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The impact of COVID-19 on patients with Parkinson disease

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ABSTRACT

Aims: Viral infections have been implicated in the development of Parkinson disease (PD). It has been observed that the presence of SARS-CoV-2 in dopaminergic cells can expedite the degeneration process and potentially exacerbate symptoms. The objective of this study was to assess the impact of the COVID-19 pandemic on individuals with PD.

Methods: A total of 60 patients were enrolled in the study. The severity of the disease was assessed using the using the Unified Parkinson's Disease Rating Scale (UPDRS), while the stage of the disease was determined using modified Hoehn &Yahr Rating Scale (m HYRS). Various measures were taken to evaluate the patients' well-being, including the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Parkinson's Disease Quality of Life Questionnaire (PDQ-39), and Impact of Events Scale (IES-R) scores. The researchers also recorded the UPDRS scores, levodopa equivalent doses (LED), and BMI of the patients before and after the lockdown period. Subsequently, the collected data were compared to identify any significant changes.

Results: The difference in UPDRS, LED and BMI of the patients before and after the lockdown was statistically significant ($p<0.05$). Furthermore, there was a significant increase in UPDRS motor score, BAI, and PDQ-39 values among female patients compared to male patients ($p<0.05$). Comparing patients with and without COVID-19 infection, it was observed that patients who had contracted COVID-19 demonstrated a statistically significant increase in m HYRS and UPDRS motor scores, and PDQ-39 values after the lockdown ($p<0.05$). To assess the impact of various factors on the quality of life, multiple linear regression analysis was performed. The analysis revealed that COVID-19-positive patients and female patients experienced a more pronounced effect on their quality of life ($p<0.05$). Moreover, quality of life was found to be affected by disease stage, depression, anxiety, the IES-R scores increase, as well as by deteriorating sleep quality ($p<0.05$).

Conclusion: During the COVID-19 pandemic, PD patients experienced a worsening of clinical symptoms and increased treatment requirements. Furthermore, their quality of life was negatively affected, particularly among females and those who contracted COVID-19 infection. It is crucial to develop supportive treatment strategies targeting neuropsychological symptoms, as these could greatly contribute to the overall management and well-being of PD patients.

Keywords: Parkinson's disease, COVID-19, quality of life, sex

INTRODUCTION

Parkinson disease (PD) is a neurodegenerative condition characterized by both motor and non-motor features.[1] Initially, patients typically respond favorably to treatment, however, as the disease progresses, medication effectiveness may decrease, and side effects can emerge from prolonged use. These complications can significantly impact patients' ability to carry out their daily activities without assistance. Consequently, caregivers play a crucial role in monitoring patients' treatment progress and managing their daily living activities.[2]

Several notable observations have been made regarding the association between COVID-19 and PD. Studies have found higher levels of autoantibodies against coronaviruses in the cerebrospinal fluid of PD patients compared to healthy individuals, indicating a potential link between viral infection and the development of PD.[3]

The angiotensin-converting enzyme 2 (ACE2) protein is primarily responsible for the cellular entry of SARS-CoV-2, serving as a receptor for the virus.[4] ACE2 receptors are prominently expressed on dopaminergic neurons in the substantia nigra and striatum. It has been observed that viral infiltration of these cells accelerate the degeneration process, worsen symptoms, and increase the need for dopaminergic treatment, particularly in individuals with advanced age and longer disease duration.[3,5] Moreover, the SARS-CoV-2 virus is believed to induce protein misfolding and aggregation.

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Recent studies on PD have suggested a potential increase in alpha-synuclein accumulation in the context of COVID-19 infection, further implicating a connection between the two conditions.[4,6]

PD patients, like the general population, have been significantly impacted by disruptions in healthcare, quarantine measures, and the global stress caused by the COVID-19 pandemic.[7] While PD patients did not face a higher risk of infection compared to the general population, those who contracted SARS-CoV-2 experienced worsened symptoms, encountered challenges in receiving regular neurological assessments and medication adjustments due to limited access to outpatient clinics, and faced delays in planned surgical interventions.[8] Moreover, the pandemic has led to lifestyle changes among patients, including decreased physical activity, inability to exercise, and increased levels of psychological stress levels.[8] As a result of these clinical and lifestyle changes, the has been a noticeable increase in anxiety, depression, and stress, accompanied by a decline in oveall quality of life for PD patients.[2]

In the current research, we aim to evaluate the impact of the COVID-19 lockdown on patients with PD by assessing changes in their clinical findings, daily habits, quality of life, and the extent to which they were affected. Additionally, we seek to determine whether the implementation of the lockdown measures is associated with a deterioration of PD symptoms.

