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Original Research Article

Comparative Clinical Spectrum of Young- and Late-Onset Parkinsonism: A Cross-Sectional Study from a Tertiary Care Hospital in Khyber Pakhtunkhwa, Pakistan

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Abstract: Background: Parkinsonism comprises a heterogeneous group of neurodegenerative disorders characterized by motor symptoms, including bradykinesia, rigidity, resting tremor, and postural instability, along with a wide range of non-motor manifestations. Clinical presentation may vary according to the age at symptom onset; however, data comparing young- and late-onset parkinsonism from Pakistan remain limited. **Objective:** To compare the demographic characteristics and clinical spectrum of young- and late-onset parkinsonism among patients presenting to a tertiary care hospital in Khyber Pakhtunkhwa, Pakistan. **Methods:** This comparative cross-sectional study included 32 consecutive patients with parkinsonism attending the Department of Neurology, Hayatabad Medical Complex, Peshawar, from June 2025 to December 2025. Participants were categorized into young-onset (<50 years) and late-onset (≥50 years) groups based on the age at symptom onset. Demographic characteristics, disease duration, family history, and motor and non-motor manifestations were recorded using a structured proforma. Comparative analyses between the two groups were performed using appropriate statistical tests, with a p-value <0.05 considered statistically significant. **Results:** Of the 32 patients, 6 (18.8%) had young-onset and 26 (81.2%) had late-onset parkinsonism. The mean age was 56.7 ± 11.7 years, and 75.0% of participants were male. Young-onset patients had a significantly lower mean age at symptom onset (38.3 ± 5.0 vs. 56.5 ± 8.6 years; p<0.001) and a longer disease duration (7.5 ± 5.6 vs. 3.1 ± 3.4 years; p=0.039). Salivation (65.6%), insomnia (46.9%), constipation (46.9%), depression/anxiety (40.6%), and fatigue (37.5%) were the most frequently reported clinical manifestations. No significant differences were observed in the frequencies of other clinical features between the two groups. **Conclusion:** Young-onset parkinsonism was associated with a longer disease duration, while the overall clinical spectrum of motor and non-motor manifestations was largely comparable between young- and late-onset groups. Larger multicenter studies are warranted to further characterize age-related differences in parkinsonism.

Keywords: Parkinsonism; Young-onset parkinsonism; Late-onset parkinsonism; Non-motor symptoms; Clinical spectrum; Pakistan

INTRODUCTION

Parkinsonism is a clinical syndrome characterized by bradykinesia in combination with resting tremor, muscular rigidity, and postural instability. It encompasses idiopathic Parkinson's disease (PD), the most common cause, as well as atypical parkinsonian disorders such as multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal degeneration, and vascular parkinsonism. Although these disorders share overlapping motor manifestations, they differ in their underlying

pathology, clinical progression, therapeutic response, and prognosis. [1–3]

Globally, Parkinson's disease affects more than 10 million people and represents the second most common neurodegenerative disorder after Alzheimer's disease. The burden of parkinsonism is expected to increase substantially due to population aging, increased life expectancy, and improved disease recognition. In low- and middle-income countries, including Pakistan, the growing burden of parkinsonian disorders presents considerable challenges because of limited neurological services, delayed diagnosis, and restricted access to specialized care. [4–6]

The age at symptom onset is an important determinant of disease phenotype and clinical outcome. Patients developing symptoms before the age of 50 years are generally classified as having young-onset parkinsonism, whereas those with symptom onset at or after 50 years are categorized as late-onset parkinsonism. Previous studies have demonstrated that younger patients tend to have a longer disease duration and may exhibit distinct clinical characteristics compared with older patients. Conversely, late-onset disease is often associated with greater functional impairment, cognitive decline, gait instability, and autonomic dysfunction. [7–9]

Beyond the classical motor manifestations, non-motor symptoms are increasingly recognized as major contributors to disability and reduced quality of life in patients with parkinsonism. Depression, anxiety, constipation, urinary dysfunction, sleep disturbances, fatigue, orthostatic hypotension, cognitive impairment, hallucinations, and pain frequently occur throughout the disease course and may precede the onset of motor symptoms. These manifestations often remain underdiagnosed despite their significant impact on daily functioning and caregiver burden. [10–12]

Several studies have compared the clinical characteristics of young- and late-onset Parkinson's disease; however, most available evidence originates from Europe, North America, and East Asia. Data from South Asian populations remain scarce, particularly regarding the broader spectrum of parkinsonian disorders encountered in routine neurological practice. Regional differences in genetics, environmental exposures, healthcare access, and socioeconomic factors may influence disease presentation and progression, highlighting the need for locally generated evidence. [13–16]

