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Profile of Motoric and Non-Motoric Symptoms Using the Indonesian Version of the Wearing-Off Questionnaire-19 in Parkinson's Patients

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ABSTRACT

Introduction: Parkinson's disease is a neurodegenerative disorder characterized by motor and non-motor symptoms. The prolonged administration of levodopa in patients may induce the wearing-off phenomenon, where symptoms recur before the next dose. Studies on the symptom profile of Parkinson's disease, especially in wearing-off conditions, are crucial for further management. **Objective:** This study aimed to determine the motor and non-motor symptom profile of patients with Parkinson's disease. **Methods:** An observational descriptive study with a cross-sectional approach was conducted. The Indonesian version of the Wearing-Off Questionnaire-19 (WOQ-19) was used to identify motor and non-motor symptoms. Data were collected from 30 Parkinson's patients at Bethesda Yogyakarta Hospital from October to December 2023 using a purposive sampling technique. The sample size was calculated using OpenEpi V3.01. **Results:** The most prevalent motor symptom among patients with Parkinson's disease was tremor (100%), followed by bradykinesia (93.33%) and rigidity (86.67%). The most common non-motor symptoms reported were abdominal discomfort (56.67%) and body aches (50%). **Conclusion:** Patients have a variety of Parkinson's disease symptoms. Parkinson's patients most commonly experienced motor symptoms such as tremors, bradykinesia, and rigidity, along with non-motor symptoms like abdominal discomfort and body aches. The significant percentage of wearing-off seen in this study underscores its common occurrence and highlights the importance of early identification and management.

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INTRODUCTION

Parkinson's disease is a neurodegenerative disorder caused by a decrease in dopamine release. The primary pathological feature of Parkinson's disease is the accumulation of alpha-synuclein in certain regions of the brain, particularly the substantia nigra. This accumulation leads to neuronal degeneration and reduces dopamine release in the basal ganglia, which controls movement and muscle tone. The resulting neurotransmitter imbalance contributes to both motor and non-motor symptoms of Parkinson's disease.¹

The prevalence and incidence of Parkinson's disease are rising. In 2016, the estimated global number of Parkinson's disease cases was 6.1 million, up from 2.5 million in 1990.² In Indonesia, the prevalence of Parkinson's disease in 2021 was estimated to be 164,000 cases, reflecting a 228% increase from 50,000 cases in 1990.³ This disease normally begins around age 60 but can develop at any time during adulthood.⁴ This condition can cause symptoms that interfere with daily activities and may lead to mortality. In 2019, Parkinson's disease was responsible for 329,000 deaths and 5.8 million disabilities.⁵

The pathogenesis of Parkinson's disease, which is characterized by progressive neurodegeneration, might worsen symptoms over time.⁴ In a study by Matthews *et al.*, fatigue, slowed movement, and decreased finger dexterity were identified as the most troubling symptoms for Parkinson's patients and their caregivers.⁶ As the disease progresses, patients may experience a poor prognosis, such as death, postural instability, and dementia.⁷

The current Parkinson's disease treatment focuses on symptom reduction and slowing disease progression. Levodopa is the most effective and widely used drug for managing Parkinson's disease symptoms.⁸ Parkinson's disease treatment can be effective in the early years. However, in the long term, patients may experience complications, such as the emergence of motor or non-motor symptoms before the next dose. These symptoms may improve after the administration of the medication, a phenomenon known as 'wearing-off'.⁹ This condition can occur in some Parkinson's patients, particularly those who have had the disease for several years and have been on treatment for a long time.¹⁰ During the wearing-off period, the emergence of motor and non-motor symptoms can disrupt daily activities and reduce the quality of life for Parkinson's patients.⁶

