ORIGINAL ARTICLE



Effects of the COVID-19 Pandemic on Patients with Schizophrenia Spectrum Disorders

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Objective: To evaluate the mental health of patients with schizophrenia spectrum disorders with the prolongation of the pandemic.

Materials and Methods: This descriptive cross-sectional study was conducted between August-October 2020. Fifty-two patients with schizophrenia spectrum disorders who were hospitalized prior to the onset of the pandemic between March 2019-March 2020 at the inpatient clinic were reassessed during the pandemic. The Positive and Negative Syndrome Scale (PANSS), the Clinical Global Impression-Severity (CGI-S) Scale, Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A) and Fear of COVID-19 Scale were used to evaluate psychopathology during the pandemic. The PANSS and the CGI severity scores at discharge from the inpatient clinic for each patient were obtained from the medical records review for comparison along with sociodemographic variables.

Results: A total of 34 patients, 33 with schizophrenia (97.1%) and 1 with schizoaffective disorder (2.9%) were included. There was no significant difference between the pre- and during the pandemic assessments in the PANSS total and the CGI severity scores. The PANSS total, the CGI, HAM-D, HAM-A and the Fear of COVID-19 scale scores, medical comorbidity and utilization of psychiatric health care services were significantly higher in patients who reported subjectively increased psychiatric symptoms during the pandemic. There was no significant difference in the change of PANSS total and CGI scores between the two groups. Fear of COVID-19 Scale and HAM-A scores were correlated positively.

Conclusion: During pandemic increase in psychiatric symptoms may be related not only to psychosis but also depression, anxiety. According to the results of patients who reported subjectively increased psychiatric symptoms during the pandemic, while the psychotic symptoms did not worsen during the pandemic, patients with higher anxiety or depression scores reported an increase in their symptoms and were more likely to seek help.

Keywords: COVID-19, Pandemic, Psychosis, Schizophrenia Spectrum Disorder, Tele-medicine

INTRODUCTION

The outbreak of the Corona Virus Disease 2019 (COVID-19) started in Wuhan /China, spread rapidly all around the world and the World Health Organization declared pandemic in March 2020. The elderly and patients with chronic disease or cancer are at higher risk in terms of negative consequences of COVID-19 [1]. From the earliest days of the pandemic, it has been thought that patients with mental illness would be among the risk groups due to their mental symptoms, side effects of psychotropic drug, medical comorbidity and smoking [2]. In a recent population-based study, the hypothesis that people with mental illness are among the risk groups for COVID-19 has been confirmed [3,4]. Cognitive dysfunction, lack of insight, sociodemographic characteristics such as living in congregate housing, homelessness and difficulty in adapting to protective measures are risk factors for patients with schizophrenia/ schizophrenia spectrum disorder to contact COVID-19. It has been shown that protective measures were less effective in these patients and negative consequences related to COVID-19 were seen in higher rates [3,4].

After the declaration of the pandemic, various protective measures such as social distancing, isolation, all of which are psychologically challenging, have been taken to prevent the spread of the disease, and a negative impact of the pandemic on mental health was expected based on previous pandemic knowledge [5]. Prevalence of depression, anxiety, sleep disorders were found to be increased in the general population [6]. The study of Wang and colleagues [7] conducted between January-February 2020 reported that the rate of moderate to severe depression and anxiety symptoms were 16.5% and 28.8%, respectively. In the study conducted between March-May 2020, the rate of depression, anxiety and/or stress at clinical levels was 65.6% [8]. These studies might indicate that the rates of psychiatric symptoms such as depression and anxiety increase with the prolongation of the pandemic [7,8]. From the beginning of the COVID-19 pandemic it has been thought that patients with severe mental illness (SMI) such as schizophrenia, bipolar disorder would be more severely affected by the physical consequences of COVID-19, as well as the psychosocial consequences associated with different aspects of the pandemic [9,10]. On the other hand, the results of a study conducted between April and June 2020 indicated that there was no increase in the psychotic symptoms of patients with schizophrenia who had been evaluated before and during the pandemic [11]. Another study evaluating the impact of the pandemic on the patients with schizophrenia between April-May 2020 showed that these patients were affected less severely than expected [12]. Similarly, an online/telephone survey conducted in a psychiatry clinic in Turkey revealed that majority of patients with schizophrenia did not report any psychotic exacerbation during the first two months of pandemic [13].

