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Non-motor Symptom Burden and Its Clinical Correlates in Parkinson's Disease: A Cross-sectional Study in Indonesia

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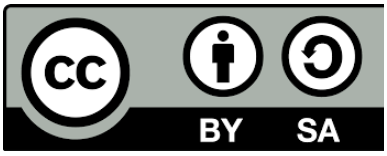

ABSTRACT

Introduction: *Non-motor symptoms (NMS) are increasingly recognized to have disabling impact on the quality of life of idiopathic Parkinson's disease (PD) patients, comparable to motor symptoms. However, their relationship with clinical and demographic factors remains obscure in local populations.* ***Purpose:*** *To determine the prevalence of NMS in idiopathic PD and evaluate their correlation with clinical variables, including disease duration, Hoehn & Yahr (H&Y) stage, and PD subtype.* ***Methods:*** *This cross-sectional study consecutively included idiopathic PD subjects evaluated between July-October 2025. Data collected included age, gender, age at onset, disease duration, H&Y stage, and PD subtype. NMS were assessed using the Indonesian version of Non-Motor Symptoms Questionnaire (NMS-Q). Correlation and multiple linear regression analyses performed.* ***Results:*** *Fifty-three subjects were included (mean age 66.9±10.5 years; 50.9% male). Median disease duration was 5 years (IQR 1–7.5), with majority in H&Y stage 2 (49%). Mean total NMS-Q score was 10.7±5.2. The most frequent NMS was urinary urgency (66%), with urinary domain being the most affected (64.2%). Total NMS-Q scores correlated with H&Y stage (r=0.427, p=0.001) and disease duration (r=0.309, p=0.025). Only H&Y stage independently predicted total NMS-Q scores (B=2.657, p=0.010).* ***Conclusion:*** *This study provides additional evidence from an Indonesian population using a standardized assessment tool, demonstrating that disease severity is an independent predictor of NMS burden, thus highlighting the importance of early and systematic evaluation of NMS in idiopathic PD.*

1. INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease (AD). It is traditionally defined by its cardinal motor symptoms (bradykinesia, resting tremor, rigidity, and postural instability).[1,2] However, the understanding of PD has evolved substantially over the past two decades, and is now recognized as a multisystem disorder encompassing a wide range of non-motor symptoms (NMS) in addition to motor symptoms.[3] These NMS, which often appear before the onset of motor symptoms, contribute significantly to disease burden and patient disability, highlighting their importance for early recognition and the development of targeted neuroprotective strategies.[4]

NMS comprise of a wide range of manifestations, such as neuropsychiatric symptoms, sleep disorders, autonomic dysfunctions, gastrointestinal disturbances, and olfactory dysfunction.[5-10] They may manifest at any stage of PD, with several symptoms appearing even before the onset of motor symptoms, such as olfactory dysfunction, Rapid Eye Movement (REM) sleep behavior disorder, depression, and constipation. Increasing evidence indicates that NMS represent some of the most disabling aspects of PD.[11]

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The Non-Motor Symptoms Questionnaire (NMS-Q), developed by the International Parkinson and Movement Disorder Society (MDS) in collaboration with the Community for Research and Involvement by People with Parkinson's (CRISP), is a self-administered screening tool designed to improve recognition of NMS in PD.[12] It comprises nine symptom domains and facilitates rapid identification of a broad range of NMS. Validation studies have shown that NMS are significantly more prevalent in PD than in healthy controls, with symptom burden increasing with disease progression; urinary symptoms are reported in approximately 60% of patients.[13,14]

Despite increasing recognition of NMS in idiopathic PD, data regarding their prevalence, distribution, and clinical correlations in Indonesian populations remain limited, Therefore, this study aimed to determine the prevalence and domain distribution of NMS in idiopathic PD using the Indonesian version of the NMS-Q, formally translated and approved by MDS, and to analyze their correlations with demographic and clinical variables, including age, gender, disease duration, Hoehn and Yahr (H&Y) stage, and PD subtype.

2. METHODS

Study Design and Participants

This cross-sectional observational study consecutively included 53 patients clinically diagnosed with idiopathic PD who attended the Neurology outpatient clinic at Siloam Hospitals Lippo Village between July 2025 - October 2025. Subjects with secondary parkinson, Parkinson plus syndrome, or comorbid neurological disorders were excluded. Demographic and clinical data were obtained prospectively through structured interviews and medical record reviews. Collected variables included age, gender, age at onset, disease duration, and Hoehn and Yahr (H&Y) stage for disease severity classification. Disease duration was defined as the time (in years) from the onset of initial symptoms to the date of examination. Motor phenotype was categorized as tremor-dominant or non-tremor dominant based on clinical presentation. Non-motor symptoms were assessed using a structured questionnaire based on the Indonesian version of Non-Motor Symptoms Questionnaire (NMS-Q), with translation provided from MDS. A limitation of this study is we did not exclude or systematically assess other potential causes of nocturia, such as obstructive sleep apnea, which may be prevalent in idiopathic PD patients and could confound the interpretation of urinary symptoms.