In Pakistan, published data describing the clinical spectrum of parkinsonism are limited, with most studies focusing on idiopathic Parkinson's disease or treatment outcomes rather than age-related differences in presentation. Understanding variations in motor and non-motor manifestations according to age at symptom onset may facilitate earlier diagnosis, improve symptom recognition, and support individualized management strategies in routine clinical practice. [17–20]

Therefore, the present study aimed to compare the demographic characteristics and clinical spectrum of young- and late-onset parkinsonism among patients presenting to a tertiary care hospital in Khyber Pakhtunkhwa, Pakistan. By evaluating both motor and non-motor manifestations, this study seeks to provide locally relevant evidence that may improve the recognition and clinical management of parkinsonian disorders across different age groups.

MATERIALS AND METHODS

This comparative cross-sectional study was conducted at the Department of Neurology, Hayatabad Medical Complex, Peshawar, Khyber Pakhtunkhwa, Pakistan. Consecutive patients presenting with parkinsonism during the study period, from June 2025 to December 2025 were enrolled using a non-probability consecutive sampling technique. Parkinsonism was diagnosed by consultant neurologists based on clinical evaluation and included idiopathic Parkinson's disease as well as related parkinsonian disorders, including multiple system atrophy (MSA), progressive supranuclear palsy (PSP), Parkinsonism-plus syndrome, and other clinically diagnosed parkinsonian disorders. Patients aged 18 years or older with a confirmed diagnosis of parkinsonism and complete clinical records were included, whereas those with incomplete medical records or insufficient clinical information were excluded.

Participants were categorized according to the age at symptom onset into young-onset parkinsonism (symptom onset <50 years) and late-onset parkinsonism (symptom onset ≥50 years). Demographic and clinical information, including age, sex, residence, age at symptom onset, disease duration, diagnosis, family history, medication history, and motor and non-motor manifestations, was collected using a structured proforma. Non-motor manifestations included depression/anxiety, constipation, urinary symptoms, insomnia, hypersomnolence, postural hypotension, reduced libido, pain, fatigue, restless legs syndrome, mild memory impairment, dementia, and hallucinations. Motor manifestations included excessive salivation, speech impairment, and swallowing difficulties.

Data were entered and analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test and are presented as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate. Categorical variables are expressed as frequencies and percentages. Comparisons between young- and late-

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onset parkinsonism were performed using the independent-samples t-test or the Mann–Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. A two-sided p-value of <0.05 was considered statistically significant.

The study was approved by the Institutional Research and Ethics Board of Hayatabad Medical Complex, Peshawar, and was conducted in accordance with the principles of the Declaration of Helsinki. Patient confidentiality was strictly maintained throughout the study, and all data were anonymized prior to analysis.

RESULTS

A total of 32 patients with parkinsonism were included in the study. The mean age was 56.7 ± 11.7 years (range: 34–71 years), while the mean age at symptom onset was 52.8 ± 11.4 years. The mean disease duration was 3.9 ± 4.1 years. Males constituted 75.0% of the study population. Based on age at symptom onset, 6 (18.8%) patients were classified as having young-onset parkinsonism and 26 (81.2%) as having late-onset parkinsonism. Idiopathic Parkinson's disease was the predominant diagnosis, accounting for 24 (75.0%) patients, whereas atypical and unclassified parkinsonian disorders comprised the remaining 8 (25.0%). Four patients (12.5%) had a positive family history of parkinsonism. Levodopa/carbidopa (Sinemet) was the most commonly prescribed medication (37.5%), followed by Kempro (31.3%). Baseline demographic and clinical characteristics are summarized in Table 1.

Table 1. Baseline demographic and clinical characteristics of patients with parkinsonism (N = 32)

Variable	Value
Age (years), Mean ± SD	56.7 ± 11.7
Age at symptom onset (years), Mean ± SD	52.8 ± 11.4
Disease duration (years), Mean ± SD	3.9 ± 4.1
Sex, n (%)	
Male	24 (75.0)
Female	8 (25.0)
Age-at-onset category, n (%)	
Young-onset (<50 years)	6 (18.8)
Late-onset (≥50 years)	26 (81.2)
Clinical diagnosis, n (%)	
Idiopathic Parkinson's disease	24 (75.0)
Multiple system atrophy (MSA)	1 (3.1)
Progressive supranuclear palsy (PSP)	1 (3.1)
Parkinsonism-plus syndrome	1 (3.1)
Unclassified parkinsonism	5 (15.6)
Positive family history of parkinsonism, n (%)	4 (12.5)
Current pharmacological treatment, n (%)	
Levodopa/Carbidopa (Sinemet)	12 (37.5)
Kempro	10 (31.3)
Levodopa/Carbidopa + Kempro	5 (15.6)
Ropinirole	4 (12.5)
No medication	1 (3.1)

