

Characteristics and Outcomes of Psychiatric Inpatients With Severe Mental Illness and COVID-19

Experience From a COVID-19-Specific Acute Psychiatric Ward in Istanbul

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Abstract: Recent studies indicated that psychiatric inpatients with severe mental illness (SMI) are at a greater risk of morbidity and mortality from COVID-19. However, there is still little data about the impact of comorbid COVID-19 infection on the course and outcome of acute exacerbations in this population. We conducted a prospective historically matched case control study. The sociodemographic and clinical characteristics of acute psychiatric inpatients with SMI and comorbid COVID-19 ($n = 21$) were compared with those of historically-matched non-COVID-19 controls with SMI ($n = 42$). The outcomes for acute inpatients with SMI and COVID-19 were also investigated. The new-onset SMI rate was relatively higher (23.8%) in the COVID-19 group, which has characteristics similar to those of the non-COVID-19 group except for working status ($p < 0.05$). The COVID-19 group had a high rate of relapse (47.6%) within 6 months of discharge. Our study suggests that patients with SMI who contracted SARS-CoV-2 may have a higher rate of new-onset mental disorder. Considering the high rate of relapse during the pandemic, chronically ill patients with SMI and COVID-19 should be closely monitored after discharge.

Key Words: Severe mental illness, COVID-19, outcome, schizophrenia, affective disorder

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The COVID-19 pandemic had a tremendous impact on the health, social, and financial life of people worldwide. As of May 10 2021, there were more than 158 million confirmed cases, including 3.29 million deaths around the world. Of these, 5.03 million cases were from Turkey and the total number of deaths in Turkey was 43,029 (WHO, 2020b). Governments had to impose nationwide preventive measures and restrictions, of which proper adoption was critical in reducing the spread (Ministry of Health, 2020a; WHO, 2020a).

The first COVID-19 case in Turkey was reported on March 11 in Istanbul, the highest and most densely populated city in Turkey (TurkStat, 2020), which has also been the hardest hit in terms of COVID-19 cases. On March 21, 2020, almost all tertiary and secondary general hospitals were obligated to serve for pandemic, which resulted in an extensive reorganization of inpatient and outpatient services in line with the new implications. This decision necessitated many psychiatric units and staff in general hospitals to serve for COVID-19, as was

happening worldwide. Hence, the burden of managing of acute psychiatric inpatients with COVID-19 had to be handled by the remaining psychiatric units, which were mostly in mental health hospitals.

Patients with severe mental illness (SMI) usually experience agitation, poor insight, lack of impulse and behavioral control, as well as impaired cognitive functions and negative health-related behaviors. Supporting patients with SMI and customizing services during the pandemic are recommended for whole community preparation facing COVID-19 as this population is more vulnerable to emotional distress, which may cause worsening or relapses of preexisting mental disorders, leading to hospitalization (Marazziti et al., 2020; Mukhtar et al., 2020; Yao et al., 2020). This population usually shows negligence of risks, lack of adequate knowledge about COVID-19, and difficulties in complying to preventive measures, which result in an increased risk for transmission and poor infection outcomes and lower treatment compliance with both psychiatric illness and COVID-19 (Kozloff et al., 2020; Muruganandam et al., 2020; Shinn et al., 2020). Thus, they might cause safety problems for other patients and staff in terms of transmission as well as agitation and aggressiveness in a standard infectious diseases unit. Furthermore, in a standard psychiatric ward, the staff has often limited experience in managing infectious diseases and their complications. Therefore, establishing a COVID-19-specific acute psychiatric ward (CSAPW) became crucial, especially for mental health epicenters with large closed inpatient wards (IWs), to reduce the spread of the infection to other psychiatric inpatients and staff as SARS-CoV-2 could easily pervade through a standard acute psychiatric inpatient unit. However, establishing a CSAPW was challenging in many levels, as it does not exactly have the qualities of a psychiatric ward or of an infectious diseases ward.

To date, there are still a limited number of studies regarding the impact of SMI on the course of COVID-19; however, there are still no studies on the sociodemographic and clinical characteristics of psychiatric inpatients with both SMI and COVID-19 admitted to CSAPWs and the impact of COVID-19 on the outcomes of this population. To address this gap, in this study, we aimed to (i) compare the sociodemographic and clinical characteristics of inpatients with SMI and COVID-19 with those of historically matched controls with SMI and without COVID-19 admitted in the past year; (ii) investigate the outcomes of inpatients with SMI and COVID-19 on the 30th day and the third and sixth months after discharge; and (iii) share the experience of frontline workers in a CSAPW and discuss the challenges for mental health hospitals serving patients with COVID-19, to improve the inpatient treatment services for these patients.

