Clinical Correlates of Non-Motor Symptoms and Quality of Life in Parkinson's Disease Patients: Analysis of Motor and Non-Motor Features

Miray Erdem[1], Derya Özdoğru[1]

1 Department of Neurology, University of Health Sciences, Adana City Training and Research Hospital, Adana, Türkiye

Abstract

Aim: Non-motor symptoms (NMS) significantly impact Parkinson's disease (PD) patients, yet their relationship with disease progression and quality of life requires further investigation. We aimed to evaluate the relationships between NMS burden, motor symptoms, disease duration and quality of life in PD patients.

Methods: In our study, 141 patients (60 females, 81 males; mean age 63.0 (33.0 - 93.0)) with PD diagnosed according to the United Kingdom Parkinson's Disease Society Brain Bank Criteria for Idiopathic PD were included. NMS were assessed using the NMS Scale. Motor symptoms were evaluated using Unified Parkinson's Disease Rating Scale Part III (UPDRS-III) and Hoehn-Yahr (H&Y) staging. Quality of life was measured using Parkinson's Disease Questionnaire-39 (PDQ-39). Disease duration was categorized into three groups: <4 years, 5-8 years, and >9 years. Statistical analyses included correlation coefficients, multivariate logistic regression, and linear regression models.

Results: NMS burden strongly correlated with quality of life (r=0.507, p<0.001) and motor symptoms (r=0.504, p<0.001). Age (p<0.001), disease duration 5-8 years (p<0.001) or 9< years (p<0.001), UPDRS-III (p<0.001), levodopa equivalent daily dose (LEDD) (p<0.001) and H&Y >3 (p<0.001) were significant in the univariate analysis. In the multivariate stage, age (p<0.001), disease duration 9< years (p=0.015) and UPDRS-III (p=0.004) remained statistically significant. Each one-unit increase in UPDRS-III increased PDQ-39 by 1.91 points and each one-point increase in NMS total score increased PDQ-39 by 3.35 points (p<0.001 for each).

Conclusion: Our study once again emphasizes the importance of non-motor symptoms in PD. Instead of the traditional approach focusing on motor symptoms, approaches that will address the quality of life of patients in a holistic manner should be developed.

***Keywords**: Parkinson's Disease, Non-Motor Symptoms, Quality of Life, Disease Progression, Movement Disorders*

1. Introduction

Parkinson's disease (PD) is a multisystem disorder associated with α-synuclein aggregates throughout the central, autonomic and peripheral nervous system, clinically characterized by motor and non-motor symptoms (NMS)[1]. Current criteria define PD as the presence of resting tremor, rigidity or bradykinesia with both. However, the clinical presentation is multifaceted and includes many non-motor symptoms[1].

Representing a preclinical phase spanning 20 or more years, NMS in PD is linked to the widespread distribution of α-synuclein pathology that is not restricted to the dopaminergic nigrostriatal system, which is responsible for the core motor features of PD[2]. There is increasing evidence that mitochondrial dysfunction, microglial activation, α-synuclein accumulation, ageing and protein misfolding contribute to the development of Parkinson's disease (PD). In addition, neuroinflammation, oxidative stress and impaired antioxidant defenses play an important role in its pathogenesis[3]. In addition to the non-nigral brainstem nuclei, α-synuclein pathology involves the sympathetic and parasympathetic, enteric, cardiac and pelvic plexuses, and many other organs, showing a topographic and chronological spread, especially in the prodromal stages of the disease[2]. In this context, symptoms such as olfactory disturbance, constipation, cardiovascular dysfunction, rapid eye movement (REM) sleep behavior disorder, depression, anxiety and others have been described[4-6]. Despite the studies, the pathophysiological mechanisms underlying NMS remain unclear and both dopaminergic (DA) and non-DA systems are thought to play a role[2]. However, it is a known fact that the severity and burden of NMS increase over time, impairing the quality of life of patients,

Corresponding Author: Miray Erdem, drmirayerdem85@gmail.com, Received: 09.01.2025, Accepted: 12.03.2025, Available Online Date: 15.03.2025 Cite this article as: Erdem M, Özdoğru D. Clinical Correlates of Non-Motor Symptoms and Quality of Life in Parkinson's Disease Patients: Analysis of Motor and Non-Motor Features. J Cukurova Anesth Surg. 2025;8(1):41-5. https://doi.org/10.36516/jocass.1616112

increasing the burden of caregivers and social costs[7,8]. Therefore, it is very important to understand that non-motor symptoms should be addressed together with motor symptoms for the proper care of PD patients.

