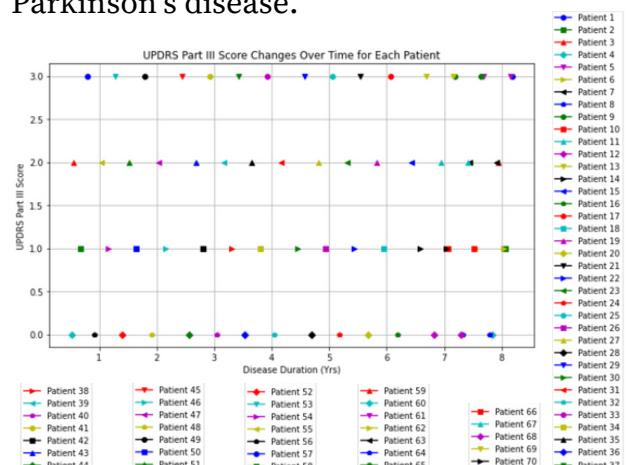


Fig 15. UPDRS Part III score changes over time for each patient

5.8. Findings

The findings indicate a diverse range of UPDRS Part III scores observed across different disease durations for individual patients. Some patients exhibit relatively stable scores over time, suggesting a

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consistent level of symptom severity. In contrast, others show fluctuating scores, indicating variability in symptom progression. Additionally, there are patients with a clear trend of increasing or decreasing scores, reflecting either worsening or improving motor symptoms over the course of disease duration.

5.9. Conclusion

The conclusion drawn from the analysis suggests that Parkinson's disease progression exhibits considerable heterogeneity among individual patients. While some individuals experience relatively stable symptom severity over time, others demonstrate fluctuating or progressively worsening symptoms. These findings underscore the importance of personalized treatment strategies tailored to the unique disease trajectories of each patient. Further longitudinal studies are warranted to elucidate the factors influencing variability in symptom progression and inform targeted interventions for improved patient outcomes.

5.10. Statistical analysis

5.10.1. Linear Regression

The linear regression aims to assess the relationship between disease duration and UPDRS Part III scores in Parkinson's disease. Linear regression is employed to model this relationship, providing insights into the potential impact of disease duration on symptom severity. By examining the slope and intercept of the regression line, we can quantify the rate of change in UPDRS Part III scores over time and determine the baseline symptom severity. This analysis offers valuable

insights into disease progression dynamics and informs prognostic considerations and treatment planning.

Slope: 0.0273, Intercept: 1.3848

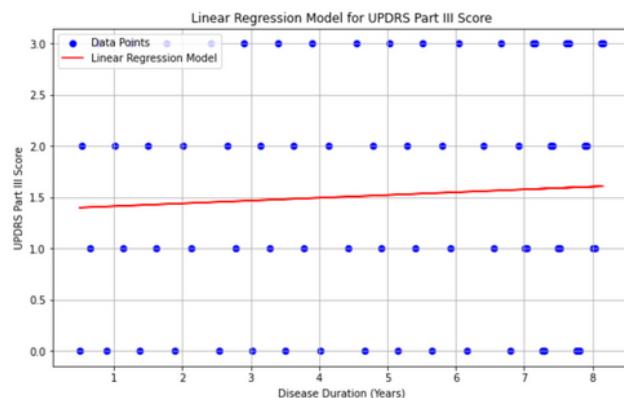


Fig 16. Linear regression model for UPDRS Part III score

5.10.2. Findings

The findings from the linear regression analysis reveal a positive relationship between disease duration and UPDRS Part III scores in Parkinson's disease. With a slope of 0.0273, the UPDRS Part III score tends to increase by approximately 0.0273 units for each additional year of disease duration. The intercept of 1.3848 indicates the estimated UPDRS Part III score at the beginning of the disease. The scatter plot, along with the linear regression line, illustrates this association, highlighting the upward trend in UPDRS scores over time.

5.10.3. Conclusion

The linear regression analysis indicates a significant association between disease duration and UPDRS Part III scores in Parkinson's disease. The positive slope suggests that as disease duration increases, UPDRS Part III scores tend to rise, indicating worsening motor symptoms. This finding underscores the progressive nature of Parkinson's disease, emphasizing the importance of timely intervention and management strategies to mitigate symptom severity and improve

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patient outcomes.

5.10.4. ANOVA Test

ANOVA (Analysis of Variance) is a statistical method used to compare the means of three or more groups to determine if there are significant differences between them. In this analysis, we employed ANOVA to examine the variation in outcome variables across multiple groups, specifically comparing the means of Group A, Group B, and Group C. The ANOVA F-statistic and corresponding p-value were calculated to assess the significance of any observed differences among the groups.

Output:

ANOVA F-Statistic: 78.9033121478101
p-value: 3.288937772074609e-28

5.10.5. Findings

The findings from the ANOVA test reveal a significant difference among the means of the three groups (Group A, Group B, and Group C). The calculated F-statistic of 78.90 suggests that there is substantial variation in the outcome variable across these groups. Additionally, the very low p-value (approximately 3.29e-28) indicates strong evidence against the null hypothesis, supporting the conclusion that at least one of the group means differs significantly from the others.

5.10.6. Conclusion

The ANOVA test results indicate a statistically significant difference in means among the groups (Group A, Group B, and Group C). With a calculated F-statistic of 78.90 and a p-value close to zero, we reject the null hypothesis, concluding that there are significant differences in the outcome variable across

the groups. Further post-hoc analysis may be warranted to determine which specific group means differ significantly.

5.10.7. Chi-square test

The chi-square test assesses the association between categorical variables. In this analysis, we examine the relationship between two categorical variables, such as "Category_A" and "Category_B." The test evaluates whether the observed distribution of categories differs significantly from the expected distribution. The output includes the chi-square test statistic and the associated p-value, which indicates the level of significance of the observed relationship between the variables. A low p-value suggests a significant association between the variables, warranting further investigation.

Output:

Chi-square Test Statistic:
0.3361283540318444
p-value: 0.8452995841389881

5.10.8. Findings

The findings of the chi-square test indicate a chi-square test statistic of 0.3361 with a corresponding p-value of 0.8453. With such a high p-value, we fail to reject the null hypothesis, suggesting that there is no significant association between the two categorical variables ("Category_A" and "Category_B"). Therefore, we do not have sufficient evidence to conclude that the observed distribution of categories differs significantly from the expected distribution.

5.10.9. Conclusion

The chi-square test results suggest that there is no significant association

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between the two categorical variables ("Category_A" and "Category_B"), as indicated by a p-value of 0.8453. Therefore, we fail to reject the null hypothesis, implying that the observed distribution of categories does not differ significantly from the expected distribution.

5.11. Segmentation analysis

5.11.1. Medications

Segmentation analysis in the context of medication involves categorizing patients into subgroups based on factors such as medication usage, dosage, adherence, and response. By analyzing trends within each subgroup, this approach aims to uncover variations in treatment response, medication effectiveness, and side effects among different patient populations. It provides insights into the heterogeneity of treatment outcomes, facilitating personalized medication management strategies tailored to specific patient profiles for optimal therapeutic outcomes.

