

Comparison of Parkinson's patients with and without COVID-19 in terms of prognosis

¹Fettah Eren MD, ¹Yagızhan Dikmen MD, ²Merve Nur Gur MD, ¹Ahmet Hakan Ekmekci MD, ³Sua Sumer MD, ¹Serefnur Ozturk MD

¹Department of Neurology, Faculty of Medicine, Selcuk University, Konya; ² School of Medicine, Necmettin Erbakan University, Konya; ³Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Selcuk University, Konya, Turkey

Abstract

Background & Objectives: This study aimed to compare PD patients with and without COVID-19 and to evaluate the associated factors about prognosis. **Methods:** The data of 37 hospitalized PD patients associated with COVID-19 pneumonia were evaluated. It was compared with the data of 40 PD patients who did not have COVID-19 in the same period. Clinical findings, prognosis, mortality and other related factors were compared in PD patients with and without COVID-19. **Results:** Hypertension was higher comorbid disease in PD patients with COVID-19 ($p = 0.005$). The duration of PD was longer in patients without COVID-19 disease (6.02 ± 2.80 vs 5.08 ± 4.59) ($p = 0.028$). In PD patients with COVID-19, the most common symptoms were myalgia-arthralgia (73.0%) and fatigue (48.6%). Intensive care was required in 17 (45.9%) patients, and invasive mechanical ventilation (IMV) was required in 9 (24.3%) patients. The in-hospital mortality rate was 29.7% ($n = 11$). Mortality and IMV requirement were higher in patients whose initial symptom was diarrhea ($p = 0.004$, $p = 0.008$, respectively). No correlation was detected between PD stage, treatment options and prognosis ($p < 0.05$).

Conclusion: Mortality rate and IMV requirement are higher in PD patients with COVID-19 pneumonia, particularly in patients with initial symptoms of diarrhea. These patients should be followed more carefully in terms of probable poor prognosis.

Keywords: Parkinson's disease, COVID-19, intensive care, mortality, mechanical ventilation

INTRODUCTION

Coronavirus disease 2019 (COVID-19), which occurs due to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has different frequencies of hospitalization and mortality rate depending on comorbid diseases and severity of symptoms. It is thought that chronic diseases such as Parkinson's disease (PD) may have a higher mortality risk and complications associated with COVID-19.¹ There is no definite consensus on whether COVID-19-related mortality in PD patients is different from the general population, but it has been reported that higher age and hypertension may increase mortality rates in these patients.^{2,3}

Many studies have been reported on the relationship between COVID-19 and PD during the pandemic process. Increased prevalence of COVID-19 has been reported in patients with

PD.⁴ However, there is no definitive conclusion if PD is a risk factor for COVID-19. Besides the increased prevalence, the higher mortality associated with COVID-19 has been reported in older patients with PD.⁵ Mortality rate in PD patients with COVID-19 disease ranges from 5.7% to 40%.^{2,4-7} There is no prognostic marker predicting mortality in these patients. The high rate of mortality is associated with hypertension in PD patients with COVID-19.³ In addition, the severity of COVID-19 disease is associated with malignancy in these patients.⁶

In the general population; increased age, male gender, some comorbid diseases such as hypertension, diabetes mellitus (DM), congestive heart failure and respiratory diseases are major risk factors for COVID-19 disease.⁸⁻¹⁰ Several studies have reported that comorbid diseases such as hypertension, DM, chronic obstructive pulmonary disease (COPD), obesity and dementia are more

Address correspondence to: Fettah Eren, Assoc. Prof., M.D., Selcuk University Faculty of Medicine, Department of Neurology, Konya, Seven street & Number 1B, Konya, 42700, Turkey. Tel: +90 (505) 860 41 46, E-mail: dreren42@hotmail.com

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common in PD patients with COVID-19.^{2,4,11} Some studies have reported that PD may be a risk factor for COVID-19.^{2,5,12} However, despite all these data concerning the COVID-19 disease and related factors are limited in patients with PD.

The primary aim of current study was to compare the demographic-clinical characteristics and comorbid diseases in PD patients with and without COVID-19. The secondary aim was to determine the characteristics in hospitalized PD patients with COVID-19. The third aim was to determine the mortality, intensive care and mechanical ventilation requirements in these patients and to evaluate the related factors.

