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Investigation of Neurological Symptoms Caused by COVID-19 in Intensive Care Unit

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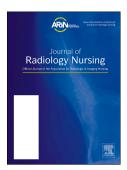
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# Impact of Neurological Symptoms Caused by COVID-19 on Quality of Life: A Retrospective Study with 1699 Patients

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Medical Practices: Y.A., Concept: Y.A., S.B., Design: Y.A., S.B., Data Collection or Processing: Y.A., S.B., AA Analysis or Interpretation: Y.A., S.B., AA Literature Search: Y.A., S.B., Writing: Y.A., S.B.

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# **Compliance with ethical standards**

Conflict of interest The authors declare that they have no conflict of interest to disclose

**Ethical approval** All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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Impact of Neurological Symptoms Caused by COVID-19 on Quality of Life after Intensive

Care

**ABSTRACT** 

**Purpose:** We examined the neurological symptoms of patients treated for COVID-19 and the

effect of these symptoms on their quality of life in this study.

**Method:** We obtained the study data retrospectively from data records of 1699 patients treated

in the COVID-19 clinics of a training and research hospital. The study is a descriptive and

cross-sectional study. Sociodemographic and Disease Information Form and Rolls Royce

Quality of Life (QoL) Scale were used for data collection. Statistical Packed for the Social

Sciences 25.0 IBM was used in Data analysis.

**Findings:** It was observed that 37% of the COVID-19 patients were between the ages of 66-80

and the quality of life was getting worse in older ages. 55.6% of the COVID-19 patients were

male and the gender difference did not statistically change the quality of life. The quality of life

of all COVID-19 patients were low. The most common neurological symptoms in the disease

process and their rates were as follows: insomnia 74.6%, taste loss 74%, smell loss 75.6%,

muscle pain 83.2%, headache 45.1%, dizziness 32.2%, weakness 20.2%, and agitation 34.7%.

The lowest quality of life was in patients with stroke and agitation among patients with

neurological symptoms (p=0.000).

Conclusion: Assessment of neurological symptoms of patients followed-up for COVID-19 is

of great importance. We suggest that neurological problems should be tried to be cured with

appropriate treatment protocols and therapy support before they progress further and the

neurological prognosis progresses.

Keywords: COVID-19, Neurological Symptoms, Sars-Cov-1, Quality of Life

# Investigation of Neurological Symptoms Caused by COVID-19 in Intensive Care Unit

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## Investigation of Neurological Symptoms Caused by COVID-19 in Intensive Care Unit

#### **ABSTRACT**

**Purpose:** We examined the neurological symptoms of patients treated in intensive care for COVID-19 in this study.

**Method:** We obtained the study data retrospectively from data records of 1699 patients treated in the COVID-19 clinics of a training and research hospital. The study is a descriptive and cross-sectional study. Sociodemographic and Disease Information Form were used for data collection. Statistical Packed for the Social Sciences 25.0 IBM was used in Data analysis.

**Findings:** It was observed that 37% of the COVID-19 patients were between the ages of 66-80 and 55.6% of the COVID-19 patients were male. The most common neurological symptoms in the disease process and their rates were as follows: insomnia 74.6%, taste loss 74%, smell loss 75.6%, muscle pain 83.2%, headache 45.1%, dizziness 32.2%, weakness 20.2%, and agitation 34.7%.

**Conclusion:** Assessment of neurological symptoms of patients followed-up for COVID-19 is of great importance. We suggest that neurological problems should be tried to be cured with appropriate treatment protocols and therapy support before they progress further and the neurological prognosis progresses.

**Implications for Clinical Practice:** The prognosis of neurological symptoms caused by COVID-19 post-ICU are unknown. These symptoms compromise independence in all aspects of patient outcomes. Nurses and physicians should include the management of these symptoms in the care plan.

**Keywords:** COVID-19, Intensive care unit, Neurological symptoms, Sars-Cov-2

#### **INTRODUCTION**

COVID-19, which causes severe acute respiratory problems, is a deadly disease that first appeared in Wuhan, China in December 2019 and caused a global pandemic. (Guan et al., 2020; World Health Organisation-WHO, 2022). Vaccination procedures is carried out as well as various treatment protocols in order to weaken the disease-causing mechanism of COVID-19. Despite the use of vaccines worldwide, COVID-19 continues to cause dire consequences. It was stated in a previous study that 2,246 out of 1,228,664 people who had the first two doses of vaccine were infected with COVID-19. In the same study, it was stated that 36 people died

among those infected with COVID-19, and 189 of them had severe symptoms (Yek et al., 2022).