METHODS

Preparations and Protocols of the CSAPW: “Psychoid Ward”

Erenköy Mental Health and Nervous Diseases Training and Research Hospital (ERSHEAH), where this study was conducted, is a

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All participants gave informed consent. The study has been carried out in accordance with 1964 Declaration of Helsinki and its later amendments and was approved by the ethics committee of Erenköy Mental Health and Nervous Diseases Training and Research Hospital and COVID-19 Scientific Review Board of the Turkish Ministry of Health.

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tertiary mental health hospital with approximately 300 inpatient beds in the Asian side of Istanbul and serving a population of 5.3 million. ERSHEAH has continued to serve as a mental health epicenter during the pandemic, with increased implementation of telepsychiatry, and provided outpatient, inpatient, and community mental health services with preventive measures such as 50% reduced outpatient and inpatient unit capacity and restricted hospitalization criteria (suicidality, self-harm, and aggression behavior). Because of the reduced inpatient unit capacity, only inpatients who required compulsory admission according to the Turkish Civil Code could be hospitalized. Patients were admitted to the wards according to their SARS-CoV-2 infection status as confirmed, suspected, or clean. The hospital had to be reorganized with preventive measures. A CSAPW, physically separate from other IWs, was also established and received patients as of April 9, 2020, the first in Turkey. In the period when the study was conducted, a sister ward in a tertiary general hospital was established shortly after in the European side of Istanbul.

A CSAPW and its protocols have many peculiarities and require special concerns regarding both psychiatric and infectious disease perspectives and shape as a compromise of both disciplines. The protocols of the CSAPW were prepared in accordance with the national and international guidelines by authorities and experts who were available at the early stage of the pandemic, including the official guideline for health institutions and psychiatric services by the Turkish Ministry of Health (Ministry of Health, 2020b, 2020c), as well as the experience shared by other colleagues from different countries including China, South Korea, Israel, Italy, and United States (Augenstein et al., 2020; Benson et al., 2020; D'Agostino et al., 2020; Fagiolini et al., 2020; Korean Society of Infectious Diseases et al., 2020; Li et al., 2020; Ministry of Health, 2020b; Shinn et al., 2020; Vlessides, 2020; Yao et al., 2020; Zhu et al., 2020). The CSAPW had high standards in terms of safety concerns and preventive measures, such as single room with a separate bathroom (two to four in standard wards of the hospital), 24-hour video surveillance, windows with shatterproof glasses, a separate garden for recreation, and medical equipment for personal use such as sphygmomanometer, and a portable pulse oximetry in each room to avoid the spread of the SARS-CoV-2.

Staff of the CSAPW consisted of a chief physician experienced in consultation-liaison psychiatry, attending psychiatrists, psychiatric trainees and nurses, patient caretakers, and security guards, a total of 30 professionals. Physicians were appointed on a voluntary basis; nurses and care staff also consisted of volunteers who were working at the ward before the pandemic. A crash course on consultation-liaison psychiatry, in terms of monitoring and management of COVID-19 symptoms, was provided to the staff by the chief physician. Ward protocols were updated at weekly meetings of the staff whenever necessary. The protocols for using personal protective equipment (PPE), social distancing and infection control, bedside rounds, and other issues are provided in Table 1.

Study Design and Sample

We conducted a prospective, historically matched case control study. A total of 23 patients consecutively admitted to the CSAPW of ERSHEAH within the period between April 9 and July 1, 2020, were included in the study. However, 2 patients were excluded as COVID-19 prediagnosis could not be confirmed; thus, 21 patients were included in the study. A COVID-19 diagnosis was made by an infectious diseases specialist, according to the official guidelines of the Turkish Ministry of Health, based on the evaluation of clinical condition and laboratory test, computed tomography, and PCR findings. All patients had SMI and were hospitalized involuntarily owing to acute psychiatric symptoms. Eighteen patients were received from the psychiatric emergency department of ERSHEAH and other hospitals and three patients were referred from the other IWs of ERSHEAH. Because of the limited medical facilities