METHODS

Study area and ethical approval

In this study, PD patients who were followed up in the hospital were included (Selcuk University Faculty of Medicine, Konya, Turkey). After Ministry of Health (Approval number: 2021-03-23T22_23_41), the study protocol was approved by Selcuk University Local Ethics Committee (Number of meetings: 2021/08, Number of Decisions: 2021/215). The study process was managed according to Helsinki Declaration and good clinical practice guidelines.

Participants and evaluation methods

In this single-center and retrospective study (between April 2020 and May 2021), PD patients with COVID-19 were studied. They had typical pneumonic infiltrates for the COVID-19 disease in thorax computed tomography. Hospitalized PD patients with active infection (bacterial, viral, or fungal) other than COVID-19 were excluded from the study. The data were compared with PD patients without active infection (COVID-19 and other infections) as control group. Patients' data were obtained from the COVID-19 service, intensive care unit, and neurology clinical archive in the University Hospital. Patients in groups with and without COVID-19 were designed to be of similar age and gender.

The COVID-19 was diagnosed according to the guidelines of the World Health Organization (WHO): with typical clinical symptoms, pneumonic infiltrates associated with COVID-19 in computed thoracic tomography and the SARS-CoV-2 positivity in the real-time reverse transcription-polymerase chain reaction (rRT-PCR) test from the nasopharynx.

Age and gender of the patients were recorded. Smoking, comorbid diseases and PD treatments were evaluated. Comorbid diseases were grouped as DM, hypertension, hyperlipidemia, congestive heart failure, stroke, dementia, cancer, COPD, renal failure and others (rheumatological, dermatological diseases, etc.). PD treatments were evaluated. Hoehn-Yahr staging scale was used to evaluate the functional disability. In this scale, the score ranged from 1 to 5. Increased scores indicated an increased disability.^{13,14}

Initial symptoms of hospitalized patients due to COVID-19 were evaluated. These were identified as fever, cough, dyspnea, myalgia-arthralgia, fatigued, anorexia, headache, diarrhea, anosmia, dizziness, cognitive disorder, visual defect, dysesthesia, facial paralysis and others (psychiatric, dermatological diseases, etc.). Respiratory supports received during hospitalization were grouped as nasal oxygen, continuous positive airway pressure (CPAP) and invasive mechanical ventilation (IMV). The requirement of intensive care was evaluated. In-hospital mortality rates were calculated.

The characteristics of PD patients with and without COVID-19, and the factors associated with prognosis in hospitalized PD patients with COVID-19 pneumonia were examined in the study.

Statistical analysis

SPSS 16.0 Package Software (Statistical Package for the Social Sciences Inc.; Armonk, NY, USA) program was utilized to analyze the data. Normality analysis of the data was performed with the Kolmogorov Smirnov test. Descriptive parameters were expressed as number (n), percentage (%), mean \pm standard deviation (minimum-maximum). The χ^2 (Chi-square) test was used to investigate the relationship between categorical variables. Two independent groups were compared using the independent sample T-test (normally distributed) or the Mann Whitney U test (not normally distributed). More than two groups were analyzed with One Way Anova test (normally distributed) or the Kruskal Wallis test (not normally distributed). The results were evaluated in the 95% confidence interval and $p < 0.05$ was considered statistical significant.

RESULTS

In the same period, 37 hospitalized PD patients with the diagnosis of COVID-19 and 40 PD patients without COVID-19 were studied.

Comparison of Parkinson's patients with and without COVID-19 disease

Of the 37 PD patients diagnosed with COVID-19, 18 (48.6%) were female and 19 (51.4%) were male. The mean age was 70.59 ± 14.06 (35-96). The data were compared with a total of 40 non-COVID-19 PD patients, 15 (37.5%) were female and 25 (62.5%) were males, with a mean age of 70.35 ± 9.51 (50-84). There was no statistical difference in age and gender between the two groups ($p = 0.752$, $p = 0.363$, respectively). Smoking frequency was also similar among these groups ($p = 0.884$). Hypertension was more common comorbid disease in PD patients with

COVID-19 (29.7% versus 5%) ($p = 0.005$). There was no statistical difference between the groups for the frequency of other comorbid diseases ($p > 0.05$).