Schizophrenia, which is characterized by chronic psychotic symptoms and lead to poor social functioning, is one of the 10 diseases that cause the greatest burden of disease in the world [14], therefore it became an important public health concern how they would be affected from the pandemic. The pandemic has also affected the follow-up and treatment of patients with schizophrenia negatively, due to the interruption of health care. Abrupt changes in mental health care induce relapse by causing decrease in treatment compliance and withdrawal from health care. In order to maintain the continuity of treatment in times of such crises, it's recommended to utilize tele-medicine methods despite some limitations [4,15].

In the majority of studies regarding the effects of the COVID-19 pandemic on mental health, the effects of uncertainty, isolation and quarantine on the general population and health-care workers have been examined. Fewer studies in the literature evaluate the effects of the pandemic on patients with existing mental illness and mental health care [16]. In the few studies which evaluate the effects of the pandemic on mental status of patients with schizophrenia and other psychotic disorders, the early effects of the pandemic on these patients

have been examined [11,12]. Considering the results of studies showing that psychological effects in the general population increase in time with the prolongation of the pandemic, it's necessary to examine how patients with schizophrenia/ schizophrenia spectrum disorders are affected by the pandemic in the long term. To our knowledge, in the literature there are no studies which evaluate the long-term effects of pandemic on the mental health of schizophrenia/schizophrenia spectrum disorder patients and their utilization of mental health care. In this study, we aimed to evaluate the effects of the pandemic on the mental health status of patients with schizophrenia/schizophrenia spectrum disorders at the end of the half year past the onset of the pandemic by comparing the psychopathological state of patients who had been hospitalized in the previous year before the onset of the pandemic, to their state at the end of 6-8 months into the pandemic. Hospitalized patients within the past year before the onset of the pandemic were particularly chosen as this would be a group with thorough assessments regarding severity of psychopathology and would be in close follow up after discharge. Our hypothesis was that psychotic symptoms would have increased during the course of the pandemic.

MATERIALS AND METHODS

Subjects

This descriptive cross-sectional study conducted between August-October 2020 at Hacettepe University Faculty of Medicine, department of psychiatry. Inclusion criteria for the sample was defined as patients with complete medical records and patients who were hospitalized prior to the onset of the pandemic between March 2019-March 2020 at the inpatient clinic with a diagnosis of schizophrenia spectrum disorders. There were no exclusion criteria for this study.

A total of 52 patients diagnosed with schizophrenia/ schizophrenia spectrum disorders were identified to be hospitalized between March 2019 - March 2020 at the inpatient clinic. Among these, 6 patients refused to participate in the study, 9 patients refused to come to the hospital or to interview via telepsychiatry methods, 3 patients could not be reached by any means. The remaining 34 patients who provided informed consent were included in the study.

Approval from the Hacettepe University Faculty of Medicine Ethics Committee was obtained for this study (Number: 2020/12-78).

Method

Patients were either interviewed face to face or via telepsychiatry methods to complete study assessments consisting of a questionnaire including sociodemographic such as age, sex and clinical characteristics. The other clinical characteristics such as diagnosis, duration of illness, pharmacological treatment, duration of treatment, length of stay in hospital, treatment compliance before the pandemic, medical and psychiatric comorbidity, Positive and Negative Syndrome Scale (PANSS) and Clinical Global Impression-Severity (CGI) scores at discharge from the inpatient clinic were obtained from the medical records for each patient. We also evaluated subjective increase in psychiatric symptoms by asking "Do you feel an increase in your psychiatric symptoms during the pandemic?". According to the subjective evaluation of the psychiatrist, patients' information level about the pandemic was graded as a high, medium and low. The PANSS [17,18], CGI [19], Hamilton Depression Rating Scale (HAM-D) [20,21], Hamilton Anxiety Rating Scale (HAM-A) [22-24] and Fear of COVID-19 Scale were used to evaluate the psychopathology. The Fear of COVID-19 Scale is a unidimensional 7 item 5-point likert type scale which was developed by Ahorsu and colleagues [25], and is used to assess the severity of fear caused by the pandemic and a higher score indicates more severe fear of COVID-19. The Turkish validity and reliability study has been recently conducted by Satici and colleagues [26].