TABLE 1. Protocols of CSAPW

- Safety should be the priority for all staff and patients. Visits and treatment hours should be planned to enter the patient room a minimal number times and to stay the shortest time as possible (<15 minutes per room for each staff). Special attention should be paid to avoid unnecessary contact with the employees from the other sites of the hospital.
- To meet social distance requirements, daily rounds should be conducted with the minimum number of participants necessary. Meeting outdoors is recommended when available.
- All team members are required to wear scrubs or medical uniforms in the ward, as well as use full PPE. A separate space should be identified for donning/doffing.
- Bedside rounds should be conducted with the participation of minimum number of participants.
- Before admission, special informed consent for hospitalization at the COVID-19 acute psychiatric unit should be taken from the patients and/or legal representatives. All visitations should be suspended to reduce the risk of transmission from the visitors.
- A diagram indicating service protocols and personal hygiene rules should be put on a visible spot in each patient room, together with personal hygiene education for all patients and relatives upon admittance and discharge.
- The PPE should be put on and off at a separate room in the ward; reusable PPE (glasses, face shields, etc.) should be sterilized in a private room.
- A distance of 2 m should be maintained while in contact with patients. In case this cannot be achieved, full PPE should be put on, including FFP2 masks.
- The CSAPW should be disinfected twice a day using a medical disinfectant.
- Smoking is banned for patients and staff.
- Use of coffee or tea machines in the common areas is banned for all staff.
- Daily online rounds should be conducted with the chief psychiatrist for the evaluation of the patients and treatment planning of psychiatric and COVID-19-related conditions.
- Patients should be examined by an internist on the first day of hospitalization and laboratory findings should be followed daily by the internist
- Theoretical training and supervision of psychiatric trainees, especially focused on consultation and liaison psychiatry, should be maintained by means of weekly online meetings with the chief psychiatrist.
- Charts of drug interactions should be prepared for all doctor rooms.
- Daily ECG monitoring and calculations of QTc intervals should be made to assess potential adverse effects due to drug interactions.
- Vital findings of the patients should be followed at least twice daily (more frequent follow-up for patients older than 50 and with chronic diseases).
- Patients with severe symptoms of COVID-19 such as blood O₂ level below 90% and who were having progressive symptoms and CT and laboratory findings despite treatment should be referred to a general hospital acute psychiatric service. Patients should be admitted to a mental health hospital unit only if considered as medically stable.
- Infectious diseases and internal medicine consultations should be made in case of complications regarding COVID-19
- Patients must be screened twice daily for symptoms of COVID-19 (cough, fever, shortness of breath, nausea, etc.)
- Two consecutive (24 hours apart) negative PCR tests should be obtained before the discharge or referral to another closed ward.
- A pre-intensive care unit, with ECG monitors and defibrillators, is prepared in a separate room, for close monitoring or resuscitation in case of emergency action.

CT indicates computed tomography; ECG, electrocardiogram; PCR, polymerase chain reaction.

of a mental health hospital, patients admitted to CSAPW were asymptomatic or had mild COVID-19 symptoms. Those with moderate and severe and/or more than two symptoms or who may need intensive care unit were referred to a general hospital. Written informed consent was obtained from patients and/or their legal representatives. This study was approved by the local institutional review board and the COVID-19 Scientific Review Board of the Turkish Ministry of Health. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The data of the sample regarding adverse drug reactions due to concurrent COVID-19 and acute psychiatric treatment admitted to CSAPW have been previously published (Sönmez Güngör et al., 2020).

The historically matched control group was designed with a detailed review of the electronic records of 2988 patients consecutively hospitalized in ERSHEAH in 2019. Of 2988 patients, a sample of 1957 subjects diagnosed with SMI in 2019 was screened. From these patients, each patient with SMI diagnosed with COVID-19 was matched (blind to any personal identifiers and outcome measures to reduce selection bias) to the controls regarding (i) diagnosis (schizophrenia, schizoaffective disorder, bipolar disorder, brief psychotic disorder, and atypical psychosis); (ii) sex (male/female); (iii) age categories of 5-year increments (e.g., 30–34, 35–39); (iv) marital status (single, married, divorced/widowed); (v) duration of illness (e.g., new onset, 1–4 years, and 5–9 years); and (vi) duration of education. This resulted in 42 controls who were matched on the above criteria. Finally, a total of 63 patients were enrolled in the study. The data of the control group were collected from the patients' electronic records between September 15 and October 1, 2020. To monitor the outcomes of the COVID-19 group, we made telepsychiatric assessments on the 30th day and the third and sixth months after discharge. The study was approved by the institutional review board of ERSHEAH and the COVID-19 Scientific Review Board of Turkish Ministry of Health.

Measures

Sociodemographic and clinical data were collected via electronic records of the patients. The severity of the mental illness of the patients was assessed for psychotic spectrum disorders and bipolar disorder via the Positive and Negative Syndrome Scale (PANSS) and Young Mania Rating Scale (YMRS). The validity and reliability of the Turkish version of the original forms of these scales were reported by Kostakoğlu et al. (1999) and Karadag et al. (2002), respectively. PANSS is rated on a 1 to 7 scale and the minimum score is 30 (for a patient with no symptoms). Thus, we subtracted 30 points to calculate the PANSS score percentage reduction before the analysis to prevent underestimation of the response rates (Leucht et al., 2010).

Statistical Analysis

We used www.e-picos.com (New York) software and the MedCalc statistical package program to analyze the data. For descriptive data, mean and standard deviation, frequency and percentage, and minimum and maximum values were used. Chi-squared and Fisher exact tests were used to compare categorical variables. Student *t* test was used to compare the mean of continuous variables of independent groups. A *p* value <0.05 was considered to be significant.

