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Factors related to non-motor symptoms in moderate to severe parkinson's disease

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ABSTRACT

Objective: To analyze factors related to non-motor symptoms in patients with moderate to severe Parkinson's disease.

Subjects and Methods: From March 2022 to September 2023, 93 patients with moderate to severe Parkinson's disease were enrolled in a cross-sectional descriptive study at the Outpatient Department of Bach Mai Hospital.

Results: Factors affecting cardiovascular symptoms: Advanced age (≥70 years) and severe disease stage increased the risk of orthostatic hypotension ($p < 0.05$). Factors affecting sleep disorders (based on NMSS and Epworth scores): Advanced age (≥70 years), disease duration of ≥5 years, and severe disease stage increased the risk of sleep disturbances ($p < 0.05$). Factors affecting mood disorders (based on NMSS and Geriatric Depression Scale - Short Form scores): Female gender was associated with an increased risk of anxiety and depression. Additionally, a disease duration of ≥5 years and severe disease stage also increased the risk of depression ($p < 0.05$).

Conclusion: Advanced age (≥70 years) and severe disease stage are factors that increase the risk of non-motor symptoms related to cardiovascular function, sleep disorders, and mood disorders.

Keywords: Parkinson's disease, non-motor symptoms, moderate to severe stage.

I. INTRODUCTION

Parkinson's disease is a common progressive neurodegenerative disorder in the elderly. Motor dysfunctions, including bradykinesia, tremors, rigidity, and postural instability characterize it. In addition, Parkinson's patients also experience non-motor symptoms such as cognitive impairment, autonomic dysfunction, sleep disorders,

urinary dysfunction, and depression. Non-motor symptoms are very common and significantly impact the quality of life of Parkinson's patients, especially in the moderate and advanced stages of the disease. In clinical practice, physicians sometimes focus solely on detecting and treating motor disorders while unintentionally overlooking non-motor symptoms, leading to suboptimal treatment outcomes. For a chronic disease like Parkinson's, comprehensive attention to all patient symptoms plays a crucial role in effective management. Several studies have investigated non-motor symptoms in Parkinson's patients, including psychiatric disorders, cognitive dysfunction, urinary disorders, and swallowing difficulties. However, there is still a lack of comprehensive research evaluating non-motor symptoms in patients with moderate to severe Parkinson's disease. Therefore, we conducted this study to analyze factors associated with non-motor symptoms in patients with moderate to severe Parkinson's disease.

II. STUDY SUBJECTS AND METHODS

2.1. Study Subjects

The study included 93 patients with moderate to severe Parkinson's disease at the Outpatient Department of Bach Mai Hospital from March 2022 to September 2023.

2.2. Inclusion Criteria

- Patients diagnosed with Parkinson's disease according to the clinical diagnostic criteria of the Movement Disorder Society (MDS).

- Patients in stages 3, 4, and 5 according to the Hoehn and Yahr classification.

2.3. Exclusion Criteria

- Patients who do not have the complete data required for the study

- Patients who do not consent to participate in the study

2.4. Research Methodology

A cross-sectional descriptive study.

2.5. Data Collection Techniques and Tools

Patients were interviewed and examined according to a standardized research medical record, which included:

- General characteristics of the study group: age, gender, age at disease onset, disease duration, disease stage, and severity of motor impairment.

- Characteristics of non-motor symptoms, assessed using the following scales: Non-Motor Symptoms Assessment Scale (NMSS), Epworth Sleepiness Scale, Geriatric Depression Scale (Short Form)

2.6. Statistical Methods and Data Processing

Data were processed and analyzed using SPSS 20.0 software.

III. RESEARCH RESULTS

3.1. General Characteristics of the Study Group

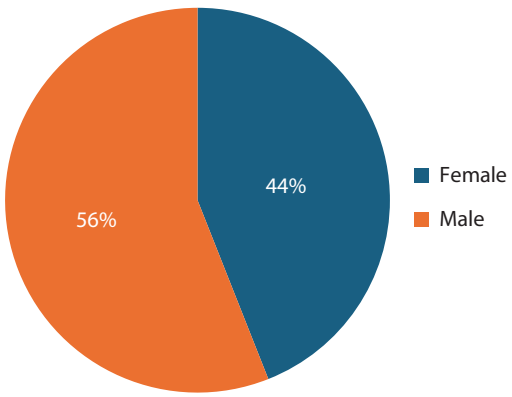

***Chart 1**. Gender Distribution*

Findings: Among the study participants, the proportions of male and female patients were 56% and 44%, respectively. The youngest patient was 46 years old, while the oldest was 86 years old. The average age of the study group was 65.11 ± 11.23 years. The most common age group was over 70 years old (38.7%).