It is reported that the clinical course of COVID-19 is worse in people with cardiovascular disease (CVD), diabetes mellitus (DM), hypertension, neurological disorder, and in older people (Benussi et al., 2020; Qin et al., 2020; Zhou et al., 2020). In addition to this, people exposed to COVID-19 have a high risk of developing central nervous system (CNS)-related disorders (Glass et al., 2004). It is stated in the literature that neurological disorders may occur in the future after the acute phase of COVID-19 has been overcome (Desforges et al., 2019). The degree and severity of the course of COVID-19 are significantly associated with the development of psychiatric and neurological disorders. Severe systemic inflammatory responses are likely to induce these disorders. The neurological vulnerability of elderly, and of those with weakened immune system, comorbidities or chronic diseases is higher (Antonini et al., 2020; Bianchetti et al., 2020; Kubota, & Kuroda, 2021). Even if they survive COVID-19, even minor injuries such as urinary tract infection or pneumonia can trigger acute confussional state, confusion, delirium, and encephalopathy, as they will have residual susceptibility.

Increasing awareness of neurological symptoms caused by COVID-19 is of great importance for the management, prevention and treatment of these symptoms. In addition to this, neurological symptoms seen during the treatment process of COVID-19 may be a sign of a poor neurological prognosis in the future. Negative emotional state and poor patient outcomes caused by neurological symptoms are also expected situations in this regard. Detection of neurological symptoms will enable us to make predictions regarding possible future neurological prognosis and learn about the areas the patients need support. We examined the neurological symptoms of patients treated in intensive care for COVID-19 in this study.

#### **MATERIALS AND METHODS**

We conducted this study as a descriptive and cross-sectional study to examine the neurological disorders experienced by patients receiving intensive care treatment for COVID-19.

#### **Research Design and Participants**

We conducted our study with the participation of patients receiving treatment in the COVID-19 intensive care of a tertiary traning and research hospital in eastern Turkey. The data regarding the hospitalization of the patients included in this study were obtained from the data records after the approval of the ethics committee. All patients who were hospitalized due to COVID-19 and met the inclusion criteria were included in the study and purposive sampling method was used. A total of 1699 patients who were hospitalized due to COVID-19 between

March 10, 2020 and January 31, 2022, in the hospital where the study was conducted were included in the sample. Neurological and pulmonary problems related to COVID-19, certain blood values, chronic diseases existing before COVID-19, diseases developing secondary to COVID-19, sociodemographic data of patients were extracted from patient files and recorded in data collection form. Sampling inclusion and exclusion criteria are provided below.

#### **Inclusion Criteria**

- i. Diagnosis of COVID-19
- ii. Being treated in the ICU due to COVID-19
- iii. Age 18 and above
- iv. Not being diagnosed with any neurological disorder prior to COVID-19

#### **Exclusion Criteria**

- i. Diagnosis other than COVID-19
- ii. Treatment at home or out of ICU for COVID-19
- iii. Patients under the age of 18
- iv. Being diagnosed with a neurological disorder prior to COVID-19

#### **Data Collection Tools**

Sociodemographic and COVID-19 Information Form were used for data collection. The sociodemographic and COVID-19 information form is a questionnaire developed by researchers in which the personal characteristics of the patients and the problems, illnesses, symptoms and clinical conditions they experienced during the period they had COVID-19 are investigated.

#### **Statistical Analysis of Data**

After the data were coded by the researchers, the statistical analysis of the data was made using the Statistical Packed for the Social Sciences (SPSS) 25.0 IBM statistical program. Descriptive statistics were used in the analysis of the data. 95% confidence interval and p<0.05 error level were taken into account in the evaluation of the results obtained.

#### **Ethical Aspect of Research**

Necessary legal permissions were obtained from Adiyaman University Training and Research Hospital and the Ethics Committee of the same university before starting the research (Decree no: 2021/10-24). Data were obtained from electronic records after ethics committee approval and we did not have access to patients' private information (name, surname, ID number, etc.).

#### **FINDINGS**

The descriptive characteristics COVID-19 patients are listed in Table 1. It was seen that 26.1% of the COVID-19 patients were 81 and older, 37% were between the ages of 66-80, and 55.6% of the COVID-19 patients were male. 76% of COVID-19 patients had a body mass index of 18-25, 78.9% have not used alcohol, 73.2% have not smoked. Of the COVID-19 patients treated in the ICU, only 20.4% had no chronic disease, the remainder had various chronic diseases (Hepatopancreatobiliary diseases, Diabetes mellitus, Chronic obstructive pulmonary disease, etc.).

