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RESEARCH ARTICLE

The Treatment of COVID-19 and Severe Mental Illness Together: Comparing Clinical Features of Patients with Bipolar Disorder and Major Depressive Disorder

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ABSTRACT

Objective: COVID-19 can be codiagnosed in people who need to be treated in psychiatry services with symptoms such as acute mood or psychotic episodes, aggression, and suicidal thoughts. The aim of the study was to compare the clinical features of patients with COVID-19 and major depressive disorder (MDD) or bipolar disorder (BD).

Materials and Methods: Of 84 patients, 60 were diagnosed with BD, and 24 were diagnosed with MDD. Patients, who were treated in a psychiatry service for COVID-19, were included in the study. The two groups were compared in terms of sociodemographic data, medications, psychiatric symptoms, comorbid diseases, progression (CALL) scores, laboratory markers of inflammation, and procoagulation.

Results: There was no significant difference between the BD and MDD groups in terms of age and gender. While self-harm/suicidal ideation was found significantly more frequently in MDD patients compared to the BD group (p=0.024), agitation/aggression and treatment refusal rates were significantly higher in the BD group (p= 0.001, p= 0.002). Lactate dehydrogenase and ferritin levels were significantly higher in the BD group (p= 0.016, p= 0.032). Finally, there was no significant difference between the two groups in terms of CALL scores (p=0.678).

Conclusion: Cases diagnosed with BD may need hospitalization for manic symptoms such as agitation/aggression/rejection of treatment during the pandemic period. BD may pose a susceptibility to inflammation associated with COVID-19 or given the underlying inflammation associated with illness. The treatment and primary prevention of these patients for COVID-19 may be of particular importance.

Keywords: Bipolar disorder, COVID-19, ferritin, lactate dehydrogenase, major depressive disorder

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INTRODUCTION

In epidemics, the prognosis of serious mental illnesses such as bipolar disorder (BD), major depressive disorder (MDD), and schizophrenia is adversely affected and the risk of relapse increases in these diseases.[1,2] COVID-19 disease, caused by the virus (SARS-CoV-2), a new agent of the coronavirus family, was declared a pandemic by the World Health Organization on March 11, 2020, and while the pandemic continued, the mental health of patients with severe mental disorders was adversely affected.[2,3] These patients showed symptoms that were severe enough to require hospitalization.[2–4] Likewise, many cases of COVID-19 were reported from psychiatric wards, and in these wards, it was noted that almost all patients quickly became COVID-19 after the first cases.[5,6] For this reason, as the COVID-19 epidemic progresses, a need for private psychiatric services for patients with severe mental illness infected with SARS-CoV-2 has arisen.

On the other hand, COVID-19 is a disease that can show variable prognoses in different age and risk groups.[7] Among the prognostic factors for COVID-19, factors such as advanced age and comorbid disease, as well as high laboratory values such as ferritin, D-dimer, fibrinogen, lactate dehydrogenase

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(LDH), and C-Reactive protein, have also been reported.[7,8] Another topic of interest is the severity of COVID-19 in those with severe psychiatric illness. In some studies, it has been found that COVID-19 has a worse prognosis in patients with severe mental illness.[9] In a recent study by Fond et al.[10] with 50,407 participants with COVID-19, 408 patients with BD and patients without serious mental disorders were compared in terms of mortality. According to the results of the study, in-hospital mortality rates were found to be higher in patients with BD than in patients without severe mental disorders.[10] Intensive care needs were found to be equal between the groups.[10] In another study conducted on patients with COVID-19, it was shown that mood or anxiety disorder was not associated with mortality, but schizophrenia was associated with mortality.[11]

Considering all this literature data and due to the need arising, "Psychiatry service special for patients infected with SARS-Cov2," which is one of the firsts in the world and the first, we know in Türkiye, was established in our hospital. Our study, it was aimed to compare the general characteristics, treatments, progression risks, inflammation, and coagulation markers in these patient groups who were hospitalized in this "COVID-19 special psychiatry service" with the diagnoses of BD and MDD. We thought that COVID-19 may have different severity in patients with BD and MDD. We also wanted to investigate whether people with BD and MDD, both mood-related disorders, show common clinical symptoms due to the common stressor, the pandemic. With the results, we aimed to provide information about the clinical features of patients with BD and MDD with COVID-19 during mood episodes.

MATERIALS and METHODS

The study was carried out in the psychiatry service of a pandemic hospital in Istanbul, which was established specifically for psychiatric patients with COVID-19. Between April 2020 and July 2021, 84 patients, 60 with BD and 24 with MDD, between the ages of 18 and 65 who were hospitalized in the special COVID-19 psychiatry service due to psychiatric disorders were included in the study. The diagnosis of COVID-19 was made with the consultation of an infectious disease specialist, confirmed by clinical findings, polymerase chain reaction test, and thoracic computed tomography. Those with comorbid psychiatric diseases such as alcohol/substance use disorder, a psychiatric disorder due to alcohol/substance use, anxiety disorder, obsessive-compulsive disorder, mental retardation, or diseases in the autistic spectrum were not included in the study.