The duration of PD (years) was longer in patients with non-COVID-19 disease (6.02 ± 2.80 vs 5.08 ± 4.59) ($p = 0.028$). The Hoehn and Yahr stage score was not different in two patient groups ($p = 0.400$). There was also no difference between the two patient groups in the options of PD treatment ($p > 0.05$). Comparison of demographic and clinical features, comorbid diseases and treatment options in patients with and without COVID-19 disease were listed in Table 1.

Table 1: Demographic, clinic and treatment characteristic in patients with Parkinson's disease with and without COVID-19 disease

| | COVID-19 patient (n = 37) | Non COVID-19 disease (n = 40) | p-value |
|---|------------------------------|----------------------------------|----------|
| Age, year | 70.59 ± 14.06 (35-96) | 70.35 ± 9.51 (50-84) | 0.752 |
| Gender | | | |
| Female | 18 (48.6) | 15 (37.5) | 0.363 |
| Male | 19 (51.4) | 25 (62.5) | |
| Smoking | | | |
| No | 31 (83.8) | 34 (85.0) | 0.884 |
| Yes | 6 (16.2) | 6 (15.0) | |
| Comorbid disease | | | |
| Diabetes mellitus | 4 (13.5) | 2 (5.0) | 0.419 |
| Hypertension | 11 (29.7) | 2 (5.0) | 0.005* a |
| Hyperlipidemia | 10 (27.0) | 5 (12.5) | 0.151 |
| Congestive heart failure | 4 (10.8) | 4 (10.0) | 0.908 |
| Stroke | 7 (18.9) | 2 (5.0) | 0.079 |
| Dementia | 6 (16.2) | 2 (5.0) | 0.144 |
| Cancer | 5 (13.5) | 1 (2.5) | 0.100 |
| COPD | 3 (8.1) | 1 (2.5) | 0.346 |
| Renal failure | 2 (5.4) | 1 (2.5) | 0.605 |
| Other | 7 (18.9) | 6 (15.0) | 0.764 |
| Disease duration, years | 4.81 ± 3.48 (1-16) | 6.02 ± 2.80 (1-13) | 0.028* b |
| Hoehn and Yahr stage, group | | | |
| Stage 1-3 | 31 (83.8) | 35 (87.5) | 0.750 |
| Stage 4-5 | 6 (16.2) | 5 (12.5) | |
| Hoehn and Yahr stage, score | 2.21 ± 1.06 (1-5) | 2.32 ± 0.93 (1-5) | 0.400 |
| Anti Parkinson's disease treatment | | | |
| Pramipexole | 20 (54.1) | 17 (42.5) | 0.365 |
| Rasajilin | 11 (29.7) | 16 (40.0) | 0.474 |
| Levodopa + benserazide | 11 (29.7) | 13 (32.5) | 0.811 |
| Levodopa+carbidopa+entacapone | 8 (21.6) | 18 (45.0) | 0.053 |
| Levodopa + carbidopa | 1 (2.7) | 3 (7.5) | 0.616 |
| Amantadine | 5 (13.5) | 11 (27.5) | 0.165 |
| Apomorphine | 4 (10.8) | 2 (5.0) | 0.419 |
| Ropinirole | 1 (2.7) | 2 (5.0) | 0.605 |

COVID-19 = Coronavirus disease 2019, n = number, COPD = Chronic obstructive pulmonary disease

* Statistically significant value, ^a χ^2 (Chi-square) Test, ^b Independent sample T-test

Clinical features of hospitalized Parkinson's patients with COVID-19 disease

The most common initial symptoms in PD patients with COVID-19 were myalgia-arthralgia (73.0%), fatigue (48.6%), cognitive disorder (48.6%), and anorexia (43.2%). All initial symptoms, clinical features and prognosis were listed in the Table 2.

Intensive care was required in 17 (45.9%) patients and IMV support was required in 9 (24.3%) patients. The in-hospital mortality rate was 29.7% (n = 11). Characteristics and in-hospital prognosis of PD patients with COVID-19 was as shown in Figure 1.

Factors associated with the prognosis in Parkinson's disease patients with COVID-19 disease

The mean age and gender were similar in intensive care and non-intensive care patient groups (p = 0.445, p = 0.858, respectively). There was

no difference between the two patient groups in terms of smoking (p = 0.383). The most common comorbid diseases were hypertension (n = 7, 41.2%) and hyperlipidemia (n = 5, 29.4%) in intensive care patient group. The frequency of comorbid chronic disease was similar in both patient groups (p > 0.05). The PD duration of the patients treated in intensive care was 4.70 ± 3.01 (1-11) years. PD duration was similar in two groups (4.90 ± 3.91 (1-16)) (p = 0.223). There was no difference between the two patient groups according to Hoehn and Yahr stage scores (p = 0.173). There was no difference between PD treatments and the frequency of initial symptoms (p > 0.05). The mortality rate was 64.7% in the intensive care group, which was significantly higher than the other group (p < 0.001).

