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Original Research

Depression and Anxiety in Parkinson's Disease: Prevalence and Associated Risk Factors

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Abstract

Objectives: Parkinson's disease (PD) is a neurodegenerative disorder with both motor and non-motor symptoms, including depression and anxiety, which significantly impact patients' quality of life. The predictors of these psychiatric symptoms remain incompletely understood. This study aims to evaluate the prevalence and potential predictors of depression and anxiety in PD.

Methods: A prospective study was conducted on 99 idiopathic PD patients. Depression and anxiety were assessed using the Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder-7 (GAD-7) scale. A range of clinical and demographic variables, including motor symptoms, sleep disturbances, and quality of life, were analyzed using regression models.

Results: Of the patients, 57.5% had depression, 48.4% had anxiety, and 36.3% had both. Significant predictors of depression included the use of apomorphine, which was associated with lower PHQ-9 scores (p=0.031), and the presence of restless legs syndrome (RLS), which was linked to higher depression scores (p=0.037). For anxiety, younger age was a significant predictor (p=0.007). Both depression and anxiety scores correlated with lower quality of life (p<0.001 for both).

Conclusion: This study highlights the high prevalence of depression and anxiety in PD, with significant predictors including RLS for depression and younger age for anxiety. Apomorphine use appears protective against depression. Both depression and anxiety disrupt quality of life. These findings underscore the importance of routine psychiatric screening and comprehensive management of depression and anxiety in PD, aiming to improve patient outcomes.

Keywords: Anxiety, depression, mental health, Parkinson's disease, psychiatric comorbidity, quality of life

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Parkinson's disease (PD) is a complex neurodegenerative disease that affects both motor and non-motor functions. While motor impairments, such as bradykinesia, rigidity, hypokinetic dysarthria, and tremor, define the disease, non-motor symptoms, including psychiatric problems, pain, and sleep disturbances, significantly contribute to disease burden and diminish patients' quality of life.[1,2] Among these non-motor symptoms, depression and anxiety are particularly prevalent, with estimates suggesting that up to 50% of PD patients experience one or both conditions during the course of their illness.[3,4] Depression and anxiety are strongly linked to impaired work and social functioning, an increased need for care, and a substantial decline in health-related life quality.[5-8] Furthermore,

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depression in PD has been linked to a faster physical and cognitive decline, an elevated risk of dementia, and higher mortality rates.[9,10] Despite their clinical importance, the predictors and underlying mechanisms of depression and anxiety in PD remain incompletely understood.

The neurological basis of depression and anxiety in PD is multi-faceted, likely involving a complex interplay of dopaminergic and non-dopaminergic dysfunction, disease-related neurodegeneration, and psychosocial stressors.[11,12] Additionally, various demographic and clinical variables, including age, sex, disorder onset time, motor symptom intensity, and comorbid conditions like sleep disturbances, have been investigated for their potential association with psychiatric symptoms. However, findings from previous studies have been inconsistent, highlighting the necessity for additional studies.[13,14]

The objective of this study was to evaluate the prevalence of depression and anxiety in patients with idiopathic PD and identify their potential predictors using validated screening tools, including the Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder-7 (GAD-7).[15,16] By examining various demographic and clinical factors, including motor symptom intensity, sleep disturbances, and life quality, we sought to provide a comprehensive evaluation of factors influencing depression and anxiety in PD. The findings aim to enhance understanding of these non-motor symptoms and inform strategies to improve the clinical management of PD.

Patients and Methods

Patients Selection

This prospective study included patients with idiopathic PD, who were evaluated at the Movement Disorders Outpatient Clinic, Department of Neurology, Sisli Hamidiye Etfal Training and Research Hospital, from August 2024 to January 2025. The Ethics Committee of Sisli Hamidiye Etfal Training and Research Hospital endorsed the study protocol (approval date and number: 11.06.2024-4439). This study was conducted in accordance with the Declaration of Helsinki. All patients gave written informed consent and were evaluated by a neurologist with expertise in movement disorders. Participants were included if they had a diagnosis of idiopathic PD. Exclusion criteria included parkinsonism due to causes other than idiopathic PD, prior treatment with levodopa-carbidopa intestinal gel or deep brain stimulation (DBS), a history of depression or anxiety, dementia, current use of medication for depression and/or anxiety, and unwillingness to participate in the study.