Statistical Analysis

Statistical analysis was conducted using the SPSS 23.0 package software for Windows. Descriptive statistics were expressed as mean \pm standard deviation for continuous variables and as number

and frequencies (percentages) for categorical variables. Participants have been categorized into two groups: Those who reported subjective increase in the severity of psychiatric symptoms during the pandemic and those who did not. The differences in categorical variables between two groups were analyzed using Chi-square test of Fisher's Exact Test and the differences in numerical variables between two independent groups were analyzed using the Mann Whitney U test for independent samples when variables were not normally distributed. Wilcoxon-signed rank test was used to compare the scores of PANSS and CGI pre- and during the pandemic. Spearman's correlation analysis was used to evaluate the relationship between fear of COVID-19 scale and other variables. The p value of < 0.05 was accepted as a statistically significant.

RESULTS

Sociodemographic and clinical characteristics

A total of 34 patients, 33 with schizophrenia (97.1%) and 1 with schizoaffective disorder (2.9%) were included. Twelve (35.3%) of the patients were female, 22 (64,7%) were male. Twenty-two patients were evaluated in the outpatient clinic face to face and 12 were evaluated via tele-psychiatry methods. The mean duration from discharge of patients until the declaration of the pandemic was 122 ($\pm 103,3$) days and the mean duration from the declaration of the pandemic to evaluation for the study was 179 (±30.49) days. Only 1 of the patients included in the study had confirmed COVID-19 infection and had survived without any problems. Eighteen patients (52.9%) were not working and 1 of these patients was dismissed from his former job due to the pandemic, 1 had left his job voluntarily. Five patients (14.7%) were living alone. While 22 patients were being treated with clozapine, 12 patients were using other antipsychotics as monotherapy or in combination with another antipsychotic. Thirty-one patients stated that they had information about the pandemic; according to the subjective evaluation of the psychiatrist, the level of the information was high in 15 (44.1%); medium in 13 (38.2%) and low in 3 (8.8%8). The patients indicated newspaper, television, internet, social media and official institutions as sources of information. Number of patients who reported

increased severity of psychiatric symptoms were 14 (41.2%). Major sociodemographic and clinical characteristics during the pandemic are shown in Table 1.

Before discharge from hospital, the mean (±SD) PANSS total score of the patients was 65.9±13.2 and CGI score was 3.6±0.7. The assessments during the pandemic revealed that the mean (±SD) PANSS total score was 62.3±16.5, CGI score 3.5±1.6, HAM-D score 7.9±8.9, HAM-A score 6,9±9,8 and the Fear of COVID-19 Scale score 17.5±7.5. There was no significant difference between the pre- and during the pandemic assessments in the PANSS Total and CGI scores (z=-1.515, p=0,130; z=-0.677, p=0.498, respectively)

When patients who reported subjectively increased psychiatric symptoms during the pandemic (Group 1, N: 14) were compared to those who did not (Group 2, N:20), age, sex, education, age of onset, duration of illness, duration of treatment, treatment compliance were not significantly different between the groups. There was also no significant change in the difference between the PANSS total and CGI scores between two groups. On the other hand, the PANSS total, CGI, HAM-D, HAM-A and the Fear of COVID-19 scale scores and utilization of psychiatric health care services were significantly higher in Group 1 (Table 2).

There were 12 patients (35.3%) with a HAM-D score of ≥8 which indicates the presence of depression. When compared to patients with HAM-D scores <8, the mean PANSS total score, CGI-S were significantly higher in patients with depression (p scores <0.001). Patients with depression reported a higher rate of subjective increase in their psychiatric symptoms (p=0.001).

There were 8 patients (23.5%) with HAM-A scores ≥8 which means anxiety. Patients with anxiety had significantly higher scores in PANSS, CGI, the Fear of COVID-19 scales compared to patients with HAM-A <8 (p scores 0.001, 0.002, <0.001, respectively). Patients with anxiety reported a higher rate of subjective increase in their psychiatric symptoms (p<0.001).

There was a positive correlation between the Fear of COVID-19 Scale and HAM-A scores (r=0.377, p=0.028).