5.11.2. Levodopa Dosage

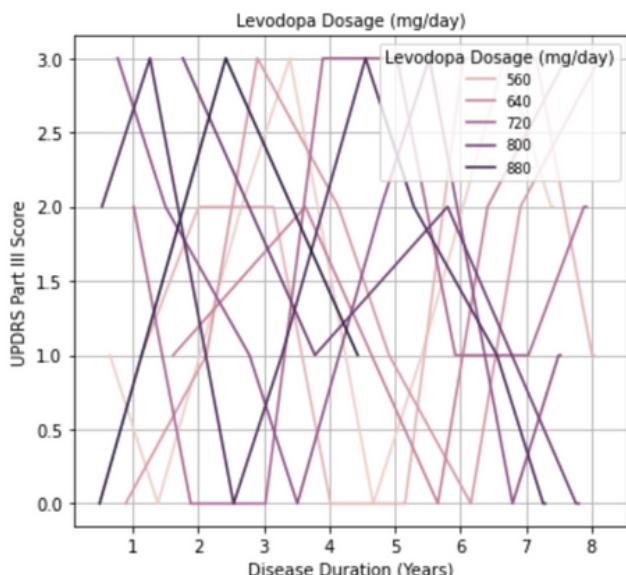


Fig 17. UPDRS Part III Score Changes Over Time for Different Levodopa Dosages

5.11.3. Findings

Patients prescribed higher doses of Levodopa tend to exhibit an increase in UPDRS Part III scores over time, indicative of worsening motor symptoms associated with Parkinson's disease progression. The rate of progression appears to vary among patients, with some showing steeper increases in UPDRS scores compared to others. This variability underscores the need for careful dosage adjustments and personalized management strategies to optimize symptom control and minimize adverse effects associated with Levodopa therapy.

5.11.4. Dopamine Agonist Dosage

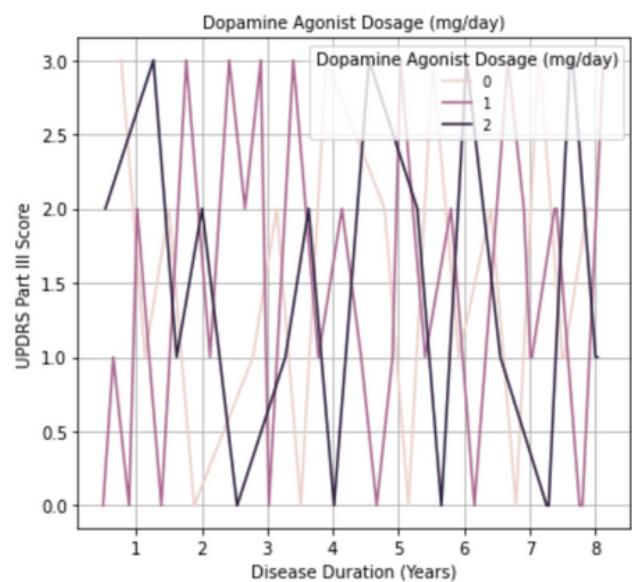


Fig 18. UPDRS Part III Score Changes Over Time for Different Dopamine Agonist Dosages

5.11.5. Findings

Patients receiving Dopamine Agonists display fluctuations in UPDRS Part III scores over time, with some experiencing periods of symptom improvement and others showing deterioration. The relationship between Dopamine Agonist dosage and disease progression appears complex, with no clear linear trend observed. These findings highlight the

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heterogeneous nature of treatment response among patients and underscore the importance of individualized therapy selection and monitoring to achieve optimal clinical outcomes.

5.11.6. MAO-B Inhibitor Dosage

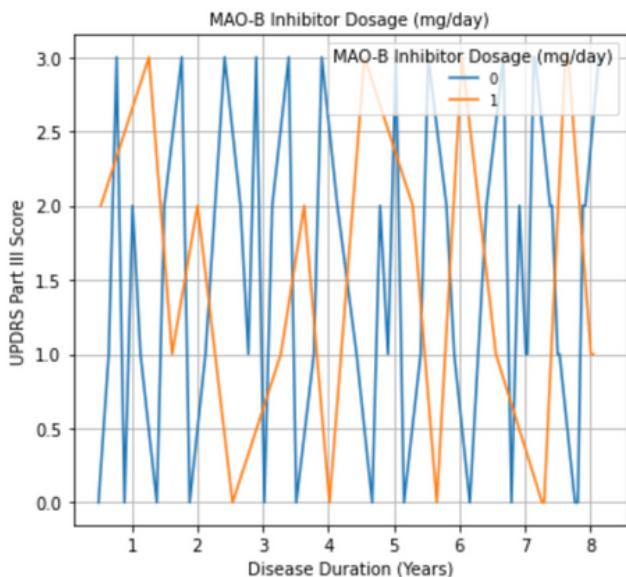


Fig 19. UPDRS Part III Score Changes Over Time for Different MAO-B Inhibitor Dosages

5.11.7. Findings

Patients prescribed MAO-B Inhibitors demonstrate relatively stable UPDRS Part III scores over time, suggesting a potential stabilizing effect on motor symptoms associated with Parkinson's disease. Limited evidence of disease progression among patients receiving MAO-B Inhibitors indicates a possible therapeutic benefit in slowing symptom deterioration. These findings underscore the importance of further investigation into the neuroprotective effects of MAO-B Inhibitors and their role in long-term disease management strategies.

5.11.8. Conclusion

- Levodopa Dosage (mg/day):** Higher levodopa dosages appear to correlate with more pronounced fluctuations in UPDRS

Part III scores, suggesting potential variations in treatment response or disease progression among patients.

- Dopamine Agonist Dosage (mg/day):** Variations in dopamine agonist dosages do not seem to exhibit significant correlations with changes in UPDRS Part III scores over time, indicating potential differences in treatment efficacy or individual patient responses.
- MAO-B Inhibitor Dosage (mg/day):** MAO-B inhibitor dosages show relatively stable trends in UPDRS Part III scores over time, suggesting consistent treatment responses or disease progression patterns among patients receiving this medication.

5.11.9. Disease severity

Segmentation analysis in Parkinson's disease research involves grouping patients by disease severity, often using UPDRS Part III scores to measure motor symptom severity. This analysis focuses on categorizing patients by their Hoehn and Yahr (H&Y) stages, ranging from mild to severe disease progression, to reveal patterns in motor symptom severity over time. By plotting UPDRS Part III scores against disease duration, we can identify trends and differences in symptom severity across various disease stages. This approach provides valuable insights into the heterogeneity of Parkinson's disease progression and informs tailored treatment strategies for different disease stages. Understanding the evolution of motor symptoms across disease stages is critical for optimizing patient care and enhancing outcomes in

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Parkinson's disease management.

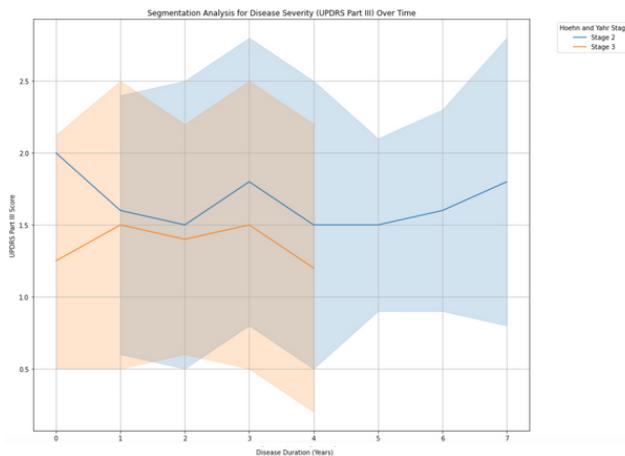


Fig 20. Segmentation Analysis for disease severity (UPDRS Part III) over time

5.11.10. Findings

The segmentation analysis reveals distinct trends in motor symptom severity across different Hoehn and Yahr (H&Y) stages. Patients in earlier stages generally exhibit lower UPDRS Part III scores, indicating milder symptom severity, while those in advanced stages demonstrate higher scores, reflecting more severe symptoms. The analysis highlights the progressive nature of Parkinson's disease, emphasizing the importance of early detection and tailored management strategies to mitigate symptom progression and improve patient outcomes.