In our study, we aimed to evaluate the relationships between NMS burden and subscale scores and motor symptoms, disease duration, levodopa equivalent daily dose (LEDD) and quality of life in PD patients.

2. Materials and Methods

2.1. Design of study and compliance

In our cross-sectional study conducted in strict adherence to the Declaration of Helsinki, the study protocol was approved by the local Ethics Committee in Adana, Turkey, at its meeting on 05 December 2024 (decision no: 250) and written informed consent was given by all participants. Informed consent complies with standards for scientific studies and includes a detailed and understandable summary of the study, the purpose of the study, confidentiality criteria, times and methods of preservation of biological material, and personal information of the participants.

2.2 Study participants

In our study, 141 patients (60 females, 81 males; mean age 63.0 (33.0 - 93.0)) with PD diagnosed according to the United Kingdom Parkinson's Disease Society Brain Bank Criteria for Idiopathic PD were included. Patients were divided into three groups according to disease duration: <4 years, 5-8 years and >9 years. Patients with Parkinson plus syndrome, those with secondary parkinsonism (drug-induced, vascular, tumoral causes), those with a previous diagnosis of dementia or psychosis, and those who could not cooperate with the tests were excluded. In addition to a detailed history and neurological examination performed by the same movement disorder specialist, demographic findings and treatments were recorded and non-motor symptoms were recorded with the NMS scale. The NMS scale[9] consists of 30 questions with a dichotomous response of present or absent for each item in six domains: neuropsychiatric symptoms (items 12-17, 30), autonomic disorders (items 1, 3-9, 18-21, 28), olfactory disorders (item 2), sleep disorders (items 22-26), sensory symptoms (item 10) and the others (items 11, 27, 29). The total NMS scale score ranges from 0-30 by counting "yes" responses. The scores indicate how many different NMS the patient has. Accordingly, patients were classified as mild (1-5 points), moderate (6-9 points), severe (10-13 points) and very severe (≥14 points). Unified Parkinson's Disease Rating Scale (UPDRS) motor scores[10] Hoehn-Yahr (H&Y) stage[10,11] and LEDD were recorded. In addition, quality of life was evaluated with the Parkinson's Disease Questionnaire – 39 (PDQ-39)[12] scale.

2.3. Statistical Method

Statistical analyses were performed using Jamovi (Version 2.3.28) and JASP (Version 0.19.2) software packages. In the analysis of demographic and clinical characteristics of Parkinson's patients, the conformity of continuous variables to normal distribution was evaluated by Shapiro-Wilk test and Q-Q plot graphs. Since the data were not normally distributed, descriptive statistics of numerical data were presented as median [minimum-maximum] and categorical data were presented as frequency (n) and percentage (%).

Kruskal-Wallis H test for continuous variables was used to compare the clinical characteristics and NMS severity of the patients according to disease duration (<4 years, 5-8 years, 9< years). When significant differences were found between the groups, post-hoc pairwise comparisons were performed with the Dwass-Steel-Critchlow-Fligner test. Pearson Chi-square test or Fisher's Exact/Fisher Freeman Halton test was used for the comparison of categorical variables (gender, educational status, H&Y scale, NMS severity classification) between the disease duration groups when the expected values were less than 5.

Spearman correlation analysis was used to analyse the relationships between the total NMS scale score, subscale scores and other clinical parameters (age, duration of education, PDQ-39, UPDRS-III, LEDD) because the variables were not normally distributed. Correlation coefficients (r) were calculated and significance levels were determined.

Univariate and multivariate logistic regression analyses were performed to determine the determinants of H&Y scale score (≤2 and >3). Model fit was analyzed by Hosmer-Lemeshow test ($p>0.05$). Variance inflation factors (VIF<10) and tolerance values (>0.2) were calculated for the multicollinearity problem between independent variables. The linearity assumption was checked by evaluating the relationship between the continuous independent variables and the logit transformed dependent variable with the Box-Tidwell test. Standardized residuals (±3), Cook's distance (<1) and leverage values were examined for outliers and influential observations. In univariate analyses, the effects of age, gender, educational status, disease duration, UPDRS-III, LEDD and NMS total score were examined. Variables with $p<0.20$ in univariate analyses were included in the multivariate model, while clinical importance was also considered in variable selection. Results were presented with odds ratio (OR) and 95% confidence intervals.