Table 1. Sociodemographic and clinical characteristics of the patients

Variables	Mean±SD	Median (25-75 percentiles)
Age	39,8±14,7	39 (26-48)
Duration of education (years)	10.8±4,7	11 (8-15)
Age of onset	24,1±10,9	22 (15-30)
Duration of illness (month)	175,5±114,5	168 (96-276)
Duration of treatment (month)	130,9±100	120 (31-204)
Length of stay in hospital (day)	49,8 ±31.2	47 (29-57)
PANSS at discharge	65.9±13.2	62 (56-74)
during pandemic	62.3±16.5	63 (47-77)
CGI at discharge	3.6±0.7	3 (3-4)
during pandemic	3.5±1.6	3 (3-5)
HAM-D	7.9±8.9	5 (1-13)
HAM-A	6,9±9.8	3 (0-7)
Fear of COVID19 scale	17.5±7.5	17 (13-22)
eal of Covid 19 scale		17 (13-22)
Marital Status	n (%)	
Marrial Status Married	6 (17.6)	
	6 (17.6)	
Single	28 (82,4)	
	n (%)	
Diagnosis of psychiatric disorders	(1)	
Schizophrenia	33 (97,1)	
Schizoaffective	1 (2.99)	
Psychiatric comorbidity		
Depression	8 (23.5)	
Anxiety Disorder	3 (8.8)	
Other	5 (14.7)	
Comorbid Medical Disease		
Diabetes mellitus	5 (14.7)	
Hypertension	2 (5.9)	
Coronary artery disease	1 (2.9)	
Asthma	1 (2.9)	
Other	5 (14.7)	
Treatment during assesment		
Clozapine	22 (64.7)	
Other antipsychotics	12 (35.3)	
Smoking		
Yes	18 (52,9)	
No	16 (47,1)	
Alcohol		
Yes	7 (20,6)	
No	27 (79,4)	
Treatment compliance before pandemic		
High	24 (70,6)	
Medium-Low	10 (29,4)	
Utilization of mental health services during pandemic		
	15 (44,1)	
Yes	12(77,1)	

SD: standard deviation, PANSS: Positive and Negative Syndrome Scale, CGI: Clinical Global Impairment, HAM-D: Hamilton Depression Rating Scale, HAM-A: Hamilton Anxiety Rating Scale

Table 2. Comparison of patients reporting subjective increase in psychiatric symptoms (Group 1) and those who did not (Group 2)

Variables	Group 1 (N=14)	Group 2 (N=20)	Statistical Analysis
	Mean±SD	Mean±SD	
Age	39.0±15.0	40.3±14.9	p=0.823*
Duration of education (year)	9.4±5.1	11.8±4.2	p=0.217*
Age of onset	22.3±10.8	25.4±11.1	p=0.377*
Duration of illness (month)	185.4±121.6	168.6±112.0	p=0.641*
Duration of treatment (month)	134.3±100.4	128.4±102.2	p=0.823*
PANSS Total	75.1±11.8	53.4±13.2	p<0.001*
CGI	4.4±0.9	2.9±0.9	p<0.001*
HAM-D	11.3±9.8	3.4±4.3	p<0.001*
HAM-A	14.3±11.6	1.7±2.3	p<0.001*
Fear of COVID-19 Scale	22.9±7.2	14.0±5.2	p=0.001*
	n (%)	n (%)	
Sex			
Female	4 (11.8)	8 (23.5)	p=0.717 [†]
Male	10 (29.4)	12 (35.3)	
Clozapine use			
Yes	9 (64.3)	13 (65.0)	p=1.000 [†]
No	5 (35.7)	7 (35.0)	
Medical comorbidity			
Yes	10 (29.4)	6 (17.6)	p=0.042 [†]
No	4 (11.8)	14 (41.2)	
Distrupted treatment compliance during pandemic			
Yes	4 (28.6)	4 (20)	p=0.689 [†]
No	10(71.4)	16 (80)	
Utilization of mental health services during pandemic			
Yes	10 (71.4)	5 (21)	p=0.020 [†]
No	4 (28.6)	15 (79)	

^{*:} Mann Whitney U Test, †: Chi-square test of Fisher's Exact Test

SD: standard deviation, PANSS:Positive and Negative Syndrome Scale, CGI: Clinical Global Impairment, HAM-D: Hamilton Depression Rating Scale, HAM-A: Hamilton Anxiety Rating Scale

DISCUSSION

The aim of this study was to reevaluate patients with schizophrenia spectrum disorders who had been hospitalized during the year before the outbreak of COVID-19 in the midst of the pandemic, and to examine the effect of this ongoing crisis on their psychopathology. The most interesting finding of the study was that there was no difference regarding the severity of psychopathology between the two time points, as indicated by the PANSS and CGI scores at discharge and in the reevaluation during the pandemic. In addition, although the patients in the group who subjectively stated that their severity of psychiatric symptoms increased during the pandemic had higher scores on all scales,

there was no significant difference in the objective change of PANSS-Total and CGI scores between the two groups.