Table 1. Descriptive Characteristics of COVID-19 Introductory Information	n	%
Age	n n	/0
Ages between 20-35	54	3.2
Ages between 36-50	143	8.4
Ages between 51-65	431	25.4
Ages between 66-80	628	37
	443	26.1
81 years old and above	443	20.1
Gender		
Female	755	44.4
Male	944	55.6
Body Mass Index	X	
between 18-25	1291	76
between 25-29.9	351	20.7
between 30-39.9	52	3.1
40 and higher	5	0.3
Alcohol Consumption		
Drinks	358	21.1
Does not drink	1341	78.9
Smoking Habit		
Smoker	455	26.8
Non-smoker	1244	73.2
Chronic Diseases before COVID-19 a		
No chronic disease	347	20.4
Hepatopancreatobiliary diseases	225	13.2
Diabetes mellitus	267	15.7
Chronic obstructive pulmonary disease	211	12.4
Chronic kidney failure	221	13
Cardiovascular disease	210	12.4
Asthma	140	8.2
Malignity	74	4.4
3 and above Comorbidity	52	3.1
Outcome		
Those recovered from COVID-19	1119	65.9
Death	422	24.8
Neurological Prognosis	158	9.3
<sup>a</sup> More than 1 problem was recorded in the same patient; X	Y Mean: SD Standard Deviation	

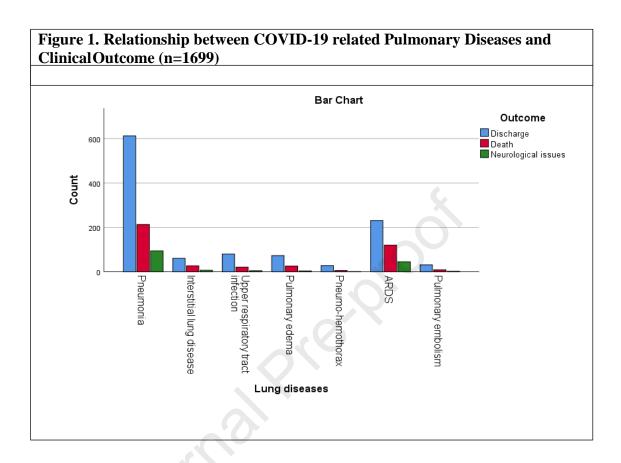
The neurological symptoms Caused by COVID-19 are presented in Table 2. The most common neurological symptoms and their rates were as follows: insomnia 74.6%, taste loss 74%, smell loss 75.6%, muscle pain 83.2%, headache 45.1%, dizziness 32.2%, weakness 20.2%, and agitation 34.7%. 71.6% of COVID-19 patients had coughing, 70.7% of them had dyspnea, and 93.2% of them had high fever.

Table 2. Neurological Symptoms Caused by COVID-19 (n=1699)		
Neurological Symptoms Caused by COVID-19 <sup>a</sup>	n	%
Peripheral nerve involvement	372	21.9
Insomnia	1267	74.6
Epileptic seizure	364	21.4
Agitation	589	34.7
Confusion	424	25.0
Lack of attention	366	21.5
Loss of taste	1257	74.0
Headache	767	45.1
Ischemic stroke	19	1.2
Blurred vision	414	24.4
Dizziness	547	32.2
Loss of smell	1285	75.6
Appetite disorder	259	15.2
Numbness in fingertips	256	15.1
Double vision	118	6.9
Muscle ache	1413	83.2
Weakness	343	20.2
Other Problems <sup>a</sup>	n	%
Cough	1216	71.6
Dyspnea	1201	70.7
GIS problems	322	19
High Fever	1583	93.2
Increase in serum CRP	1399	82.3
Increase in serum Procalcitonin	1528	89.9
Increase in serum d-Dimer	786	46.3
<sup>a</sup> More than 1 problem was recorded in the same patient		

The comorbid and pulmonary diseases are presented in Table 3. It was determined that the most common pulmonary disease caused by COVID-19 was pneumonia with a rate of 54.1% and the rate of ARDS was 23.3%. When the health problems that develop secondary to COVID-19 during the ICU period are examined; it was seen that 9.2% of the patients developed CVD, 6% of them developed Acute Renal Failure, and 8.7% of them developed metabolic acidosis.