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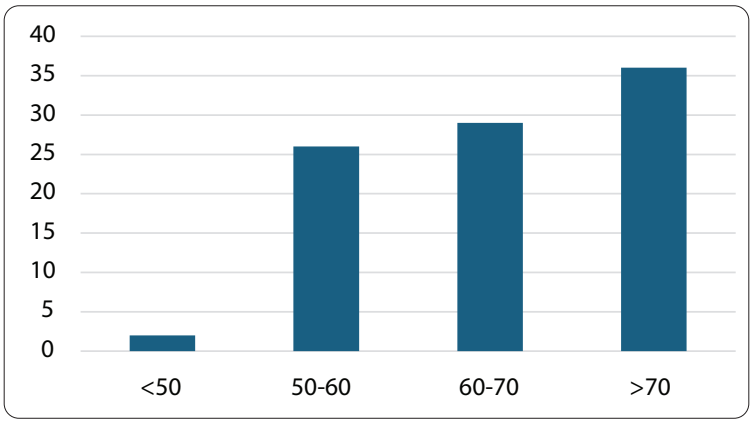

***Chart 2**. Age Group Distribution*

***Table 1**. Disease Duration*

Disease Duration	Number of Patients	Percentage (%)
< 5 years	20	21.5%
5 – 9 years	45	48.4%
≥ 10 years	28	30.1%
Average disease duration	8,13 ± 4,39	

Findings: The average disease duration among the study group was 8.13 ± 4.39 years. The majority of patients had a disease duration of 5–9 years (48.4%), followed by those with 10 years or more (30.1%).

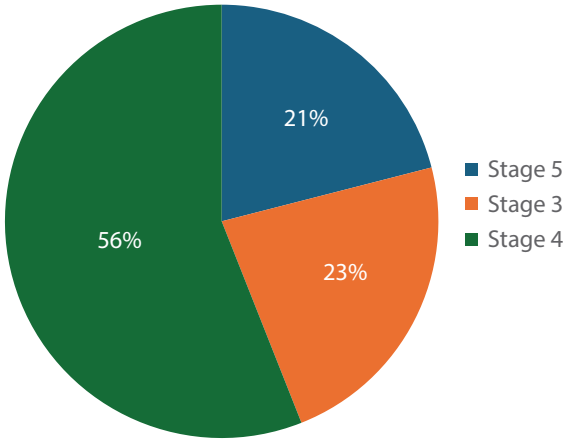

***Chart 3**. Disease Stage Characteristics*

Findings: All 93 patients in the study were in disease stages 3 to 5. Stage 4 had the highest proportion (56%), stage 3 accounted for 23%, and stage 5 accounted for 21%.

3.2. Factors Related to Non-Motor Symptoms in the Study Group

3.2.1. Comparison Between Disease Status and Cardiovascular Symptoms

***Table 2**: Comparison Between Disease Status and Cardiovascular Symptoms*

Factor \ Cardiovascular Symptoms		Orthostatic Hypotension		Syncope	
		p-value	OR	p-value	OR
Age	<70	0,003	2,04	0,024	1,96
	≥70				
Gender	Male	0,75	1,15	0,31	1,23
	Female				
Disease Duration	<5 years	0,23	1,05	0,97	1,52
	≥5 years				
Disease Stage	3	0,025	3,03	0,037	2,17
	4-5				

Findings: Age and disease stage were significant factors affecting orthostatic hypotension: Patients aged ≥70 years had a 2.04 times higher risk of orthostatic hypotension compared to those under 70 (p = 0.003). Patients in stages 4 and 5 had a 3.03 times higher risk than those in stage 3 (p = 0.025). No significant difference was found between genders (p = 0.75) or disease duration (p = 0.23) with orthostatic hypotension. For syncope, age, and disease stage also had significant effects: Patients aged ≥70 years had a 1.96 times higher risk of syncope (p = 0.024). Patients in stages 4 and 5 had a 2.17 times higher risk than those in stage 3 (p = 0.037). No significant difference was observed between genders (p = 0.31) or disease duration (p = 0.97) regarding syncope.

3.2.2. Comparison Between Disease Status and Sleep Disorders

a) Comparison of Disease Status and Sleep Disorders Based on NMSS

***Table 3**. Comparison Between Disease Status and Sleep Disorders (NMSS)*

Factor \ Sleep Disorders (NMSS)		Excessive Daytime Sleepiness		Insomnia		Restless Legs Syndrome	
		p-value	OR	p-value	OR	p-value	OR
Age	<70	0,046	2,04	0,037	2,65	0,86	1,25
	≥70						
Gender	Male	0,67	1,76	0,56	1,06	0,89	1,25
	Female						
Disease Duration	<5 years	0,006	3,08	0,026	2,87	0,86	1,45
	≥5 years						
Disease Stage	3	0,07	1,34	0,65	1,08	0,56	1,07
	4-5						