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 27.0. Descriptive statistics were expressed as mean ± standard deviation (SD) and median with interquartile range (IQR) for normally distributed and non-normally distributed variables, respectively. Categorical data were presented as frequencies and percentages. Normality of the data was assessed using the Shapiro–Wilk test. As the data were not normally distributed, non-parametric tests were applied, including Spearman's rank correlation and the Mann–Whitney U test. The Spearman's correlation test was used to assess relationships between total NMS-Q scores and continuous clinical variables (age, age at onset, disease duration, and H&Y stage). The Mann–Whitney U test was used to assess the association between NMS-Q scores and categorical variable (gender). Variables with p-values <0.20 in the bivariate analysis were included in the multiple linear regression model to identify independent predictors of total NMS-Q score. A two-tailed $p < 0.05$ was considered statistically significant.

Ethical approval

Protocol and consent form were approved by the Research Ethics Committee of Faculty of Medicine Universitas Pelita Harapan and Siloam Hospitals Lippo Village (224/K-LKJ/ETIK/VI/2025).

3. RESULTS

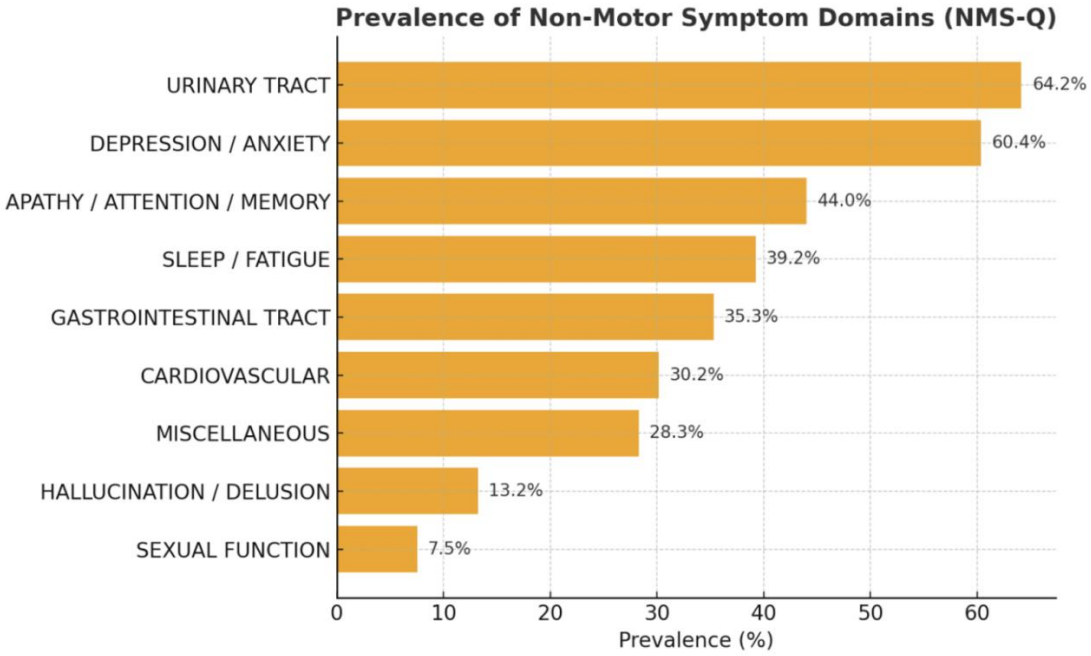
A total of 53 participants with idiopathic PD were included in the analysis, comprising 27 males (50.9%) and 26 females (49.1%). The mean age of participants and age at onset were 66.94±10.53 and 61.77±12.78 years, respectively. The median disease duration was 5 years (IQR 1-7.5). Most participants were in H&Y stage 2 (n = 26, 49.0%). No patients with H&Y stage 4 were encountered during the recruitment period. Regarding PD subtypes, 37.7% were classified as tremor-dominant, whereas 62.3% were identified as non-tremor dominant. The mean total NMS-Q score was 10.68±5.18 (Table 1).