Assessment Procedures

All evaluations were conducted when patients were in the 'on' state. The Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III was administered to assess motor symptoms.[17] Disease severity was classified based on the Hoehn and Yahr Scale.[18]

The PHQ-9 and GAD-7 scales were used to assess depression and anxiety, respectively. A score of 5 or higher was used as the cut-off for the existence of depression and anxiety disorder.[15,16] The EQ-5D-3L, a three-level version of EQ-5D developed by the EuroQol Group, was used to assess health-related quality of life.[19]

Additionally, data on patient demographic information, age of disorder onset, disease duration, and the presence of sleep disorders such as rapid eye movement sleep behavior disorder (RBD) and restless legs syndrome (RLS) were collected. Information regarding the existence of pain and other comorbidities was also recorded.

Statistical Analysis

The PHQ-9 and GAD-7 scores were evaluated to determine their associations with various demographic and clinical variables, including age, sex, age at disease onset, PD duration, medication use, MDS-UPDRS III scores, EQ-5D-3L scores, H&Y stage, RLS, RBD, and insomnia. All analyses were conducted with the R statistical programming language, version 4.3.1 (Vienna, Austria: R Foundation for Statistical Computing). Data distribution was evaluated through the Kolmogorov-Smirnov test, skewness, and kurtosis. Given that none of the variables followed a normal distribution, descriptive statistics were reported as median, interquartile range (IQR), and frequency counts. Group comparisons were conducted using the Chi-squared test for categorical variables and the Mann-Whitney U test for continuous variables. Additionally, multiple linear regression models were developed to identify significant predictors of depression and anxiety. A 95% confidence level ($p<0.05$) was used to assess statistical significance.

An a priori power analysis was conducted using G*Power (version 3.1) to determine the required sample size for detecting individual predictors in a multiple regression model. Assuming a medium effect size ($f^2=0.15$), a significance level of $\alpha=0.05$, desired statistical power of 0.80, and 12 predictors included in the model, the analysis indicated a required minimum sample size of approximately 55 participants. Our final sample of 99 participants exceeded this requirement, resulting in an achieved power of approximately 97%, confirming that the study was sufficiently powered to detect statistically significant effects of individual predictors.

Results

Clinical and Demographic Findings

During the study period, 123 patients with PD were evaluated. Of these, 24 patients were excluded for various reasons: 3 had undergone DBS, 6 had a history of depression or anxiety, 8 had been diagnosed with dementia, and 7 were receiving treatment for depression and/or anxiety. The study sample comprised 99 patients, consisting of 37 females and 62 males. The median age of patients was 66 years (IQR:56–73), the median age of disease onset was 59 years (IQR:50.5–67.0), and the median disease duration was 5 years (IQR:3–8). The median MDS-UPDRS III score was 15 (IQR:12–24).

Among the participants, 6 patients (6.06%) reported insomnia, 16 (16.2%) had RLS, 28 (28.3%) had RBD, and 9 patients (9.1%) experienced excessive daytime sleepiness. The most frequently prescribed medications included levodopa with benserazide (n=63), rasagiline (n=50), dopamine agonists (n=48), levodopa with carbidopa and entacapone (n=27), levodopa with carbidopa (n=25), amantadine (n=13), and apomorphine (n=3).

Findings from Questionnaires and Depression/ Anxiety-Related Factors

The median PHQ-9 score among participants was 5 (IQR:3–11), while the median GAD-7 score was 4 (IQR:1–8.5). A total of 57 patients (57.5%) (27 females, 30 males) had a PHQ-9 score of 5 or higher, while 48 patients (48.4%) (20 females, 28 males) had a GAD-7 score of 5 or higher. A total of 36 patients (36.3%) (17 females, 19 males) had both PHQ-9 and GAD-7 scores of 5 or higher. To identify factors associated with depression and anxiety in patients with PD, two multiple linear regression models were constructed. The first model assessed predictors of PHQ-9 scores, while the second focused on GAD-7 scores. A summary of the results from both models is provided in Table 1.

No significant associations were observed between sex, MDS-UPDRS III scores, Hoehn and Yahr stage, PD duration, dopamine agonists, rasagiline, levodopa combinations, amantadine, the presence of chronic pain, RBD, insomnia, excessive daytime sleepiness, and either GAD-7 or PHQ-9 scores.

The regression model predicting PHQ-9 scores explained 60.7% of the variance (r^2=0.607). Significant predictors included the use of apomorphine, which was associated with lower PHQ-9 scores (β=-6.25, p=0.031), and the presence of RLS, which was linked to higher PHQ-9 scores (β=2.91, p=0.037) (Fig. 1). Higher EQ-5D-3L scores, indicating poorer quality of life, were associated with increased depression scores (β=1.50, p<0.001). Additionally, higher GAD-7 scores showed a positive relationship with higher PHQ-9 scores (β=0.26, p=0.018) (Table 1).