RESULTS

Sociodemographic and Clinical Characteristics of the Patients Admitted to CSAPW

Of the 21 patients, 18 (85.7%) were male. The mean age was 38 ± 11.7 years, and five patients had comorbid medical conditions.

Regarding COVID-19 symptoms, 10 patients were asymptomatic, whereas the others had cough (28.5%), fever (14.3%), headache (14.3%), fatigue (9.5%), and diarrhea (4.8%). The COVID-19 treatment regimen included hydroxychloroquine (95.8%), azithromycin (33.3%), ceftriaxone (28.6%), and oseltamivir (4.8%). In our ward, no patient received favipiravir, during the study period because it could be administered only to patients with a blood O₂ saturation below 90% according to the guidelines of Turkish Ministry of Health.

Seventeen patients were diagnosed with psychotic spectrum disorders and four with bipolar disorder, and five of them (23.8%) were first-episode patients (two patients with brief psychotic disorder, two patients with atypical psychosis, and one patient with bipolar disorder). The most common psychiatric symptoms were lack of insight, verbal/physical aggression, disturbed sleep and paranoid delusions, and affective symptoms. A female patient had delirium during the first days of hospitalization. A detailed presentation of the symptoms of the patients is provided in Table 2. All patients received antipsychotic drugs (100%); 16 (76.2%) and 9 (43%) of them received hypnotic sedatives and mood stabilizers, respectively. The mean chlorpromazine drug equivalent dose was 576.1 ± 209.5 mg/day. Long-acting antipsychotic medication was administered to 14 patients (66%) with psychotic spectrum disorders. New-onset mental severe mental disorders were found in five (23.8%) patients; two of them had brief psychotic disorder, two had atypical psychosis, and one was diagnosed with bipolar disorder.

We found no significant differences in the comparison of the COVID-19 and non-COVID-19 historically matched control groups in terms of sociodemographic and clinical characteristics, except for working status (*p* < 0.05). Table 3 summarizes the data of the comparison of the COVID-19 and historically matched control groups.

Measures and Outcomes

Of the 21 patients, all recovered from COVID-19; 19 of them had good outcomes for psychiatric conditions, and 2 patients who still

TABLE 2. Symptoms of Patients Admitted in the CSAPW (*N* = 21)

Symptom Category	<i>n</i>	%
Affective symptoms	15	71.4
Manic/dysphoric mood	11	52.3
Depressive mood	4	19.1
Refusal to eat/drink	6	28.5
Cognitive impairment	8	38.1
Delusions		
Paranoid type	17	80.9
Grandiose type	6	28.5
Disorganized speech or behavior	11	52.4
Dissociative symptoms	2	9.5
Hallucinations		
Visual	6	28.5
Auditory	11	52.4
Other	2	9.5
Impaired orientation	5	23.8
Lack of insight	21	100.0
Negative symptoms (poor self-care, social withdrawal, etc.)	11	52.3
Psychomotor agitation	13	61.9
Disturbed sleep	17	80.9
Somatic anxiety	3	14.2
Suicidal ideation/attempt	1	4.7
Treatment noncompliance	15	71.4
Verbal/physical aggression	17	80.9

TABLE 3. Sociodemographic and Clinical Characteristics of COVID-19 and Non-COVID-19 Groups (*n* = 63)