Assessment for wearing-off can be performed by healthcare professionals using tools such as the Wearing-Off Questionnaire-19 (WoQ-19 or QUICK).⁹ This examination evaluates the symptoms of Parkinson's disease that patients experience during

wearing-off phenomenon. The Wearing-Off Questionnaire-19 (WOQ-19) is a sensitive tool for assessing Parkinson's disease complications and the wearing-off phenomenon. It was developed in 2007 and has been translated and validated in multiple languages, including Portuguese, Japanese, Filipino, Italian, and Vietnamese.¹¹ The questionnaire has nine motor symptoms and ten non-motor symptoms. In practice, patients complete the questionnaire by marking the symptoms that improve after the next dose of Parkinson's medication. Wearing-off is detected when two or more symptoms improve following the next dose.¹²

Further research is needed on the symptoms of Parkinson's disease, as early treatment is important for managing both motor and non-motor symptoms, which can significantly impact patients' daily lives. Therefore, the authors did a study titled "Profile of Motoric and Non-Motoric Symptoms Using Indonesian Version of Wearing-Off Questionnaire-19 in Parkinson's Patients" to find out the distribution of motor and non-motor symptoms in Parkinson's disease.

OBJECTIVE

This study aimed to identify motor and non-motor symptoms using the Indonesian version of the Wearing-Off Questionnaire-19. This would enable patients and clinicians to better assess these symptoms, allowing for adjustments in therapy and improving the quality of life for patients with Parkinson's disease.

METHODS

In this descriptive observational study, motor and non-motor symptoms in Parkinson's patients were identified using the Indonesian version of the Wearing Off Questionnaire-19 (WoQ-19) at Bethesda Hospital Yogyakarta. The questionnaire has been translated into Indonesian and found to be reliable (*Cronbach's α* = 0.67) and accurate in symptom diagnosis (*Kappa value* = 0.72). It has 82% sensitivity and 74% specificity.¹³ The study analyzed both numerical and categorical data. Patient age was recorded as numerical data, while sex, disease duration, disease stage, and motor and non-motor symptoms were recorded as categorical data. This study used a cross-sectional design.

The study conducted between January and February 2024 used medical records from October to December 2023. The inclusion criteria for this study were Parkinson's patients who had treatment at Bethesda Hospital Yogyakarta, as evidenced by medical records. The patients also needed to be conscious and able to communicate. Parkinson's

patients with incomplete medical records and those with dementia were excluded from the study. The study involved 30 Parkinson's patients who were experiencing the recurrence of symptoms, as assessed by neurologists and recorded in medical records. Secondary data from these records were analyzed by purposive sampling. To obtain a comprehensive understanding of the symptoms, data analysis was performed using R and R Studio. The Health Research Ethics Committee of Bethesda Hospital Yogyakarta granted ethical clearance for this study, with approval number No.01/KEPK-RSB/I/24.

RESULTS

Table 1. Demographics of Parkinson's patients at Bethesda Hospital (October – December 2023)

Characteristics	Mean (n = 30)
Age	70.73 ± 8.685
Gender	
- Male	20 (66.67%)
- Female	10 (33.33%)
Duration of Parkinson's disease	5.2 ± 1.471
Hoehn-Yahr stage	
- Stage I	0 (0%)
- Stage II	11 (36.67%)
- Stage III	16 (53.33%)
- Stage IV	3 (10%)
- Stage V	0 (0%)
Pharmacological therapy	
- Levodopa	16 (53.33%)
- Levodopa & dopamine agonist	3 (10%)
- Levodopa & COMT inhibitors	4 (13.33%)
- Levodopa & trihexyphenidyl	6 (20%)
- Levodopa, COMT inhibitors, trihexyphenidyl	1 (3.33%)
Experiencing Wearing Off	
- Yes	17 (56.67%)
- No	13 (43.33%)

Motor symptoms

Tremor (100%) was the most commonly reported motor symptom, followed by bradykinesia (93.33%) and rigidity (86.67%). Several motor symptoms improved with the second dose of medication, with tremor having the greatest improvement (100%),

Demographic and clinical characteristics

The study included 30 patients with Parkinson's disease from Bethesda Hospital Yogyakarta, with a mean age of 70.73 ± 8.685 years. The majority of patients (66.67%) were male, with a male-to-female ratio of 2:1. The mean duration of Parkinson's disease among patients was 5.2 ± 1.471 years. According to the Hoehn-Yahr scale, most patients were in stage III (53.33%). All patients were treated with levodopa, and some were also given dopamine agonists, COMT inhibitors, and/or trihexyphenidyl. Of the patients, 56.67% experienced the wearing-off.

followed by rigidity (9 out of 26 people) and bradykinesia (9 out of 18 people). Other motor symptoms included difficulty rising from a chair (70%), decreased dexterity (60%), weakness (50%), balance issues (46.67%), speech difficulties (23.33%), and muscle cramps (13.33%).