METHODS

This study was conducted with the approval of the Ethics Committee of the University of Health Sciences Fatih Sultan Mehmet Training and Research Hospital (Date: 11.03.2021, Decision No: 2021/29). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

A total of 60 patients in the neurology outpatient clinic at the University of Health Sciences, Fatih Sultan Mehmet Research and Training Hospital were included in the study. These patients were diagnosed with PD based on the Movement Disorder Association Parkinson's Disease Clinical Diagnostic Criteria. The study period encompassed December 2019 to December 2021.

To assess the impact of the COVID-19 lockdown, we divided the study period into two phases. The pre-lockdown period, referred to as "pre-COVID", included data collected until March 2020. The post-lockdown period, referred to as "post-COVID", included data collected from July 2021 onwards.

During these periods, we collected various data points including demographic information, daily levodopa equivalent doses (LED), scores from the Beck depression inventory (BDI), Beck anxiety inventory (BAI), Pittsburgh sleep quality index (PSQI), Epworth sleepiness inventory (ESI), Parkinson's disease quality of life questionnaire (PDQ-39) and impact of events scale (IES-R).

Disease severity was assessed using the Unified Parkinson's Disease Rating Scale (UPDRS), while disease stage was determined using the modified Hoehn & Yahr Rating Scale (mHYRS). We recorded UPDRS scores, LED, and BMI of patients both before and after the lockdown, and compared the data obtained during these periods.

Statistical Analysis

For statistical analysis, we utilized IBM SPSS Statistics 25 software provided by IBM SPSS, Turkey. Descriptive methods such as mean, standard deviation, median, frequency, ratio, minimum, and maximum were employed to summarize the data. The Shapiro-Wilk Test was used to assess the distribution of the data.To compare qualitative data between the two groups we utilized the Mann-Whitney U Test. For comparisons between two time periods, the Wilcoxon test was employed. A chi-square analysis was performed to determine the association concerning qualitative data. Linear regression analysis was utilized to establish the parameters affecting the dependent variables. The significance level was set at $p<0.05$ to determine statistical significance.

RESULTS

The study included a total of 60 patients, of which 43.4% (n=26) were female and 56.7% (n=34) were male. The age range of the participants was between 32 and 83 years, with a mean age of 63.2±11.55 years. Detailed demographic and clinical information, such as disease duration, UPDRS and mHYRS scores, disease dominancy, educational status, habits, comorbid diseases, and lifestyle of the patients can be found in Table 1.

Table 1. Demographic and clinical data of patients with Parkinson's disease

		mean+SD	median (min-max)
Age		63.2±11.55	32-83 (67)
Sex	Female Male	26 (43.4%) 34 (56.7%)	
Disease Duration (year)		7.09±4.3	2-23 (6)
Disease Dominancy	Bradykinesia Tremor	44 (73.3%) 16 (26.7%)	
UPDRS		33.65±9.73	13-48 (35)
mHYRS		2.57±0.74	1-4 (2.5)
LED		527.33±290.4	110-1650 (450)
Person living together	With family Alone	55 (91.7%) 5 (8.3%)	
Comorbid diseases	Yes No	40 (66.7%) 20 (33.3%)	
Smoking	Yes No	9 (15%) 51 (85%)	
Education	Primary school High school University	40 (66.7%) 13 (21.7%) 7 (11.7%)	

UPDRS: Unified Parkinson's Disease Rating Scale, LED: levodopa equivalent dose, mHYRS: modified Hoehn-Yahr Rating Scale

When comparing the clinical findings of the patients before and after the COVID-19 pandemic lockdown, statistically significant differences were observed in UPDRS motor scores, daily levodopa intake, and BMI values after the lockdown (p=0.001, p=0.001, p=0.001, p=0.001; p<0.05). Detailed information regarding these findings can be found in Table 2.