Table 1.
Baseline demographic and clinical characteristics of study participants

Variable	Characteristics
Age (years), mean ± SD	66.94±10.53
Gender, n (%)	
Male	27 (50.9)
Female	26 (49.1)
Age at onset (years), mean ± SD	61.77±12.78
Disease duration (years), median (IQR)	5 (1-7.5)
H&Y Stage, n (%)	
1	10 (18.9)
2	26 (49)
3	17 (32.1)
PD subtype, n (%)	
Tremor dominant	20 (37.7)
Non-tremor dominant	33 (62.3)
Total NMS-Q Score, mean ± SD	10.68±5.18

Abbreviations: H&Y, Hoehn & Yahr; NMS-Q, Non-Motor Symptoms Questionnaire; PD, Parkinson's disease

Figure 1.
Prevalence of non-motor symptom domains (NMS-Q)



The frequency of individual questions assessed by the NMS-Q is presented in Table 2. The most commonly reported symptoms waere urinary urgency (66%) and anxiety (66%). Less frequently reported symptoms included bowel incontinence (18.9%), daytime sleepiness (17%), nausea/vomiting (15.1%), sweating (15.1%), lower limb edema (9.4%), sexual performance difficulties (7.5%), and delusions (3.8%). The domains which accounted for most positive answers were urinary tract (64.15%) and depression/anxiety (60.38%). The sexual function domain had the least reported symptoms (7.55%) (Figure 1). Overall, these findings highlight that autonomic and neuropsychiatric symptoms were the most prevalent NMS in this cohort.

Table 2.
Individual non-motor symptoms from NMS-Q

Question No.	Symptoms	Yes (%)	Question No.	Symptoms	Yes (%)
1	Sialorrhea	18 (34)	16	Sad / Depression	29 (54.7)
2	Reduced taste/smell	14 (26.4)	17	Anxiety	35 (66)
3	Dysphagia	26 (49.1)	18	Lack of sexual drive	4 (7.5)
4	Nausea/vomiting	8 (15.1)	19	Sexual performance difficulties	4 (7.5)
5	Constipation	29 (54.7)	20	Dizziness	21 (39.6)
6	Bowel incontinence	10 (18.9)	21	Falls	11 (20.8)
7	Incomplete bowel emptying	26 (49.1)	22	Daytime sleepiness	9 (17)
8	Urinary urgency	35 (66)	23	Insomnia	20 (37.7)
9	Nocturia	30 (62.5)	24	Intense vivid dreams	19 (35.8)
10	Pain	33 (62.3)	25	REM Sleep Behavior Disorder	27 (50.9)
11	Weight changes	12 (22.6)	26	Restless leg syndrome	29 (54.7)
12	Memory impairment	23 (43.4)	27	Lower limb edema	5 (9.4)
13	Anhedonia	26 (49.1)	28	Sweating	8 (15.1)
14	Hallucinations	12 (22.6)	29	Diplopia	17 (32.1)
15	Difficulty concentrating	21 (39.6)	30	Delusions	2 (3.8)

Correlation and comparative analyses were performed to evaluate the relationship between demographic and clinical characteristics with total NMS-Q scores, as presented in Table 3. Total NMS-Q scores showed significant correlation with H&Y stage (r = 0.427, p = 0.001) and disease duration (r = 0.309, p = 0.025), respectively indicating that higher disease severity and longer disease duration are associated with greater NMS burden. In contrast, no significant correlations were found between total NMS-Q scores with gender (U = 337.50, Z = –0.241, p = 0.810), age (r = –0.025, p = 0.860), and age at onset (r = –0.124, p = 0.377).

A multiple linear regression analysis was conducted to examine the independent association of disease duration and H&Y stage with total NMS-Q scores. Multicollinearity was assessed using the variance inflation factor (VIF), with values >5 indicating potential concern. In this model, VIF values were low (VIF = 1.162 for both variables), suggesting no evidence of multicollinearity between predictors. Among the predictors, H&Y stage was a significant independent predictor of

total NMS-Q score (B = 2.657, β = 0.363, *t* = 2.691, *p* = 0.010), indicating that higher disease stage was associated with more severe NMS (Table 4).

Table 3.
Association of demographic and clinical variables with total NMS-Q scores

Variable	Statistical Test	Test Value	p-value
H&Y stage	Spearman's correlation	r = 0.427	**0.001**
Disease duration	Spearman's correlation	r = 0.309	**0.025**
Age	Spearman's correlation	r = -0.025	0.860
Age at onset	Spearman's correlation	r = -0.124	0.377
Gender	Mann–Whitney U	U = 337.50, Z = -0.241	0.810
PD Subtype	Mann–Whitney U	U = 320, Z = -0.184	0.854

Abbreviations: H&Y, Hoehn & Yahr.