Table 3. Comorbid and Pulmonary Diseases Caused by COVID-19 (n=	:1699)	
Diseases Developing Secondary to COVID-19 in the Intensive Care Unit <sup>a</sup>	n	%
Acute Renal Failure	102	6
Gastric bleeding	123	7.2
Hypertension	125	7.4
Metabolic acidosis	147	8.7
Cardiovascular disorders	156	9.2
Peritonitis	104	6.1
Subdural hemorrhage	94	5.5
Pressure ulcer	45	2.6
Cerebrovascular event	81	4.8
Skin problems (Echymosis, petechiae etc.)	64	3.8
Necrotizing fasciitis	67	3.9
Sepsis	58	3.4
Pain (Head, chest, muscle)	78	4.6
Nutritional disorders	81	4.8
Hypoalbuminemia	68	4
Pulmonary Diseases Caused by COVID-19	n	%
Pneumonia	919	54.1
Interstitial lung disease	95	5.6
Upper respiratory tract infection	106	6.2
Pulmonary edema	103	6.1
Pneumo-hemithorax	35	2.1
Acute respiratory distress syndrome	396	23.3
Pulmonary embolism	42	2.5
Other	3	0.2
<sup>a</sup> More than 1 problem was recorded in the same patient		

The relationship between the pulmonary diseases caused by COVID-19 and their outcome of clinical (death, discharge, and neurological issues) is shown in Figure 1.



As per Figure 1, it is seen that clinical outcomes, and pulmonary diseases had varying rates. It was established that ARDS and pneumonia patients developed the most neurological prognosis.

#### **DISCUSSION**

Our study which was carried out with 1699 patients diagnosed with COVID-19 who were treated at a hospital is an important source of information. We examined the neurological symptoms of patients treated for COVID-19 in this study. It was stated in a systematic review that headache, dizziness and confusion were the most common neurological findings associated with COVID-19. It was also stated in the same systematic review that ischemic stroke, CNS problems, CVA, polyneuropathy, muscle coordination weakness and encephalopathy were less common (Bulbuloglu & Gurhan, 2022). The most common neurological symptoms in our study were muscle pain (83.2%), loss of smell (75.6%), insomnia (74.6%), loss of taste (74%), headache (45.1%), agitation (34.7%), dizziness (32.2%) and weakness (20.2%) and the least common neurological symptoms were ischemic stroke (1.2%), diplopia (6.9%), appetite

disorder (15.2%), and fingertip numbness (15.1%). Our results are similar to those reported in the literature.

COVID-19-related neurological diseases are usually recognized when symptoms appear. Sometimes, neurological diseases or problems may delay the onset of symptoms in proportion to the location and size of the lesions in the brain, or the neurological disease may generate any symptoms. It was reported in a previous study that in people who had COVID-19, viruses remained in the CNS later on and these viruses later led to post-infectious neurological complications (Desforges et al., 2019). Our study also highlights the onset of neurological symptoms during the acute phase of COVID-19. In addition to the foregoing, it was observed that during the acute phase of COVID-19, 4.8% of the patients had a CVA and 5.5% had subdural hemorrhage. In our study, it was established that 9.3% of the patients who survived the acute phase of COVID-19 experienced neurological prognosis. Previous studies reported that neurological diseases seen in more than 30% of the patients (Karadaş, Öztürk & Sonkaya, 2020; Mao et al., 2017). The difference may be due to the fact that the diseases diagnosed with neurological symptoms were not separately specified in previous studies.

Upon review of the studies in the literature it is seen that; in a study conducted with the participation of n=239 COVID-19 patients, it was reported that 26.7% of the patients had headaches, 6.7% of them had dizziness, 9.6% of them had confusion, 12.6% of them had sleep disturbance and 15.1% of them had muscle pain (Karadaş, Öztürk & Sonkaya, 2020). In a study conducted in China with the participation of n=214 patients, it was reported that 25% of the patients had CNS problems, 13% of them had headache, 17% of them had dizziness and 8% of them had confusion (Mao et al., 2017). Case reports in the literature have generally addressed 1 or 2 findings. These findings include dramatic issues such as Guillain-Barré syndrome, ischemic stroke, encephalopathy, and cerebral venous sinus thrombosis (Alberti et al., 2020; Beyrouti et al., 2020; Cavalcanti et al., 2020; Oxley et al., 2020; Padroni et al., 2020; Paterson et al., 2020). In addition to that, it is stated in literature that patients with at least one neurological symptom have a significantly higher blood D-dimer level (p<0.05) than patients without any neurological symptoms (Karadaş, Öztürk & Sonkaya, 2020). It was emphasized in literature that the level of D-dimer, leukocytes, neutrophils and C-reactive protein (CRP) increased due to COVID-19 (Li et al., 2020). 82.3% of the patients included in our study had an increase in CRP and 46.3% of them had an increase in d-dimer levels. Our results are similar to those reported in the literature.