Table 2. The impact of the COVID-19 pandemic on the clinical manifestations of patients with Parkinson's disease

	Before Lockdown mean+SD median (min-max)	After Lockdown mean+SD median (min-max)	p
UPDRS	33.65±9.73 13-48 (35)	49.53±14.24 20-78 (48)	0.001**
Levodopa equivalent dose	527.33±290.4 110-1650 (450)	695.92±299.55 150-1700 (650)	0.001**
Body mass index	27.6±4.65 20.76-43.28 (26.23)	28.62±5.34 20.76-48.93 (27.16)	0.001**

Wilcoxon test, *p<0.05, **p<0.01, UPDRS: Unified Parkinson's Disease Rating Scale

The study found a statistically significant rate of increase in UPDRS motor scores, BAI, and PSQI values among female patients compared to males (p=0.001, p=0.001, p=0.001, p=0.001; p<0.05). Moreover, there was a significant difference in the quality of life assessed by PDQ-39, and total score, with women exhibiting significantly higher scores than men (p=0.001; p<0.05). Specifically, women showed significantly higher scores in the "mobility" and "physical discomfort" domains of PDQ-39 compared to men (p=0.001, p=0.001; p<0.05). Detailed analyses of these findings can be found in Tables 3a and 3b.

We found statistically significant increases in mHYRS, post-lockdown UPDRS-motor scores and PDQ-39 values among patients with COVID-19 infection (p=0.001, p=0.001, p=0.001, p=0.001, p=0.001, p=0.001; p<0.05). A detailed analysis of these findings can be found in Table 4.

Table 3a. Comparison of clinical and neuropsychological findings of male and female patients

	Female (n=26) Mean±SD /Min-Max (Median)	Male (n=34) Mean±SD /Min-Max (Median)	p
UPDRS increase rate	17.54±6.64/8-31 (16)	14.62±7.06/4-34 (12.5)	0.047*
LED increase rate	167.88± 294.9/-700-1115 (175)	169.12± 168.56/-250-550 (150)	0.976
BMI increase rate	1.28±1.47/0-5.65 (0.82)	0.71±0.83/0-2.42 (0)	0.165
BDI	13.46±8.98/1-36 (14.5)	12.62±9.89/0-40 (10)	0.627
BAI	22.62±13.38/3-59 (21.5)	16.5±14.1 /1-56 (12)	0.028*
PSQI	13.38±3.9/4-21 (13)	10.29±4.14/2-17 (11)	0.007**
ESS	10.5±11.79/0-59 (7)	7.97±4/2-16 (8)	0.911
IES-R	35.08±12.27/12-58 (34.5)	32.94±15.1/4-58 (32.5)	0.591

Mann Whitney U Test , *p<0.05, **p<0.01, UPDRS: Unified Parkinson's Disease Rating Scale, LED: levodopa equivalent dose, BMI: body mass index, BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, PSQI: Pittsburgh Sleep Quality Index, ESS: Epworth Sleepiness Scale, IES-R: Impact of Events Scale

Table 3b. Comparison of Quality of Life (PDQ-39) scales of male and female patients

	Female (n=26) Mean±SD /Min-Max (Median)	Male (n=34) Mean±SD /Min-Max (Median)	p
PDQ-39 total	64.77±29.56/4-124 (70)	43.59±28.37/6-124 (37.5)	0.004**
Mobility	21.69±11.02/0-44 (22.5)	11.82±11.51/0-44 (8.5)	0.001**
Activities of daily living	11±6.75/0-24 (11)	8.5±6.95/0-24 (6.5)	0.178
Emotional well-being	10.38±6.82/0-24 (9)	7.29±5.27/0-24 (6)	0.078
Stigma	3±3.25/0-11 (2)	2.32±3.01/0-12 (1)	0.293
Social support	2.96±2.92/0-12 (2.5)	2.5±2.3/0-8 (2)	0.649
Cognition	5.58±3.62/0-12 (5.5)	4.29±2.58/0-11 (4)	0.207
Communication	2.69±3.3/0-14 (2)	2.41±2.49/0-9 (2)	0.976
Bodily discomfort	7.19±3.63/0-12 (7)	4.56±3.58/0-12 (4)	0.007**

Mann Whitney U Test, *p<0.05, **p<0.01, PDQ-39: Parkinson's Disease Quality of Life Questionnaire