Patients were divided into 3 groups (nasal oxygen, CPAP, IMV) according to respiratory support. The mean age, gender and frequency of smoking were similar between three groups

Table 2: Clinical features in Parkinson's patients with COVID-19 disease (n = 37)

| Parameters | Number (n) | Percentage (%) |
|--|------------|----------------|
| Initial symptom* | | |
| Fever | 12 | 32.4 |
| Cough | 8 | 21.6 |
| Dyspnea | 9 | 24.3 |
| Myalgia-arthralgia | 27 | 73.0 |
| Fatigued | 18 | 48.6 |
| Anorexia | 16 | 43.2 |
| Headache | 9 | 24.3 |
| Diarrhea | 8 | 21.6 |
| Anosmia | 7 | 18.9 |
| Taste disorder | 10 | 27.0 |
| Dizziness | 5 | 13.5 |
| Cognitive disorder | 18 | 48.6 |
| Visual defect | 2 | 5.4 |
| Dysesthesia | 12 | 32.4 |
| Facial paralysis | 1 | 2.7 |
| Others | 3 | 8.1 |
| Treatment in intensive care unit | | |
| Yes | 17 | 45.9 |
| No | 20 | 54.1 |
| Invasive or noninvasive respiratory support | | |
| Nasal oxygen | 15 | 40.6 |
| Continuous positive airway pressure | 13 | 35.1 |
| Invasive mechanical ventilation | 9 | 24.3 |
| Mortality | | |
| Yes | 11 | 29.7 |
| No | 26 | 70.3 |

* Multiple initial symptoms may coexist in the same patient

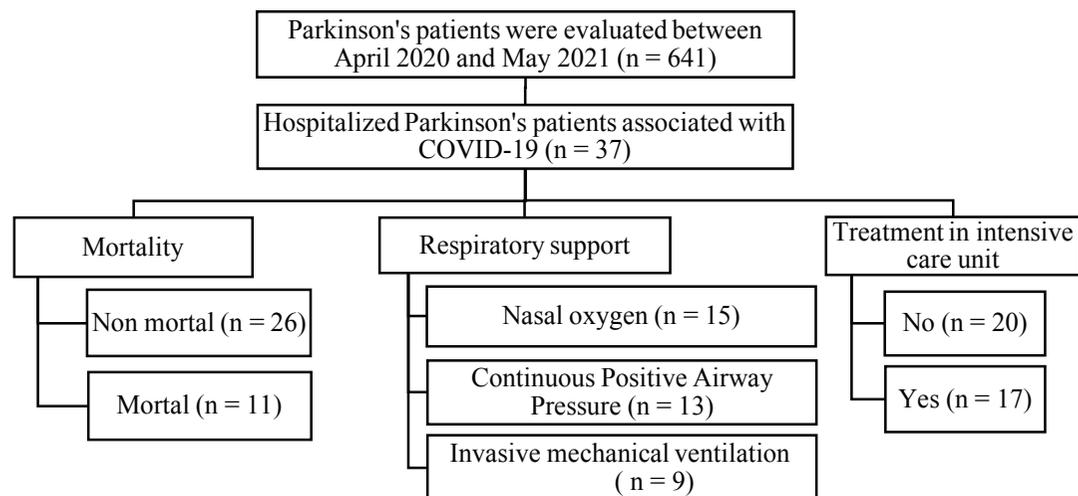


Figure 1. Characteristics of Parkinson's patients with Coronavirus disease 2019 (COVID-19)

($p = 0.801$, $p = 0.705$, $p = 0.271$, respectively). The frequency of comorbid chronic diseases was similar in three groups ($p > 0.05$). The PD duration was 5.0 ± 3.74 (1-11) years in IMV patient group, which was similar to the other patient groups ($p = 0.794$). There was no difference between the groups according to Hoehn and Yahr stage scores ($p = 0.926$). There was no difference between the frequencies of PD treatment options in three patient groups ($p > 0.05$). It was detected that diarrhea was more common symptom in the CPAP and IMV patient groups ($p = 0.008$). There was no statistical difference between the groups in terms of the frequency of other symptoms ($p > 0.05$). The mortality rate in IMV patient group was 88.9%, which was significantly higher than the other groups ($p < 0.001$). Comparison of demographic and clinical features, comorbid diseases and PD treatments according to the respiratory support were listed in Table 3.a.