The study was planned as cross-sectional. Sociodemographic information, drugs used, psychiatric symptoms, comorbid diseases, LDH, ferritin, fibrinogen, and D-dimer values were recorded for each patient. The CALL (C="comorbidity," A="age," L="lymphocyte count," and L="LDH") score was calculated based on the participants' age, comorbidity, absolute lymphocyte count, and serum LDH level. The CALL score is a parameter scored between 4 and 13 and has been shown to predict the risk of COVID-19 pneumonia.[7]

Before starting the study, an application was made to the COVID-19 Scientific Research Evaluation Commission of the Ministry of Health of the Republic of Türkiye, the General Directorate of Health Services, and the necessary approvals were obtained. In our study, the principles of human experiments determined in the Helsinki Agreement adopted in 1975 were followed and Local Ethics Committee approval was obtained (number: 2021.07.217).

All statistical analyses were performed in the Statistical Package for the Social Sciences version 24 (IBM Corporation, Armonk, New York). The normal distribution of continuous variables was tested using skewness and kurtosis values. Normally distributed data in continuous variables were compared using Student's t-test. Continuous variables that did not show normal distribution were compared with the Mann–Whitney U-test. Welch correction was made when the variances were not equal in the t-test applied to independent samples. Categorical variables were compared using the Chi-square test and reported as percentage frequency with the number of participants. Fisher's exact test was used instead of the chi-square test when the cell number was less than 5. Statistical significance was set at 0.05 for all comparisons.

RESULTS

The study sample consisted of 84 participants, 60 of whom were diagnosed with BD and 24 with MDD. In Table 1, the group with BD and the group with MDD were compared in terms of sociodemographic data and clinical characteristics (Table 1). Both groups were similar in terms of age, gender, length of hospital stay, presence of comorbid disease, and COVID-19 treatments ($p>0.05$). Disease duration was significantly higher in the BD group than in the MDD group ($p<0.001$). While the use of antipsychotics and mood stabilizers was significantly higher in the BD group than in the MDD group ($p=0.022$, $p<0.001$), the antidepressant use rate was significantly higher in the MDD group ($p<0.001$). Benzodiazepine use was similar in both groups ($p=0.238$). When hospitalization indications are examined; self-harm/suicidal ideation was found significantly more frequently in the

Table 1. Comparison of sociodemographic data and clinical features of patients with major depressive disorder and bipolar disorder hospitalized in a COVID-19-specific psychiatry service

	MDD (n=24)		BD (n=60)		t/U/X²	p
	n	%	n	%		
Age, year, mean±SD	43.2±15.1		42.6±14.8		0.2	0.875
Sex						
Women	7		31		3.5	0.061
Men	17		29			
Hospitalization, days, median (IQR)	14 (11–25)		19 (14–30)		530.5	0.074
Disease duration, years, median (IQR)	1 (0–6)		10 (4–21)		210.0	**<0.001**
Medicine, (n=83)						
Antipsychotics	21	87.5	59	100.0	Fisher's exact test	**0.022**
Mood stabilizers	3	12.5	41	69.5	22.2	**<0.001**
Antidepressants	18	75.0	4	6.8	40.8	**<0.001**
Benzodiazepines	14	58.3	26	44.1	1.4	0.238
Comorbid diseases, (n=83)						
Hypertension	4	16.7	9	15.3	Fisher's exact test	1.0
Chronic obstructive pulmonary disease	1	4.2	1	1.7	Fisher's exact test	0.497
İmmunosuppressive diseases	0	0.0	2	3.4	Fisher's exact test	1.0
Diabetes mellitus	4	16.7	4	6.7	Fisher's exact test	0.217
Hospitalization indication						
Self-harm/suicidal thoughts	14	58.3	19	31.7	5.1	**0.024**
Agitation/aggression	1	4.2	25	42.4	11.6	**0.001**
Clinical worsening with treatment refusal	3	12.5	29	48.3	9.3	**0.002**
Forensic case	2	8.3	2	3.3	0.9	0.331
COVID-19 treatment						
Hydroxychloroquine	1	4.2	5	8.5	Fisher's exact test	0.667
Heparin	20	83.3	52	88.1	Fisher's exact test	0.772
Favipiravir	18	75.0	39	66.1	Fisher's exact test	0.428
Oxygen	0	0.0	3	5.0	Fisher's exact test	0.554

MDD: Patients with Major Depressive Disorder; BD: Patients with Bipolar Disorder, n: Number of Individuals; SD: Standard deviation; IQR: InterQuartile Range; M: Median

group with MDD compared to the group with BD (MDD= 14 [58.3%], BD= 19 [31.7%], p=0.024), while the rate of agitation/aggression and treatment rejection was found to be significantly higher in the group with BD (agitation: BD=25 [42.4%], MDD=1 [%] 4.2), p=0.001, treatment rejection: BD=29 (48.3%), MDD=3 (12.5%), p=0.002).