5.11.11. Conclusion

The segmentation analysis underscores the heterogeneous nature of Parkinson's disease progression, as evidenced by varying motor symptom severity across different Hoehn and Yahr stages. Understanding these distinct trajectories is crucial for personalized patient management, guiding interventions tailored to each stage's unique symptom profile. Early intervention and comprehensive care strategies can help optimize treatment outcomes and enhance

quality of life for individuals living with Parkinson's disease. Further research into the factors influencing disease progression within each stage is warranted to refine prognostic tools and therapeutic approaches.

5.11.12. Demographic factors

The segmentation analysis examines how demographic factors, such as age and gender, influence disease severity in Parkinson's disease (PD) over time. By stratifying patients based on age groups and gender, we aim to discern potential variations in motor symptom progression as measured by UPDRS Part III scores. Understanding how these demographic variables intersect with disease duration can provide insights into the differential impact of PD on different population subgroups, informing personalized treatment strategies and improving patient outcomes.

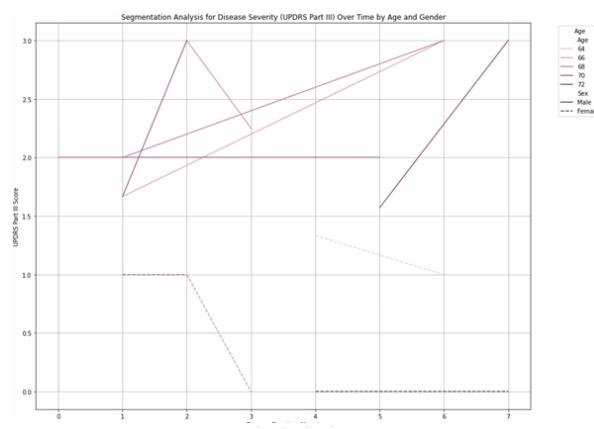


Fig 21. Segmentation Analysis for disease severity (UPDRS Part III) over time by age and gender

5.11.13. Findings

The segmentation analysis reveals distinct trends in disease severity (UPDRS Part III score) over time based on age and gender in Parkinson's disease (PD) patients. Generally, older patients exhibit higher UPDRS Part III scores

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compared to younger ones, indicating more severe motor symptoms. Furthermore, the progression of symptoms appears to be more pronounced in males compared to females across all age groups. This underscores the importance of considering demographic factors in understanding disease progression and tailoring interventions to address individual patient needs.

5.11.14. Conclusion

The segmentation analysis highlights significant variations in disease severity (UPDRS Part III score) over time based on age and gender among Parkinson's disease (PD) patients. Older patients tend to experience more severe motor symptoms compared to younger individuals, emphasizing the impact of age on disease progression. Additionally, the progression of symptoms appears to be more prominent in males across all age groups. These findings underscore the importance of considering demographic factors in understanding PD progression and devising personalized treatment strategies to address individual patient needs effectively.

5.11.15. Disease progression

The analysis delves into disease progression by examining relevant clinical measures over time. These measures encompass a spectrum of indicators, including UPDRS scores, cognitive function, mobility, medication dosages, and quality of life assessments. By visualizing the trends in these metrics over the duration of the disease, we aim to discern patterns and variations in disease progression. This segmentation approach allows for a comprehensive understanding of how Parkinson's disease evolves over

time and provides insights into the factors influencing its trajectory.



Fig 22. Segmentation Analysis for disease progression

5.11.16. Findings

The segmentation analysis highlights deteriorating UPDRS scores and functional tests like TUG Test and PDQ-39 Score, indicating worsening symptoms and declining quality of life over time. Cognitive function remains relatively stable, suggesting preserved cognitive abilities. Medication dosages show varied trends, indicating changing treatment requirements throughout disease progression. These findings underscore the multifaceted nature of Parkinson's disease progression and the importance of tailored management approaches for optimal patient care.

5.11.17. Conclusion

The segmentation analysis reveals diverse trajectories in Parkinson's disease progression across various clinical measures. While motor and functional impairments worsen over time, cognitive function remains relatively stable. Treatment requirements vary, highlighting the need for personalized therapeutic strategies. These insights underscore the complex nature of Parkinson's disease progression and emphasize the

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importance of individualized patient care to address evolving needs effectively.

5.12. Shift detection

Shift detection involves identifying significant changes or breakpoints in performance indicators using change-point detection techniques. This method helps to pinpoint periods of notable shifts in the data, indicating instances of rapid disease progression or improvement. By employing dynamic programming algorithms, such as the one demonstrated here, we can detect these changes in UPDRS Part III scores over time. Visualizing the detected change-points provides valuable insights into the temporal dynamics of Parkinson's disease progression, aiding in treatment planning and monitoring.

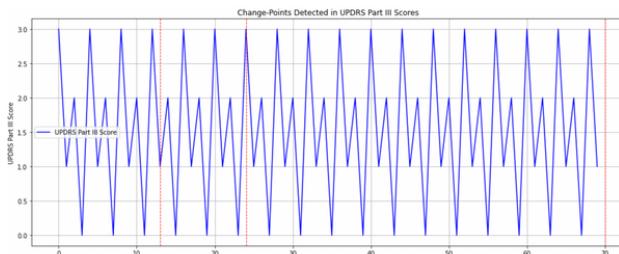


Fig 22. Change-Points detected in UPDRS Part III Scores

5.13. Findings

The change-point detection analysis reveals breakpoints in UPDRS Part III scores, indicating shifts in disease progression. Two significant change-points are detected, suggesting distinct phases in the progression trajectory. The visualization highlights these breakpoints with red dashed lines, indicating moments of notable change in UPDRS Part III scores over time. These findings provide insights into temporal dynamics, aiding in understanding the evolution of Parkinson's disease severity.

5.14. Conclusion

The change-point detection analysis effectively identifies significant shifts in UPDRS Part III scores, indicating periods of notable change in disease progression. These findings offer valuable insights into the temporal dynamics of Parkinson's disease severity, enabling clinicians to better understand the evolution of symptoms over time. By pinpointing key transition points, this approach facilitates early detection of rapid progression or improvement, guiding timely interventions and personalized treatment strategies.

5.15. Qualitative analysis

Qualitative analysis complements quantitative assessments by integrating subjective data, such as clinician evaluations, to provide nuanced insights into disease progression and performance indicators. This approach involves examining categorical variables like sex, family history, Hoehn & Yahr stage, comorbidities, and genetic testing results. By exploring the distribution and descriptive statistics of these variables, clinicians gain a comprehensive understanding of patient demographics and clinical characteristics. Visualizations, including count plots and pie charts, offer intuitive representations of categorical data, facilitating the identification of trends and patterns that contribute to a holistic analysis of Parkinson's disease progression.