	Total	COVID-19 Group (<i>n</i> = 21)	Non-COVID-19 Group (<i>n</i> = 42)	<i>p</i>
	<i>N</i> (%)	<i>n</i> (%)	<i>n</i> (%)	
Gender				
Female	9 (14.3)	3 (14.3)	6 (14.3)	0.99 ^a
Male	54 (85.7)	18 (85.7)	36 (85.7)	
Age, mean ± SD	37.5 ± 11.7	38 ± 11.7	37 ± 11.1	0.81 ^b
Marital status				
Single	42 (66.7)	15 (71.4)	27 (64.3)	0.76 ^c
Married	9 (14.3)	3 (14.3)	6 (14.3)	
Divorced	10 (15.9)	3 (14.3)	7 (16.7)	
Widowed	2 (3.2)	–	2 (4.8)	
Habitation				
Alone	12 (19.0)	5 (23.8)	7 (16.7)	0.27 ^c
Family	50 (79.4)	15 (71.4)	35 (83.3)	
Homeless/nursing home	1 (1.6)	1 (4.8)	–	
Working status				
Working	18 (28.6)	10 (47.6)	7 (16.66)	0.03^c
Not working	40 (63.5)	10 (47.6)	31 (73.8)	
Retired	5 (7.9)	1 (4.8)	4 (9.5)	
Diagnosis				
Schizophrenia	21 (33.3)	7 (33.3)	14 (33.3)	0.99 ^c
Schizoaffective disorder	13 (20.6)	4 (19)	9 (21.4)	
Bipolar disorder	12 (19.0)	4 (19)	8 (19.0)	
Atypical psychosis	12 (19.0)	4 (19)	8 (19.0)	
Brief psychotic disorder	5 (7.9)	2 (9.5)	3 (7.1)	
Length of hospitalization, mean ± SD, days	63 (100)	28.5 ± 17.6	26.9 ± 12.6	0.68 ^b
First episode				
Yes	13 (20.6)	5 (23.8)	8 (19.0)	0.74 ^a
No	50 (79.4)	16 (76.2)	34 (81.0)	
Previous hospitalization				
No	18 (28.6)	6 (28.6)	12 (28.6)	1.0 ^c
Yes	45 (71.4)	15 (71.4)	30 (71.4)	
Remission				
No	22 (41.5)	8 (50)	14 (37.8)	0.41 ^c
Yes	31 (58.5)	8 (50)	23 (62.2)	
Regular outpatient follow-up before admission				
No	37 (69.8)	9 (56.3)	28 (75.7)	0.19 ^a
Yes	16 (30.2)	7 (43.8)	9 (24.3)	
Community mental health center follow-up before admission				
No	46 (86.8)	13 (81.3)	33 (89.2)	0.41 ^a
Yes	7 (13.2)	3 (18.8)	4 (10.8)	
Alcohol use				
No	56 (90.3)	19 (90.5)	37 (90.2)	1.0 ^a
Yes	6 (9.7)	2 (9.5)	4 (9.8)	
Substance use				
No	46 (74.2)	14 (66.7)	32 (77.0)	0.33 ^c
Yes	16 (25.8)	7 (33.3)	9 (22.0)	

TABLE 3. (Continued)

Comorbid physical illness				
No	52 (82.5)	16 (76.2)	36 (85.7)	0.48 ^a
Yes	11 (17.5)	5 (23.8)	6 (14.3)	
Family history of psychiatric disorders				
No	43 (68.3)	15 (71.4)	28 (66.7)	0.70 ^c
Yes	20 (31.7)	6 (28.6)	14 (33.3)	

Bold indicates statistical significance at the 0.05 level.

^aFisher exact test.

^bStudent *t* test.

^cChi-square test.

needed inpatient psychiatric treatment after the recovery from COVID-19 treatment were transferred to standard wards of the hospital.

Among the COVID-19 patients with psychotic spectrum disorders (*n* = 17), two (12%) had an improvement of less than 25%, six (35%) had an improvement in the range of 25% to 49%, and nine (53%) had an improvement of greater than 50% in PANSS scores. Among the COVID-19 patients with bipolar disorders (*n* = 4), all had a greater than 50% improvement in YMRS scores.

Mean PANSS scores in patients with psychotic spectrum disorders at the hospital admission were 74.29 ± 23.31 for the COVID-19 group (*n* = 17) and 84.61 ± 24.91 for the non-COVID-19 group (*n* = 34). At discharge from hospital, PANSS scores improved to 35.29 ± 24.5 in the COVID-19 group and 39.20 ± 14.5 in the non-COVID-19 group. No statistically significant difference was found between groups in terms of PANSS scores at admission and discharge (*p* = 0.16 and *p* = 0.55, respectively). Mean YMRS scores in the hospital admission were 36.75 ± 9.74 and 38.0 ± 10.62 for the COVID-19 (*n* = 4) and non-COVID-19 (*n* = 8) groups, respectively. At discharge, improvement in YMRS scores was achieved as 13.5 ± 12.3 and 10.75 ± 6.88 in the COVID-19 and control groups, respectively. Although the COVID-19 group had higher YMRS scores at discharge, the difference was not significant for admission or discharge (*p* = 0.84 and *p* = 0.65, respectively). Table 4 summarizes the comparison of PANSS and YMRS scores of the COVID-19 and non-COVID-19 groups.

TABLE 4. PANSS and YMRS Scores of COVID-19 and Non-COVID-19 Groups (*n* = 63)

	Scores		
	Mean ± SD	%95 Lower-Upper Confidence Interval	<i>p</i>
PANSS score at admission			
COVID-19 (<i>n</i> = 17)	74.29 ± 23.31	62.31–86.28	0.16
Non-COVID-19 (<i>n</i> = 34)	84.61 ± 24.91	76.24–92.98	
PANSS score at discharge			
COVID-19 (<i>n</i> = 17)	35.29 ± 24.5	22.69–47.89	0.55
Non-COVID-19 (<i>n</i> = 34)	39.20 ± 14.5	34.33–44.07	
YMS score at admission			
COVID-19 (<i>n</i> = 4)	36.75 ± 9.74	21.24–52.25	0.84
Non-COVID-19 (<i>n</i> = 8)	38.0 ± 10.62	30.64–45.36	
YMRS score at discharge			
COVID-19 (<i>n</i> = 4)	13.5 ± 14.3	1.44–25.55	0.65
Non-COVID-19 (<i>n</i> = 8)	10.75 ± 6.88	5.98–15.52	

Student *t* test was used for all comparisons.