Patients were divided into 2 groups as mortal ($n = 11$) and non-mortal ($n = 26$). The mean age and gender frequency were similar in two groups ($p = 0.447$, $p = 0.543$, respectively). The frequency of smoking was higher in mortal group. However, the difference was not statistically significant (36.4% vs. 7.7%, $p = 0.051$). Hypertension ($n = 4$, 36.4%) and hyperlipidemia ($n = 4$, 36.4%) were the most common comorbid diseases in mortal group. There was no difference between the frequency of comorbid chronic diseases in two patient groups ($p > 0.05$). Disease duration was 5.09 ± 3.61 (1-11) years in the mortal group and 4.69 ± 3.49 (1-16) years in the non-mortal group ($p = 0.731$). There was no difference between the two patient groups according to Hoehn and

Yahr stage scores ($p = 0.523$). There was no difference between PD treatment options in two patient groups ($p > 0.05$). Diarrhea was higher as initial symptom in the mortal group than the non-mortal group ($p = 0.004$). The frequency of other symptoms was similar between the two groups ($p > 0.05$). The comparison of demographic and clinical characteristics, comorbid diseases and PD treatments according to mortality were listed Table 3.b.

DISCUSSION

According to our literature review, this is the first study in hospitalized PD patients with COVID-19 from Turkey. In this study, PD patients with COVID-19 were compared with non-COVID-19 patients. In-hospital prognosis in these patients and the associated factors were also analyzed.

Social restrictions and preventions during the COVID-19 pandemic have created differences for daily life in patients and healthcare professionals. In a recent online survey study, PD patients stated that they were worried about COVID-19 pandemic and some patients have cancelled their medical follow up.¹⁵ Elective procedures (including deep brain stimulation or the infusion treatments) have been delayed to provide for greater hospital capacity to handle the pandemic and reduce the risk of infection.¹⁶ PD patients with longer disease duration and higher stage were generally treated at home or in the geriatrics unit. In this way, patients were protected from SARS-CoV-2.¹⁵⁻¹⁷ In our study, it was demonstrated that patients with COVID-19 disease had lower PD duration (4.81 ± 3.48 in patients with COVID-19 and 6.02

Table 3: The comparison in hospitalized Parkinson's patients with COVID-19 according to respiratory support and mortality