Table 4.
Multiple linear regression analysis of factors associated with total NMS-Q scores

Predictor Variable	B	SE	β	t	p-value	VIF
(Constant)	3.954	2.056	—	1.923	0.060	—
Disease duration	0.190	0.141	0.182	1.349	0.184	1.162
H&Y stage	2.657	0.987	0.363	2.691	**0.010**	1.162

4. DISCUSSION

Our findings reinforce the high prevalence of NMS in PD and are consistent with prior studies showing that autonomic and neuropsychiatric symptoms are among the most frequent and clinically significant manifestations.[15,16] In this study, urinary and neuropsychiatric domains were particularly prominent, underscoring their contribution to overall disease burden. Urinary urgency, nocturia, and other bladder symptoms likely reflect early autonomic involvement, which often goes unrecognized in clinical practice.[11] Previous studies have similarly identified urinary dysfunction as one of the most prevalent NMS, affecting more than half of PD patients.[17-21] Conversely, the relatively low frequency of sexual dysfunction observed in our sample may reflect underreporting or reluctance to disclose intimate symptoms rather than a true lower prevalence, as several studies have documented higher rates of sexual disturbances in PD.[22] Nonetheless, consistent with our findings, Karri et al. observed sexual dysfunction to be among the least reported NMS, with a prevalence of approximately 3%.[23]

In addition to urinary urgency, anxiety was one of the most frequently reported NMS (66%) in our study, with the depression/anxiety domain emerging as the second most commonly affected (60.38%). While many previous studies have reported comparable or slightly lower rates of anxiety and depression in PD,[7,24,25] some have observed even higher prevalence, with anxiety affecting up to 73% of patients.[26,27] These symptoms are believed to arise from disruptions in serotonergic, dopaminergic, and noradrenergic pathway.[10] Consistent with our results, large multicenter studies such as the PRIAMO study have identified neuropsychiatric symptoms as among the most frequent and burdensome NMS in PD populations.[24] These findings highlight the clinical importance of routinely screening for anxiety and mood disturbances as part of comprehensive PD management, given their significant contribution to disability and reduced quality of life.

Similar to previous studies, our findings demonstrated that higher NMS burden was significantly correlated with increasing H&Y stage (r = 0.427, p = 0.001) and longer disease

duration (r = 0.309, p = 0.025). This pattern suggests that as PD progresses, both the variety and severity of non-motor symptoms escalate, a trend similarly reported by Fernandes et al. and Vongvaivanich et al.[25,28] In multivariate analysis, H&Y stage remained a significant independent predictor of total NMS-Q score (B = 2.657; β = 0.363; t = 2.691; p = 0.010), whereas disease duration did not (B = 0.190; β = 0.182; t = 1.349; p = 0.184). While findings across studies are heterogeneous, most literature report that both disease stage and duration contribute to NMS burden,[25] with few identifying H&Y stage as the dominant predictor as consistent with our results.[15] Differences in sample, assessment instrument (NMS-Q vs NMSS), and analytic approach likely explain these variations. In effect, our findings imply that patients in more advanced PD stages are more likely to manifest greater NMS burden, irrespective of how long they have had the disease.

From a pathophysiological standpoint, this finding is plausible. NMS in PD reflect widespread neurodegeneration beyond the nigrostriatal dopaminergic system, including noradrenergic, serotonergic, cholinergic, and autonomic pathways, thus correlating more closely with global brain involvement and disease stage rather than simply disease duration.[11] The fact that disease duration did not independently predict NMS burden may reflect heterogeneity in disease progression and the influence of other factors, such as medication effects, or comorbidities in NMS development.

Several limitations of this study should be acknowledged. Its single-center, cross-sectional design prevents determination of causal relationships or the temporal sequence of NMS development. The modest sample size and predominance of participants in H&Y stage 2 may limit the external validation of the findings and reduce sensitivity for detecting between-group differences. Moreover, the NMS-Q, while useful for screening, does not capture the severity, frequency, or longitudinal evolution of individual symptoms. The use of self-reported data may also introduce recall or reporting bias, particularly for socially sensitive domains such as sexual or psychiatric symptoms. Future studies should adopt longitudinal designs with larger and more diverse samples to track NMS progression across disease stages

5. CONCLUSION

This study highlights the substantial burden of NMS among individuals with PD, emphasizing the high prevalence of autonomic and neuropsychiatric disturbances in our Indonesian observational study. The strong association between higher H&Y stage and greater NMS burden underscores the progressive nature of these symptoms as disease severity advances. These findings emphasize the importance of systematic NMS screening across all disease stages to facilitate early detection and intervention, ultimately contributing to better patient outcomes and quality of life.

6. ACKNOWLEDGEMENTS

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