Regarding inflammatory markers, the C-reactive protein (CRP) levels of the COVID-19 group was found to be higher than that of the control group, as expected (2.48 ± 3.44 vs. 0.85 ± 1.19 ; $p < 0.05$). Mean ferritin, white blood cell (WBC), and lymphocyte percentage levels did not differ between groups ($p = 0.38$, $p = 0.96$, $p = 0.31$, respectively). The findings related to inflammatory markers are summarized in Table 5.

In the telepsychiatric assessment on the 30th day after discharge, we observed that the psychiatric conditions of the patients have not changed and two patients who were transferred to standard wards were still hospitalized while the others were stable. Upon the assessment on the third month of discharge, we were able to contact 20 patients and/or their relatives; of 20 patients, 2 who were still hospitalized at the first telepsychiatric assessment were discharged but still nonremitted, and 6 other (5 male and 1 female) patients (in a total of 38.1%) were found to have relapsed and 4 (19%) of them were rehospitalized. The diagnoses of the patients who had relapse were schizophrenia in five patients, bipolar disorder in one patient, schizoaffective disorder in one patient, and atypical psychosis in one patient. On the sixth-month assessment after discharge, we were able to contact all of the patients, and 10 (47.6%) of them were found to have relapsed within 6 months (3 schizophrenia patients who had relapsed on the third-month assessment were still nonremitted). The diagnoses of the patients who had a relapse in the sixth-month assessment were schizophrenia in five patients, schizoaffective disorder in two patients, atypical psychosis in two patients, and bipolar disorder in one patient. A total of seven (33.3%) patients were rehospitalized within 6 months after discharge, and one (4.7%) of these patients was hospitalized twice. Seven (33.3%) patients were attending routine psychiatric follow-up in community mental health centers and none of these patients had relapsed within 6 months after discharge. Four patients were attending routine psychiatric follow-up in the hospital's outpatient unit and only one patient had relapsed and was hospitalized. Ten patients did not attend routine psychiatric follow-up and nine of them had relapsed.

DISCUSSION

Summary of the Main Findings

This study was performed in a CSAPW during the lockdowns in Istanbul, Turkey. To the best of our knowledge, this preliminary study is the first to provide data on the sociodemographic and clinical characteristics

and outcomes of acute psychiatric inpatients with SMI diagnosed with COVID-19. The main findings of our study were as follows: (i) acute psychiatric inpatients with SMI and COVID-19 were mostly middle-aged men with psychotic spectrum disorders who were working during the pandemic. New-onset SMI rate was relatively higher. The most common psychiatric symptoms were lack of insight, paranoid delusions, verbal or physical aggression, sleep disturbances, and affective symptoms, and the most common symptom of COVID-19 was cough. (ii) Most of the COVID-19 group had good outcomes in both COVID-19 and psychiatric illness during the hospitalization. The COVID-19 group had similar sociodemographic and clinical characteristics compared with control group except for working status. (iii) The inpatients diagnosed with COVID-19 had high rates of relapse on the assessment on the third and sixth months after discharge. (iv) And the establishment of a solid organization and a collaboration among the staff in CSAPW may lead to good outcomes, for both psychiatric and COVID-19 treatment of psychiatric inpatients with SMI and COVID-19 in mental health hospitals, which are at a disadvantage in terms of liaison services, and to lower transmission rates for the staff of the ward.

Sociodemographic and Clinical Characteristics of Patients Admitted to CSAPW

Most patients admitted to the CSAPW were male and diagnosed with psychotic spectrum disorders. The most common diagnosis was schizophrenia (33%), and schizoaffective disorders, bipolar disorders, and atypical psychosis had similar rates (19%), and 2 (10%) patients were diagnosed with brief psychotic disorder. Despite the predominance of psychotic spectrum disorders, affective symptoms were also prominent in approximately 70% of the patients. In a study from Wuhan with a similar sample size consisting of patients with first-onset mental disorders, the authors reported that adjustment disorder and acute and transient psychotic disorder were found as the two main clinical diagnoses (Xie et al., 2020). The difference regarding the diagnosis rates was probably because of the fact that patients with SMI were underrepresented in the sample of this study.