| Parameters | Table 3.a | | | p-value | Table 3.b | | p-value |
|---|------------------------|------------------------|------------------------|---------|------------------------|------------------------|---------|
| | Nasal oxygen, n = 15 | CPAP, n = 13 | IMV, n = 9 | | Nonmortal, n = 26 | Mortal, n = 11 | |
| Age, year | 69.4 ± 13.1 (42-88) | 71.2 ± 15.8 (35-96) | 71.7 ± 14.5 (50-90) | 0.801 | 69.5 ± 14.5 (35-96) | 73.3 ± 13.3 (50-90) | 0.447 |
| Gender | | | | | | | |
| Female | 7 (46.7) | 6 (46.2) | 5 (55.6) | 0.705 | 13 (50.0) | 5 (45.5) | 0.543 |
| Male | 8 (53.3) | 7 (53.8) | 4 (44.4) | | 13 (50.0) | 6 (54.5) | |
| Smoking | | | | | | | |
| No | 14 (93.3) | 10 (76.9) | 7 (77.8) | 0.271 | 24 (92.3) | 7 (63.6) | 0.051 |
| Yes | 1 (6.7) | 3 (23.1) | 2 (22.2) | | 2 (7.7) | 4 (36.4) | |
| Comorbid disease | | | | | | | |
| Diabetes mellitus | 1 (6.7) | 2 (15.4) | 2 (22.2) | 0.275 | 3 (11.5) | 2 (18.2) | 0.659 |
| Hypertension | 3 (20.0) | 4 (30.8) | 4 (44.4) | 0.211 | 7 (26.9) | 4 (36.4) | 0.699 |
| Hyperlipidemia | 4 (26.7) | 4 (30.8) | 2 (22.2) | 0.861 | 6 (23.1) | 4 (36.4) | 0.442 |
| Congestive heart failure | 2 (13.3) | - | 2 (22.2) | 0.668 | 2 (7.7) | 2 (18.2) | 0.567 |
| Stroke | 3 (20.0) | 3 (23.1) | 1 (11.1) | 0.650 | 5 (19.2) | 2 (18.2) | 0.941 |
| Dementia | 1 (6.7) | 3 (23.1) | 2 (22.2) | 0.271 | 3 (11.5) | 3 (27.3) | 0.335 |
| Cancer | 1 (6.7) | 2 (15.4) | 2 (22.2) | 0.276 | 3 (11.5) | 2 (18.2) | 0.623 |
| COPD | 1 (6.7) | - | 2 (22.2) | 0.263 | 2 (7.7) | 1 (9.1) | 0.888 |
| Renal failure | - | 1 (7.7) | 1 (11.1) | 0.229 | - | 2 (18.2) | 0.083 |
| Other | 3 (20.0) | 2 (15.4) | 2 (22.2) | 0.943 | 4 (15.4) | 3 (27.3) | 0.403 |
| Disease duration, years | 5.46 ± 4.17 (1-16) | 3.92 ± 2.32 (2-9) | 5.0 ± 3.74 (1-11) | 0.794 | 4.69 ± 3.49 (1-16) | 5.09 ± 3.61 (1-11) | 0.731 |
| Hoehn and Yahr stage, score | 2.36 ± 1.28 (1-5) | 2.07 ± 0.95 (1-4) | 2.16 ± 0.86 (1-4) | 0.926 | 2.13 ± 1.03 (1-5) | 2.40 ± 1.15 (1-4) | 0.523 |
| Hoehn and Yahr stage, group | | | | | | | |
| Stage 1-3 | 12 (80.0) | 11 (84.6) | 8 (88.9) | 0.567 | 23 (88.5) | 8 (72.7) | 0.335 |
| Stage 4-5 | 3 (20.0) | 2 (15.4) | 1 (11.1) | | 3 (11.5) | 3 (27.3) | |
| Anti Parkinson's disease treatment | | | | | | | |
| Pramipexole | 7 (46.7) | 7 (53.8) | 6 (66.7) | 0.636 | 13 (50.0) | 7 (63.6) | 0.495 |
| Rasajilin | 7 (24.7) | 3 (23.1) | 1 (11.1) | 0.058 | 8 (30.8) | 3 (27.3) | 0.834 |
| Levodopa + benserazide | 4 (26.7) | 5 (38.5) | 2 (22.2) | 0.923 | 9 (34.6) | 2 (18.2) | 0.445 |
| Levodopa + carbidopa + entacapone | 2 (13.3) | 4 (30.8) | 2 (22.2) | 0.517 | 4 (15.4) | 4 (36.4) | 0.203 |
| Levodopa + carbidopa | 1 (6.7) | - | - | 0.288 | 1 (3.8) | - | 0.515 |
| Amantadine | 1 (6.7) | 2 (15.4) | 1 (11.1) | 0.276 | 1 (3.8) | 4 (36.4) | 0.070 |
| Apomorphine | 2 (13.3) | 1 (7.7) | 1 (11.1) | 0.816 | 2 (7.7) | 2 (18.2) | 0.567 |
| Ropinirole | 1 (6.7) | - | - | 0.288 | 1 (3.8) | - | 0.515 |
| Initial symptom | | | | | | | |
| Fever | 5 (33.3) | 4 (30.8) | 3 (33.3) | 0.981 | 7 (26.9) | 5 (45.5) | 0.443 |
| Cough | 1 (6.7) | 5 (38.5) | 2 (22.2) | 0.251 | 4 (15.4) | 4 (36.4) | 0.203 |
| Dyspnea | 4 (26.7) | 3 (23.1) | 2 (22.2) | 0.796 | 6 (23.1) | 3 (27.3) | 0.789 |
| Myalgia-arthralgia | 10 (66.7) | 10 (76.9) | 7 (77.8) | 0.523 | 18 (69.2) | 9 (81.8) | 0.688 |
| Fatigued | 5 (33.3) | 7 (53.8) | 6 (66.7) | 0.107 | 10 (38.5) | 8 (72.7) | 0.079 |
| Anorexia | 4 (26.7) | 7 (53.8) | 5 (55.6) | 0.136 | 10 (38.5) | 6 (54.5) | 0.475 |
| Headache | 4 (26.7) | 4 (30.8) | 1 (11.1) | 0.460 | 7 (26.9) | 2 (18.2) | 0.695 |
| - | - | - | - | - | - | - | - |