It was determined that 65.9% of 1699 COVID-19 patients included in our study recovered from COVID-19, 24.8% of them died, and 9.3% were transferred to the neurology

clinic due to neurological prognosis. Patients who recovered from COVID-19 continued to struggle with the diseases they contracted during the time they had COVID-19. It was established in or study that COVID-19 plays an active role in the development of not only neurological issues, but also many other problems and diseases such as CVD, Acute Renal Failure, metabolic acidosis, gastric bleeding, and hypoalbuminemia. COVID-19 is an extremely dangerous disease that causes mass deaths, especially before vaccination. The problems caused by COVID-19 have not been fully understood yet. Our study is an important source of information in this sense. That being said, the fact that all patients were not examined by neuroimaging methods in our study and interleukin and other cytokine values could not be checked were deemed as limitations of this study.

#### **Conclusion**

The findings of our study revealed that the neurological issues associated with COVID-19 should not be ignored and are seen at a high rate. It was found out in our study that at least one neurological finding occurred in every COVID-19 patient. Our study is an important source of information for a full understanding of the effects of COVID-19 disease. Unfortunately, due to the pandemic, not all of the available evidence could be confirmed by advanced diagnostic methods, due to financial problems and a lack of workforce. Therefore, additional studies are needed to be conducted. It should also be considered that not all COVID-19 patients undergo a neurological examination. This is an indication that some issues and symptoms may go undetected. Clinicians should be aware of possible psychiatric and neurological issues, and these issues should be diagnosed and treated at an early stage.

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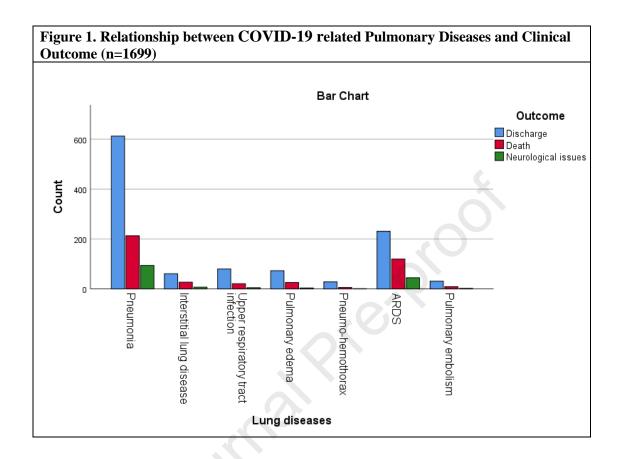
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Introductory Information	Table 1. Descriptive Characteristics of COVID-19	Patients (n=1699)	
Ages between 20-35     54     3.2       Ages between 36-50     143     8.4       Ages between 51-65     431     25.4       Ages between 66-80     628     37       81 years old and above     443     26.1       Gender       Female     755     44.4       Male     944     55.6       Body Mass Index     5     6       between 18-25     1291     76       between 25-29.9     351     20.7       between 30-39.9     52     3.1       40 and higher     5     0.3       Alcohol Consumption       Drinks     358     21.1       Does not drink     1341     78.9       Smoker     455     26.8       Non-smoker     1244     73.2       Chronic Diseases before COVID-19 and the color of t	*		%
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81 years old and above   343   26.1		628	37
Gender         755         44.4           Male         944         55.6           Body Mass Index		443	26.1
Male         944         55.6           Body Mass Index         Between 18-25         1291         76           between 25-29.9         351         20.7           between 30-39.9         52         3.1           40 and higher         5         0.3           Alcohol Consumption         Drinks         358         21.1           Does not drink         1341         78.9           Smoking Habit         Smoker         455         26.8           Non-smoker         1244         73.2           Chronic Diseases before COVID-19 a         No chronic disease         347         20.4           Hepatopancreatobiliary diseases         225         13.2           Diabetes mellitus         267         15.7           Chronic obstructive pulmonary disease         211         12.4           Chronic kidney failure         221         13           Cardiovascular disease         210         12.4           Asthma         140         8.2           Malignity         74         4.4           3 and above Comorbidity         52         3.1           Outcome         20         24.8           Those recovere	•		
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40 and higher       5       0.3         Alcohol Consumption       358       21.1         Drinks       358       21.1         Does not drink       1341       78.9         Smoking Habit       Smoker       455       26.8         Non-smoker       1244       73.2         Chronic Diseases before COVID-19 a       No chronic disease       347       20.4         Hepatopancreatobiliary diseases       225       13.2         Diabetes mellitus       267       15.7         Chronic obstructive pulmonary disease       211       12.4         Chronic kidney failure       221       13         Cardiovascular disease       210       12.4         Asthma       140       8.2         Malignity       74       4.4         3 and above Comorbidity       52       3.1         Outcome			
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Neurological Prognosis 158 9.3	Those recovered from COVID-19	1119	65.9
	Death	422	24.8
	Neurological Prognosis	158	9.3
		X, Mean; SD, Standard Deviation	n