Linear regression analyses were performed separately to determine the factors affecting PDQ-39 quality of life scale, UPDRS-III motor symptom score, LEDD and NMS total score. Univariate analyses were performed for each dependent variable. In multivariate models, enter method was used and variables with $p<0.20$ in univariate analyses were evaluated. Regression coefficients (β) and 95% confidence intervals were calculated. Assumptions (normality, linearity, equivariance, multicollinearity, multicollinearity) were checked for the suitability of the models.
The significance level was accepted as $p\leq0.05$ in all statistical analyses. In post-hoc analyses for inter-group comparisons, p values corrected for multiple comparisons were used.

3. Results

The median age of the PD (n=141) who participated in the study was 63 years (33-93), 57.4% were male (n=81) and 42.6% (n=60) female. Formal education was available in 76.6% of the patients and the median duration of education was 5 years (3-15). The median disease duration was 1 year (1-3), PDQ-39 quality of life scale score was 51 (4-134), UPDRS-III motor symptom score was 16 (6-40) and LEDD was 400 mg/g (150-1700). 72.3% (n=102) of the patients had H&Y stage ≤2. According to the total score of the NMS scale, 22% of the patients had mild (1-5 points), 27% moderate (6-9 points), 25.5% severe (10-13 points) and 25.5% very severe (≥14 points) non-motor symptoms (**Table 1**).

Significant positive correlations were found between NMS scale total score and age (r=0.380), PDQ-39 (r=0.507), UPDRS-III (r=0.504) and LEDD (r=0.473) ($p<0.001$ for all). When the subscales were analysed, gastrointestinal symptoms correlated with LEDD (r=0.352, $p<0.001$) and UPDRS-III (r=0.248, p=0.003); urinary symptoms correlated with age (r=0.431, $p<0.001$) and LEDD (r=0.381, $p<0.001$); sexual dysfunction with UPDRS-III (r=0.353, $p<0.001$) and age (r=0.290, $p<0.001$); cardiovascular/falling symptoms with UPDRS-III (r=0.480, $p<0.001$) and PDQ-39 (r=0.282, $p<0.001$); attention/memory problems with PDQ-39 (r=0.411,

p<0.001) and age (r=0.272, p=0.001); sleep disorders showed significant correlations with PDQ-39 (r=0.414, p<0.001) and UPDRS-III (r=0.323, p<0.001) (**Table 2**).

Linear regression analyses for the PDQ-39 score showed a higher score of 27.25 points (p<0.001) in patients with a disease duration of 5-8 years and 13.43 points (p=0.029) in patients with a disease duration of 9< years compared to the <4 year group. Each one-unit increase in UPDRS-III increased PDQ-39 by 1.91 points and each one-point increase in NMS total score increased PDQ-39 by 3.35 points (p<0.001 for each). In multivariate analysis, UPDRS-III (p<0.001) and NMS total score (p<0.001) remained significant, whereas the significance of disease duration and LEDD variables disappeared (**Table 3**).

Age (p<0.001), disease duration 5-8 years (p<0.001) or 9< years (p<0.001), UPDRS-III (p<0.001), LEDD (p<0.001) and H&Y >3 (p<0.001) were significant in the univariate analysis. In the multivariate stage, age (p<0.001), disease duration 9< years (p=0.015) and UPDRS-III (p=0.004) remained statistically significant; the effects of LEDD and H&Y were not significant at this level (p>0.05) (**Table 4**). These results showed that the progressive increase of both motor and non-motor symptoms in PD was associated with prolonged disease duration and an increase in UPDRS-III score, whereas quality of life was more under the integrated effect of motor and non-motor burden.

Table 1

Descriptive statistics on demographic and clinical characteristics in patients with Parkinson's disease