| Parameters | Table 3.a | | | p-value | Table 3.b | | |
|------------------|----------------------|--------------|------------|---------------------|-------------------|----------------|---------------------|
| | Nasal oxygen, n = 15 | CPAP, n = 13 | IMV, n = 9 | | Nonmortal, n = 26 | Mortal, n = 11 | p-value |
| Diarrhea | - | 4 (30.8) | 4 (44.4) | 0.008* ^a | 2 (7.7) | 6 (54.5) | 0.004* ^a |
| Anosmia | 4 (26.7) | 3 (23.1) | - | 0.133 | 7 (26.9) | - | 0.080 |
| Taste disorder | 3 (20.0) | 5 (38.5) | 2 (22.2) | 0.774 | 6 (23.1) | 4 (36.4) | 0.442 |
| Dizziness | 2 (13.3) | 2 (15.4) | 1 (11.1) | 0.909 | 4 (15.4) | 1 (9.1) | 0.614 |
| Cognitive | 6 (40.0) | 9 (69.2) | 3 (33.3) | 0.973 | 14 (53.8) | 4 (36.4) | 0.476 |
| Visual defect | 2 (13.4) | - | - | 0.288 | 2 (7.6) | - | 0.515 |
| Dysesthesia | 5 (33.3) | 4 (30.8) | 3 (33.3) | 0.981 | 9 (34.6) | 3 (27.3) | 0.667 |
| Facial paralysis | - | 1 (7.7) | - | 0.837 | 1 (3.8) | - | 0.515 |
| Others | 1 (6.7) | 1 (7.7) | 1 (11.1) | 0.714 | 2 (7.7) | 1 (9.1) | 0.888 |

CPAP = Continuous Positive Airway Pressure, IMV = Invasive mechanical ventilation, SD = Standard deviation, n = number, COPD = Chronic obstructive pulmonary disease

* Statistically significant value, ^a χ^2 (Chi-square) Test

± 2.80 in patients non-COVID-19 patients). PD patients with lower disease duration period may be more active socially, this patient group may undergo less isolation. More studies are needed on the relationship between PD characteristics and social interaction.

Some recent studies have reported that PD is an important risk factor for mortality and disability after SARS-CoV-2.^{18,19} The rate of COVID-19-related mortality in patients with PD is between 5.7% and 40%.^{2,4,7} In the current study, the mortality rate was 29.7% in hospitalized PD patients with COVID-19. The rate was similar to previous report in the literature. It has been reported that increased age is a risk factor for poor prognosis in PD patients with COVID-19.^{3,5,19} In a study it was reported that with multivariate regression, the risk of in-hospital mortality was associated with higher age after COVID-19.⁸ Another study reported that poor prognosis in PD patients with COVID-19 was associated with comorbid medical diseases, rather than higher age.¹ In a recent study, the mean age in patients with mortal PD associated with COVID-19 was 77.06 ± 7.46 years, not different to the patients with non-mortal PD.¹⁸ In our study, the mean age of PD patients with mortality was higher than non-mortal group, but the difference was not statistically significant.

Some previous studies have reported that male gender is a risk factor for poor prognosis in patients with COVID-19^{10,20}, but no association has been reported between gender and COVID-19 in studies with PD patients.⁹ Similarly, in our study, no gender difference was detected between the PD groups with and without COVID-19. In addition, there was no difference between poor prognosis and gender. Dementia have been