Patients were categorized into young-onset parkinsonism (n=6, 18.8%) and late-onset parkinsonism (n=26, 81.2%). As shown in Table 2, the young-onset group had a significantly lower mean age at symptom onset than the late-onset group (38.3 ± 5.0 vs. 56.5 ± 8.6 years; p<0.001) and a significantly longer disease duration (7.5 ± 5.6 vs. 3.1 ± 3.4 years; p=0.039). Although male predominance was observed in both groups (83.3% vs. 73.1%), the difference was not statistically significant (p=0.602). Similarly, family history of parkinsonism was more frequent among patients with young-onset disease (33.3% vs. 7.7%), but the difference did not reach statistical significance (p=0.100).

Table 2. Comparison of demographic and clinical characteristics between young- and late-onset parkinsonism

Variable	Young-onset (n=6)	Late-onset (n=26)	p-value
Current age (years), Mean ± SD	43.2 ± 8.1	59.8 ± 9.3	<0.001
Age at symptom onset (years), Mean ± SD	38.3 ± 5.0	56.5 ± 8.6	<0.001
Disease duration (years), Mean ± SD	7.5 ± 5.6	3.1 ± 3.4	0.039
Male sex, n (%)	5 (83.3)	19 (73.1)	0.602
Positive family history, n (%)	2 (33.3)	2 (7.7)	0.100

The distribution of motor and non-motor manifestations is summarized in Table 3. Excessive salivation was the most frequently reported clinical feature, affecting 65.6% of participants, followed by insomnia (46.9%), constipation

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(46.9%), depression/anxiety (40.6%), and fatigue (37.5%). Urinary symptoms, pain, and speech problems were each reported by 21.9% of patients, while swallowing difficulties and mild memory impairment were observed in 18.8% and 15.6%, respectively. Hallucinations, postural hypotension, and restless legs syndrome each occurred in 9.4% of participants, whereas dementia was identified in 6.3%.

Table 3. Comparison of clinical manifestations between young- and late-onset parkinsonism

Clinical manifestation	Young-onset (n=6)	Late-onset (n=26)	p-value
Depression/Anxiety	3 (50.0)	10 (38.5)	0.607
Constipation	3 (50.0)	12 (46.2)	0.865
Urinary symptoms	2 (33.3)	5 (19.2)	0.465
Insomnia	2 (33.3)	13 (50.0)	0.465
Hypersomnolence	1 (16.7)	3 (11.5)	0.742
Postural hypotension	1 (16.7)	2 (7.7)	0.533
Reduced libido	1 (16.7)	3 (11.5)	0.742
Pain	2 (33.3)	5 (19.2)	0.465
Fatigue	2 (33.3)	10 (38.5)	0.816
Restless legs syndrome	1 (16.7)	2 (7.7)	0.533
Excessive salivation	5 (83.3)	16 (61.5)	0.320
Speech problems	3 (50.0)	4 (15.4)	0.079
Swallowing problems	2 (33.3)	4 (15.4)	0.345
Mild memory impairment	1 (16.7)	4 (15.4)	0.982
Dementia	0 (0.0)	2 (7.7)	0.470
Hallucinations	1 (16.7)	2 (7.7)	0.533

DISCUSSION

The present study compared the demographic characteristics and clinical spectrum of young- and late-onset parkinsonism among patients attending a tertiary care hospital in Khyber Pakhtunkhwa, Pakistan. The principal findings were a marked male predominance, a significantly longer disease duration among patients with young-onset parkinsonism, and a high prevalence of non-motor manifestations, particularly excessive salivation, insomnia, constipation, depression/anxiety, and fatigue. Although several clinical features were more frequently observed in the young-onset group, most differences between the two groups were not statistically significant.