Several risk factors such as advanced age, chronic disease, smoking and immunosuppression have been determined for COVID-19, and patients with mental illness were also included in these risk groups [2]. It was found that patients with a new psychiatric diagnosis in the previous year before the pandemic have more COVID-19 than those without mental illness and that mortality is higher in these patients [7]. It has also been argued that there are different risk factors for each mental disorder [7]. When it has been stated that the high rates for COVID-19 in patients with schizophrenia

may have resulted from difficulties in applying protective measures such as isolation, quarantine due to delusions, cognitive dysfunctions, poor insight or/and the role of similar mechanisms such as inflammation in both diseases [4,7]. Smoking habits, medical comorbidities which are common in patients with schizophrenia also lead to high mortality rates [2,7]. In addition, since the beginning of the pandemic, it has been mentioned that both the disease itself and its consequences along with mandatory protective measures all have negative effects on mental health in the general population, and that people with preexisting mental illness will be affected even more negatively [27]. Nevertheless, in the current literature, studies showing the relationship of these risk factors with psychotic exacerbations include only case reports [28,29]. On the contrary, in one study, it has been shown that the prevalence of psychosis among university students did not increase during the pandemic compared to pre-pandemic period [30]. Similarly, majority of patients with schizophrenia didn't report any psychotic exacerbation in a study conducted in Turkey [13]. In our study, no significant difference was found between the pre- and during the pandemic psychopathology severity scores consisting of PANSS and CGI evaluations, this finding is consistent with the evidence showing that the COVID-19 pandemic does not cause a significant increase in psychotic symptoms. These results have previously been interpreted as those with SMI are more resilient to the psychological effects of a pandemic [11,31].

In the literature several variables that protect patients with schizophrenia from being negatively affected by disasters in acute and subacute period are defined [32]. Psychopathology -related (i.e., negative symptoms, lack of insight, or drug treatment) and treatment related variables (qualified and competent follow-up process during and after the disaster, as in the present case of pandemic) may play a compensating role in the negative ef-fects of the event. Parallel to this opinion, Katz and colleagues [33] have previously reported that patients with schizophrenia may remain clinically stable after disasters. They offered the vulnerability stress coping model as the mechanism of sustaining clinical stability. This coping model suggests that the subjective perception of distressing events in clinically stable schizophrenia patients does not form an immediate negative interpretation.

In addition various studies show that individuals using the avoidance strategy to cope with the negative effects of distressing events generally have more severe psychopathology compared to patients who mainly use other coping mechanisms [34,35]. These mechanisms, which have been suggested to lead to protective effects, in the acute and subacute periods of disasters, may have also contributed to the resilience of schizophrenia patients in terms of psychotic symptoms in our study. To our knowledge, there are no studies evaluating long term effects of disasters or other mass events like a pandemic on the psychotic symptom severity of patients with schizophrenia.

Stigmatization in schizophrenia is an important problem in patients' access to treatment, and it is divided into public stigma and self-stigma [36]. It is argued that self-stigmatization in schizophrenia patients may decrease with the increase in perceived similarities with the general population [36]. In this context, the applying of restrictions to prevent the spread of the disease to the world reduces the internal stigmatization of patients with schizophrenia, and therefore may have been protective against increase in psychotic symptoms. However, in order to support this interpretation, studies investigating how self-stigma has been affected by the pandemic in patients with schizophrenia are needed.

In studies conducted in the general population at different time points, it has been shown that negative effects on mental health increase with the prolongation of the pandemic [6,8]. Studies suggesting schizophrenia patients are more resilient to the mental effects caused by the pandemic have been conducted in the earlier period of the COVID-19 [11,12]. When compared to other studies, in our study patients were evaluated at a later period of the pandemic and it was found that there was no increase in psychotic symptoms parallel to the results of the studies conducted in the early periods of pandemic. This result suggests that resilience may not be limited to the early period of the pandemic for patients with schizophrenia.