Table 2. Proportion of patients experiencing motor symptoms

Variable	Number (n = 30)	Percentage (%)
Tremor	30	100
Bradykinesia	28	93.33
General stiffness	26	86.67
Difficulty getting out of the chair	21	70
Reduced dexterity	18	60
Weakness	15	50
Problems with balance	14	46.67
Difficulty in speech	7	23.33
Muscle cramping	4	13.33

The median number of motor symptoms per patient was 5.5 (IQR: 1.75), with a range of 3 to 8 symptoms. Each patient experienced an improvement in 1 to 3 motor symptoms after medication, with most patients (30%) experiencing six motor symptoms.

Table 3. Proportion of patients based on the number of motor symptoms

Variable	Number (n = 30)	Percentage (%)
Number of motor symptoms experienced per patient		
- 3 symptoms	2	6.67
- 4 symptoms	6	20
- 5 symptoms	7	23.33
- 6 symptoms	9	30
- 7 symptoms	4	13.33
- 8 symptoms	2	6.67
Number of motor symptoms experienced per patient		
- 1 symptoms	13	43.33
- 2 symptoms	13	43.33
- 3 symptoms	7	13.33

Non-motor symptoms

The most prevalent non-motor symptom was abdominal discomfort (56.67%), followed by aching (50%). Other non-motor symptoms included mood changes (30%), dullness thinking (30%), pain (20%), feeling hot and cold (16.67%), anxiety (6.67%), and panic attacks (6.67%).

Table 4. Proportion of patients experiencing non-motor symptoms

Variable	Number (n = 30)	Percentage (%)
Abdominal discomfort	17	56.67
Aching	15	50
Mood changes	9	30
Cloudy mind / dullness thinking	9	30
Pain	6	20
Experience hot and cold	5	16.67
Anxiety	2	6.67
Numbness	2	6.67
Experiencing panic attacks	2	6.67
Experiencing sweating	0	0

Four patients (13.33%) did not experience any non-motor symptoms. The average number of non-motor symptoms per patient was 2.23 ± 1.47 , with patients experiencing between 0 and 6 symptoms. Most patients (33.33%) experienced two non-motor symptoms. The next dose of medication did not improve any non-motor symptoms.

Table 5. Proportion of patients based on the number of non-motor symptoms

Variable	Number (n = 30)	Percentage (%)
Number of non-motor symptoms experienced by patients		
- No symptoms	4	13.33
- 1 symptom	4	13.33
- 2 symptoms	10	33.33
- 3 symptoms	9	30
- 4 symptoms	1	3.33
- 6 symptoms	2	6.67
Number of improved non-motor symptoms		
- No symptoms	30	100

DISCUSSION

Demographic and clinical characteristics

The demographic findings align with previous studies indicating age as a significant risk factor for Parkinson's disease.¹⁴ The male predominance is consistent with other research, which suggest hormonal and genetic differences as underlying factors.¹⁵ The average disease duration of 5.2 ± 1.471 years, with most patients in stage III, aligns with the typical progression timeline of Parkinson's, where significant deterioration develops within 3 to 7 years post-onset.¹⁶

Motor symptoms

The predominance of tremor in this study is consistent with findings from the Philippines and Indonesia,^{17,18} while studies from Italy and Vietnam reported bradykinesia as more common.^{11,19} The elevated incidence of tremor could be attributed to its noticeable nature, increasing the likelihood of patients pursuing medical attention for this symptom.²⁰