Table 1. Regression analysis results for PHQ-9 and GAD-7

Variable	PHQ-9 Coefficient (β)	PHQ-9 p	GAD-7 Coefficient (β)	GAD-7 p
Age	-0.01	0.760	-0.11	0.007*
Sex	-0.23	0.820	-0.29	0.772
Parkinson's disease duration	-0.17	0.151	-0.04	0.743
Apomorphine	-6.25	0.031*	-4.59	0.110
Dopamine agonists	-0.767	0.437	1.433	0.142
Rasagiline	0.541	0.578	-0.589	0.543
Levodopa combinations	-1.642	0.313	1.281	0.428
Amantadine	-1.073	0.464	-1.080	0.457
MDS-UPDRS III	-0.03	0.606	0.04	0.521
Hoehn &Yahr Stage	1.07	0.284	-0.87	0.378
Existence of pain	-1.68	0.167	0.84	0.486
Rapid eye movement sleep behavior disorder	-0.56	0.614	-0.16	0.881
Insomnia	0.48	0.805	0.53	0.784
Restless leg syndrome	2.91	0.037*	-0.47	0.738
Daytime Sleepiness	-1.17	0.446	0.92	0.546
EQ-5D-3L	1.50	<0.001**	1.10	<0.001**
GAD-7	0.26	0.018*	–	–
PHQ-9	–	–	0.25	0.018*

*Significant at p<0.05; **Significant at p<0.001. MDS-UPDRS III: The Movement Disorders Society-Unified Parkinson's Disease Rating Scale part III; Euroqol EQ-5D-3L: 3-level version of EQ-5D (EQ-5D-3L) by the EuroQol Group; GAD-7: General Anxiety Disorder-7 scale; PHQ-9: Patient Depression Questionnaire-9 scale.

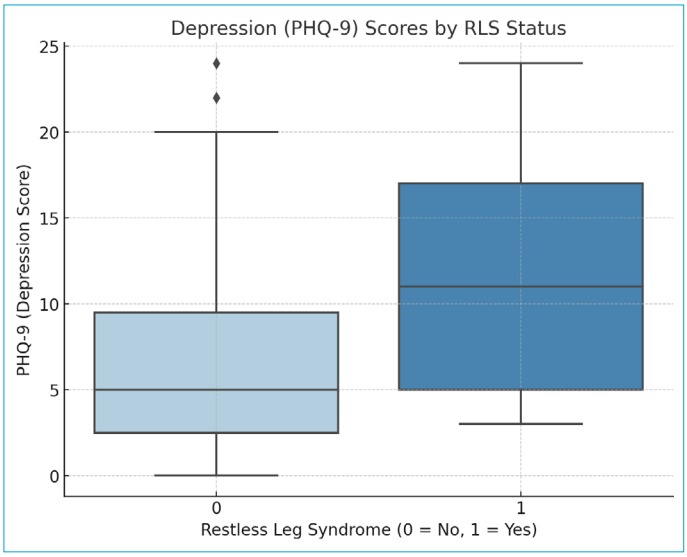

Figure 1. Relationship between restless leg syndrome and depression.

**PHQ-9: Patient Depression Questionnaire-9 scale; RLS: Restless leg syndrome.*

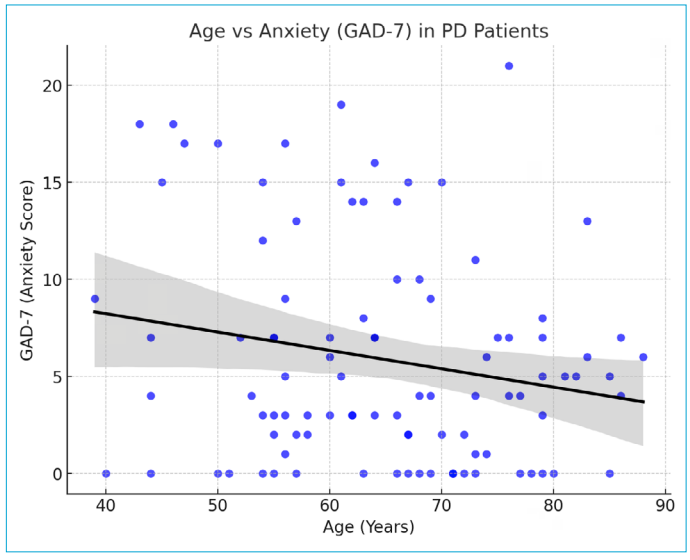

Figure 2. Relationship between age and anxiety.