Table 4. Comparison of clinical data of patients with and without COVID-19

	COVID-19 (+) (n=17) Mean±SD/Min-Max (Median)	COVID-19 (-) (n=43) Mean±SD/Min-Max (Median)	p
Sex (f/m)	7/10	19/24	[a]0.533
Presence of comorbidities	13	27	[a]0.242
Smokers	3	6	[a]0.499
Dominancy (bradykinesia /tremor)	14/3	30/13	[a]0.256
Age	64.24±11.84/43-83 (65)	62.79±11.55/32-77 (67)	0.870
mHYRS	3±0.81/1.5-4 (3)	2.4±0.64/1-4 (2.5)	0.009**
Post-lockdown UPDRS	56.65±11.76/24-72 (58)	46.72±14.27/20-78 (46)	0.006**
Post-lockdown LED	803.24±350.57/150-1700 (800)	653.49±269.68/300-1300 (600)	0.075
Post-lockdown BMI	27.93±4.81/20.76-36.21 (26.81)	28.9±5.57/21.33-48.93 (27.82)	0.530
IES-R	34.35±14.51/8-58 (41)	33.67±13.78/4-58 (32)	0.812
PDQ-39	68.71±31.09/6-124 (66)	46.47±28.26/4-124 (42)	0.013*
Disease Duration	7.93±3.83/3-15 (7.5)	68±4.46/2-23 (6)	0.202

a Chi-square test, Mann Whitney U Test, *p<0.05, **p<0.01, UPDRS: Unified Parkinson's Disease Rating Scale, mHYRS: modified Hoehn-Yahr Rating Scale, LED: levodopa equivalent dose, BMI: body mass index, IES-R: Impact of Events Scale, PDQ-39: Parkinson's Disease Quality of Life Questionnaire

When comparing the habits of those who had COVID-19 during the pandemic with those who did not, no statistically significant changes were observed in terms of exercising, weight gain, worsening of clinical findings, disruption in treatment, reaching a doctor and using telemedicine (p=0.499, p=0.403, p=0.428, p=0.163, p=0.605, p=0.283; p>0.05). However, it was found that COVID-19-positive PD patients had significantly higher exposure to COVID-19-positive individuals compared to COVID-19-negative PD patients (p=0.001; p<0.01).

Upon examining **Table 5**, the multiple linear regression analysis conducted to assess the influence of independent variables on quality of life yielded statistically significant (F=13.064 p<0.05). A positive and highly statistically significant association was observed between independent variables and quality of life (R=0.866, p<0.05). The independent variables included in the model accounted for 75% of the total variance in quality of life (p<0.05). In the multivariate analysis of regression coefficients, it was found that COVID-19 status (β=-0.174, p<0.05) and gender (β=-0.197, p<0.05) had a negative impact on quality of life. Conversely, m HYRS (β=0.356, p<0.05), BDI (β=0.191, p<0.05), BAI (β=0.256, p<0.05), PSQI (β=0.189, p<0.05), and IES-R (β=0.281, p<0.05) had a positive and significant influence.

DISCUSSION

In this study, we investigated the clinical and neuropsychiatric effects of the COVID-19 lockdown on patients with PD. Our findings indicate that there was a deterioration in the clinical condition of individuals, as evidenced by worsening symptoms, weight gain, and increased daily LED doses during the post-lockdown period. Notably, clinical deterioration was more pronounced in female patients. Our observations revealed that the quality of life of the patients, particularly those who had COVID-19 infection and were female, experienced a more significant decline compared to male patients. Furthermore, we noted a significant increase in depression and anxiety levels among the patients following the lockdown. Additionally, their sleep quality deteriorated, and there was a progression in the disease stage. The overall impact of the COVID-19 pandemic situation further contributed to the deterioration of their quality of life.

The COVID-19 outbreak has had a significant unfavorable effect on individuals worldwide. To contain the spread of the virus, healthy individuals have been mandated to adhere to various social distancing rules, while those who have contact with the SARS-CoV-2 virus have been compelled to undergo isolation. Previous pandemics have demonstrated that a considerable number of people experienced ongoing psychological distress even after the pandemic had subsided. This highlights the crucial need for psychological support for susceptible individuals.[8-10] Moreover, the pandemic and associated lockdown measures may trigger or exacerbate neuropsychiatric symptoms such as anxiety, depression, and sleep disturbances among patients with PD. Given that physical activity has been shown to alleviate motor symptoms in PD, the sedentary nature of the lockdown measure is particularly unfortunate for this population and may exacerbate their motor symptoms.[8,9,11,12]

Likewise, in this study, we observed a parallel deterioration in motor symptoms, along with a notable increase in depression and anxiety levels, as well as a decline in sleep quality among our patients. Female patients have been found to be more pronounced to experience these deteriorations.