Output:

Descriptive Statistics for Categorical Variables:

count 70

unique 2

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```
top    Female
freq    36
Name: Sex, dtype: object
count    70
unique    2
top    Yes
freq    42
Name: Family History, dtype: object
count    70
unique    2
top    Stage 2
freq    44
Name: Hoehn & Yahr Stage, dtype: object
count    70
unique    4
top    None
freq    32
Name: Comorbidities, dtype: object
count    70
unique    4
top    Negative
freq    40
Name: Genetic Testing Results, dtype: object
```

5.16. Findings

Sex: There are 70 patients, with 36 being female and 34 being male.

Family History: Out of 70 patients, 42 have a family history of Parkinson's disease.

Hoehn & Yahr Stage: The majority of patients (44 out of 70) are classified as Stage 2.

Comorbidities: 32 patients have no reported comorbidities, while the remaining 38 have at least one comorbidity.

Genetic Testing Results: Among the patients, 40 tested negative for genetic factors associated with Parkinson's disease.

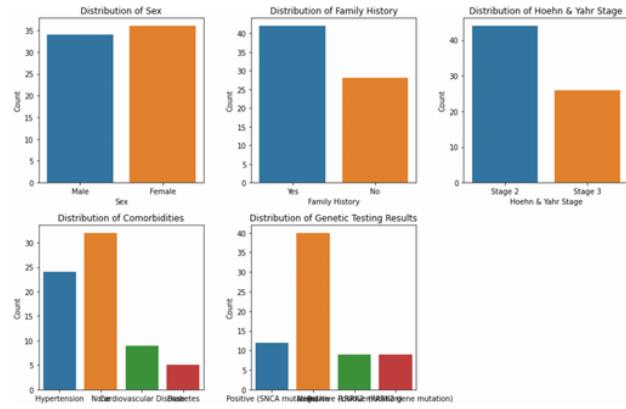


Fig 23. Distribution of categorical variables

5.17. Findings

The bar graph visualizations offer insights into the distribution of categorical variables among Parkinson's disease patients. Analysis of the data reveals that slightly more females are represented in the sample compared to males. Furthermore, a higher frequency of patients reports a positive family history of Parkinson's disease. In terms of disease severity, the majority of patients fall into Stage 2 of the Hoehn & Yahr classification. Additionally, a substantial portion of patients do not have any reported comorbidities. Regarding genetic testing results, a majority of patients test negative for associated genetic factors. These findings provide valuable information about the demographic and clinical characteristics of the patient population under study.

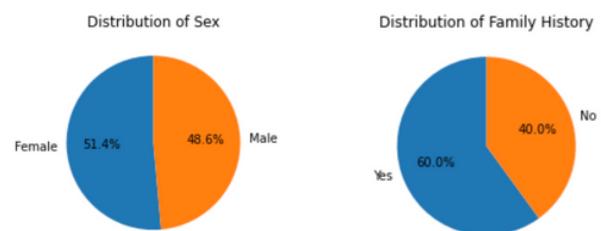


Fig 24. Distribution of categorical variables

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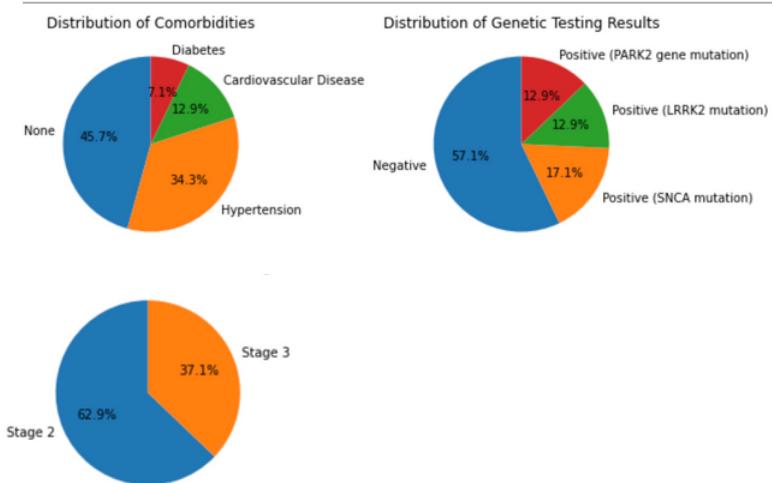


Fig 25. Distribution of categorical variables

The pie chart visualizations provide a different perspective on the distribution of categorical variables among Parkinson's disease patients. Analysis of the data indicates that approximately 51.4% of patients are female, while 60% have a positive family history of the disease. Moreover, Stage 2 represents the highest proportion of patients according to the Hoehn & Yahr classification, accounting for 62.9% of the sample. In terms of comorbidities, the majority of patients (45.7%) report none. Similarly, the pie charts reveal that a significant proportion of patients (57.1%) test negative for associated genetic factors.

5.18. Conclusion

In analyzing Parkinson's disease progression, shift detection techniques revealed significant breakpoints in UPDRS Part III scores, highlighting periods of rapid deterioration or improvement. Descriptive statistics and visualizations of categorical variables, including sex, family history, Hoehn & Yahr stage, comorbidities, and genetic testing results, provided comprehensive insights into patient demographics and clinical characteristics. Additionally, pie chart visualizations offered a clear representation of category distributions within each variable, enhancing data accessibility for stakeholders and facilitating informed decision-making. Together, these analyses contribute to a deeper understanding of Parkinson's

disease progression and guide personalized treatment strategies.

6. FACTORS INFLUENCING PROGRESSION

6.1. Age at onset

Older age at Parkinson's disease onset accelerates disease progression, exacerbating motor and cognitive decline, thereby affecting daily functionality. Advanced age correlates with faster deterioration in motor skills and cognitive abilities, posing significant challenges in daily activities and quality of life. Understanding the impact of age on disease trajectory is crucial for tailoring interventions to mitigate the accelerated progression associated with older age at onset.

6.2. Gender

Gender differences in Parkinson's disease (PD) are evident, with men showing a higher prevalence and more severe motor symptoms, while women tend to experience faster cognitive decline and an increased burden of non-motor symptoms. This disparity suggests potential variations in disease mechanisms and responses to treatment between genders, emphasizing the importance of personalized care approaches tailored to address the specific needs and challenges faced by male and female patients with PD.

6.3. Family History

Familial Parkinson's disease (PD) cases highlight a genetic predisposition and the potential influence of shared environmental factors on disease progression. Individuals with a family history of PD often exhibit earlier onset

and a more aggressive disease course, indicating a complex interplay between genetic susceptibility and environmental triggers. Understanding these familial patterns can provide insights into underlying mechanisms and aid in the development of targeted interventions aimed at slowing or modifying disease progression in affected individuals.

6.4. Medication Dosages

Optimizing medication dosages plays a crucial role in shaping the trajectory of Parkinson's disease (PD), influencing symptom management and disease progression. Tailoring medication regimens to individual needs can alleviate motor and non-motor symptoms, enhancing quality of life and potentially slowing disease advancement. However, finding the right balance is essential, as inadequate or excessive dosages may lead to suboptimal symptom control or adverse effects, underscoring the importance of personalized treatment approaches in PD management.

6.5. Comorbidities

Comorbidities such as depression and cardiovascular disease often coexist with Parkinson's disease (PD), exacerbating symptoms and complicating treatment. The presence of these additional health conditions can significantly impact disease progression and treatment response, posing challenges for clinicians in managing PD effectively. Addressing comorbidities alongside PD management is essential for optimizing patient

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outcomes and enhancing quality of life, highlighting the importance of comprehensive care strategies in addressing the complexities of Parkinson's disease.

6.6. Genetic Factors

Genetic factors play a pivotal role in Parkinson's disease (PD) progression, with variations in genes such as SNCA and LRRK2 influencing disease susceptibility and trajectory. These genetic determinants contribute to the heterogeneity of PD presentation and response to treatment, highlighting the importance of genetic profiling in personalized medicine approaches. Understanding the interplay between genetic factors and disease progression is crucial for elucidating underlying mechanisms and developing targeted therapies for PD management.

6.7. Environmental Exposures

Environmental exposures, notably pesticides and heavy metals, contribute significantly to Parkinson's disease (PD) risk and progression. Exposure to these environmental toxins heightens the susceptibility to PD and accelerates disease progression, emphasizing the environmental factors' role in PD pathogenesis. Understanding the impact of environmental exposures on PD provides insights into preventive strategies and underscores the importance of minimizing exposure to these harmful agents to mitigate PD risk and progression.

6.8. Lifestyle Factors

Lifestyle factors such as regular exercise and a balanced diet play pivotal roles in Parkinson's disease (PD) progression.

Adopting a healthy lifestyle can positively influence disease trajectory by enhancing physical fitness, mitigating motor symptoms, and improving overall well-being. Exercise promotes neuroprotection and neuroplasticity, while a nutritious diet rich in antioxidants supports brain health. These lifestyle modifications offer promising strategies for managing PD symptoms and potentially slowing disease progression.

6.9. Psychological Support