Male patients constituted three-quarters of the study population, which is consistent with the well-recognized male predominance reported in parkinsonism worldwide. Recent epidemiological studies have demonstrated that men have approximately 1.5 times higher risk of developing Parkinson's disease than women, possibly because of interactions between genetic susceptibility, environmental exposures, and the neuroprotective effects of estrogen. Recent multicenter studies from Asia and Europe have similarly reported a male predominance ranging from 60% to 70%, supporting our findings. [1,2,3]

One of the major findings of this study was the significantly longer disease duration among patients with young-onset parkinsonism. This observation is expected because younger individuals develop symptoms earlier and consequently live with the disease for a longer period. Previous investigations have shown that young-onset patients generally experience slower disease progression but are exposed to dopaminergic therapy for longer durations, increasing the likelihood of long-term treatment-related complications such as motor fluctuations and dyskinesias. Recent cohort studies have similarly demonstrated prolonged survival and longer disease duration among younger patients compared with those with late-onset disease. [4–6]

Non-motor manifestations were highly prevalent in the present study. Excessive salivation was the most frequently reported clinical feature, followed by insomnia, constipation, depression/anxiety, and fatigue. Increasing evidence suggests that non-motor symptoms are major determinants of disability and impaired quality of life in parkinsonism, often exceeding the impact of motor symptoms. Recent systematic reviews have highlighted constipation and sleep disturbances as common prodromal manifestations that may precede motor symptoms by several years, reflecting early involvement of autonomic and brainstem pathways. Likewise, depression and anxiety are increasingly recognized as important contributors to poor functional outcomes, caregiver burden, and reduced treatment adherence. [7–10]

Although depression/anxiety, constipation, speech impairment, and positive family history were numerically more frequent among patients with young-onset parkinsonism, none of these differences reached statistical significance. This may largely reflect the relatively small sample size of the present

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study rather than the absence of clinically meaningful differences. Nevertheless, previous studies have reported similar trends, suggesting that younger patients may exhibit distinct clinical characteristics while sharing many core motor and non-motor manifestations with patients who develop symptoms later in life. [11–13]

Our findings are clinically relevant because recognition of non-motor manifestations remains suboptimal in routine neurological practice, particularly in resource-limited settings. Early identification and appropriate management of symptoms such as depression, constipation, sleep disturbances, autonomic dysfunction, and fatigue have been shown to improve quality of life and reduce overall disease burden. Recent international guidelines therefore emphasize comprehensive multidisciplinary assessment of both motor and non-motor symptoms throughout the course of parkinsonism rather than focusing solely on motor disability.[14–16]

The present study contributes important regional data from Khyber Pakhtunkhwa, where published evidence on the clinical spectrum of parkinsonism remains scarce. Inclusion of patients with both idiopathic Parkinson's disease and related parkinsonian disorders reflects the spectrum of cases encountered in routine tertiary neurological practice and provides valuable information regarding their demographic and clinical characteristics. These findings may assist clinicians in recognizing age-related differences in presentation and support more individualized patient management.

This study has several limitations. First, the single-center design and relatively small sample size may limit the generalizability of the findings. Second, the cross-sectional nature of the study precludes assessment of disease progression and temporal changes in clinical manifestations. Third, symptom assessment was based primarily on routine clinical evaluation rather than validated rating scales, such as the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) or the Non-Motor Symptoms Scale (NMSS). Future multicenter prospective studies with larger sample sizes and standardized assessment tools are needed to validate these findings and further clarify differences between young- and late-onset parkinsonism.

Despite these limitations, the study provides one of the few comparative evaluations of young- and late-onset parkinsonism from Pakistan. The findings highlight the importance of comprehensive assessment of both motor and non-motor manifestations and underscore the need for early diagnosis and individualized management strategies, particularly for younger patients who are likely to experience a longer disease course.[17,18]

CONCLUSION

This study provides a comparative evaluation of the clinical spectrum of young- and late-onset parkinsonism in patients presenting to a tertiary care hospital in Khyber Pakhtunkhwa, Pakistan. Young-onset parkinsonism was associated with a significantly longer disease duration, whereas the overall distribution of motor and non-motor manifestations was largely comparable between the two groups. Excessive salivation, insomnia, constipation, depression/anxiety, and fatigue were the most frequently observed clinical manifestations, emphasizing the substantial burden of non-motor symptoms in routine clinical practice. These findings highlight the importance of comprehensive clinical assessment irrespective of age at onset and support the need for multidisciplinary management strategies that address both motor and non-motor aspects of the disease. Larger multicenter prospective studies are warranted to validate these findings and further characterize age-related differences in parkinsonism within the Pakistani population.

Abbreviations

Abbreviation	Definition
PD	Parkinson's Disease
IPD	Idiopathic Parkinson's Disease
MSA	Multiple System Atrophy
PSP	Progressive Supranuclear Palsy
SD	Standard Deviation
IQR	Interquartile Range
SPSS	Statistical Package for the Social Sciences

Authors' Contributions

All authors contributed substantially to the conception and design of the study. Data collection, statistical analysis, interpretation of results, manuscript drafting, and critical revision were performed collaboratively. All authors read and approved the final manuscript.

Competing Interests

The authors declared that they have no competing interests.

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