reported to be a risk factor for mortality in PD patients with COVID-19.^{5,18,21} Several studies have reported that dementia and hypertension are important risk factors for COVID-19-related mortality in PD patients^{3,5,218}, but a recent study in hospitalized PD patients with a diagnosis of COVID-19 demonstrated that mortality is lower in patients with dementia and hypertension. In the study, it was also reported that the frequency of heart failure and DM was lower in the PD patient cohort.²¹ Other studies have reported that the same comorbid diseases are risk factors for COVID-19-related mortality.^{20,22,23} The results were thus inconsistent. In our study, the percentage of comorbid chronic diseases was generally higher in hospitalized PD patients with COVID-19, but only the frequency of hypertension was statistically significantly higher (5% vs. 29.7%). Similarly, the frequency of chronic diseases was higher in patients with poor prognosis in the in-hospital period, but no statistical difference was detected between them. There is an association between smoking and poor prognosis in PD, but there are conflicting results about smoking and poor prognosis in PD patients with COVID-19.^{3,21,24} In our study, there was no difference between the frequency of smoking in the patient groups with and without COVID-19. The frequency of smoking was higher in the patient group with mortality (36.4% vs 7.7%), but the difference was not statistically significant ($p = 0.051$). This may be due to low number of patients. These results need to be confirmed by further studies with larger number of patients.

The clinical data about COVID-19 disease in PD patients are limited, but it is considered that PD is associated with severe symptoms of COVID-19.^{16,25} In a recent study, no difference

was detected between COVID-19 symptoms in patients with and without PD. The most common symptoms in PD have been reported as fever, cough, nasal congestion, fatigue, and myalgia-arthralgia.² In our study, the most common symptoms in PD patients were myalgia-arthralgia, fatigue, and cognitive disorder. Parkinson's patients with neurological manifestations (a change in mental status, physical neurological deficit, or general weakness) had higher mortality rates than patients with respiratory or gastrointestinal manifestations.¹⁹ In our study, no association was found between initial symptoms and mortality, other than diarrhea. Concerning the relationship between gastrointestinal symptoms and prognosis in patients with COVID-19; Pan *et al.* reported that the hospitalization period was longer in COVID-19 patients with diarrhea and vomiting. Besides, this study noted that gastrointestinal symptoms may be associated with poor prognosis in COVID-19 disease.²⁶ Another study did not support the association of gastrointestinal symptoms and poor prognosis in COVID-19 patients.²⁷ In a study from Hong Kong, RNA positivity was detected higher in patients with diarrhea as the initial symptom.²⁸ In addition, it has been reported that viral infection can cause malabsorption by changing intestinal permeability. Cytokine storm can cause intestinal ischemia and this may be associated with a poor prognosis.²⁹ In our literature review, we could not determine any data about the association of COVID-19 and diarrhea with poor prognosis in PD patients. Our study has shown an increased frequency of diarrhea was associated with the indication for CPAP and IMV. In addition, diarrhea was also associated with mortality. These results demonstrated that there was an association between diarrhea and poor prognosis in PD patients with COVID-19.

Because of the pandemic process, new treatment options for protection and treatment of SARS-CoV-2 were explored. In addition to the new treatment options, current medical drugs were also searched for in COVID-19. It was thought that anti-PD drugs may have a therapeutic role in COVID-19. This theory was put forward especially considering the relationship between dopamine and angiotensin-converting enzyme II (ACE-II).³⁰ Entacapone, a catechol-O-methyltransferase (COMT) inhibitor, has a potential effect on viral biology.³¹ Amantadine, which is a prophylactic agent for influenza, has also been thought to change the lysosomal structure in the SARS-CoV-2 replication.³²

However, there is no randomized study in the literature concerning the effects of PD treatments on SARS-CoV-2 infection. Studies are retrospective and observational. In previous studies, the effect of PD treatments on COVID-19 disease could not be demonstrated.^{2,3,33} In our PD patient cohort, we could not detect an effectiveness of these drugs during the COVID-19, but more studies are needed.

Limitations of the study are; First, it is a retrospective and single-center study. Second, the number of patients in the groups is relatively small. Third, all Parkinson's patients with typical pneumonic infiltrates associated with COVID-19 in computed thoracic tomography were included in the study; however, data on patients who were positive rRT-PCR and not- pulmonary infiltration were not included in the study.

In conclusion, PD patients are sensitive to infectious diseases. Therefore, it is important to evaluate PD patients with and without COVID-19 disease. Hypertension is more common comorbid disease in hospitalized patients with COVID-19 disease. Particularly in patients with diarrhea as the initial symptom, the frequency of mortality and CPAP/IMV requirement is higher. In hospitalized PD patients with COVID-19, total mortality rate was 29.7% (64.7% in the intensive care unit, and 88.9% in patients with IMV). Considering the mortality rate of the COVID-19 and its effects on PD patients, randomized and (further and larger) multicenter studies are needed.

DISCLOSURE

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