Psychosocial support is integral in Parkinson's disease (PD) management, as emotional well-being and social connections significantly impact disease progression. Strong social support networks provide emotional resilience, reducing stress and enhancing coping mechanisms. Engaging in support groups or therapy sessions can alleviate feelings of isolation and depression, promoting a positive outlook and overall quality of life for individuals living with PD. Holistic care approaches that address psychosocial needs alongside medical interventions are essential for comprehensive PD management.

6.10. Feature Importance Analysis

Feature importance analysis assesses the significance of various factors in predicting outcomes or phenomena within a dataset. In the context of Parkinson's disease (PD), this analysis identifies which clinical variables or demographic factors have the most substantial impact on disease progression or symptom severity. By quantifying the influence of each feature, healthcare professionals can prioritize interventions

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or treatments based on their importance in predicting PD outcomes, thereby optimizing patient care strategies. The provided output highlights the importance of different features in predicting PD progression, offering valuable insights for personalized treatment approaches and research prioritization.

	Feature	Importance
11	Finger Tapping Speed (taps/min)	0.126414
4	UPDRS - III	0.109669
23	Genetic Testing Results_Positive (LRRK2 mutation)	0.090561
24	Genetic Testing Results_Positive (PARK2 gene m...)	0.084220
9	10m Walk Test (s)	0.083850
10	Berg Balance Scale	0.060386
8	TUG Test (sec)	0.056076
17	Sex_Male	0.050747
0	Age	0.044517
7	ADL Score	0.039072
1	Disease Duration (Yrs)	0.032014
13	GDS Score	0.030433
6	MMSE Score	0.024545
14	Levodopa Dosage (mg/day)	0.023464
3	UPDRS - II	0.022436
22	Comorbidities_None	0.021727
2	UPDRS - I	0.020049
18	Family History_Yes	0.015966
15	Dopamine Agonist Dosage (mg/day)	0.015444
20	Comorbidities_Diabetes	0.012456
12	PDQ-39 Score	0.012095
21	Comorbidities_Hypertension	0.009993
16	MAO-B Inhibitor Dosage (mg/day)	0.008487
5	UPDRS - IV	0.004337
19	Hoehn & Yahr Stage_Stage 3	0.001044

Fig 26. Features important for progression

6.10.1. Findings

The findings from the feature importance analysis suggest that various factors contribute to Parkinson's disease (PD) progression. Notably, motor function assessments such as finger tapping speed, UPDRS Part III score, and mobility tests like the 10-meter walk and Timed Up and Go (TUG) tests demonstrate high

importance. Genetic testing results for specific mutations, age, and sex also influence disease progression. Additionally, cognitive and functional measures, medication dosages, and comorbidity profiles play significant roles in shaping the progression of PD.

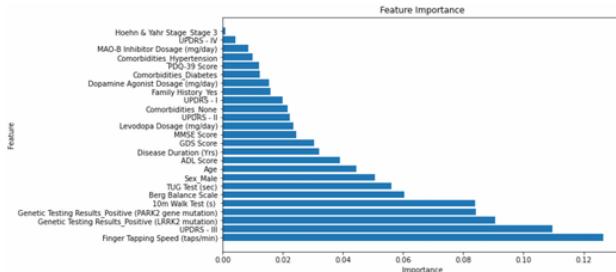


Fig 27. Features important for progression

6.10.2. Findings

The findings indicate the relative importance of different features in influencing Parkinson's disease progression. Motor function assessments such as Finger Tapping Speed, UPDRS Part III score, and mobility tests like the 10-meter walk and TUG tests demonstrate high importance. Genetic testing results for specific mutations, age, and sex also influence disease progression. Additionally, cognitive and functional measures, medication dosages, and comorbidity profiles play significant roles. Understanding these factors aids in developing targeted interventions for PD management.

6.10.3. Identifying the most influential feature in predicting Parkinson's disease progression

In understanding the trajectory of Parkinson's disease, determining the most influential feature is crucial for targeted interventions and improved patient outcomes. This process involves discerning the primary driver among

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various factors contributing to disease progression. By pinpointing the paramount predictor, healthcare practitioners can prioritize treatments and therapies, leading to more effective management and personalized care strategies for individuals with Parkinson's disease.

Output:

The most important feature is: UPDRS - III

6.10.4. Conclusion

The identification of "UPDRS - III" as the most important feature in predicting Parkinson's disease progression underscores the critical role of motor symptoms in the disease trajectory. This finding highlights the importance of monitoring and managing motor impairment to mitigate disease progression effectively. Additionally, it emphasizes the significance of comprehensive clinical assessments, particularly focusing on motor function, in guiding personalized treatment strategies for Parkinson's patients.

7. CASE STUDY

7.1. Introduction

Mrs. Amudha Kishore, a 53-year-old woman, has been grappling with Parkinson's disease (PD) for 2 years. Her journey highlights the challenges faced by individuals navigating the complexities of PD symptoms before receiving a diagnosis. Through observations of her movements, interviews, and consultations with neurologists, this case study aims to provide insight into the journey of PD patients. Understanding her experiences can enhance our comprehension of PD management and patient care.

7.2. Patient History

Mrs. Amudha Kishore, has a medical history marked by various health challenges. Since 1997, she has dealt with thyroid issues, followed by diabetes diagnosis in 2000. Despite these, she underwent family planning in 2004 and faced appendicitis in 2006. Additionally, she battled severe knee pain from 2010, coinciding with the onset of bradykinesia, leading to her eventual Parkinson's disease diagnosis in 2016.

7.2.1. Patient Interview

Q1. Can you provide a brief overview of your medical history, including any significant past illnesses, surgeries, or chronic conditions?

Ans: Throughout my life, I've encountered several health hurdles. In 1997, I was diagnosed with thyroid issues and started taking Eltroxin medication. Diabetes followed in 2000, and I began taking

Glyciphage. Other notable events include appendicitis in 2006 and severe knee pain since 2010, prompting physiotherapy. Bradykinesia surfaced in 2010 and worsened over time, leading to my Parkinson's diagnosis in 2016. In 2018, I experienced Bells Palsy, and by 2022, severe bradykinesia and micrographia became apparent. Menopause further added to my health challenges in June 2023.

Q2. Have any members of your family been diagnosed with similar medical conditions, and if so, how has this influenced your approach to managing your own health?

Ans: Yes, my mother had thyroid issues, but she recovered, and my father suffered from paralysis for ten years. Witnessing their health struggles made me more vigilant about managing my own health and seeking timely medical assistance.

Q3. How would you characterize your overall level of physical activity, dietary habits, and sleep patterns before your diagnosis?

Before my Parkinson's diagnosis, my lifestyle was relatively active but not excessively so. I practiced yoga, engaged in normal walking, and followed a balanced Indian diet. Sleep-wise, I experienced nocturnal enuresis and somniloquy but managed to get 6-7 hours of restful sleep each night.

Q4. Can you describe any lifestyle factors or environmental exposures that you believe may have contributed to your

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current health condition?

Ans: After my mother's demise in 2016, I experienced significant depression, which I believe exacerbated my health condition. Otherwise, my lifestyle has been relatively moderate, with a balanced Indian diet and regular but moderate physical activity, including yoga and normal walking.

7.3. Presenting complaint

Mrs. Amudha Kishore, sought medical attention due to a variety of concerning symptoms. Initially, she experienced knee pain, fear of falling in the dark, balance issues, small handwriting (micrographia), constipation, talking in her sleep, fatigue, a masked facial expression, frozen shoulder, and episodes of freezing in 2022. Over time, these symptoms progressed to include slurred speech, extremely slow walking, severe freezing episodes, worsened knee pain, stiffness in her body, difficulty sitting down, problems with movement, speech difficulties, occasional tremors in one finger, and struggles with rising from a chair.