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Findings: Age and disease duration significantly affected excessive daytime sleepiness: Patients aged ≥70 years had a 2.04 times higher risk (p = 0.046). Patients with a disease duration of ≥5 years had a 3.08 times higher risk compared to those with <5 years (p = 0.006). No significant difference was found between genders or disease stages. For insomnia, age, and disease duration were also significant factors: Patients aged ≥70 years had a 2.65 times higher risk (p= 0.037). Patients with a disease duration of ≥5 years had a 2.87 times higher risk (p=0.026).

b) Comparison Between Disease Status and Sleep Disturbance Severity Based on Epworth Sleepiness Scale (ESS)

Table 4*. Comparison Between Disease Status and Sleep Disturbance Severity (ESS)*

Factor \ Sleep Disturbance (ESS)		p-value	OR
Age	<70	0,0035	2,59
	≥70		
Gender	Male	0,83	1,05
	Female		
Disease Duration	<5 years	0,002	3,78
	≥5 years		
Disease Stage	3	0,026	3,15
	4-5		

Findings: Age, disease duration, and disease stage significantly influenced sleep disturbances: Patients aged ≥70 years had a 2.59 times higher risk of sleep disturbances compared to those under 70 (p = 0.0035). Patients with a disease duration of ≥5 years had a 3.78 times higher risk compared to those with <5 years (p = 0.002). Patients in stages 4 and 5 had a 3.15 times higher risk of sleep disturbances compared to those in stage 3 (p = 0.026). No significant difference was found between genders regarding sleep disturbance severity (p = 0.83).

3.2.3. Comparison Between Disease Status and Mood Symptoms

a) Comparison Between Disease Status and Mood Symptoms Based on NMSS

Table 5*. Comparison Between Disease Status and Mood Symptoms Based on NMSS*

Factor \ Mood Symptoms		Anxiety		Depression	
		p-value	OR	p-value	OR
Age	< 70	0,45	1,12	0,78	1,27
	≥ 70				
Gender	Male	0,035	3,15	0,006	2,23
	Female				

Factor \ Mood Symptoms		Anxiety		Depression	
		p-value	OR	p-value	OR
Disease Duration	< 5 years	0,26	1,08	0,95	1,22
	≥ 5 years				
Disease Stage	3	0,07	1,03	0,23	1,17
	4-5				

Findings: Gender significantly influences anxiety and depression symptoms: Women have a 3.15 times higher risk of anxiety than men (p = 0.035). Women have a 2.23 times higher risk of depression than men (p = 0.006). No significant association was found between age, disease duration, or disease stage with anxiety and depression symptoms.

b) Comparison Between Disease Status and Depression Severity Based on the Geriatric Depression Scale (GDS-SF)

Table 6*. Comparison Between Disease Status and Depression Severity Based on GDS-SF*

Factor \ Depression Severity		p-value	OR
Age	< 70	0,24	1,01
	≥ 70		
Gender	Male	0,538	1,45
	Female		
Disease Duration	< 5 years	0,003	2,73
	≥ 5 years		
Disease Stage	3	0,026	3,14
	4-5		

Findings: Disease duration and disease stage significantly influence depression severity: Patients with ≥5 years of disease duration have a 2.73 times higher risk of depression compared to those with <5 years (p = 0.003). Patients in stages 4 and 5 have a 3.14 times higher risk of depression compared to those in stage 3 (p = 0.026). No significant difference was found between age groups (p = 0.24) or between genders (p = 0.538) regarding depression severity.

IV. DISCUSSION

4.1. General Characteristics of the Study Group

In our study, 93 patients with moderate to severe Parkinson's disease were included. The number of male patients was higher than that of female patients, with a male-to-female ratio of 1.27 (56% male, 44% female). This result is similar to findings from other studies, such as Nguyen The Anh (male-to-female ratio: 1.77) and Truong Thi Thu Huong (male-to-female ratio: 1.38).The mean age of the study group was 65 ± 11 years, with most patients being over 70 years old. This result aligns with both domestic and international studies.The mean disease duration was 8.13 ± 4.39 years. The majority of patients had a disease duration of 5–9 years (48.4%), followed by ≥10

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years (30.1%). These findings are consistent with other studies, such as P. Martinez-Matin, where the mean disease duration was 8.1 ± 5.7 years.

4.2. Comparison Between Disease Status and Cardiovascular Symptoms

We analyzed the relationship between disease status and two cardiovascular symptoms: orthostatic hypotension (OH) and syncope.