		Overall (n=141)
Age		63.0 [33.0 - 93.0]
Gender (%)	Woman	60 (42.6)
	Male	81 (57.4)
Education Status (%)	None	33 (23.4)
	There is	108 (76.6)
Duration of Education (year)		5.0 [3.0 - 15.0]
Duration of Illness		1.0 [1.0 - 3.0]
PDQ-39		51.0 [4.0 - 134.0]
H&Y Scale (%)	≤ 2	102 (72.3)
	>3	39 (27.7)
UPDRS-III		16.0 [6.0 - 40.0]
LEDD		400.0 [150.0 - 1700.0]
NMS Scale Total Score Classification	Light (1-5)	31 (22.0)
	Medium (6-9)	38 (27.0)
	Heavy (10-13)	36 (25.5)
	Very severe (≥14)	36 (25.5)
NMS Scale Total Score		10.0 [2.0 - 17.0]
Gastrointestinal		2.0 [0.0 - 5.0]
Urinary		2.0 [0.0 - 2.0]
Sexual function		0.0 [0.0 - 2.0]
Cardiovascular/Fall		0.0 [0.0 - 2.0]
Attention/Memory		1.0 [0.0 - 3.0]
Perception problems		0.0 [0.0 - 2.0]
Mood		1.0 [0.0 - 2.0]
Sleep		1.0 [0.0 - 4.0]
Other		1.0 [0.0 - 3.0]

‡: n (%), §: Median [Min.-Max.], H&Y Scale: Hoehn-Yahr Scale, LEDD: Levodopa Equivalent Daily Dose, NMS: Non-Motor Symptom, PDQ-39: Parkinson's Disease Questionnaire-39, UPDRS-III: Unified Parkinson's Disease Rating Scale Part III.

Table 2

Correlation of demographic and clinical characteristics with non-motor symptom severity in patients with Parkinson's disease

	Age		Training Duration		PDQ-39		UPDRS-III		LEED	
	r	p	r	p	r	p	r	p	r	p
NMS Scale Total Score	0.380	<0.001	-0.054	0.580	0.507	<0.001	0.504	<0.001	0.473	<0.001
Gastrointestinal	0.171	0.042	0.023	0.815	0.188	0.026	0.248	0.003	0.352	<0.001
Urinary	0.431	<0.001	-0.255	0.008	0.138	0.102	0.222	0.008	0.381	<0.001
Sexual function	0.290	<0.001	0.056	0.564	0.180	0.033	0.353	<0.001	0.261	0.002
Cardiovascular/Fall	0.240	0.004	-0.131	0.178	0.282	<0.001	0.480	<0.001	0.205	0.015
Attention/Memory	0.272	0.001	-0.108	0.267	0.411	<0.001	0.243	0.004	0.210	0.012
Perception problems	-0.051	0.545	0.178	0.066	0.134	0.114	-0.013	0.875	0.123	0.145
Mood	0.067	0.432	0.153	0.115	0.370	<0.001	0.152	0.072	0.181	0.031
Sleep	0.222	0.008	-0.132	0.172	0.414	<0.001	0.323	<0.001	0.300	<0.001
Other	0.093	0.275	0.047	0.632	0.293	<0.001	0.310	<0.001	0.230	0.006

Spearman's rho correlation coefficient was used., Notes: Bold p-values indicate statistical significance (p≤0.05).
LEDD: Levodopa Equivalent Daily Dose, NMS: Non-Motor Symptoms, PDQ-39: Parkinson's Disease Questionnaire-39, UPDRS-III: Unified Parkinson's Disease Rating Scale Part III.

Table 3

Linear regression analysis results for factors affecting quality of life in patients with Parkinson's disease

Linear regression predicting PDQ-39	Univariate Linear Regression		Multivariate Linear Regression	
	β [95% CI]	p	β [95% CI]	p
Age	0.18 [-0.35 - 0.71]	0.510	-	-
Gender Man vs. Female	4.16 [-6.71 - 15.04]	0.454	-	-
Education Status: Yes vs. No	-3.51 [-16.22 - 9.2]	0.589	-	-
Disease Duration: ref.=<4 years				
5-8 years	27.25 [12.29 - 42.2]	<0.001	9.38 [-6.57 - 25.32]	0.251
9< year	13.43 [1.53 - 25.33]	0.029	-1.7 [-15.42 - 12.02]	0.808
UPDRS-III	1.91 [1.37 - 2.44]	<0.001	1.52 [0.91 - 2.14]	<0.001
LEDD	0.02 [0.01 - 0.03]	0.007	-0.01 [-0.03 - 0.01]	0.257
NMS Scale Total Score	3.35 [2.24 - 4.46]	<0.001	2.3 [1.09 - 3.5]	<0.001

β: Unstandardised regression coefficient, CI: Confidence interval, LEDD: Levodopa Equivalent Daily Dose, NMS: Non-Motor Symptoms, PDQ-39: Parkinson's Disease Questionnaire-39, UPDRS-III: Unified Parkinson's Disease Rating Scale Part III.