Brief psychotic disorder is relatively rare in clinical settings even among the first-admission psychosis. The higher rate of brief psychotic disorder diagnosis (9.5%) in our sample, as a stress-related psychotic disorder, is consistent with previous data that emphasize increased rates of brief psychotic disorder during the pandemic as recently reported in other countries (D'Agostino et al., 2021; Schwartz et al., 2000). The

TABLE 5. Inflammatory Markers of the COVID-19 and Non-COVID-19 Groups

N = 42	Outcome of Laboratory Assessment		
	Mean ± SD	%95 Lower-Upper Confidence Interval	p
CRP level, mg/L			
COVID-19 (n = 21)	2.48 ± 3.44	0.37–3.51	0.04
Non-COVID-19 (n = 42)	0.85 ± 1.19	0.49–1.21	
Ferritin level, mg/L			
COVID-19 (n = 21)	132.5 ± 136.23	70.48–194.51	0.38
Non-COVID-19 (n = 42)	107.74 ± 84.80	82.09–133.4	
WBC count			
COVID-19 (n = 21)	9757.76 ± 3714.94	8,066.74–11,448	0.96
Non-COVID-19 (n = 42)	9718.09 ± 2672.31	8,909.9–10,526.3	
Lymphocyte, %			
COVID-19 (n = 21)	36.77 ± 38.81	19.09–54.43	0.31
Non-COVID-19 (n = 42)	23.33 ± 7.30	21.12–25.54	

Student *t* test is used for all comparisons.

CRP indicates C-reactive protein; WBC, white blood cell.

relatively high rate of SMI (23.8%) was another remarkable finding, which was probably associated with the literature indicating an increased risk of psychosis during the pandemic (Brown et al., 2020). However, the difference of this rate with non-COVID-19 group was not statistically significant, and this was probably due to the small sample size of our study. Considering our results and recent reports from other countries, we suggest that COVID-19 could be a potential risk factor for new-onset SMI.

Comparison of the COVID-19 Group With the Non-COVID-19 Historically Matched Control Group

The comparison of the COVID-19 and control groups revealed that the acute psychiatric inpatients with COVID-19 did not significantly differ from the control group regarding sociodemographic and clinical characteristics and length of hospitalization, except for working status. The negative impact of SMI on the course of COVID-19 was previously reported (De Hert et al., 2021; Nemani et al., 2021). However, to the best of our knowledge, there are still no clinical or case studies regarding the impact of COVID-19 on the course of SMI and also clinical characteristics, length of hospitalization and outcomes of patients with SMI diagnosed with COVID-19. Our results indicated that patients admitted to the CSAPW had higher rates of employment than the historically matched control group. Individuals with SMI were previously found to be under greater risk of COVID-19 infection than other mental disorders and the general population (Wang et al., 2021). Patients with SMI are vulnerable to many environmental risk factors for COVID-19 infection, such as socioeconomic deprivation and working in unsafe environments. Thus, working seems to be a conflictual condition as both an important need and a risk for transmission in this population during the pandemic period. This finding suggests that policy makers should provide additional public support (*i.e.*, social, vocational and economic) for patients with SMI and confirms previous reports suggesting that patients with SMI should be prioritized for COVID-19 vaccination (De Hert et al., 2021; De Picker et al., 2021).

Despite the increased levels of ferritin, WBC count, and lymphocyte percentage, no significant difference was observed in terms of inflammatory markers except, CRP. This was probably related to our small sample size. In a study focusing on the relationship between clinical correlates of COVID-19 and mental health, levels of inflammatory markers such as interleukin-1 β and neutrophil-to-lymphocyte ratio were found to be correlated with COVID-19 patients' mental symptoms (Hu et al., 2020). However, the rate of delirium due to COVID-19 as another condition related to the severity of the infection was 4.7% in our sample, similar to the rates reported in the literature (Kotfis et al., 2020; Xie et al., 2020).

When it comes to the impact of COVID-19 on the severity of mental illness, researchers from the United States reported that individuals with SMI were not reporting a worsening of symptoms or affective experiences (Pinkham et al., 2020). In our study, COVID-19 and historically matched control groups were similar in terms of clinical characteristics in acute psychotic episode and had similar lengths of hospitalization. Hence, we suggest that contracting COVID-19 does not increase the severity of the psychotic or affective symptoms of acute psychiatric inpatients with SMI. However, the small sample size with mild COVID-19 symptoms and relatively large margin of standard deviation in means of scale scores might have contributed to the statistical similarities between COVID-19 and historically matched control groups and have limited the generalizability of our findings.