Orthostatic Hypotension (OH) Age and disease stage significantly influenced OH: Patients aged ≥ 70 years had a 2.04 times higher risk of OH than those < 70 years (p = 0.003). Patients in stages 4–5 had a 3.03 times higher risk of OH than those in stage 3. A high percentage of patients in the study had OH, and its severity increased with age and disease progression. According to W. Poewe, OH occurs in 20–60% of Parkinson's disease (PD) cases. It is associated with: Dopaminergic medications, disease severity, and disease duration. Patients with Parkinson's disease dementia are at a higher risk of OH than those without dementia. Levodopa, dopamine agonists, and MAO-B inhibitors can contribute to OH.

With syncope symptoms: Age and disease stage significantly influenced syncope: Patients aged ≥ 70 years had a 1.96 times higher risk of syncope than those < 70 years (p = 0.024). Patients in stages 4–5 had a 2.17 times higher risk of syncope than those in stage 3 (p = 0.037). No significant difference was found between genders (p = 0.31) or disease duration (p = 0.97) regarding syncope. Like OH, syncope was more common in older patients and those with advanced disease. Syncope represents a more severe form of OH, increasing fall-related injuries. Clinicians should monitor and manage this symptom in elderly patients with advanced PD to improve safety and quality of life.

4.3. Comparison Between Disease Status and Sleep Disorders

We analyzed the relationship between disease status and sleep disorder symptoms using the NMSS (Non-Motor Symptoms Scale) and Epworth Sleepiness Scale (ESS). Sleepiness (Daytime Sleepiness) Age and disease duration influenced daytime sleepiness: Patients aged ≥ 70 years had a 2.04 times higher risk of excessive daytime sleepiness (EDS) than those < 70 years (p = 0.0046). Patients with ≥ 5 years of disease duration had a 3.08 times higher risk of EDS than those < 5 years (p = 0.006). No significant difference was found between genders or disease stages regarding EDS.

Insomnia: Age and disease duration influenced insomnia: Patients aged ≥ 70 years had a 2.65 times higher risk of insomnia than those < 70 years (p = 0.037). Patients with ≥ 5 years of disease duration had a 2.87 times higher risk of insomnia than those < 5 years (p = 0.026). No significant difference was found between genders or disease stages regarding insomnia. Restless legs syndrome (RLS) was not significantly associated with disease status.

Epworth Sleepiness Scale (ESS) Analysis: Age, disease duration, and disease stage influenced sleep disorders: Patients aged ≥ 70 years had a 2.59 times higher risk of sleep disorders than those < 70 years (p = 0.0035). Patients with ≥ 5 years of disease duration had a 3.78 times higher risk of sleep disorders than those < 5 years (p = 0.002). Patients in stages 4–5 had a 3.15 times higher risk of sleep disorders than those in stage 3. No significant difference in sleep disorder severity was found between genders (p = 0.83).

We find that: Sleep disorders worsen with age, disease duration, and disease progression, consistent with dopamine deficiency in PD. Common PD-related sleep disorders include: Insomnia (difficulty falling asleep, sleep maintenance issues, fragmented sleep) Excessive daytime sleepiness (50% prevalence

in PD patients), REM sleep behavior disorder (RBD), sleep-disordered breathing, restless legs syndrome (RLS), periodic limb movement disorder (PLMD), dopaminergic medications (e.g., dopamine agonists) may contribute to excessive daytime sleepiness.

4.4. Comparison Between Disease Status and Mood Symptoms

We analyzed the relationship between disease status and mood symptoms, including anxiety and depression. Anxiety and Depression (NMSS Analysis)

Gender significantly influenced anxiety and depression: Women had a 3.15 times higher risk of anxiety than men ($p = 0.035$). Women had a 2.23 times higher risk of depression than men ($p = 0.006$). Age, disease duration, and disease stage did not significantly influence anxiety or depression. Depression Severity (GDS-SF Analysis). Disease duration and disease stage influenced depression severity: Patients with ≥5 years of disease duration had a 2.73 times higher risk of depression than those <5 years ($p = 0.003$). Patients in stages 4–5 had a 2.14 times higher risk of depression than those in stage 3 ($p = 0.026$). No significant difference was found between age groups ($p = 0.24$) or genders ($p = 0.538$) regarding depression severity. Depression often emerges early in PD but is frequently overlooked. Symptoms include low libido, sadness, pessimism, and loss of interest in surroundings. In moderate to advanced stages, depression worsens, affecting: Quality of life, disease progression, self-care abilities and cognition, treatment adherence, and caregiver burden. Our results align with global studies on PD and depression.

CONCLUSION

Our study on 93 patients with moderate to severe Parkinson's disease indicates that, in addition to motor disorders, non-motor symptoms are also common and severe. Therefore, clinicians should pay more attention to these symptoms in clinical practice. Advanced age (70 years and older) and severe disease stages are key factors that increase the risk of non-motor symptoms, particularly cardiovascular disorders, sleep disturbances, and mood disorders.

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