Table 4

Linear regression analysis results for the factors affecting NMS total scores in patients with Parkinson's disease

Linear regression predicting NMS Score	Univariate Linear Regression		Multivariate Linear Regression	
	β [95% CI]	p	β [95% CI]	p
Age	0.17 [0.11 - 0.24]	<0.001	0.16 [0.1 - 0.21]	<0.001
Gender Man vs. Female	-0.82 [-2.27 - 0.63]	0.270	-	-
Education Status: Yes vs. No	-0.51 [-2.21 - 1.19]	0.555	-	-
Disease Duration: ref.=<4 years				
5-8 years	3.83 [1.94 - 5.71]	<0.001	1.66 [-0.37 - 3.68]	0.111
9< year	3.93 [2.43 - 5.43]	<0.001	2.2 [0.45 - 3.96]	0.015
UPDRS-III	0.22 [0.14 - 0.29]	<0.001	0.17 [0.06 - 0.28]	0.004
LEDD	0.01 [0.01 - 0.02]	<0.001	0.01 [0.01 - 0.02]	0.060
H&Y Scale: >3 vs. ≤ 2	3.14 [1.62 - 4.67]	<0.001	-1.37 [-3.54 - 0.8]	0.218

β: Unstandardised regression coefficient, CI: Confidence interval, H&Y Scale: Hoehn-Yahr Scale, NMS: Non-motor symptom scale, LEDD: Levodopa Equivalent Daily Dose, UPDRS-III: Unified Parkinson's Disease Rating Scale Part III.

4. Discussion

The most Although NMS manifestations of PD are less noticeable than motor symptoms, they have a critical impact on quality of life during the disease process. In our study, the effect of NMS on quality of life and its relationship with disease duration, motor symptom severity and the total dose of dopaminergic treatment received by the patient were analyzed. The findings suggest that NMS is an important determinant of quality of life in PD and these symptoms become more prominent with disease progression.

In our study, significant positive correlations were found between NMS total score and age, UPDRS-III, PDQ-39 and LEDD. These findings confirm that the burden of NMS increases with increasing age and motor symptom severity, thus confirming the effect of disease progression on NMS. Focusing on the subparameters of NMSs, gastrointestinal, urinary and cardiovascular symptoms were found to reflect this relationship more strongly. For example, each one unit increase in NMS total score was associated with a significant increase in LEDD dose, suggesting that NMS may also influence dopaminergic treatment requirements.

The existing literature shows that NMS profoundly affects not only quality of life but also disease management in PD. Chaudhuri et al.[13] reported that NMS is common even in the early stages of PD and that these symptoms become more severe in the later stages. Our study also supports these findings; especially the fact that NMS total scores were significantly higher in patients with age and H&Y score >3 suggests that these symptoms constitute a burden that cannot be ignored at every stage of the disease. Furthermore, the strong correlation between PDQ-39 and NMS total score is consistent with the literature emphasizing the impact of NMS on quality of life[14].

When the subparameters of NMS were analyzed, it was observed that gastrointestinal, urinary and sexual function symptoms increased remarkably. In Cankaya's study, the effect of these symptoms on patients' activities of daily living was emphasised[15]. However, our study also draws attention to the relationship between these symptoms and LEDD and reveals that high dose levodopa treatment alleviates some symptoms and exacerbates others. The effect of LEDD on NMS is discussed in the literature. Pekel et al. reported that high dose treatment had a favorable effect especially on gastrointestinal symptoms[16]. However, in our study, this effect was found to differ according to individual NMS types.

The limitations of our study include the limited number of participants and the lack of long-term follow-up data. In addition, it is thought that a more detailed analysis on the effects of NMS in different age groups should be performed. However, our findings have important implications for clinical management. It is clear that NMS should be addressed not only in the advanced stages of PD but also in the early stages and should be treated with a multidisciplinary approach. In our study, in which the effects of follow-up and early recognition of non-motor symptoms as well as motor symptoms of Parkinson's disease on quality of life were clearly demonstrated, it is thought that quality of life is an important criterion for managing

the treatment strategies of patients and intervening at the right time.

For future studies, it is recommended to investigate in more depth how NMS change in different disease stages, the mechanisms of their relationship with LEDD, and the effects of these symptoms at the individual level. Identification of latent structures between NMS subparameters by advanced statistical methods such as structural equation modelling may help us to better understand the effects of these symptoms on quality of life in PD.