In Table 2, the patient groups with MDD and BD were compared in terms of laboratory values (Table 2). While no significant difference was found between D-dimer and fibrinogen between the two groups, LDH and ferritin levels were found to be significantly higher in the group of patients with BD (for LDH; 266±100.1 U/L vs. 213±64 U/L, p=0.016 and for ferritin 1470±1367 ng/mL vs. 759±895 ng/mL, p=0.032). There was no significant difference between the two groups in terms of CALL scores (MDD= 5.9±1.9, BD= 5.7±1.9, p=0.678).

DISCUSSION

In the results of our study, we found that the symptoms of the patients with BD were generally agitation/aggression and treatment rejection, whereas the patients with MDD had more thoughts of self-harm. The results were similar to the reported indications for hospitalization for cases admitted to psychiatric services during the pandemic.[2,3,12,13] However, the point that caught our attention in this result was the prominent symptoms in patients with BD. Because cases with BD

Table 2. Comparison of laboratory values of patients with major depressive disorder and bipolar disorder hospitalized in the COVID-19 special psychiatry service. Data are given as mean±standard deviation (Mean±SD)

	n	MDD	n	BD	t/U	p
LDH[a] U/L	20	213±64	41	266±100.1	t=2.5	0.016
D-dimer mg/L	22	95±173	48	72±102	U=457.0[b]	0.369
Fibrinogen mg/L	20	404±122	41	405±115	t=0.1	0.985
Ferritin[a,c] ng/mL	15	759±895	42	1470±1367	t=2.2	0.032
CALL score	20	5.9±1.9	41	5.7±1.9	t=0.4	0.678

[a]: Welch correction for unequal variances; [b]: Mann–Whitney U-test; [c]: An extreme value above the mean was eliminated in the BB group. MDD: Patients with major depressive disorder; BD: Patients with bipolar disorder, LDH: Lactate dehydrogenase; CALL: Progression score, Ji et al.[7]

showed more frequent symptoms such as aggression/agitation, which would suggest a manic episode, rather than depressive symptoms. In a recent study by Koenders et al.,[14] conducted with 70 patients with BD, it was shown that the mania symptoms of patients with BD increased significantly with the pandemic, but the pandemic had no effect on depressive symptoms and anxiety symptoms. Considering the results of our study, we can say that patients with BD may have more manic episode symptoms during the pandemic period, and it may be important to follow these patients more closely in terms of manic episodes.

Another result of the study was on laboratory parameters predicting the severity of COVID-19. While patients with BD were similar to patients with MDD in terms of D-dimer, fibrinogen, and CALL scores, LDH and ferritin levels were higher. Many studies have shown the relationship of BD with cell damage and inflammatory processes.[15,16] LDH and ferritin, which are inflammation markers recently shown to predict the prognosis of COVID-19, may also be associated with the increased inflammatory response in these patients with BD.[17–19] In a study, it was also shown that serum LDH levels are higher in patients with BD than in patients with MDD.[19] In light of all this information, our study suggests that elevated LDH and ferritin values in patients with BD may be related to the increased response to COVID-19 in patients with BD. It can also be considered that the primary prevention and treatment of this patient group require special attention.

Considering that the drugs used in BD also have an effect on the inflammation processes as well as the BD itself, the use of multiple drugs in our study sample and the inability to divide those receiving monotherapy treatments into subgroups are limitations of our study. If the subgroups receiving monotherapy can be compared in future studies, the effects of drugs on inflammation in cases with COVID-19 and BD can be discussed and more comprehensive recommendations can be made. Other limitations of our study are: Being single-centered, cross-sectional, small sample size, unknown pre-COVID-19 period, and inability to present causality.

CONCLUSION

The results of our study showed the clinical features of the patients treated in the special psychiatry service for COVID-19. It can be said that ferritin and LDH parameters, which were found to be higher in patients with BD compared to patients with MDD, may be associated with the increased inflammatory response of BD to COVID-19; therefore, clinical follow-up and protection of patients with BD during the COVID-19 period is important.

Disclosures

Ethics Committee Approval: The study was approved by the University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee (No: 2021.07.217, Date: 08/07/2021).

Informed Consent: Patient consent was not deemed necessary because of the retrospective study design.

Peer-review: Externally peer reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

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