Outcomes in the COVID-19 Group

In previous studies, patients with SMI were reported to be more prone to have impaired immunity, poor nutrition and self-care, and associated metabolic disorders. Anxiety, fear of infection, and negative symptoms could cause a reduced physical activity and lead to

dysfunctional immunity, which may result in a higher risk of morbidity and mortality in the course of COVID-19, and this negative impact on prognosis could be bidirectional (Khandaker et al., 2015; Kozloff et al., 2020; Lazzari et al., 2020; Muller et al., 2015; Nemani et al., 2021; Shinn et al., 2020). Regarding comorbid medical condition as an important factor related with COVID-19 prognosis, five (23.8%) patients were having comorbid physical conditions such as hypertension, chronic obstructive pulmonary disease, epilepsy, hyperparathyroidism, and chronic hepatitis C infection. Nevertheless, in our sample, none of the patients had a complication due to the course of COVID-19 and all recovered from COVID-19. When treating COVID-19 patients in a CSAPW, severe and critical cases must be detected at an early stage. Early-warning indicators should be monitored closely to prevent severe complications and negative outcomes (Adorjan et al., 2021). The relatively younger age and asymptomatic or mild disease course and lower rates of comorbid medical conditions of our sample are the possible explanations of the better outcomes. On the other hand, weekly updated protocols regarding the needs of the patients and the staff, the collaborative teamwork among the staff, and the close monitoring in our unit have probably contributed to good outcomes regarding COVID-19.

In our sample, 19 patients (90.5%) had good outcome for psychiatric conditions as they have had at least a 25% or greater improvement, and regarding their symptoms, and only two (9.5%) were transferred to standard IWs as they still need psychiatric treatment after the recovery from COVID-19. However, we observed high rates of relapse as 38.1% and 47.6% via telepsychiatric assessment on the third- and sixth-month assessments after discharge, respectively, which were greater than relapse rates with schizophrenia and bipolar disorders that were previously reported (Perlis et al., 2006; Weiden et al., 1995). These findings suggest that acute psychiatric inpatients with SMI diagnosed with COVID-19 may have a higher risk of relapse during the pandemic period. This could be explained as follows; patients with both COVID-19 and mental illness were reported to be at higher risk of being stigmatized. Therefore, psychiatric patients with SMI diagnosed with COVID-19 might suffer from an even higher stigma and may have disadvantage in health care, and also social isolation, and worse health outcomes (Anmella et al., 2020). Discontinuing drug therapy has been reported as one of the main predictors of relapse in both schizophrenia and bipolar disorder (Goodwin et al., 2016; Lieberman et al., 1993). Although we administered long-acting injectable second-generation antipsychotic medication to 14 patients (66%) diagnosed with a psychotic spectrum disorder, 9 of these patients had relapsed. On the other hand, among 11 patients who attended routine psychiatric follow-up in community mental health centers or hospital, only one patient had relapsed. Almost all the patients who had relapse and/or their relatives reported that they could not be able to arrange an appointment for routine visits and prescriptions because of the decreased number of appointments in the hospitals and community mental health centers during the pandemic. Unfortunately, psychiatric units were among the first transformed to serve to COVID-19 emergency in Turkey as in, worldwide, and remaining units worked with limited capacity. This caused important difficulties in the utilization of psychiatric services for patients with SMI as well as the general population. Being chronically ill with a history of cycles of relapse was probably another reason for the high rate of relapse as 9 of the 10 patients who had relapse within 6 months after discharge were not first-episode patients and were chronically ill.

These alarming results indicate that a limitation of psychiatric services due to pandemic-related arrangements of governments may cause a significant disadvantage for patients with SMI diagnosed with COVID-19 to reach psychiatric services, and these patients should be closely monitored after discharge as they may have a high rate of relapse owing to the probable impact of the pandemic.

Limitations

The small sample size is the main limitation of our study; however, we consider that the historically matched design of our study is an important factor that may strengthen the validity of our results. Another important limitation is that our data were collected from a sample consisting of asymptomatic patients or those with mild COVID-19 symptoms, which underrepresents the characteristics of acute psychiatric inpatients with severe COVID-19 symptoms. Our data were collected in a relatively earlier period of the pandemic, which can be a limitation when assessing the impact of later periods of COVID-19 on the clinical characteristics and outcome of psychiatric inpatients with SMI. We were not able to reach the relapse rates of the historically matched controls on the third and sixth months after discharge to compare with the COVID-19 group.

CONCLUSIONS

Our results suggest that working could be a potential risk factor for transmission in patients with SMI and those continuing to work during the pandemic should be prioritized in vaccination. The rate of the new-onset SMI among inpatients with COVID-19 were relatively higher compared with the previous prepandemic studies on SMI. Hence, COVID-19 could be a potential risk factor for new-onset SMI. Our results also indicate that chronically ill inpatients with SMI diagnosed with COVID-19 should be closely monitored after discharge as they are found to have a high rate of relapse. To avoid undertreatment of patients with SMI and COVID-19, we believe that the role of consultation-liaison psychiatry is crucial during the pandemic. Finally, this preliminary study suggests that additional longitudinal investigations are needed with larger samples on patients with SMI with COVID-19.

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DISCLOSURE

The authors declare no conflict of interest.

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