**GAD-7: General Anxiety Disorder-7 scale.*

The regression model predicting GAD-7 scores accounted for 55.3% of the variance (r^2=0.553). Significant predictors included higher PHQ-9 scores, demonstrating a positive association between depression and anxiety (β=0.25, p=0.018). Younger age was linked to higher GAD-7 scores (β=-0.11, p=0.007) (Fig. 2). Higher EQ-5D-3L scores, indicating poorer quality of life, were associated with higher GAD-7 scores (β=1.10, p<0.001) (Table 1).

Discussion

Our key findings were as follows: (i) 57.5% of patients with PD had depression, 48.4% had anxiety, and 36.3% had both conditions; (ii) apomorphine use was associated with lower depression scores; (iii) RLS was associated with higher depression scores; (iv) younger age was linked to higher anxiety levels; and (v) both depression and anxiety were found to negatively impact quality of life.

A total of 57 patients (57.5%) in our study had depression, 48 patients (48.4%) had anxiety, and 36 patients (36.3%) experienced both depression and anxiety. These results highlight the high prevalence of these psychiatric comorbidities in PD and their potential under-recognition in clinical practice.[3,13,20] Moreover, the co-occurrence of depression and anxiety in approximately one-third of patients with PD aligns with existing literature, emphasizing the need for comprehensive mental health assessments in this population.[4]

Even though the number of patients using apomorphine was low, our regression analyses revealed that the use of apomorphine was associated with lower depression scores. Apomorphine, a dopamine agonist, may alleviate depressive symptoms by enhancing dopaminergic activity, which plays a central role in mood regulation.[21,22] Dopamine agonists, such as pramipexole and rotigotine, have been shown to effectively treat depression in patients with PD.[21,23,24] Our findings align with previous research, suggesting that dopaminergic treatments may have a beneficial effect on mood in PD.

RLS was identified as a significant contributor to depressive symptoms, reinforcing previous evidence that sleep disturbances exacerbate mood disorders in PD.[25] Although our study did not reveal a notable link between insomnia and depression, the presence of RLS correlated with higher depression scores, suggesting that sleep disruptions may amplify the neuropsychiatric burden by impairing restorative processes and exacerbating fatigue.[26,27]

Poorer quality of life was strongly linked to higher PHQ-9 and GAD-7 scores, underscoring the bidirectional relationship between psychiatric symptoms and overall well-being in PD.[5,13] These findings highlight the importance of addressing psychosocial and functional impairments to improve mental health outcomes in this population. Given that PD progressively impairs motor function, autonomy, and social participation, the presence of psychiatric symptoms may further exacerbate disease burden, leading to greater disability and reduced life satisfaction.[1,5-8] This underscores the critical need for a comprehensive, multidisciplinary approach to PD management, incorporating both pharmacological and non-pharmacological interventions aimed at improving psychosocial and functional well-being. Addressing the interplay between mental health and quality of life is essential to optimizing patient-centered care and enhancing overall outcomes in this population.

Interestingly, younger age was a predictor of higher anxiety scores, consistent with studies suggesting that younger patients with PD may face greater psychological challenges related to disease adaptation, social roles, and employment concerns.[4] This underscores the need for targeted interventions to address the unique challenges faced by younger patients with PD.

Contrary to expectations, no significant associations were found between anxiety or depression and motor symptom severity (MDS-UPDRS III), Hoehn and Yahr stage, PD duration, or comorbidities such as pain and RBD. These observations imply that psychiatric symptoms in PD may not directly correlate with motor symptom severity or disease duration, highlighting the need for multidimensional approaches to understanding and managing these non-motor symptoms.[11,14]

The strengths of this study include its comprehensive assessment of demographic, clinical, and psychosocial factors using validated scales and its focus on idiopathic PD patients. However, several limitations should be considered. First, the small number of patients using apomorphine limits the generalizability of the observed association between apomorphine use and lower depression scores. Second, the cross-sectional design precludes causal inferences, and the exclusion of patients with a history of depression or anxiety may have led to an underestimation of the frequency of psychiatric diseases in PD. Future research with a longitudinal design is necessary to explore the temporal dynamics of these relationships and the potential impact of interventions.

Conclusion

Our study reinforces the high prevalence of depression and anxiety in PD and identifies significant predictors, including RLS for depression and younger age for anxiety. Apomorphine use seems to be protective against depression in PD. Both depression and anxiety disrupt quality of life. These findings underscore the need for routine evaluation for psychiatric signs and the need for holistic management strategies that address both motor and non-motor aspects of PD to optimize patient care.

Disclosures

Ethics Committee Approval: The study was approved by the Sisli Hamidiye Etfal Training and Research Hospital Clinical Research Ethics Committee (date: 11.06.2024, number: 439).

Conflict of Interest: None declared.

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Informed Consent: Written informed consents were obtained from the patients.

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