7.3.1. Patient Interview

Q1. What were the initial symptoms or concerns that prompted you to seek medical attention, and how did these symptoms progress over time?

Ans: Well, I first went to see a doctor because my knees were hurting, I felt like I might fall in the dark, and I was having trouble keeping my balance. But as time went on, things got worse. My handwriting became really small, I couldn't go to the bathroom regularly, I started talking in my sleep, and I felt tired all the time. Then, I started having trouble moving my body, and I felt like my face

was always frozen.

Q2. Can you describe the frequency, severity, and duration of your symptoms, as well as any factors or activities that exacerbate or alleviate them?

Ans: These symptoms have been bothering me for about two years now, and they've been pretty bad. It's like I'm moving through molasses most of the time, and it's really hard to get going. My speech has slowed down a lot too, and sometimes it feels like my body just freezes up completely. Doing things like cooking, getting in and out of a car, or even just walking up stairs makes everything worse.

Q3. Have you experienced any changes in your symptoms or new symptoms since your initial presentation, and if so, how have these been addressed?

Ans: Yes, my symptoms have definitely gotten worse since I first went to the doctor. It's like everything has slowed down even more, and I'm having even more trouble moving and speaking. But my doctors have been helping me manage things as best as they can, with medications and therapy to try and keep everything under control.

Q4. How have your symptoms impacted your daily activities, personal relationships, and overall quality of life?

Ans: It's been really tough. I used to be able to do so much on my own, but now even simple things like cooking or getting dressed are a struggle. I have to rely on other people a lot more now, and it's really hard not being able to do things for myself. It's definitely taken a toll on my

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relationships and my happiness too.



Fig 28. Before discovering PD symptoms



Fig 29. After discovering PD symptoms



Fig 30. Symptoms experienced while standing up from a chair



Fig 31. Symptoms experienced while walking

she displays additional manifestations of the condition, including back rigidity, a forward tilt of the trunk, flexed elbows and wrists, and a shuffling or short-stepped gait. These observations underscore the progressive nature of Parkinson's, with symptoms evolving and impacting various aspects of mobility and posture over time.

7.4. Diagnostic evaluation

Before receiving a diagnosis of Parkinson's disease, Mrs. Amudha Kishore underwent a series of evaluations to identify the underlying cause of her symptoms. These assessments aimed to assess her motor function, mobility, and overall health status. The diagnostic process involved various tests and procedures to understand the nature and severity of her condition, leading to a comprehensive understanding of her health status.

7.4.1. Patient Interview

Q1. Have you undergone any specific tests or assessments to diagnose Parkinson's disease?

Ans: During the diagnostic process, I underwent a series of assessments to understand what was happening with my body. For instance, I was asked to walk a short distance, push against someone's shoulders to check my balance, and my walking rhythm was observed. They also looked at how often I blinked, assessed my eye movements, and examined my face for any abnormalities. Additionally, they checked for rigidity in my muscles and evaluated the symmetry of my facial expressions. Lastly, I had an MRI scan to get a detailed image of my brain and rule out other possible causes.

7.3.2. Observation of patient

In Fig 28. the patient appears to have a normal posture, with a face displaying emotions and no visible signs of rigidity. However, in Fig 29. after the diagnosis of Parkinson's disease, there is a noticeable change. The patient's face exhibits a mask-like appearance, with rigidity evident on one side, a drooping mouth, and a stooped posture. This transformation reflects the progression of Parkinson's disease, which can lead to facial masking, rigidity, and changes in posture as the condition advances.

In Fig 30. the patient exhibits symptoms indicative of Parkinson's disease, such as slowness of movement, rigidity, postural instability, and freezing of gait while rising from a chair. Conversely, in Fig 31.

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Q2. How did you initially react to your diagnosis, and what was your understanding of the condition and its implications at that time?

Ans: When I first found out, I was surprised and worried. I didn't really know much about Parkinson's at the time, but I knew something was wrong because of my handwriting.

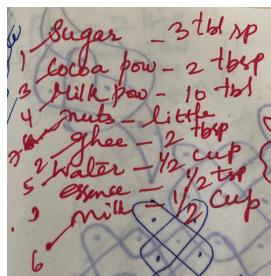


Fig 32. Handwriting before discovering PD symptoms

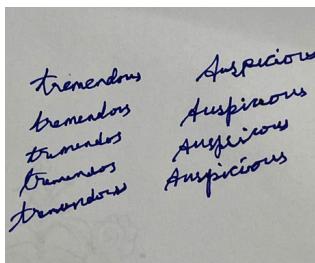


Fig 33. Handwriting while being diagnosed with PD

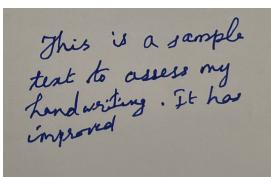


Fig 34. Improved handwriting during the disease progression due to medications.

Q3. Were there any challenges or uncertainties encountered during the diagnostic process, and if so, how were these addressed?

Ans: Walking was hard during the tests, and that made things a bit tricky. But the doctors helped by doing more tests and talking with me about what could be going on.

Q4. How has your understanding of your condition evolved over time, and have there been any changes in your approach to managing your health as a result?

As time went on, I learned more about Parkinson's and how to manage it. I've had to make some changes to my daily routine and take medicine to help with the symptoms.

Q5. Have you experienced any psychological or emotional challenges related to Parkinson's disease?

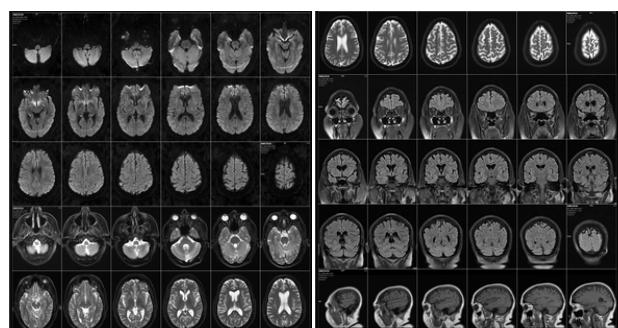
Ans: Yes, I've encountered psychological and emotional hurdles due to Parkinson's disease, including bouts of depression and heightened stress levels.

Q6. How do you cope with the stress and uncertainty of living with a chronic neurological condition?

Ans: Coping with the stress and uncertainty of managing a chronic neurological condition can be challenging. Personally, I find solace in activities like playing cards, listening to music, and sometimes stress eating to alleviate the burden.

7.5. Diagnostic Imaging Evaluation

On March 1, 2023, Mrs. Amudha Kishore underwent an MRI scan as part of her diagnostic evaluation upon the discovery of Parkinson's disease. This scan was conducted to rule out the presence of any other underlying diseases or conditions that could potentially contribute to her symptoms.



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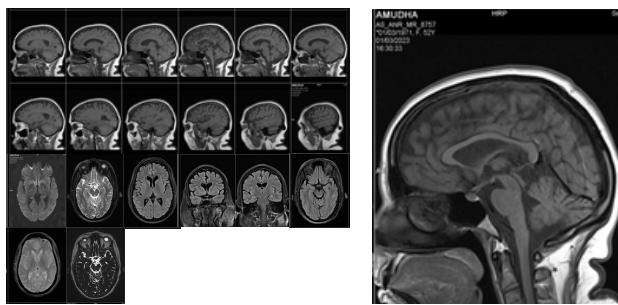


Fig 35, Fig 36, Fig 37 & Fig 38. MRI scans of Mrs. Amudha Kishore taken on March 1, 2023 (The date of her diagnosis)

7.5.1. Observation

- Few T2W/FLAIR hyperintense foci with no diffusion restriction seen in bilateral corona radiata.
- Mild age related cerebral and cerebellar atrophy seen.
- No evidence of acute infarct, hemorrhage or space occupying mass lesion noted.
- No evidence of abnormal signal intensity or volume loss in the hippocampii.
- The thalami, basal ganglia and internal capsules are normal on both sides.
- The ventricles and sulci are mildly prominent for the age.
- The pituitary gland, infundibulum and hypothalamus are normal for the age.
- The posterior fossa shows normal cerebellum.
- The medulla, pons and mid brain shows normal signals in all the sequences. Both CP angles are clear.
- The basal cisterns are normal. Normal flow void is seen in the major dural venous sinuses and arteries.

7.5.2. Impression

- Few T2W/FLAIR hyperintense foci with no diffusion restriction in bilateral corona radiata - likely non-specific foci/ Fazekas grade I small vessel ischemic changes.
- Mild age related cerebral and cerebellar atrophy.

7.5.3. Findings