Cilia et al.[12] suggested that the exacerbation of motor symptoms could be attributed to either the degeneration of dopaminergic systems or changes in pharmacokinetics. They also found that patients required higher doses

Table 5. Results of multiple linear regression analysis for independent variables and Quality of Life (PDQ-39)

Independent variables	Univariable					Multivariable				
	B	S.Error	Standard (B)	t	p	B	S. Error	Standard (B)	t	p
COVID Status	-22.241	8.327	-0.331	-2.671	0.001**	-11.725	5.472	-0.174	-2.143	0.037*
Sex	-21.181	7.527	-0.347	-2.814	0.001**	-12.035	4.941	-0.197	-2.436	0.019*
Exercise Status	26.102	8.313	0.381	3.14	0.001**	2.068	6.09	0.03	0.34	0.736
Clinical worsening	-18.06	8.5	-0.269	-2.125	0.001**	-3.989	5.287	-0.059	-0.754	0.454
UPDRS	1.105	0.386	0.352	2.864	0.001**	-0.56	0.381	-0.178	-1.47	0.148
mHYRS	18.147	4.874	0.439	3.723	0.001**	14.707	4.913	0.356	2.993	0.004**
BDI	1.846	0.349	0.57	5.287	0.001**	0.617	0.294	0.191	2.096	0.041*
BAI	1.335	0.225	0.615	5.933	0.001**	0.555	0.204	0.256	2.722	0.009**
PSQI	3.531	0.812	0.496	4.352	0.001**	1.346	0.66	0.189	2.041	0.047*
ESS	1.655	0.429	0.452	3.854	0.001**	0.238	0.315	0.065	0.757	0.453
IES-R	0.891	0.264	0.405	3.371	0.001**	0.619	0.174	0.281	3.553	0.001*

UPDRS: Unified Parkinson's Disease Rating Scale, mHYRS: modified Hoehn-Yahr Rating Scale, BDI: Beck Depression Inventory, BAI:Beck Anxiety Inventory, PSQI: Pittsburgh Sleep Quality Index, ESS: Epworth Sleepiness Scale, IES-R: Impact of Events Scale

of dopaminergic therapy.[13] Similarly, Suzuki et al.[11] demonstrated a correlation between disease severity, disease duration, and the decline in the quality of life. The BMI revealed an increase, suggesting that a sedentary lifestyle has resulted in weight gain. However, it is important to note that this consequence may not be specific to PD.[14] Consistent with the aforementioned studies, we observed an increase in patients' UPDRS part III and PDQ-39 scores, m HYRS stages, and BMI among patients following the lockdown.

Although PD is more commonly diagnosed in men than in women, it is noteworthy that women tend to experience more accelerated disease progression and higher mortality rates.[15,16] The manifestation and diagnosis of PD predominantly rely on motor symptoms, which exhibit remarkable differences between men and women in terms of clinical progression and treatment outcomes.[17]

Regarding the impact on quality of life, studies have found that female gender has a detrimental effect on physical functioning and socio-emotional well-being. On the other hand, males have reported a more pronounced impact on the cognitive domain.[18] Consistent with these findings, our study demonstrated that female patients experienced a greater increase in UPDRS-motor scores, along with higher levels of depression, sleep disorders, and a decline in overall quality of life compared to males.

PD patients require regular outpatient visits for follow-up examinations and prescription management. However, due to the lockdown, these visits have been insufficient. Consequently, the patients had to change their daily routines and habits, leading to weight gain and worsening clinical symptoms. There were also disruptions in their treatment regimens, making it challenging for them to communicate effectively with their neurologists. In an attempt to overcome these obstacles, many patients resorted to utilizing telemedicine services.[12]

When examining the habits of PD patients with and without COVID-19 infection during the lockdown, we did not observe any remarkable difference. However, it is important to note that these changes in habits had an impact on their quality of life. The only notable difference between the patients was that PD patients who had been in contact with confirmed COVID-19 individuals were more susceptible to contracting the infection compared to COVID-19-negative PD patients. Our findings revealed a significant deterioration in the clinical stages of the disease, quality of life, and an increase in UPDRS scores following the lockdown among patients who had contracted COVID-19 compared to those who had not.

CONCLUSION

This paper sheds light on the undesirable outcomes of the COVID-19 outbreak on the quality of life of PD patients. The findings of this investigation have important implications for understanding and potentially managing the changes in clinical outcomes among these patients. We strongly believe that these results underscore the significance of multidisciplinary approaches for PD patients, enabling them to learn and employ self-management strategies effectively.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the University of Health Sciences, Fatih Sultan Mehmet Research and Training Hospital Ethics Committee (Date: 11.03.2021, Decision No: 2021/29).

Informed Consent: Written consent was obtained from the patient participating in this study.

Referee Evaluation Process: Externally peer reviewed.

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Author Contributions: All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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