Parkinson's disease motor symptoms are primarily due to basal ganglia dysfunction caused by reduced dopaminergic activity.²¹ Specific symptoms, such as difficulty rising from a seated position, are associated with impaired postural control and force transmission.²² Rigidity, bradykinesia, and postural instability all contribute to balance issues, increasing the risk of falls.²³ Speech difficulties result from motor coordination and sensory issues,²⁴ while muscle cramps are often due to poor posture.²⁵

Non-motor symptoms

The prevalence of abdominal discomfort and aching among non-motor symptoms in this study

differs from findings in other regions. Sweating and cloudy mind were the most common non-motor symptoms in Vietnam,¹¹ but insomnia was prevalent in the Philippines.¹⁷ According to Italian studies, mood changes and anxiety were the most common non-motor symptoms.¹⁹ In previous Indonesian studies, pain and insomnia were the most commonly reported non-motor symptoms.¹⁸

Non-motor symptoms vary between regions, highlighting Parkinson's disease complexity and heterogeneity. These symptoms are frequently underreported and undiagnosed due to a lack of comprehensive patient interviews and detailed symptom questionnaires thus significantly reduce the patient's quality of life.²⁶ Non-motor symptoms such as mood changes, anxiety, and panic attacks can be linked to dopaminergic dysfunction and structural changes in the brain.²⁷ Autonomic nerve system dysfunction can cause symptoms such as abdominal discomfort and sweating.²⁸ Pain in Parkinson's patients is often caused by basal ganglia dysfunction, which impairs sensory input modulation, whereas cognitive issues might be caused by neurotransmitter imbalances and structural brain changes.²⁹

Study implication

The high incidence of wearing off (56.67%) aligns with existing literature, highlighting both the prevalence of this phenomenon and its detrimental effect on patients' quality of life.³⁰ Adjunct therapies such as dopamine agonists and COMT inhibitors, playing a critical role in maintaining dopamine levels and enhancing levodopa efficacy, as shown by their common use among the people in the study.^{11,31,32}

The persistence of non-motor symptoms, even with comprehensive motor symptom management, highlights a significant gap in current clinical treatment protocols for Parkinson's disease. Previous studies have similarly noted that while levodopa and adjunct therapies effectively address motor symptoms, non-motor symptoms frequently remain untreated. This persistent gap in care may significantly impact overall patient well-being.³³ The study's findings underscore the need for a more holistic approach to Parkinson's disease management, integrating targeted therapies for non-motor symptoms.

This study's strengths include the use of the validated Indonesian version of the Wearing-Off Questionnaire-19 (WOQ-19), ensuring accurate symptom identification. The cross-sectional design and purposive sampling effectively capture the symptom profiles of Parkinson's patients. Ethical approval and informed consent further enhance its credibility.

This study looked at motor and non-motor symptoms in Parkinson's patients using the Indonesian

version of the Wearing Off Questionnaire 19, but it did not assess quality of life and comorbidity profiles. Adding these aspects could provide additional information about how symptoms affect patients and what management they need, but their absence doesn't lessen the value of what this study reveals about the symptoms of Parkinson's patients.

CONCLUSION

Tremor was shown to be the most common motor symptom among Parkinson's disease patients, while abdominal discomfort was the most common non-motor symptom. Levodopa was effective in managing motor symptoms; however, the prevalence of "wearing off" necessitated the use of additional therapies. These findings emphasize the need for a holistic approach to symptom management, addressing both motor and non-motor symptoms. The recommendations include improving healthcare practitioners' attention to patient symptoms and treatment strategies.

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Conflict of Interest

The authors have no conflict of interests

Ethic Consideration

The study received ethical clearance from the Health Research Ethics Committee of Bethesda Hospital Yogyakarta, under the certification number No.01/KEPK-RSB/I/24. All participants provided informed consent.

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Author Contributions

BM led the study design, conducted the data analysis, and drafted the manuscript. RTP collected the data and contributed to organizing and designing the analysis. RTP and YCP assisted in the analysis design and participated in revising the manuscript. All authors reviewed and approved the final version of the manuscript.

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