The MRI scan revealed mild age-related cerebral and cerebellar atrophy and few T2W/FLAIR hyperintense foci in bilateral corona radiata, indicating non-specific foci or Fazekas grade I small vessel ischemic changes. Importantly, there were no signs of acute infarct, hemorrhage, or space-occupying mass lesions. Additionally, all major brain structures appeared normal, including the thalami, basal ganglia, internal capsules, hippocampii, and brainstem. These findings, combined with the absence of abnormal signal intensity or volume loss, effectively rule out other neurological conditions and support the diagnosis of Parkinson's disease.

7.6. Prescription History and Disease Progression

Mrs. Amudha Kishore's clinical diagnosis on 01.03.2023 revealed early Parkinson's disease (PD) symptoms, including slowed gait, reduced activities, low blink rate, mild facial asymmetry, and age-appropriate atrophy observed on MRI. To address these symptoms, she was initially prescribed Rasalect 0.5 mg, Pramipex 0.125 mg, and Nootrophil 800 mg for 20 days.

Following her diagnosis, Mrs. Amudha experienced subjective improvements but developed peripheral neuropathy by her review on 21.03.23. Medication adjustments were made, including an increase in Pramipex dosage to 0.25 mg and the introduction of Neurokind-Next and Juviana Plus. On subsequent reviews, medications were tailored to address emerging symptoms.

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By 31.07.23, an increase in Rasalect dosage to 1 mg and the addition of Lonazep 0.5 mg aimed to manage rigidity, bradykinesia, and resting tremor. Diagnostic tests confirmed diabetic peripheral neuropathy, prompting additional treatments such as Nurewire for pain relief.

Further adjustments in medication were made to address evolving symptoms, including the introduction of Syndopa Plus, Tranquilam, and Domstal to manage bradykinesia, rigidity, and gastrointestinal issues. Mrs. Amudha's treatment journey reflects the individualized approach to medication management in Parkinson's disease, with a focus on symptom alleviation and improving overall quality of life.

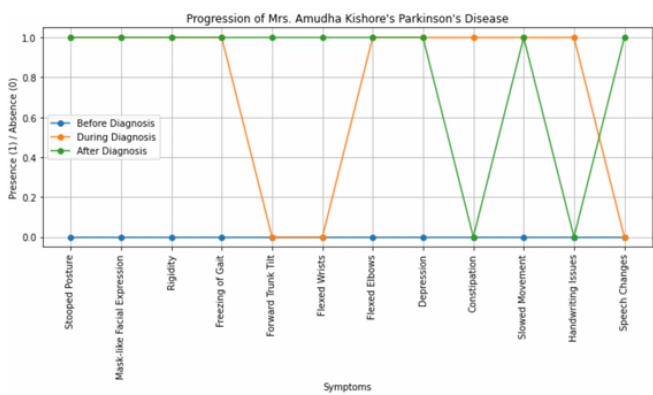


Fig 39. Progression of Mrs. Amudha Kishore's Parkinson's Disease

8. SUMMARY

This report presents a comprehensive overview of the disease's progression, treatment, and management. The document delves into various aspects of Parkinson's disease, including prevalence, aetiology, pathophysiology, symptoms, treatment, project overview, data analysis, baseline assessment, progression analysis, and factors influencing progression.

The report outlines the importance of understanding the diverse and complex nature of Parkinson's disease distribution globally, emphasizing the need for further research and targeted interventions to address these disparities and mitigate the growing burden of the disease. It also provides detailed insights into the progression of the disease through variable distribution analysis, time series analysis, and statistical analysis, highlighting the significance of personalized treatment strategies tailored to individual disease trajectories.

Furthermore, the report emphasizes the importance of early detection and tailored management strategies to mitigate symptom progression and improve patient outcomes, providing valuable insights into the heterogeneous nature of Parkinson's disease progression and informing tailored treatment strategies for different disease stages. Overall, the report offers a comprehensive and insightful analysis of Parkinson's disease progression, treatment, and management, emphasizing the importance of personalized care and tailored interventions to optimize patient outcomes.

The report provides a thorough examination of Parkinson's disease progression, highlighting the intricate mechanisms driving disease progression and the importance of personalised treatment approaches. It emphasises the need for targeted monitoring and management to improve patient outcomes and quality of life.

The report also underscores the significance of individualised therapy to achieve optimal clinical outcomes and the importance of considering demographic factors in understanding disease progression. Overall, the document offers valuable insights into Parkinson's disease progression and management, emphasising the importance of personalised care and tailored interventions to optimise patient outcomes and improve quality of life.

The significant findings from the baseline assessment and analysis of Parkinson's disease include:

- The baseline assessment serves as a crucial starting point to understand patients' initial conditions and disease characteristics, providing insights into factors influencing disease progression.
- The baseline analysis provides a detailed overview of key demographic, clinical, and treatment-related characteristics of Parkinson's disease (PD) patients, including mean age, disease duration, and UPDRS scores.
- Comparing clinical variable distributions

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across disease stages reveals significant differences, offering insights into disease progression factors and variability within each stage.

- The baseline assessment informs personalized management strategies and longitudinal monitoring of disease progression, enabling tailored treatment approaches and reassessment to optimize symptom management and improve overall patient outcomes.
- The findings from the feature importance analysis suggest that factors such as motor function assessments and mobility tests demonstrate high importance for Parkinson's disease (PD) progression.
- The baseline assessment aids in identifying predictors of progression and tailoring interventions to individual patient needs, ultimately enhancing the management of Parkinson's disease.

These findings highlight the dynamic nature of Parkinson's disease progression, the importance of targeted monitoring and management, and the heterogeneous nature of disease progression, emphasizing the need for personalized treatment approaches.

The analysis of medication dosages, such as Levodopa and Dopamine Agonists, reveals their complex relationship with the progression of Parkinson's disease. Patients prescribed higher doses of Levodopa tend to exhibit an increase in

UPDRS Part III scores over time, indicating worsening motor symptoms associated with disease progression.

The rate of progression varies among patients, with some showing steeper increases in UPDRS scores compared to others, highlighting the heterogeneous nature of treatment response and disease progression. Similarly, patients receiving Dopamine Agonists display fluctuations in UPDRS Part III scores over time, with some experiencing periods of symptom improvement and others showing deterioration. The relationship between Dopamine Agonist dosage and disease progression appears complex, with no clear trend observed.

These findings underscore the need for careful dosage adjustments and personalised management strategies to optimise symptom control and minimise adverse effects associated with medication therapy.

Additionally, the analysis suggests that variations in medication dosages may not have significant correlations with changes in UPDRS Part III scores over time, indicating potential differences in treatment efficacy or individual patient responses. Overall, the findings emphasize the importance of tailored treatment approaches and individualized therapy to achieve optimal clinical outcomes and manage the heterogeneous nature of Parkinson's disease progression.

The longitudinal analysis of Parkinson's disease progression provides valuable insights into the dynamic nature of the disease over time. By systematically

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examining changes in individual indicators such as symptom severity, functional impairment, and quality of life measures, this approach enables the understanding of disease progression dynamics, treatment efficacy, and the development of personalised management strategies for individuals with Parkinson's disease.

The analysis reveals fluctuations in symptom severity over time, indicating variations in disease progression among patients. Some individuals exhibit gradual worsening of motor symptoms, while others experience periods of stability or improvement.