5. Conclusion

Our study once again emphasizes the importance of non-motor symptoms in PD. Instead of the traditional approach focusing on motor symptoms, approaches that will address the quality of life of patients in a holistic manner should be developed.

Statement of ethics

Ethical approval was obtained from the Adana City Training and Research Hospital Ethics Committee and the study was conducted by the principles of the Declaration of Helsinki (05/12/24, no:250). Informed consent forms were obtained from all patients and control subjects.

Author Contributions

Concept: ME/DO, Design: ME/DO, Literature search: ME, Data Collection and Processing: ME/DO, Analysis or Interpretation: ME/DO, Writing: ME/DO.

Source of Finance

The authors declare that they have received no financial support for this study.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

References

1.Bloem BR, Okun MS, Klein C. Parkinson's disease. Lancet. 2021 Jun 12;397(10291):2284-2303.
https://doi.org/10.1016/S0140-6736(21)00218-X
2.Jellinger KA. Neuropathobiology of non-motor symptoms in Parkinson's disease. Neural Transm (Vienna). 2015 Oct;122(10):1429-40.
https://doi.org/10.1007/s00702-015-1405-5
3.Güzelad Ö, Özkan A, Parlak H, et al. Protective mechanism of Syringic acid in an experimental model of Parkinson's disease. Metabolic Brain Disease, 2021;36(5), 1003–14.
https://doi.org/10.1007/s11011-021-00704-9
4.Postuma RB, Aarsland D, Barone P, et al. Identifying prodromal Parkinson's disease: pre-motor disorders in Parkinson's disease. Mov Disord. 2012; 27:617-26.
https://doi.org/10.1002/mds.24996
5.Stern MB, Lang A, Poewe W. Toward a redefinition of Parkinson's disease. Mov Disord. 2012; 27:54-60.
https://doi.org/10.1002/mds.24051
6.Berg D, Postuma RB, Adler CH, et al. MDS research criteria for prodromal Parkinson's disease. Mov Disord. 2015;30: 1600-11.
https://doi.org/10.1002/mds.26431
7.Poewe W, Seppi K, Tanner CM, et al. Parkinson's disease. Nat Rev Dis Primers. 2017;3:17013.
https://doi.org/10.1038/nrdp.2017.13
8.Martinez-Martin P, Rodriguez-Blazquez C, Paz S, Paz S, et al. Parkinson's symptoms and health related quality of life as predictors of costs: a longitudinal observational study with linear mixed model analysis. PLoS One. 2015;10: e0145310.
https://doi.org/10.1371/journal.pone.0145310
9.Chaudhuri KR, Martinez-Martin P, Schapira AH et al. International multicentre pilot study of the first comprehensive self completed nonmotor symptoms questionnaire for Parkinson's disease: the NMSQuest study. Mov Disord 2006;21:916-23.
https://doi.org/10.1002/mds.20844
10.Balaban H. Scales used in the evaluation of Parkinson's disease. Türkiye Klinikleri Nöroloji 2003;1:231-6.
11.Siderowf A, McDermott M, Kieburtz K, et al. Test-retest reliability of the unified Parkinson's disease rating scale in patients with early Parkinson's disease: results from a multicenter clinical trial. Mov Disord 2002; 17:758-63.
https://doi.org/10.1002/mds.10011
12.Kayapınar T. Parkinson hastalığı yaşam kalitesi anketi (PDQ-39) güvenilirlik ve geçerlilik çalışması (Yüksek Lisans Tezi). T.C. Haliç Üniversitesi Sağlık Bilimleri Enstitüsü, İstanbul,2018.
13.Chaudhuri KR, Healy DG, Schapira AHV. Non-motor symptoms of Parkinson's disease: diagnosis and management. Lancet Neurology. 2006 Mar;5(3):235-45.
https://doi.org/10.1016/S1474-4422(06)70373-8
14.Marinus J, Zhu K, Marras C, et al. Risk factors for non-motor symptoms in Parkinson's disease. Lancet Neurology. 2018 Jun;17(6):559-68.
https://doi.org/10.1016/S1474-4422(18)30127-3
15.Cankaya S, Altınayar S. Evaluation of non-motor findings in Parkinson's patients using the NMSQ questionnaire. 2020;1;47-55.
16.Pekel NB. The effect of diabetes mellitus on non-motor symptoms in Parkinson's disease. Acta Medica Alanya. 2019;3:293-9.
https://doi.org/10.30565/medalanya.569168