Another finding of this study is that the patients who reported an increase in their psychiatric symptoms during the pandemic had higher scores in all psychopathology severity rating scales in the pandemic period. Although these patients also had

higher PANSS total scores before discharge from the hospital compared to those who did not report an increase in their symptoms during the pandemic, no difference between two groups in terms of change in the PANSS total scores were found. This finding may suggest that the symptoms which patients claim to be exacerbated may not be the psychotic symptoms, but other mental symptoms that may occur during the pandemic period. Patients who had more anxiety and depression symptoms at follow up, as indicated by higher HAM-D and HAM-A scores, reported a subjective increase in their psychiatric symptoms and their total PANSS scores were found to be higher. This finding is most likely due to the fact that PANSS evaluation includes multiple domains of psychopathology including depression and anxiety, and not only psychotic symptoms. We suggest that this subjective increase could be related with higher depression and anxiety symptoms assessed during the pandemic. In our clinic, baseline HAM-A and HAM-D are not used in the routine of patients with a diagnosis of schizophrenia, and therefore we could not compare the pre-pandemic and pandemic depression and anxiety scores. The lack of HAM-D and HAM-A baseline evaluations to further support the view that the subjective increase of symptoms during the pandemic could be related with increasing depressive and anxiety symptoms, is an important limitation.

Previously, higher levels of avoidance predicted higher residual stress symptoms at 5 weeks after an earthquake in schizophrenia patients [32]. Subacute effects of these particular coping mechanism may also have contributed to the observed anxiety symptoms in our study group. One study showed that patients with SMI had more anxiety associated with the COVID-19 pandemic [38] and the higher anxiety scores of patients who reported an increase in their symptoms supports this finding. Since anxiety may have unfavorable outcomes in patient with SMI, screening anxiety in patients with psychiatric disorders is important in terms of early interventions [38]. In our study, we determined that although the pandemic did not affect the positive psychotic symptoms negatively, patients having higher anxiety or depression scores reported an increase in their symptoms and were more likely to seek mental health services than others. This finding supports the importance of screening for anxiety and depression in patients

with schizophrenia spectrum disorders in periods of crisis such as a pandemic.

With the pandemic, measures such as postponing appointments and reducing patient quota in healthcare services have been taken which cause disruptions in health care [39]. On the other hand, some patients have avoided referral to hospitals because of COVID-19 even if they have complaints [40]. In this study, the rate of referral to psychiatry was significantly higher in patients who reported an increase in their psychiatric symptoms during the pandemic, this finding is important in terms of showing that these patients had the opportunity of utilizing a health care service during the pandemic. Since the beginning of the pandemic, the use of telemedicine methods has been suggested in order to prevent disruptions in health care, in our clinic a telephone line and a triage system has been established with the declaration of the pandemic. Our results supported that telepsychiatry interventions are important to facilitate the utilization of mental health care in patients with increased psychiatric symptoms [41].

Previous studies conducted during the pandemic evaluated psychopathology by self-report scales and one of the strengths of this study is that evaluation and rating of psychopathology of the patients was mainly based on psychiatric interview and structured scales. The relatively small sample size and the subjective evaluation of whether there is an increase in the symptoms of the psychiatric disorder and whether treatment compliance is kept and access to psychiatric services is present during the pandemic, are among the limitations of the study.

In conclusion, although studies with larger samples are needed to explore the impact of the pandemic on patients with schizophrenia spectrum disorders, it appears that this group of patients are more resilient to the effect of stress related to the pandemic and this resilience continues into the 6-8 months into the pandemic. However, it should be kept in mind that the prolongation of the pandemic could still cause negative consequences upon daily life and mental health care. Although positive psychotic symptoms do not appear to be exacerbated, patients report discomfort and morbidity due to an increase in depressive and anxiety symptoms. The overall effect of the pandemic on the psychopathology of the schizophrenia spectrum patients could lead to

more substantial change in the months to follow and therefore should be reexamined. In addition, the importance of tele-medicine applications for accessing to health care during the pandemic is evident, despite limitations they should be utilized in the follow up of seriously mentally ill patients in different clinical settings.

Author contribution

Study conception and design: EÖE, MİY, AEAY, AE, and MKY; data collection: OKY and ÖT; analysis and interpretation of results: SK, EÖE, MİY, AEAY, AE, and MKY. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the Hacettepe University Faculty of Medicine Ethics Committee (Protocol no. 2020/12-78/23.06.2020).

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Conflict of interest

The authors declare that there is no conflict of interest.

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