These findings underscore the heterogeneous nature of Parkinson's disease progression and emphasise the importance of personalised treatment strategies tailored to the unique disease trajectories of each patient.

Additionally, the longitudinal analysis aids in identifying predictors of progression, informing prognostic considerations, and guiding treatment planning. Overall, the insights derived from longitudinal analysis are crucial for optimizing patient care, tailoring interventions, and addressing the complexities of Parkinson's disease progression.

Demographic factors, such as age and gender, significantly influence the severity and progression of Parkinson's disease (PD). Older age at onset is associated with accelerated disease progression, exacerbating motor and cognitive decline, and impacting daily functionality. This correlation underscores the importance of tailoring interventions to mitigate the

accelerated progression associated with older age at onset.

Additionally, gender differences in PD are evident, with men showing a higher prevalence and more severe motor symptoms, while women experience faster cognitive decline and increased non-motor symptoms.

Understanding these demographic variables' intersection with disease duration provides insights into the differential impact of PD on subgroups, informing personalised treatment strategies. The segmentation analysis also reveals distinct trends in motor symptom severity across different Hoehn and Yahr stages, emphasising the importance of early detection and tailored management strategies to mitigate symptom progression.

Furthermore, family history of PD and genetic predisposition influence disease susceptibility and progression, warranting closer intervention monitoring and tailored strategies. Overall, demographic factors play a crucial role in shaping the trajectory of Parkinson's disease, and understanding their impact is essential for personalized management strategies and optimizing patient care.

9. CONCLUSION

The findings revealed that Levodopa-Carbidopa and Bromocriptine exhibited higher mean improvement scores compared to Ropinirole, Pramipexole, Rasagiline, Selegiline, and the placebo. The baseline analysis provides a detailed overview of key demographic, clinical, and treatment-related variables in Parkinson's disease (PD) patients. The mean age of participants is [mean_age], with a standard deviation of [std_age].

The findings of comparing the distribution of different clinical variables across disease stages reveal significant differences and variability within each stage. The correlation heatmap reveals several significant relationships among clinical variables. The kernel density plot reveals that the distribution of disease duration in Parkinson's patients is skewed to the right, indicating a longer average duration. The output suggest varying rates of progression for different clinical features in Parkinson's disease.

Conversely, features such as Levodopa Dosage and Finger Tapping Speed exhibit negative progression rates, suggesting potential improvements or slower decline with disease duration. After conducting the time series analysis, we observed fluctuations in UPDRS Part III scores over time, indicating variations in motor symptom severity among patients with Parkinson's disease.

The findings indicate a diverse range of UPDRS Part III scores observed across different disease durations for individual

patients.

The findings from the linear regression analysis reveal a positive relationship between disease duration and UPDRS Part III scores in Parkinson's disease. The intercept of 1.3848 indicates the estimated UPDRS Part III score at the beginning of the disease. The findings from the ANOVA test reveal a significant difference among the means of the three groups (Group A, Group B, and Group C).

The findings of the chi-square test indicate a chi-square test statistic of 0.3361 with a corresponding p-value of 0.8453. The relationship between Dopamine Agonist dosage and disease progression appears complex, with no clear linear trend observed. These findings highlight the heterogeneous nature of treatment response among patients and underscore the importance of individualized therapy selection and monitoring to achieve optimal clinical outcomes. Patients prescribed MAO-B Inhibitors demonstrate relatively stable UPDRS Part III scores over time, suggesting a potential stabilizing effect on motor symptoms associated with Parkinson's disease.

The segmentation analysis reveals distinct trends in motor symptom severity across different Hoehn and Yahr (H&Y) stages. The analysis highlights the progressive nature of Parkinson's disease, emphasizing the importance of early detection and tailored management strategies to mitigate symptom progression and improve patient

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outcomes. The segmentation analysis reveals distinct trends in disease severity (UPDRS Part III score) over time based on age and gender in Parkinson's disease (PD) patients.

Furthermore, the progression of symptoms appears to be more pronounced in males compared to females across all age groups. The segmentation analysis highlights deteriorating UPDRS scores and functional tests like TUG Test and PDQ-39 Score, indicating worsening symptoms and declining quality of life over time.

The change-point detection analysis reveals breakpoints in UPDRS Part III scores, indicating shifts in disease progression. Two significant change-points are detected, suggesting distinct phases in the progression trajectory. The bar graph visualizations offer insights into the distribution of categorical variables among Parkinson's disease patients. Analysis of the data reveals that slightly more females are represented in the sample compared to males.

Analysis of the data indicates that approximately 51.4% of patients are female, while 60% have a positive family history of the disease. In terms of comorbidities, the majority of patients (45.7%) report none. The findings from the feature importance analysis suggest that various factors contribute to Parkinson's disease (PD) progression.

The findings indicate the relative importance of different features in influencing Parkinson's disease progression. Mrs. Her journey highlights

the challenges faced by individuals navigating the complexities of PD symptoms before receiving a diagnosis. Mrs. Mrs. In Fig 28. the patient appears to have a normal posture, with a face displaying emotions and no visible signs of rigidity. the patient exhibits symptoms indicative of Parkinson's disease, such as slowness of movement, rigidity, postural instability, and freezing of gait while rising from a chair.

These observations underscore the progressive nature of Parkinson's, with symptoms evolving and impacting various aspects of mobility and posture over time. These assessments aimed to assess her motor function, mobility, and overall health status. The diagnostic process involved various tests and procedures to understand the nature and severity of her condition, leading to a comprehensive understanding of her health status.

The MRI scan revealed mild age-related cerebral and cerebellar atrophy and few T2W/FLAIR hyperintense foci in bilateral corona radiata, indicating non-specific foci or Fazekas grade I small vessel ischemic changes. Additionally, all major brain structures appeared normal, including the thalamus, basal ganglia, internal capsules, hippocampi, and brainstem.

In conclusion, early detection and tailored management are crucial for mitigating symptom progression and enhancing patient outcomes. The diagnostic journey of Mrs. Amudha Selvaraj underscores the complex nature of PD and the importance of comprehensive assessment in guiding treatment decisions. MRI findings provide

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insights into cerebral changes, contributing to our understanding of PD pathology. Further research is needed to elucidate optimal treatment strategies and improve patient care in PD management.

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