Table 2. Neurological Symptoms Caused by COVID-19 (n=1699	)	
Neurological Symptoms Caused by COVID-19 <sup>a</sup>	n	%
Peripheral nerve involvement	372	21.9
Insomnia	1267	74.6
Epileptic seizure	364	21.4
Agitation	589	34.7
Confusion	424	25.0
Lack of attention	366	21.5
Loss of taste	1257	74.0
Headache	767	45.1
Ischemic stroke	19	1.2
Blurred vision	414	24.4
Dizziness	547	32.2
Loss of smell	1285	75.6
Appetite disorder	259	15.2
Numbness in fingertips	256	15.1
Double vision	118	6.9
Muscle ache	1413	83.2
Weakness	343	20.2
Other Problems <sup>a</sup>	n	%
Cough	1216	71.6
Dyspnea	1201	70.7
GIS problems	322	19
High Fever	1583	93.2
Increase in serum CRP	1399	82.3
Increase in serum Procalcitonin	1528	89.9
Increase in serum d-Dimer	786	46.3
<sup>a</sup> More than 1 problem was recorded in the same patient		

Table 3. Comorbid and Pulmonary Diseases Caused by COVID-19 (n=	1699)	
Diseases Developing Secondary to COVID-19 in the Intensive Care Unit <sup>a</sup>	n	%
Acute Renal Failure	102	6
Gastric bleeding	123	7.2
Hypertension	125	7.4
Metabolic acidosis	147	8.7
Cardiovascular disorders	156	9.2
Peritonitis	104	6.1
Subdural hemorrhage	94	5.5
Pressure ulcer	45	2.6
Cerebrovascular event	81	4.8
Skin problems (Echymosis, petechiae etc.)	64	3.8
Necrotizing fasciitis	67	3.9
Sepsis	58	3.4
Pain (Head, chest, muscle)	78	4.6
Nutritional disorders	81	4.8
Hypoalbuminemia	68	4
Pulmonary Diseases Caused by COVID-19	n	%
Pneumonia	919	54.1
Interstitial lung disease	95	5.6
Upper respiratory tract infection	106	6.2
Pulmonary edema	103	6.1
Pneumo-hemithorax	35	2.1
Acute respiratory distress syndrome	396	23.3
Pulmonary embolism	42	2.5
Other	3	0.2
<sup>a</sup> More than 1 problem was recorded in the same patient		



# Highlights

- Post-COVID-19 issues are not yet fully known.
- Life-threatening diseases can occur after COVID-19.
- Symptoms caused by COVID-19 should be diagnosed and treated early.

Availability of data and material: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interests: The authors declare that they have no conflicts of interest related to the publication of this manuscript.

Funding: No funding was received for this research.

Informed Consent: Written informed consent was obtained from the parents or guardians of all patients.

Ethical Consideration: This research has been approved by Adiyaman University Medical Faculty, Department of Neurology Institutional Review Board (IRB). Before starting the study, the necessary permissions were obtained from Adiyaman University Research and Training Hospital's Clinical Research Ethics Committee.

Dac	laration	of interests
Dec	iaration	or interests

☐ The authors declare that they have no known competing financial interests or personal relationships
nat could have appeared to influence the work reported in this paper.
☐The authors declare the following financial interests/personal relationships which may be considered
s potential competing interests: